Exceptional Access Program (EAP)
EAP Reimbursement Criteria for Frequently Requested Drugs

Updated – February 20, 2019
Disclaimer

The information in this document is updated on a regular basis. Although we strive to ensure that all information is accurate at the time of posting, please be aware that some items may be subject to change from time-to-time.

The following list of drugs and indications that will be considered for funding under the Exceptional Access Program is not exhaustive. Physicians may wish to contact the EAP directly by phone at 416-327-8109 or 1-866-811-9893 or by email at EAPFeedback.MOH@ontario.ca to see if a specific drug product and or indication not listed below may be considered for EAP funding.

The information provided in this document and website is intended for information purposes only and does not provide any medical diagnosis, symptom assessment, health counselling or medical opinion for individual users. This information also does not constitute medical advice for physicians or patients. For more detailed information on prescription drugs, please consult a qualified healthcare professional.
Reimbursement Criteria for Frequently Requested Drugs and Indications

For a drug to be considered for funding, the EAP reimbursement criteria must always be met and the request approved prior to the initiation of treatment with the drug being requested, unless otherwise specified within the criteria. This includes:

- funding for continued treatment that was previously supplied through a clinical trial, or paid for by other means (such as a third party payer)
  
  Note: First time applications for the funding of ongoing treatments must meet both initial and renewal criteria for the drug being requested (unless otherwise specified)

- funding for a renewal beyond the previously approved initial period, unless otherwise specified.

Note that the terms “fund”, “funded”, or “funding” within this document are interpreted and applied by the Ministry in accordance with the clinical evidence used to establish the reimbursement criteria. The Ministry does not distinguish between the source of the drug funding (e.g. public or private payer[s]) in administering the EAP reimbursement criteria.

Consider the following:

The “non-funding” of specific combination treatments as identified by the criteria will not be reimbursed regardless of the funding source(s) of either therapy. The funding criteria are established based on the reviewed clinical evidence through the submission process and are not to be misconstrued with the source(s) of funding.

Example 1: If drug A has approved reimbursement criteria and drug B has approved reimbursement criteria but the combination therapy of drug A plus drug B has not been reviewed through the established process and/or has no reimbursement criteria, the EAP will not fund either drug individually or as combination therapy if the intended use is for combination therapy, regardless of the actual source of funding of either drug A or drug B.

Example 2: If drug A has approved reimbursement criteria and drug B does not have approved reimbursement criteria, and drug A used in combination with drug B does not have approved reimbursement criteria, funding for drug A will not be provided if the intent is to use drug A as combination with drug B, regardless of the source of funding for drug B.

The duration of funding of a regimen identified in the criteria is in accordance with the duration of therapy supported by the clinical evidence and is not related to or dependent on source(s) of funding.

Example 1: If the approved reimbursement criteria states that “The Ministry will fund drug C for a period of 3 years” and drug C was already used by the patient for 2 years funded by another payer (e.g. private payer, manufacturer, out-of-pocket), the Ministry will only be obliged to fund drug C for the remaining one year if the request meets the approved EAP reimbursement criteria. Such a limitation in the duration of funding is aligned with the clinical evidence provided to the Ministry at the time of the review.

For a limited number of requests where expert opinion is required, the requests are reviewed by an external reviewer who is a medical expert in the field.

Where available, a link has been provided to the information page containing details of the Committee to Evaluate Drugs (CED) review and subsequent the Executive Officer’s funding.
decision for the particular drug and indication. Information on whether the drug and indication can be considered through the Telephone Request Service (TRS) is also included.

EAP requests may be submitted for numerous other drugs not listed below, or for drugs listed below but for different indications. However, EAP funding will only be considered for drugs and indications that have been reviewed by the CED and approved for funding by the Executive Officer. For more information, please refer to the main EAP webpage.

Some of the drugs considered through EAP are also listed on the ODB Formulary for a different indication as Limited Use (LU) benefit. You can check whether the drug is listed by searching the e-Formulary.

For details on how the EAP reimbursement criteria are developed, please refer to the main EAP webpage.

To assist physicians applying for exceptional access, the ministry has developed a standard form. Use of form is not mandatory but does facilitate provision of all relevant information. Where applicable, please ensure that all relevant clinical information is provided demonstrating that the patient meets the reimbursement criteria.

Note: The dosage form and strength of the product that has been approved for reimbursement consideration are those that have been approved by the Committee to Evaluate Drugs (CED). In most cases, these are the dosage forms and strengths submitted to the CED by the manufacturer for consideration, however, it may not be inclusive of all dosage forms and strengths available through the manufacturer.
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ANEMIA

Darbepoetin
Brand(s): Aranesp
DOSAGE FORM/ STRENGTH: Prefilled syringes: 150 mcg, 200 mcg, 300 mcg, 500 mcg

(Requests for the treatment of chemotherapy-induced anemia in patients with malignant cancer DO NOT require an EAP submission. Please refer to the ODB e-formulary to determine if the patient satisfies the criteria for use.)

For the treatment of anemia secondary to chronic renal disease in those who are not eligible under the Special Drugs Program, approval can be given if the patient meets the following criteria:
Estimated glomerular filtration rate (GFR) less than 30 mL/min AND
Baseline hemoglobin level less than 100 g/L AND
Mean corpuscular volume (MCV) level between 75 fL and 120 fL
All requests MUST indicate the reason why the patient is ineligible for the Special Drugs Program.
**Duration of Approval: 6 months**

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.
Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date(s) that the transfusion(s) occurred.
**Duration of Approval: 12 months**

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:
- MDS confirmed by the bone marrow report AND
- With a hemoglobin count less than 100 g/L AND
- Endogenous erythropoietin level of less than 500 U/L AND
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL.
Submissions must include the date(s) for the above blood work.
For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission.
**Duration of Approval: 6 months**

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.
Darbepoetin
Brand(s): Aranesp
DOSAGE FORM/ STRENGTH: Prefilled syringes: 150 mcg, 200 mcg, 300 mcg, 500 mcg

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date(s) that the transfusion(s) occurred.

Duration of Approval: 12 months

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:

- MDS confirmed by the bone marrow report AND
- With a hemoglobin count less than 100 g/L AND
- Endogenous erythropoietin level of less than 500 U/L AND
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL.

Submissions must include the date(s) for the above blood work.

For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission.

Duration of Approval: 6 months

Renewals will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with darbepoetin and the date(s) that the transfusion(s) occurred.

Duration of Approval: 12 months
Epoetin Alpha
Brand(s): Eprex
DOSAGE FORM/ STRENGTH: Prefilled syringes: 5,000 IU/0.5 mL, 6,000 IU/0.6 mL, 8,000 IU/0.8 mL, 10,000 IU/mL, 20,000 IU/0.5 mL, 40,000 IU/mL

For the treatment of anemia secondary to chronic renal disease in those who are not eligible under the Special Drugs Program, approval can be given if the patient meets the following criteria:

- Estimated glomerular filtration rate (GFR) less than 30 mL/min \textbf{AND}
- Baseline hemoglobin level less than 100 g/L \textbf{AND}
- Mean corpuscular volume (MCV) level between 75 fL and 120 fL

All requests MUST indicate the reason why the patient is ineligible for the Special Drugs Program.

**Renewals** will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with epoetin alpha and the date(s) that the transfusion(s) occurred.

For the treatment of anemia secondary to myelodysplastic syndrome (MDS) in patients who meet the following criteria:

- MDS confirmed by the bone marrow report \textbf{AND}
- With a hemoglobin count less than 100 g/L \textbf{AND}
- Endogenous erythropoietin level of less than 500 U/L \textbf{AND}

Mean corpuscular volume (MCV) level between 75 fL and 120 fL.

Submissions must include the date(s) for the above blood work.

For patients with an MCV level below 75 fL or above 120 fL, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission

**Duration of Approval:** 6 months

**Renewals** will be provided to patients where the hemoglobin levels have improved by 15 g/L after 3 months of therapy.

Renewals must specify the name of the drug and dose requested and MUST be accompanied by bloodwork that includes a recent hemoglobin level. Also, please identify if the patient has received transfusions after the first 2 weeks of therapy with epoetin alfa and the date(s) that the transfusion(s) occurred.

**Duration of Approval:** 6 months
Epoetin Alpha

Brand(s): Eprex

DOSAGE FORM/ STRENGTH: Prefilled syringes: 5,000 IU/0.5 mL, 6,000 IU/0.6 mL, 8,000 IU/0.8 mL, 10,000 IU/mL, 20,000 IU/0.5 mL, 40,000 IU/mL

For treatment of anemia secondary to hepatitis C therapy in patients who meet the following criteria:

- Patient is diagnosed with Hepatitis C and is undergoing treatment with pegylated interferon and ribavirin AND
- Current hemoglobin is >100 g/L but patient has experienced a drop in hemoglobin of at least 40 g/L since treatment OR
- Current hemoglobin count is < 100 g/L

Submissions must include the following:

1) Details of therapy with pegylated interferon and ribavirin (ie: Start date, duration of treatment, patient response etc)
2) Bloodwork (full CBC preferred) that includes the hemoglobin and mean corpuscular volume (MCV) as well as the date(s) for the above blood work.

For patients with an MCV level below 75 fl or above 120 fl, the physician must provide a discussion of how reversible causes of anemia were ruled out to enable further consideration of the submission.

Submissions not meeting the above criteria will be considered on a case-by-case basis. All submissions should be accompanied by

- Baseline and current bloodwork (full CBC with MCV)
- Baseline clinical status and current symptoms from anemia that were not present at baseline
- Details of any complications from anemia

Duration of Approval: Full duration of treatment with pegylated interferon/ribavirin treatment

Renewals will be granted for the full period of pegylated interferon and ribavirin treatment in those who show significant response to therapy. Renewals should be accompanied by bloodwork that includes a recent hemoglobin and must identify if the patient has required transfusions after the first 2 weeks of therapy.

Duration of Approval: Full duration of treatment with pegylated interferon/ribavirin treatment

Pre-operative use at a dose up to 40,000 IU weekly prior to single hip, double knee, or single (“redo”) knee surgery in patients who meet the following criteria;

- Hemoglobin between 100 – 130 g/L inclusive AND
- Mean corpuscular volume (MCV) level between 75 fl and 120 fl inclusive

Request not meeting these criteria will be assessed on a case-by-case basis.

Duration of Approval: Up to 4 doses preoperatively
Epoetin Alpha

Brand(s): Eprex

DOSAGE FORM/ STRENGTH: Prefilled syringes: 5,000 IU/0.5 mL, 6,000 IU/0.6 mL, 8,000 IU/0.8 mL, 10,000 IU/mL, 20,000 IU/0.5 mL, 40,000 IU/mL

For the treatment of anemia in palliative cancer patients. Individuals will be assessed on a case-by-case basis. Submissions must include the rationale for using epoetin alpha over transfusion.

Requests for the treatment of chemotherapy-induced anemia in patients with malignant cancer DO NOT require an EAP submission. Please refer to the e-formulary to determine if the patient satisfies the criteria for use.

Iron dextran complex

Brand(s): Dexiron

DOSAGE FORM/ STRENGTH: 50 mg/mL Injectable

For the treatment of iron-deficiency anemia confirmed by bloodwork where the patient has a demonstrated intolerance\(^1\) to oral iron therapy\(^2\) OR has not responded to adequate therapy with oral iron\(^2\).

\(^1\)Intolerance must be described.

\(^2\)Provide name of iron salt, dose, duration of therapy, response etc.

Duration of Approval: 1 year

Renewals will be considered on a case-by-case basis.

Duration of Approval: 2 years
Iron sucrose  
Brand(s): Venofer  
DOSAGE FORM/STRENGTH: 20 mg/mL Injectable  

For the treatment of iron-deficiency anemia confirmed by bloodwork where the patient has a demonstrated intolerance\(^1\) to oral iron therapy\(^2\) OR has not responded to adequate therapy with oral iron\(^2\).  
\(^1\)Intolerance must be described.  
\(^2\)Provide name of iron salt, dose, duration of therapy, response etc.  

**Duration of Approval:** 1 year  

**Renewals** will be considered on a case-by-case basis.  

**Duration of Approval:** 2 years

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Lenalidomide  
Brand(s): Revlimid  
DOSAGE FORM/STRENGTH: 5 mg, 10 mg capsule  

For the treatment of anemia due to myelodysplastic syndrome (MDS) for patients who meet all the following clinical criteria;  
- Demonstrated diagnosis of MDS on bone marrow aspiration; AND  
- Presence of del[5q] documented by standard cytogenetic or fluorescence in situ hybridization; AND  
- International Prognostic Scoring System (IPSS) risk category low or intermediate-1; AND  
- Transfusion-dependent symptomatic anemia.  

**Duration of Approval:** 6 Months  

**Renewal** will be considered for patients who are transfusion-dependent and who have demonstrated at least a fifty percent (50%) reduction in transfusion requirements.  

**Duration of Approval:** Up to 1 Year  

Note: Patients with anemia due to MDS who are not transfusion-dependent will be assessed on a case-by-case basis.  
- Physicians submitting initial requests for non-transfusion-dependent patients must provide clinical evidence of symptomatic anemia affecting the patient’s quality of life and the rationale for why transfusions are not being used.  
- Renewal requests for non-transfusion-dependent patients will be considered on a case-by-case basis. In such cases, the requesting physician will be required to provide the patient’s serial clinical blood culture (CBC) pre- and post-lenalidomide therapy in addition to any other objective evidence of the patient’s response to lenalidomide therapy.
Lamotrigine (chewable)
Brand(s): Lamictal
DOSAGE FORM/ STRENGTH: 5 mg chewable tablet

For the adjunctive therapy for children over 2 years of age who are suffering from refractory seizures associated with Lennox-Gastaut syndrome, and who have previously tried other antiepileptic drugs.

Duration of Approval: 1 year
Oxcarbazepine
Brand(s): Trileptal
DOSAGE FORM/ STRENGTH: 150 mg, 300 mg, and 600 mg tablet 60 mg/mL

For the treatment of partial seizures in adults and in children aged 6 years and older who have had an inadequate response or intolerance* to at least 3 other formulary agents (prior or current use) including carbamazepine.

* Intolerance must be described in detail.

Warning: Life-threatening dermatological reactions, including Stevens Johnson Syndrome and toxic epidermal necrolysis, and multi-organ hypersensitivity reactions have been associated with the use of oxcarbazepine. More information may be found on the Health Canada webpage: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/trileptal_hpc-cps_e.html

Duration of Approval: Lifetime

Phenobarbital
Brand(s): PMS-Phenobarbital
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg, 60 mg, 100 mg tablet; 5 mg/mL oral liquid; 120mg/mL Injection

Effective January 31, 2018, Phenobarbital tablets, oral liquid, and injection are made available as General Benefits on the Ontario Drug Benefit Formulary.
Rufinamide
Brand(s): Banzel
DOSAGE FORM/ STRENGTH: 100 mg, 200 mg, 400 mg

For the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in patients who meet the following criteria:

- Patient is 4 years of age or older; AND
- the Patient is currently on two or more anti-epileptic drugs (AEDs) without optimal seizure control; AND
- the Patient has failed an adequate trial\(^1\) of lamotrigine AND topiramate; AND
- the Patient is in the care of a physician experienced in managing seizures.

\(^1\)If an adequate trial of lamotrigine and/or topiramate is not possible due to intolerance or contraindication, a less costly AED that is listed as a benefit on the Ontario drug benefit formulary must be tried in its place

Dose: Maximum daily dose is 1,300 mg per day for patients less than 30 kg; and 3,200 mg per day for patients 30 kg or greater

Exclusion Criteria.

Funding will not be approved for the following circumstances:
- Banzel used first line for LGS; OR
- Treatment of partial seizures

Duration of Approval: Lifetime
Stiripentol
Brand(s): Diacomit
DOSAGE FORM/ STRENGTH: 250 mg capsule, 250 mg/pack powder for suspension, 500 mg capsule, 500 mg/pack powder for suspension

For the treatment of patients with severe myoclonic epilepsy in infancy (Dravet syndrome) who meet the following criteria;

i) the patient has refractory generalized tonic-clonic seizures; AND

ii) the patient requires Diacomit (Stiripentol) for use in combination with clobazam and valproate as adjunctive therapy for the seizures; AND

iii) the patient’s seizures are not adequately controlled with clobazam and valproate alone; AND

iv) the request is submitted by a neurologist or pediatrician.

Case-by-case consideration through external review will be permitted for circumstances not meeting the above criteria.

**Duration of Approval:** Lifetime

ANTIDIABETIC AGENTS

Pioglitazone
Brand(s): Actos, Generics
DOSAGE FORM/ STRENGTH: 15 mg, 30 mg, 45 mg tablet

For the treatment of type 2 diabetes in patients who require;

- Dual combination therapy of diabetes AND demonstrate inadequate glycemic control (HbA1c of >7%) on maximal doses of metformin (2000 mg/day) OR
- Dual combination therapy of diabetes AND demonstrate inadequate glycemic control (HbA1c of >7%) on maximal* doses of sulfonylurea and demonstrated intolerance / contraindication to metformin OR
- Triple combination therapy of diabetes and who demonstrate inadequate glycemic control on maximal** doses of metformin and a sulfonylurea AND only if the physician has offered insulin as an alternative option first, and the patient has refused or is not able to take insulin. Note: Both the physician and patient must be aware that thiazolidinediones (TZDs), are not indicated for use in triple therapy.

***Those with one or more of the following contraindications/ precautions to therapy with pioglitazone/rosiglitazone will not be considered.
Pioglitazone
Brand(s): Actos, Generics
DOSAGE FORM/STRENGTH: 15 mg, 30 mg, 45 mg tablet

- Patients with type 1 diabetes
- Patients who will be using this as monotherapy
- Combination use with a nitrates
- Combination use with insulin
- Patients with any stage of heart failure (i.e. NYHA Class I, II, III, IV)
- Patients at high risk for bone fracture (i.e. post-menopausal women with previously confirmed osteoporosis or osteopenia)
- Patients with recent history (in the past 3 months) of an ischemic cardiovascular event (myocardial infarction, unstable angina)

* Note: For the purpose of the EAP submission, maximal dose of sulfonylurea is considered to be glyburide 10 mg/day, gliclazide 160mg/day OR Diamicron MR 60mg/day, OR glimepiride (Amaryl) 4 mg/day.

**Note: For the purpose of the EAP submission, maximal dose of metformin is considered to be 2000 mg/day.

Duration of Approval: 5 years

Renewals as well as requests for ongoing treatment in patients previously provided these drugs by other means will be considered for those patients who have NOT developed a contraindication/precautionary use*** in the intervening period AND have demonstrated a recent HbA1c level ≤7% while on treatment

Duration of Approval: 5 years

Repaglinide
Brand(s): GlucoNorm
DOSAGE FORM/STRENGTH: 0.5 mg, 1 mg, 2 mg tablet

For the treatment of type 2 diabetes in patients with:

- Inadequate glycemic control (HbA1c >7%) using maximal* doses of a sulfonylurea AND metformin (2000mg/day) OR
- Inadequate glycemic control and demonstrated intolerance or contraindication to metformin and who are on maximal* doses of a sulfonylurea OR
- Inadequate glycemic control and demonstrated intolerance or contraindication to a sulfonylurea (glyburide, gliclazide or glimepiride) and are on maximal** doses of metformin OR
- Demonstrated intolerance or contraindication to both a sulfonylurea (glyburide, gliclazide or glimepiride) AND metformin OR
**Repaglinide**

**Brand(s):** GlucoNorm  
**DOSAGE FORM/ STRENGTH:** 0.5 mg, 1 mg, 2 mg tablet

- Adequate glycemic control (HbA1c ≤ 7%) who develops intolerance or contraindication to sulfonylurea (glyburide, gliclazide or glimepiride) or metformin OR
- HbA1c ≤ 7% but with greater than 50% of fasting blood glucose (FBG >7mmol/L) or post-prandial plasma glucose (PPG >10mmol/L) levels not within target range and using maximally tolerated doses of a sulfonylurea and metformin.

* **Note:** For the purpose of the EAP submission, maximal dose of sulfonylurea is considered to be glyburide 10mg/day, gliclazide 160 mg/day or Diamicron MR 60 mg/day, OR glimepiride (Amaryl ) 4 mg/day.

**Note:** For the purpose of the EAP submission, maximal dose of metformin is considered to be 2000 mg/day  
**Duration of Approval:** 5 years

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**Rosiglitazone**

**Brand(s):** Avandia  
**DOSAGE FORM/ STRENGTH:** 2 mg, 4 mg, 8 mg tablet

For the treatment of type 2 diabetes mellitus in patients with:

- Inadequate glycemic control (HbA1c >7%) from ALL other oral antidiabetic agents* funded through one of the Ontario Drug Benefit Programs, in monotherapy or in combination OR
- Where ALL other oral antidiabetic agents are inappropriate due to contraindications or intolerance AND
- The patient has refused or is not able to take insulin AND
- There is no known contraindication to rosiglitazone.

* Oral antidiabetics include the following agents:
  - glyburide
  - metformin
  - gliclazide (Diamicron, Diamicron MR)
  - sitagliptin (Januvia)
  - saxagliptin (Onglyza)
  - repaglinide (GlucoNorm)
  - pioglitazone (Actos)
Note: A trial with acarbose is not a mandatory requirement.

Note: It is not necessary for patients to have tried the following oral antidiabetic agents that are currently not funded by the OPDP for the purposes of obtaining rosiglitazone:

- glimepiride (Amaryl)
- nateglinide (Starlix)

**Duration of Approval:** 5 years

**Renewals** will be considered where patients have benefited and continue to benefit from rosiglitazone treatment as demonstrated by recent HbA1c levels ≤7% while on treatment with rosiglitazone AND in those who continue to have no known contraindication(s) to rosiglitazone.

**Duration of Approval:** 5 years

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**Orlistat**

**Brand(s):** Xenical

**DOSAGE FORM/ STRENGTH:** 120 mg capsule

For the treatment of type 2 diabetes in a patient with:

- Inadequate glycemic control (i.e., HbA1c > 7.0%) on maximal oral antidiabetic medications* **AND**
- Body Mass Index ≥ 27 **AND**
- Demonstrated failure to a trial of nutritional/dietary counselling and exercise programs

* Note: Maximal dose of sulfonylurea is considered to be glyburide 10mg/day, gliclazide (160mg/day or Diamicron MR 60 mg/day) OR glimepiride (Amaryl ) 4mg/day.

Note: Maximal dose of metformin is considered to be 2000 mg/day

**Duration of Approval:** 1 year

**Renewals** will be considered for those with demonstrated response to treatment reported as at least 5% weight loss and improvement in glycemic control (i.e., HbA1c <7.0% or HbA1c reduction of more than 0.5%)

**Duration of Approval:** 12 months (First Renewal)
ANTI-INFECTIVES

Aztreonam
Brand(s): Cayston

**DOSAGE FORM/ STRENGTH:** 75 mg/vial powder for solution

For the treatment of chronic infection with *Pseudomonas aeruginosa* (PsA) infection in patients with a diagnosis of Cystic Fibrosis who meet all the following criteria:

(a) Patient has a documented diagnosis of cystic fibrosis;
(b) Patient has a chronic infection with *Pseudomonas aeruginosa* (PsA) that has been confirmed by 2 (two) positive sputum cultures taken at least 1 month apart that are both positive for PsA;
(c) the Patient’s clinical condition is deteriorating despite treatment with inhaled tobramycin;
(d) the Patient has moderate to severe impairment of lung function defined by baseline FEV1 < 75% of predicted; and
(e) the Patient is ≥ 6 years old.

**Exclusion Criteria:** Aztreonam (Cayston) will not be funded in the following circumstances.

- Aztreonam will not be funded in combination with tobramycin inhalation
- Aztreonam will not be funded for bronchiectasis indications outside of proven cystic fibrosis
- Aztreonam will not be funded outside of the cystic fibrosis population
- Aztreonam will not be funded for patients with mild cystic fibrosis;
- Aztreonam will not be funded for the purpose of convenience

**Approved Dosage.** The approved dosage for Aztreonam (Cayston) under the EAP is as follows:

Inhale 75 mg three times daily used in a repeated 28 day cycle that involves administration of aztreonam for 4 weeks of treatment followed by 4 weeks off aztreonam therapy.

**Duration of Approval:** 1 year

**Renewals** will be considered in patients who demonstrate ongoing response to therapy.

**Duration of Approval:** 1 year

**Approved Dosage.** The approved dosage for Aztreonam (Cayston) under the EAP is as follows:

Inhale 75 mg three times daily used in a repeated 28 day cycle that involves administration of aztreonam for 4 weeks of treatment followed by 4 weeks off aztreonam therapy.

**Renewals** will be considered in patients who demonstrate ongoing response to therapy.

**Duration of Approval:** 1 year
**Dapsone**
*Brand(s): Dapsone*

**DOSAGE FORM/ STRENGTH:** 100 mg tablet

Note that Effective on July 31, 2018, Dapsone has been moved to the Ontario Drug Benefit (ODB) Formulary as a general benefit.

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**Daptomycin**
*Brand(s): Cubicin*

**DOSAGE FORM/ STRENGTH:** 500 mg/10 mL powder for injection

Note that initial requests for Daptomycin may be accessed through the EAP’s Telephone Request Service.

For the treatment of patients experiencing the following types of infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria:

1. Staphylococcus aureus bloodstream (SAB) infection including right-sided *Staphylococcus aureus* infective endocarditis (SARIE); AND/OR
2. Osteomyelitis; AND/OR
3. Device-related osteoarticular or prosthetic joint infections; AND/OR
4. Diabetic foot infections.

Additionally, the patient must have failed to adequately respond to, be intolerant\(^1\) to, or have a contraindication to vancomycin.

\(^1\)Intolerance due to Red Man Syndrome. If the physician asserts that the patient is intolerant to vancomycin due to red man’s syndrome, additional clinical details of the patient’s intolerance, including rate of infusion and the use of antihistamines and other histamine blockers prior to therapy with vancomycin.

**Duration of Approval:** Up to 8 weeks

**Renewals** will be considered on a case-by-case basis. (Physicians must submit adequate clinical information to justify the need for ongoing therapy with daptomycin.)

**Duration of Approval:** Case-by-case

**Exclusion Criteria:**
- Daptomycin is not funded for patients with MRSA-related pneumonia;
- Daptomycin is not funded for patients with skin/skin structure infections other than diabetic foot infections caused by MRSA.
Fidaxomicin (May be accessed through the telephone request service)
Brand(s): Dificid
DOSAGE FORM/ STRENGTH: 200 mg tablet

For the treatment of Clostridium difficile infection (CDI) in patients who meet the EAP criteria for vancomycin use, but where the patient:

- has experienced a third or subsequent episode within 6 months of treatment with vancomycin for prior episode(s), with no previous trial of fidaxomicin; OR
- has experienced treatment failure* with oral vancomycin for the current CDI episode; OR
- has had a documented allergy (immune-mediated reaction) to oral vancomycin; OR
- has experienced a severe adverse reaction or intolerance** to oral vancomycin treatment that resulted in the discontinuation of vancomycin therapy.

*Treatment failure is defined as 7 days of vancomycin therapy without acceptable clinical improvement.

**Details of severe adverse reaction or intolerance must be provided and should be clinically related to oral administration of vancomycin.

Re-treatment criteria:

- Re-treatment with fidaxomicin will only be considered for an early relapse occurring within 30 days of the completion of the most recent fidaxomicin course.
- Relapse/ recurrence occurring beyond 30 days after the completion of the most recent fidaxomicin course will require a trial with vancomycin, unless there is a documented allergy, severe adverse reaction or intolerance to prior oral vancomycin use.

Note: Fecal biotherapy ("stool transplantation"), if available, should be encouraged for this patient population.

Approved dose and duration: 200 mg twice a day for 10 days.
Fluconazole
Brand(s): Diflucan, Generics
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg, tablets, 150 mg capsule, 10mg/mL oral solution

Effective with the June 2018 formulary update, fluconazole tablets are made available as a General Benefit on the Ontario Drug Benefit (ODB) Formulary and fluconazole oral solution is made available as a Limited Use Benefit on the ODB formulary.

Levofloxacin hemihydrate
Brand(s): Quinsair
DOSAGE FORM/ STRENGTH: 240mg/ 2.4mL solution for inhalation

For the management of adult cystic fibrosis patients with chronic pulmonary Pseudomonas aeruginosa (P.aeruginosa) infections who meet the following criteria:

- Documented diagnosis of Cystic Fibrosis; AND
- Patient is 18 years of age or older; AND
- Chronic infection with Pseudomonas aeruginosa (PsA) [confirmed by 2 (two) PsA positive sputum cultures taken at least 1 month apart]; AND
- Patient has failed treatment with inhalational tobramycin and demonstrates deteriorating clinical condition despite treatment with inhaled tobramycin; AND
- Request is from a prescriber experienced in the diagnosis and treatment of cystic fibrosis.

Exclusion criteria:

- Use in combination (sequential or cycled during off-treatment periods) with other inhaled antibiotics to treat P.aeruginosa will not be funded.

- Funding will not be provided for conditions outside of cystic fibrosis.

Approval duration: 1 year

Renewal requests:

Patient demonstrates response to therapy.

Approval duration: 1 year
Posaconazole
Brand(s): Posanol
DOSAGE FORM/ STRENGTH: 40 mg/mL Suspension

For the prophylaxis of Aspergillus and Candida infections in patients who have recently (within the past 3 months) undergone an allogeneic bone marrow transplant.

Duration of Approval: Limited to 4 months

For the prophylaxis of invasive fungal infections in patients who have previously (3 months or longer) undergone an allogeneic stem cell transplant and are experiencing moderate to severe graft-versus-host-disease (GVHD) will be considered on a case-by-case basis.

Note: Please provide details of the patient’s clinical condition including all medications used to treat the condition with your request application.

Duration of Approval: Up to 4 months

Renewals will be considered on a case-by-case basis for patients who continue to experience ongoing symptoms of moderate to severe GVHD. Please provide information regarding infections that were experienced while on therapy (as applicable) including the names of medications and treatments being used to manage GVHD.

Duration of Approval: Case-by-case

For the treatment of invasive aspergillosis* in patients who are refractory or intolerant to voriconazole OR who have documented contraindication to voriconazole.

*Invasive aspergillosis should be confirmed by fungal culture.

Note: Requests without a positive fungal culture must be accompanied by a consultation note from an infectious disease expert with details of how the diagnosis was made and will be considered on a case-by-case basis.

Duration of Approval: 3 months

Renewals will be considered on a case-by-case basis.
Posaconazole
Brand(s): Posanol
DOSAGE FORM/ STRENGTH: 40 mg/mL Suspension

For the treatment of mucormycosis** in patients who have failed, have a contraindication to, or experienced intolerance to amphotericin B; OR

Duration of Approval: 3 months

For the step-down treatment of mucormycosis** in patients who have been initially treated with amphotericin B but cannot tolerate long-term therapy with this agent.

**Mucormycosis infection must be confirmed by fungal culture.

Note: Requests without a positive fungal culture but where the diagnosis of mucormycosis is documented by an infectious diseases consult and other tools (e.g, radiology reports, histopathology, etc.) will be considered on a case-by-case basis.

Duration of Approval: 3 months

Renewals will be considered for patients who are responding to therapy but who have not experienced clinical resolution of their condition. Note that requests for renewal must be accompanied by supporting clinical information ( Infectious disease consultation/radiology report)

Duration of Approval: 3 months

Duration of Approval of subsequent renewal: Case-by-case
Vancomycin (May be accessed through the telephone request service)
Brand(s): Vancocin and other generics (Note that only specific DINs are reimbursed by the EAP)
DOSAGE FORM/ STRENGTH: 125 mg capsules, 250 mg capsules

For the treatment of patients with symptomatic Clostridium difficile-associated diarrhea (CDAD) with diagnosis confirmed by:
- Positive toxin assay; or
- Typical endoscopic appearance; or
- Typical histologic pattern on biopsy; or
- Pending toxin results and clinical suspicion of CDAD; or
- Clinical suspicion and less than 30 days since last CDAD episode that was diagnosed by any of the above 3 criteria (quick relapse).

AND meeting one of the below criteria:
- Documentation of Severe CDAD*
- 3 or more episodes in the last 6 months
- Relapse within 60 days of completion of previous vancomycin therapy
- Contraindication or current/previous intolerance to metronidazole
- Failure (inadequate clinical response) with metronidazole for the current episode

*Indicators of Severe CDAD: If patient has ≥ two indicators from column 1 OR ≥ one indicator from column 2, then failure of a standard course of metronidazole is NOT required.

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<thead>
<tr>
<th>Column 1 (Two Of):</th>
<th>Column 2 (One Of):</th>
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<tbody>
<tr>
<td>• Age ≥ 65 years old</td>
<td>• Toxic megacolon</td>
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<td>• Renal failure SrCr ≥ 200 umol/L</td>
<td>• Septic shock/hypotension</td>
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<td>• High leukocyte count &gt;15x109 cells/L</td>
<td>• Bowel perforation</td>
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<td>• Serum albumin &lt; 25 g/L</td>
<td>• Ileus</td>
</tr>
<tr>
<td>• Temperature &gt; 38.3°C</td>
<td>• Need for colectomy</td>
</tr>
<tr>
<td></td>
<td>• Treatment in the ICU</td>
</tr>
</tbody>
</table>
Vancomycin (May be accessed through the telephone request service)
Brand(s): Vancocin and other generics (Note that only specific DINs are reimbursed by the EAP)
DOSAGE FORM/ STRENGTH: 125 mg capsules, 250 mg capsules

Approved Dose and Duration:
1st episode:
- Severe CDAD: 125mg-250 mg four times daily for 2 weeks
- Non-severe CDAD: 125 mg four times daily for 2 weeks

2 episodes in 6 months:
- Severe CDAD or Early Relapse: 125 mg-250 mg four times daily for 4 weeks
- Non-severe CDAD: 125mg four times daily for 4 weeks

3 or more episodes in 6 months:
- 125mg-250mg four times daily for 8 weeks

Duration of Approval:
Duration is provided based on the clinical history of the CDI infection provided. Range of 2 to 8 weeks based on clinical details which include the number of episodes for the infection

Voriconazole
Brand(s): VFend
DOSAGE FORM/ STRENGTH: 50 mg, 200 mg tablets, 200 mg/vial injection

For the treatment of patients who have culture positive candidemia, due to Candida species, AND with documented resistance to fluconazole.

This will be for patients whose therapy is initiated in the hospital by a hospital physician and who require continuation of therapy when they are discharged as an outpatient. Oral tablets will be authorized for those with a properly functioning gastrointestinal (GI) tract and the parental injection will be authorized for those who do not have a properly functioning GI.

Case-by-case consideration for other indications will be provided.

Duration of Approval: 1 month
### ANKYLOSING SPONDYLITIS DRUGS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand(s)</th>
<th>DOSAGE FORM/ STRENGTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>Brand(s): Humira</td>
<td>40mg/0.8mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>Brand(s): Cimzia</td>
<td>200 mg/mL prefilled syringe</td>
</tr>
<tr>
<td>Etanercept*</td>
<td>Brand(s): Enbrel</td>
<td>25mg/vial and 50mg prefilled syringe for subcutaneous injection</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Brand(s): Simponi</td>
<td>50 mg/0.5 ml prefilled syringe and autoinjector</td>
</tr>
<tr>
<td>Infliximab*</td>
<td>Brand(s): Remicade</td>
<td>100mg/10mL intravenous infusion</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>Brand(s): Cosentyx</td>
<td>150 mg/mL prefilled syringe and 150 mg/mL prefilled pen</td>
</tr>
</tbody>
</table>

Biosimilars are available on the formulary as Limited Use Benefits and all patients treatment naïve to the innovator biologics for which a funded biosimilar exists should refer to the EO announcements as a guide to public funding for the innovator and biosimilar products.
Effective February 25, 2016, Infliximab as Inflectra can be considered for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis will only be considered for funding for existing EAP renewals.

Effective on September 27, 2018, Infliximab as Renflexis can be considered for adult and pediatric rheumatology conditions. Refer to the Limited Use criteria on the Ontario Drug Benefit Formulary.

Effective July 31, 2017, etanercept as Enbrel for the treatment of ankylosing spondylitis (AS) and rheumatoid arthritis (RA) will only be considered for funding for existing EAP renewals. Etanercept as Brenzys can be considered through Limited Use criteria on the Ontario Drug Benefit Formulary.

Effective December 21, 2017 etanercept as Erelzi for the treatment of ankylosing spondylitis (AS), rheumatoid arthritis (RA), and polyarticular juvenile idiopathic arthritis (pJIA) will only be considered for funding for existing EAP renewals. Etanercept as Brenzys can be considered through Limited Use criteria on the Ontario Drug Benefit Formulary.

For the treatment of ankylosing spondylitis (AS) OR psoriatic spondylitis (PS) in patients who have severe active disease with:

- Age of disease onset 50 years of age or younger; **AND**
- Low back pain and stiffness for greater than 3 months that improves with exercise and not relieved by rest; **AND**
- Failure to respond to or documented intolerance to adequate trials of 2 non-steroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks each; **AND**
- BASDAI score of ≥ 4 for at least 4 weeks while on standard therapy; **AND**
- A list of current concomitant medications related to the AS/PS, including pain medications (if relevant) with dosing regimens provided.

*NSAIDs include coxibs; use of DMARDS instead of NSAIDs not acceptable

The information submitted with the request must include the following:

- A list of current concomitant medications related to the AS/PS, including pain medications (if relevant). Please include dosing regimens.
- Details of review of radiographic reports for severe active disease.
  - X-ray or CT scan report stating the presence of “SI joint fusion” or “SI joint erosion” **OR**
  - MRI report stating the presence of “inflammation” or “edema” of the SI joint
  - Actual radiographic reports must be submitted with the request. If the radiographic reports do not specify the above, the request will be reviewed by external medical experts.

Additional information that should be provided if applicable:

- Schober measurement and chest expansion measurement
- Evidence of restricted spinal mobility
• If the patient has AS/PS with predominantly peripheral joint involvement, additional information pertaining to trials of DMARDs must be provided, and these requests will be reviewed by external medical experts.

**Duration of Approval:** 1 year

**Renewal** will be considered for patients with objective evidence of at least a 50% reduction in BASDAI score or ≥ 2 absolute point reduction in BASDAI score. Please provide an update on concomitant medications for AS/PS and whether there has been a reduction in pain medication for AS/PS since initiating the biologic (if applicable).

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The planned dosing regimen for the requested biologic should be provided.

The recommended doses for the treatment of AS/PS are:

- Adalimumab 40 mg every two weeks
- Certolizumab 400mg at 0, 2, and 4 weeks followed by maintenance therapy of 200 mg every 2 weeks or 400 mg every 4 weeks.
- Etanercept 25 mg twice weekly or 50 mg once weekly
- Golimumab 50mg once a month
- Infliximab 3-5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of up to 5mg/kg/dose every 6 to 8 weeks
- Secukinumab 150 mg sc at weeks 0, 1, 2, and 3 followed by monthly maintenance dosing starting at week 4.

**Duration of Approval:** First renewal: 1 year, Second and subsequent renewals: 2 years
### ASTHMA

**Zafirlukast**
Brand(s): Accolate  
**DOSAGE FORM/ STRENGTH:** 20 mg tablet

**Montelukast**  
Brand(s): Singulair  
**DOSAGE FORM/ STRENGTH:** 5 mg, 10 mg tablet

For the treatment of asthma patients who cannot manage the use of an inhalation device despite assistance with a spacer (e.g. physically or mentally disabled patients or pediatric patients).

**Duration of Approval:** 5 years

OR

For the treatment of asthma in children and adolescents whose asthma cannot be controlled on ICS alone and where the condition remains uncontrolled despite using full doses of ICS with addition of LABA, and with assurance of good adherence and inhaler technique.

**Duration of Approval:** 5 years (up until age of 18)

**Renewal** of requests that meet the above criteria will be provided where the following apply:
- Current medications and dosages must be clearly specified; AND  
  Objective evidence of positive response from treatment (spirometry OR decrease in health care utilization) must be provided

**Duration of Approval:** 5 years (up until age of 18)

**Omalizumab**
Brand(s): Xolair  
**DOSAGE FORM/ STRENGTH:** 150 mg/ vial

For the treatment of severe uncontrolled asthma in patients who meet the following criteria:
- Has required hospitalization for asthma within the past 12 months; OR
- Has required two or more urgent visits for asthma to a physician or an emergency department within the past 12 months; OR
-
Omalizumab
Brand(s): Xolair
DOSAGE FORM/ STRENGTH: 150 mg/ vial

- Has had two or more courses of high-dose oral corticosteroids in the past 12 months; AND
- Is age 12 years or older; AND
- Has demonstrated a positive skin test or in vitro reactivity to a perennial aeroallergen; AND
- Has a baseline IgE level between 30 and 700 IU/mL (inclusive); AND
- Has an actual body weight between 20 kg to 150 kg (inclusive); AND
- Is receiving treatment with a high-dose inhaled corticosteroid* in addition to a long-acting inhaled beta 2-agonist. (Note: the patient can be on other concomitant therapies as well); AND
- Is deemed to be adherent and is using his/her inhaled corticosteroid and long-acting beta agonist daily as prescribed; AND
- Is using proper inhaler technique (with a spacer if required); AND
- The request for Xolair is made by the patient’s specialist in respirology or allergy/clinical immunology. (Note: Individual consideration can be given for extenuating circumstances where access to these specialists is not possible.)

* High-dose inhaled corticosteroids is considered the use of more than 1000 mcg of beclomethasone dipropionate (BDP) equivalents daily.

To avoid delays in the assessment of the request, physicians should provide the following information within their request submission.

1. The number of hospitalizations for asthma in the past 12 months.
2. The number of asthma exacerbations requiring urgent visits to a physician or emergency department in the past 12 months.
3. The average number of night-time awakenings in a one week period. (reflective of control in last 12 months).
4. The average number of puffs/day of short-acting beta-agonists within a one week period (reflective of control in last 12 months).
5. The number of courses of prednisone (or acute increases in prednisone dose if the patient is already using chronic daily prednisone) for asthma exacerbation in the past 12 months.
6. The FEV₁ pre and post bronchodilator.
8. The serum IgE level.
9. Results of a positive allergy testing by skin prick test or IgE RAST.
10. A list of all of the patient’s current asthma medications including drug name and doses.
11. Confirmation that the patient’s asthma is currently uncontrolled despite optimal therapy (including confirmation of proper inhaler technique), patient adherence to current therapy, and the removal of allergic and environmental triggers or the reduction of such triggers to the fullest extent possible.
Omalizumab
Brand(s): Xolair
DOSAGE FORM/ STRENGTH: 150 mg/ vial

Note that contraindications and intolerance to inhaled corticosteroids and/or long-acting beta agonists will not be considered as a justification to request Xolair funding.

Duration of Approval: 1 year

Renewal of requests for Xolair will be considered in patients who have a positive clinical response to the drug and who are expected to continue to do so. Renewals will be considered on a case-by-case basis and should be accompanied by the following information:

1. The number of hospitalizations for asthma in the past 12 months
2. The number of asthma exacerbations requiring urgent visits to a physician or Emergency Department in the past 12 months
3. The number of courses of prednisone (or acute increases in prednisone dose if patient is already using chronic daily prednisone) for asthma exacerbations in the past 12 months.

4. The number of nighttime awakenings (over a several week period post-introduction of therapy)
5. The average number of puffs/day of short-acting beta-agonists used per day (over a several week period post-introduction of therapy)
6. The FEV₁ pre and post bronchodilator

7. All current asthma medications taken by the patient including drug names and dosing schedule.

Duration of Approval: Up to 1 year
Mepolizumab
Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Injection

For the treatment of adult patients with severe eosinophilic asthma who meet ALL the following criteria:

i) Mepolizumab is being used as an add-on maintenance therapy; AND

ii) Patient is inadequately controlled with high dose inhaled corticosteroids (ICS) (greater than or equal to 500 mcg of fluticasone propionate (FP) equivalents daily) used with one or more asthma controller(s) (e.g., a long-acting beta-agonist [LABA], leukotriene receptor antagonist [LTRA], theophylline); AND

iii) Demonstrates a blood eosinophil count greater than or equal to 150 cell/mcL prior to start of mepolizumab (levels must be drawn within 3 months prior to the start of treatment) OR a count greater than or equal to 300 cell/mcL within the 12 months prior to start of mepolizumab; AND

iv) Patient must have experienced two or more clinically significant asthma exacerbations in the past 12 months and show reversibility on pulmonary function tests/laboratory spirometry (i.e. at least 12% and 200 mL in FEV1 or FVC from baseline/pre-bronchodilator values) OR is being treated with daily oral corticosteroids for their asthma; AND

v) Request is from a specialist in respirology, or allergy/clinical immunology, or by a physician with expertise in the treatment of asthma. Individual consideration can be given for extenuating circumstances where access to these specialists is not possible.

Duration of approval: 1 year

Renewals will be considered on a case-by-case basis for patients who do not meet any of the stopping criteria.

1Stopping criteria are defined as:

• Failure to achieve a decrease in any clinically significant exacerbations (defined as worsening of asthma resulting in administration of systemic corticosteroids for at least 3 days, or an emergency room visit, or hospitalization) within 12 months of initial funding; OR
Mepolizumab
Brand(s): Nucala
DOSAGE FORM/ STRENGTH: 100 mg/mL Injection

- Failure to achieve at least a 25% decrease in the maintenance oral corticosteroid dose at 12 months of initiation of mepolizumab.

Duration of renewals: 1 year

Approved dose: 100 mg subcutaneous every 4 weeks.

**BLOOD MODIFIERS**

**Deferasirox**
Brand(s): Exjade
DOSAGE FORM/ STRENGTH: 125 mg, 250 mg, 500 mg tablet

Brand(s): Jadenu
DOSAGE FORM/ STRENGTH: 90 mg, 180 mg, 360 mg tablet

For the treatment of patients with chronic iron overload in transfusion-related anemia due to B-thalassemia or sickle cell disease in patients who meet the following criteria;

i) Patient is 6 years of age or older; OR

ii) The patient is between 2 to 5 years of age (inclusive) and cannot be adequately treated with deferoxamine.

Combination therapy (i.e., Deferasirox (Exjade or Jadenu) in addition to another iron chelating agent) will not be approved.

Note, that therapy should be initiated and maintained by physicians experienced in the treatment of chronic iron overload due to blood transfusions.

**Renewals** will be considered in patients who continue to require iron chelation therapy and has had a consistent response to therapy (demonstrated by a reduction in baseline liver iron concentration (LIC) levels).

The following documentation is required for renewals:

- A transfusion record from the past year; AND

LIC levels – baseline (pre-treatment) and since initiation of treatment. The most recent LIC level should be from within the previous year.
### Deferasirox

**Brand(s):** Exjade

**DOSAGE FORM/ STRENGTH:** 125 mg, 250 mg, 500 mg tablet

**Brand(s):** Jadenu

**DOSAGE FORM/ STRENGTH:** 90 mg, 180 mg, 360 mg tablet

For the treatment of chronic iron overload in transfusion-dependent anemia in those with low-risk myelodysplastic syndrome (MDS) or other rare anemias (e.g. Diamond Blackfan) in patients who have a contraindication or severe intolerance to deferoxamine.

Contraindications may include one or more of the following:

- known or suspected hypersensitivity to deferoxamine
- recurrent injection or infusion-site reactions (e.g., cellulitis)
- concomitant bleeding disorder
- immunocompromised patients with a documented risk of significant infections with parenteral administration (e.g. neutropenia)

**Duration of Approval:** 1 year

**Renewals** will be considered on a case-by-case basis. Physicians must provide adequate information to support the request for renewal.

Note: If switching between brands of deferasirox, please include the reasons for switching (e.g. description of the intolerance etc.) with your request application.

**Duration of Approval:** 5 years

### Deferiprone

**Brand(s):** Ferriprox

**DOSAGE FORM/ STRENGTH:** 1000 mg Tablets, 100 mg/mL oral solution

For the treatment of patients with transfusional iron overload due to thalassemia syndromes who cannot be adequately treated with deferoxamine or deferasirox.

Notes:

Combination iron chelation therapy with Ferriprox will be considered on a case-by-case basis.

Therapy should be initiated and maintained by physicians experienced in the treatment of chronic iron overload due to blood transfusions.

**Duration of Approval:** 5 years
Renewals will be considered for Patients who continue to require iron chelation therapy and has had a consistent response to therapy (demonstrated by a reduction in baseline liver iron concentration (LIC) levels).

The following documentation is required:

- A transfusion record from the past year; and
- LIC levels – baseline (pre-treatment) and since initiation of treatment. The most recent LIC level should be from within the previous year.

Duration of Approval: 5 years

Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

For the treatment of patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) meeting the following criteria:

The diagnosis of Paroxysmal Nocturnal Hemoglobinuria (PNH) has been made based on the following confirmatory results:

- Flow cytometry/FLAER exam with granulocytes clone ≥ 10% AND
- LDH > 1.5 ULN

AND at least one of the following:

- A thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy,
- Minimum transfusion requirement of 4 units of red blood cells in the previous 12 months,
- Chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70 g/L or by more than one measure of less than or equal to 100 g/L with concurrent symptoms of anemia,
- Pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded,
- Renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73 m², where causes other than PNH have been excluded,
- Smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded.

The dose of eculizumab that will be considered is:

600 mg once per week for the first 4 weeks, then from week five of treatment, 900 mg once every 2 weeks

Duration of Approval: 6 months
Eculizumab
Brand(s): Soliris
DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

Renewals will be considered for patients who:

- Demonstrate clinical improvement while on therapy or
- Where therapy has been shown to stabilize the patient's condition.

Requests for renewal should be accompanied by confirmation of granulocyte clone size (by flow cytometry).

Further, subsidized treatment may continue unless one or more of the following situations apply:

i) The patient or treating physician fails to comply adequately with treatment or measures, including monitoring requirements, taken to evaluate the effectiveness of the therapy;

ii) If therapy fails to relieve the symptoms of disease that originally resulted in the patient being approved for subsidized treatment;

Other eligibility requirements:

Note: All patients must receive meningococcal vaccination with a tetravalent vaccine at least two weeks prior to receiving the first dose of eculizumab.

Exclusion criteria for both initial and renewal requests:

i) Small granulocyte clone size - the treatment of patients with a granulocyte clone size below 10% will not be eligible for treatment; OR

ii) Aplastic anemia with two or more of the following: neutrophil count below 0.5 x 10^9/L, platelet count below 20 x 10^9/L, reticulocytes below 25 x 10^9/L, or severe bone marrow hypocellularity; OR

iii) Patients afflicted with PNH and another life-threatening or severe disease where the long term prognosis is unlikely to be influenced by therapy (for example acute myeloid leukemia or high-risk myelodysplastic syndrome); OR

iv) The presence of another medical condition that might reasonably be expected to compromise a response to therapy.

Preamble:
A confirmed diagnosis of atypical hemolytic uremic syndrome (aHUS) is required for eculizumab funding. The information below is to provide clinicians with context for how a diagnosis of aHUS will be assessed for funding consideration. Details to address these issues should be provided in the funding request.
Eculizumab

Brand(s): Soliris

**DOSAGE FORM/ STRENGTH:** 10 mg/mL (300 mg per vial)

While some patients may already have a confirmed aHUS diagnosis, by clinical history and/or genetic testing, the majority of patients presenting with thrombotic microangiopathy (TMA) have no prior diagnosis of aHUS. For most patients presenting with a TMA, it is not possible to confidently separate aHUS from the vast majority of other conditions causing TMA until after appropriate testing and treatment have occurred. The majority of patients who have TMA suffer from Thrombotic Thrombocytopenic Purpura (TTP) (30-40%), or a secondary form of TMA (e.g., pregnancy, HIV, collagen vascular disease, drugs, malignancy, stem cell transplant, malignant hypertension) (> 50%), or hemolytic uremic syndrome due to a Shiga toxin (>5%). In most cases, patients who suffer from TTP will have an ADAMTS-13 of less than 10%. If TTP has been ruled out and any secondary causes have been treated and the patient still has a persisting unexplained TMA with ADAMTS-13 ≥10%, the patient would be presumed to suffer from aHUS. Patients who present with ADAMTS-13 of ≥10% and who are unresponsive to plasma therapy (>4 plasma exchanges) and do not have a known secondary explanation would also be presumed to suffer from aHUS.

In the absence of a confirmed diagnosis of aHUS, there is nothing in these criteria that changes the clinical expectation for appropriate use of plasma exchange/plasma infusion in the management of patients presenting with TMA.

**Initiation Criteria**

A patient must meet all three of the following criteria to obtain funding for initial treatment with eculizumab:

1. Confirmed diagnosis* of atypical hemolytic uremic syndrome (aHUS) at initial presentation, defined by:
   a. Presence of an unexplained non-disseminated intravascular coagulation thrombotic microangiopathy (TMA); AND
   b. Baseline ADAMTS-13 activity ≥ 10% on blood samples taken prior to plasma exchange or plasma infusion (PE/PI);

   **Note:**
   If the sample for ADAMTS-13 was not collected prior to PE or PI, platelet counts > 30 x 109/L and eGFR < 50 mL/min/1.73m² at TMA presentation will be accepted as predictive of ADAMTS-13 ≥10% in TMA patients. In this case, measurement of ADAMTS-13 can
Eculizumab

Brand(s): Soliris

DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)

be taken 1-2 weeks following the last PE. The ADAMTS-13 result must be provided within 30 days of commencement of eculizumab and at least 1 week after the last PE. A one-month interim funding for eculizumab will be provided.

AND

c. STEC-negative test in patients with a history of bloody diarrhea in the preceding two weeks; AND

d. Other diagnoses and causes of TMA must be ruled out, as per preamble.

2. Evidence of ongoing active and progressing TMA as defined by:
   a. Thrombocytopenia (platelet count <150 x 10^9/L) that is not explained by some other cause including secondary TMA; AND hemolysis as indicated by the documentation of two of the following: red blood cell (RBC) fragmentation (schistocytes) on the blood film; low or absent haptoglobin; or lactate dehydrogenase (LDH) above normal; OR
   b. Tissue biopsy confirming TMA in patients who do not have evidence of platelet consumption and hemolysis.

   Note: Review by external clinical expert may be required to assess requests for patients with ongoing TMA that may not clearly meet the above criteria.

3. Evidence of at least one of the following documented clinical features of active organ damage or impairment:
   a. Kidney impairment as demonstrated by one of the following:
      o A decline in estimated glomerular filtration rate (eGFR) or a rise in serum creatinine (SrCr) of >20% in a patient with pre-existing renal impairment; OR
      o SrCr > upper limit of normal (ULN) for age or eGFR < 60mL/min in patients who have no history of pre-existing renal impairment (i.e., who have no baseline eGFR measurement); OR
      o SrCr > the age-appropriate ULN in pediatric patients (subject to advice from a pediatric nephrologist); or
      o Renal biopsy;
   OR
**Eculizumab**

**Brand(s):** Soliris

**DOSAGE FORM/ STRENGTH:** 10 mg/mL (300 mg per vial)

b. Onset of neurological impairment related to TMA (e.g., visual field defect, hemiparesis, sensory loss, asymmetric limb weakness, confusion, loss of consciousness/coma, new onset seizure).

Note: Patients who have extra-renal complications related to TMA (e.g., TMA-related cardiac impairment, TMA-related gastrointestinal impairment, or TMA-related pulmonary impairment) will be reviewed by an external clinical expert.

**Continuation Criteria (at 6 months)**

After six months of eculizumab therapy, a further six month of funding will be considered if the patient demonstrates treatment response, defined as:

Hematological normalization (platelet count, LDH, haptoglobin); AND

- An improvement or stabilization of eGFR (or SrCr); AND

- Stabilization of neurological or extra-renal impairment if these complications were originally present.

Continued treatment with eculizumab will not be funded beyond six months if a patient has experienced treatment failure, defined as:

- Dialysis-dependent at six months, and failed to demonstrate resolution or stabilization of neurological or extra-renal complications if these were originally present; OR
- On dialysis for ≥ four of the previous six months while receiving eculizumab and failed to demonstrate resolution or stabilization of neurological or extra-renal complications if these were originally present; OR
- Worsening of kidney function with a reduction in eGFR or increase in SrCr ≥ 25% from baseline.

Approval duration: 6 months

**Continuation Criteria (at 12 months):**

1. Ongoing treatment response as defined in the 6-month continuation criteria; AND
2. The patient has limited organ reserve defined as:
**Eculizumab**

**Brand(s): Soliris**

**DOSAGE FORM/ STRENGTH: 10 mg/mL (300 mg per vial)**

- Significant cardiomyopathy, neurological, gastrointestinal or pulmonary impairment related to TMA; or
- Grade 4 or 5 chronic kidney disease (eGFR <30mL/min). (Note: Patients who are dialysis-dependent with no significant extra-renal manifestations persisting are not considered).

There may be other exceptional circumstances where the patient has a high risk of recurrence and in whom consequences of a relapse are significant (e.g., complement Factor H genetic mutation, multiple clinical presentations of active TMA). These will be reviewed on a case-by-case basis by an external clinical expert.

For patients in whom a pause in therapy is recommended, funding will be left in place for 3 months so that eculizumab can be quickly restarted upon evidence of recurrence per recommencement criteria.

Approval duration: 12 months

**Recommencement Criteria:**

A patient previously diagnosed with aHUS and who responded to treatment with eculizumab and has not failed eculizumab is eligible to restart eculizumab if the following clinical conditions are met:

- Significant hemolysis as evidenced by presence of schistocytes on the blood film, or low or absent haptoglobin, or LDH above normal;

AND EITHER

- Platelet consumption as measured by either ≥ 25% decline from patient baseline or thrombocytopenia (platelet count <150,000 x 10^9/L);

OR

- TMA-related organ impairment (e.g., unexplained rise in serum creatinine with onset of urine dipstick positive for hemoglobin) including on recent biopsy.

Note:

1. Raised LDH alone is not a sufficient reason to recommence eculizumab, but thrombocytopenia with one marker of hemolysis (such as raised LDH, presence of schistocytes, or low/absence of haptoglobin) is an accepted reason to recommence.
2. Kidney transplantation/dialysis is not a contraindication to recommencement.

A patient who becomes eligible to restart eculizumab, in accordance with the above criteria, will be assessed every 6 months for treatment response or failure.
Approval duration: 6 months

**Patients undergoing kidney transplantation:**
For patients with a confirmed aHUS diagnosis who are undergoing kidney transplantation, eculizumab funding will be provided for the time period immediately prior to (or at time of) transplant. Treatment must be started immediately prior to or at time of transplant.

Approval duration: 6 months

All funding requests must come from, or be submitted in consultation with, a pediatric nephrologist, a nephrologist, a pediatric hematologist or a hematologist.

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**Eltrombopag**

**Brand(s): Revolade**

**DOSAGE FORM/ STRENGTH:** 25 mg, 50 mg tablet

For the treatment of refractory chronic idiopathic thrombocytopenic purpura (ITP) with bleeding complications in patients who meet the following criteria:

- Patient has undergone a splenectomy\(^1\); AND
- Patient has tried and is unresponsive to other treatment modalities\(^2\).

\(^1\)Requests for Revolade where the requesting physician has stated that the patient is not a candidate for splenectomy will be assessed on a case-by-case basis. The requesting physician must provide rationale for why a splenectomy cannot be considered, and where possible, to include a preoperative/surgical evaluation on the patient’s surgical risks to splenectomy, to include consideration of risks of laparoscopic and open surgical interventions if these are available. This evaluation must come from a physician who is not the requesting physician.

\(^2\)Appropriate first-line treatment modalities may include:
- Corticosteroids
- IV anti-D
- Intravenous immune globulin (IVIG)

Appropriate second-line treatment modalities include:
- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate
- Rituximab
- Danazol
- Dapsone
Eltrombopag
Brand(s): Revolade
DOSAGE FORM/ STRENGTH: 25 mg, 50 mg tablet

Note: Patients need to have failed at least two of the second-line therapies listed above prior to requesting Revolade. Dosage: 50 mg once daily to a maximum of 75 mg once daily.

Duration of Approval: 1 year

Renewal of requests for Revolade will be assessed on a case-by-case basis

Note: Revolade therapy beyond 1 year of continuous treatment has not been studied. After 1 year of continuous treatment, therapeutic options should be reassessed.

Duration of Approval: 1 year

Icabitant
Brand(s): Firazyr
DOSAGE FORM/ STRENGTH: 30 mg/3 mL prefilled syringe

For the treatment of acute attacks of type I or type II hereditary angioedema (HAE) in adults with lab confirmed c1-esterase inhibitor deficiency if the following conditions are met:

a. Treatment of acute non-laryngeal attacks of at least moderate severity; OR
b. Treatment of acute laryngeal attacks; AND
c. Must be prescribed by physicians (e.g. immunologists, allergists or hematologists) with experience in the treatment of HAE.

Notes:

- Documentation of diagnosis (e.g. patient and family history, symptoms, lab test results) must be provided.
- For acute non-laryngeal attacks, documentation of severity (frequency, location, and degree of swelling) must be provided

Doses for acute treatment are limited to a single dose for self-administration per attack.

Duration of Approval: Lifetime
Romiplostim  
Brand(s): Nplate  
DOSAGE FORM/STRENGTH: 250 mcg/0.5 mL 500 mcg/mL

For the treatment of refractory chronic idiopathic thrombocytopenic purpura (ITP) with bleeding complications in patients who meet the following criteria;

i) Patient has undergone a splenectomy
ii) Patient has tried and is unresponsive to other treatment modalities.

Requests for romiplostin where the requesting physician has stated that the patient is not a candidate for splenectomy will be assessed on a case-by-case basis. The requesting physician must provide rationale for why a splenectomy cannot be considered, and where possible, to include a preoperative evaluation on the patient’s surgical risks to splenectomy to include consideration of risks of laparoscopic and open surgical interventions if these are available.

Note: The Executive Officer (EO) may revise the criteria if the frequency of patients who are not eligible for splenectomy exceeds published estimates.

Appropriate first-line treatment modalities may include;
- Corticosteroids
- IV anti-D
- Intravenous immune globulin (IVIG)

Appropriate second-line treatment modalities may include;
- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate
- Rituximab
- Danazol
- Dapsone

Patients need to have failed at least two second-line therapies prior to requesting Nplate.

Duration of Approval: 1 year

Renewal of requests will be considered in patients who have a stable platelet response and reduced symptoms of ITP-related bleeding events.

Duration of Approval: 1 year
CARDIOLOGY DRUGS

Eplerenone
Brand(s): Inspra
DOSAGE FORM/ STRENGTH: 25 mg, 50 mg tablets

For the treatment of patients who have heart failure and left ventricular systolic dysfunction due to acute myocardial infarction. Patients must have:

- An ejection fraction ≤ 40% AND
- Prior trial of spironolactone but experienced severe symptomatic (painful) gynecomastia

Duration of Approval: Lifetime

CENTRAL NERVOUS SYSTEM DRUGS

Modafanil
Brand(s): Alertec
DOSAGE FORM/ STRENGTH: 100 mg tablet

For the symptomatic treatment of excessive daytime sleepiness in patients with narcolepsy who have demonstrated a lack of response to or an inability to tolerate dextroamphetamine AND methylphenidate.

Note: See also Multiple Sclerosis Drugs

Duration of Approval: 2 years (Initials and Renewals)

Riluzole
Brand(s): Rilutek
DOSAGE FORM/ STRENGTH: 50 mg tablet

Approvals will be provided for:

Patients who have probable or definite amyotrophic lateral sclerosis (ALS) as defined by World Federation of Neurology (WFN) criteria with onset within 5 years, who have a vital capacity of >60% predicted and do not have a tracheostomy.

Approval period: 12 months

Discontinuation Criteria:

Reimbursement will be discontinued if the patient progresses to require permanent assisted ventilation. This is defined as assisted ventilation required for 23 out of 24 hours for greater than or equal to 14 consecutive days.
Tetrabenazine
Brand(s): Nitoman
DOSAGE FORM/ STRENGTH: 25 mg tablet

For the treatment of Huntington's chorea, tic and Gille’s de la Tourette syndrome and tardive dyskinesia in patients meeting the following criteria:

i) is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND

ii) have disabling Huntington's chorea OR tic and Gille’s de la Tourette syndrome and have documented evidence of failure to respond, intolerable side effects or contraindication to at least one agent presently available on the Formulary.

**Note that for patients with disabling tardive dyskinesia, a trial of a Formulary agent is NOT required (ie. tetrabenazine can be considered for use as a first-line agent)**

Duration of Approval: 1 year

Renewals will be considered for patients whose request is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND who provide written confirmation that movements and functional status are stabilized on tetrabenazine therapy.

Duration of Approval: 5 years

For the treatment of Hemiballismus, senile chorea, or other disabling hyperkinetic movement disorders (HKMD) will be considered on a case-by-case basis in patients meeting the following criteria:

- is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND

- have documented evidence of failure to respond, intolerable side effects or contraindication to at least one agent presently available on the Formulary.

Duration of Approval: 1 year
Tetrabenazine
Brand(s): Nitoman
DOSAGE FORM/ STRENGTH: 25 mg tablet

Renewals will be considered for patients whose request is prescribed by (or in consultation with) physicians who are experienced in the treatment of hyperkinetic movement disorders (e.g. specialists practicing in a Movement Disorder Clinic, neurologists, psychiatrists, physiatrists, geriatricians, pediatricians); AND who provide written confirmation that movements and functional status are stabilized on tetrabenazine therapy.

Duration of Approval: 5 years

Please note that information MUST BE provided about why a patient has not tried or cannot try a formulary alternative.

Requests not meeting the above criteria for HKMD will be considered through a case-by-case review and the physician must provide adequate clinical information to enable this assessment.
DERMATOLOGY DRUGS

Adalimumab
Brand(s): Humira

DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection

For the treatment of adult patients with active moderate to severe hidradenitis suppurativa who have not responded to conventional therapy (including systemic antibiotics) and who meet all of the following:

- A total abscess and nodule count of 3 or greater
- Lesions in at least two distinct anatomic areas, one of which must be Hurley Stage II or III
- An inadequate response to a 90-day trial of oral antibiotics
- Prescribed by a practitioner with expertise in the management of patients with HS

Note: Treatment with adalimumab should be discontinued if there is no improvement after 12 weeks of treatment

First renewal:
- Requests for renewal should provide objective evidence of a treatment response, defined as at least a 50% reduction in abscesses and inflammatory nodule count with no increase in abscess count or draining fistula count relative to baseline at week 12.

Subsequent renewal:
- For renewals beyond the second year, objective evidence of the preservation of treatment effect should be provided (i.e. the current AN (abscess and inflammatory nodule) count and draining fistula count should be compared to the count prior to initiating treatment with adalimumab).

Approval duration:
- Initial approval: 3 months
- First renewals: 1 year
- Subsequent renewals: 2 years

Recommended dose:
- The recommended dose is 160 mg initially (week 0), followed by 80 mg at week 2, then 40 mg at week 4, and 40 mg weekly thereafter
**Imiquimod**  
*Brand(s):* Apo-Imiquimod  
**DOSAGE FORM/ STRENGTH:** 5% Cream

*For the treatment of external genital and perianal warts/condyloma acuminata* in patients who;

- Have documented failure to a trial of podophyllum resin and one other treatment modality (including cryotherapy, surgical excision, or electrosurgery).

Duration of Approvals: 1 year  (Maximum of 16 weeks for each treatment course)

*For the treatment of biopsy-confirmed primary superficial basal cell carcinoma* in patients meeting the following criteria;

- Tumour diameter of ≤ 2 cm  AND  
- Tumour location on the trunk, neck or extremities (excluding hands and feet)  AND  
- Surgery or irradiation therapy is not medically indicated (e.g. recurrent lesions in previously irradiated area, number of lesions too numerous to irradiate or remove surgically)

Duration of Approvals: 6 weeks  
**Renewals** for the same tumour will not be considered.

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**Omalizumab**  
*Brand(s):* Xolair  
**DOSAGE FORM/ STRENGTH:** 150 mg Inj

*Initial Criteria:*

*For the treatment of moderate to severe chronic idiopathic urticaria (CIU) when prescribed by a specialist (i.e. an allergist, an immunologist, a dermatologist)* in patients who meet ALL the following criteria;

(i) Patient must be 12 years of age or older; AND  
(ii) Patient must remain symptomatic despite optimum management with available oral therapies.

Approved regimen: Up to 300 mg every 4 weeks

**Duration of Approval:** 24 weeks
Omalizumab

Brand(s): Xolair

DOSAGE FORM/ STRENGTH: 150 mg Inj

Renewals will be considered for patients who demonstrate one of the following responses to treatment;

i) Patient has had a trial of stopping omalizumab treatment after having achieved symptom control for at least 12 weeks while on therapy but who experience symptom relapse during the stoppage period; OR

ii) Patient has demonstrated improvement but has not been able to achieve complete symptom control for more than 12 consecutive weeks; OR

iii) Patient has demonstrated a partial response to treatment defined as at least a greater than or equal to 9.5 point reduction in the baseline urticaria activity score over 7 days (UAS7).

Approved regimen: Up to 300 mg every 4 weeks

Duration of Approval: 24 weeks

Propranolol

Brand(s): Hemangiol

DOSAGE FORM/ STRENGTH: 3.75mg/mL oral solution

Initial Criteria:

For the treatment of infants and children with any of the following proliferating infantile hemangiomas;

- Life or function-threatening hemangioma OR
- Ulcerated hemangioma in those experiencing pain and/or lack of response to simple wound care measures; OR
- Hemangiomas deemed to put the patient at risk of permanent scarring or disfigurement.

Requests must be from a dermatologist or a physician experienced in the care of infantile hemangiomas.

Duration of approval: up to 12 months

Note that the treatment duration is typically 6 months and consideration should be made to discontinue the product in the absence of improvement within the first 2 months.

Renewals: Renewals will be considered on a case-by-case basis. If wounds are not healing, please provide clinical information as to why ongoing reimbursement is required.
Rituximab
Brand(s): Rituxan

**DOSAGE FORM/ STRENGTH:** 10 mg/mL intravenous injection

**For the treatment of severe pemphigus vulgaris** in patients who meet the following criteria.

- Patient has failed combination therapy with high-dose systemic steroids\(^1\) and a steroid-sparing immunosuppressant\(^2\) trialed in combination for a minimum of 3 months.
- The request must be made by a dermatologist/specialist familiar with the management of pemphigus vulgaris and with the use of rituximab in this condition.

\(^1\)Patients must have used a steroid dose equivalent to a 1 mg/kg prednisone dose equivalent (or a minimum of 60 mg/day for patients > 60 kg) for at least 4 to 6 weeks before attempting to taper to a lower dose.

\(^2\)Patients must try at least one of the following at therapeutic doses: azathioprine, mycophenolate, cyclophosphamide, or methotrexate (in combination with a steroid).

**Dose:**
One course of treatment with rituximab is considered

375 mg/m\(^2\) administered weekly for 4 weeks (for a total of 4 doses) OR

1000 mg of rituximab administered at week 0 and week 2 (for a total of 2 doses).

Re-treatment may be provided if the patient responded to rituximab therapy then experiences disease flare, as long as the request is made no less than 6 months after the last dose of the patient’s last treatment course/cycle with rituximab.

**Rejection Criteria:**

- Other dermatology diagnoses, such as pemphigus foliaceus and bullous pemphigoid
- Maintenance infusions (i.e. regular maintenance doses to keep disease in remission)

**Duration of Approval:** 1 year

Maintenance Treatment is not funded.

First Renewal: 1 year

Subsequent Renewals after first renewal: 2 years

(Rituxan is funded for course of therapy to be given at an interval of at least 6 months only upon flare of the condition.)
**ENDOCRINOLOGY AGENTS**

**Cinacalcet**

**Brand(s): Sensipar**

**DOSAGE FORM/ STRENGTH:** 30 mg, 60 mg, 90 mg tablets

**For the treatment of severe hyperparathyroidism* in patients with chronic kidney disease who are on dialysis** who meet the following criteria;

i) the patient is refractory to other treatments; AND

ii) the patient has symptoms clearly related to hyperparathyroidism that are causing significant impairment in quality of life (e.g. calciphylaxis or bone pain); AND

iii) additionally, **ONE** of the following criteria is present:

- the patient has been reviewed by a surgeon, anesthetist or nephrologist and has been deemed not to be a candidate for parathyroidectomy due to high surgical risk or anesthetic risk. [Please note: This must be accompanied by a clinical note explaining the high surgical risk or anesthetic risk and the patient’s parathyroid hormone (PTH) level]; OR

- the patient has been wait-listed for a parathyroidectomy and requires Sensipar for bridge therapy; OR

- the patient is awaiting an imminent renal transplant and a nephrologist indicates a preference for pre-transplant treatment with Sensipar instead of a parathyroidectomy.

*Severe hyperparathyroidism is considered to be patients with PTH levels greater than 88 pmol/L confirmed on two laboratory tests for PTH taken at least 1 month apart.

**Exclusion Criteria**

- Patients with primary hyperparathyroidism or parathyroid carcinoma.

**Initial Approval duration**

Patients who are not a candidate for parathyroidectomy due to high surgical or anesthetic risk: 1 year

ii) Patients wait-listed for a parathyroidectomy requiring bridge therapy with Sensipar or awaiting an imminent renal transplant will be approved to the estimated date of the surgery.
Cinacalcet  
**Brand(s): Sensipar**  
**DOSAGE FORM/ STRENGTH:** 30 mg, 60 mg, 90 mg tablets  

**Duration of Approval:** 1 year or to the estimated date of the procedure for those using for bridge therapy and awaiting surgery  

**Renewals** will be considered for patients who are not candidates for parathyroidectomy and who continue to benefit from therapy. Requests for renewals should include the patient’s PTH level.  

**Renewals** will **NOT** be considered for patients who have had a parathyroidectomy.  

**Duration of Approval:** 1 year  

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Sodium Thiosulfate  
**Brand(s): Seocalphyx**  
**DOSAGE FORM/ STRENGTH:** 250mg/mL Injection  
**Brand(s): (Hospira brand)**  
**DOSAGE FORM/ STRENGTH:** 12.5 g/50mL Injection  

**Approval of sodium thiosulfate for the treatment of calciphylaxis** will be provided where all of the following criteria have been met:  

Patients with G4 or G5 chronic kidney disease; **AND**  

i) Have been diagnosed with calciphylaxis either by:  
   a) 99m Technicium scintigraphy (bone scan) showing deposits that correspond to clinical lesions; **OR**  
   b. Biopsy; **OR**  
   c. Where scintigraphy negative and biopsy is not feasible, then diagnosis must be confirmed by nephrologist with submission of anonymized photographs of lesions **AND** a differential diagnosis checklist (e.g. warfarin-induced necrosis if on warfarin; lipohypertrophy if on insulin; cellulitis, nephrogenic sclerosing dermopathy, emboli, thrombi, fibrointimal hyperplasia and so on which depends on the site of lesion); **AND**  

ii) Patient has either:  
   a. Ulcerated lesions; **OR**  
   b. Non-ulcerated lesions which have not improved after 2 weeks of multimodal treatment with replacement of calcium-containing phosphate binders with non-calcium containing binders (i.e. sevelamer), discontinuation of vitamin D analogs and initiation of calcimimetic (i.e. cinacalcet), changes in dialysis prescription (reduction in dialysate calcium; consideration of increased dialysis intensity),
**Sodium Thiosulfate**
Brand(s): Seacalphyx
DOSAGE FORM/ STRENGTH: 250mg/mL Injection
Brand(s): (Hospira brand)
DOSAGE FORM/ STRENGTH: 12.5 g/50mL Injection

replacement of warfarin with alternative anticoagulants where possible, wound management strategies, and analgesia for lesion pain.

Requests for patients with calciphylaxis who do not meet the above criteria will be considered on a case-by-case basis.

**Duration of Approval:** 2 months

**Renewals** will be considered for patients responding to treatment with improved pain control AND reduction in lesion number or size, reduction in ulcer size, or complete ulcer healing.

**Recommended dose:** 25g three times weekly.

**Duration of Approval:** Two months at a time until lesions are completely resolved, and for additional 2 months after complete healing.

**GOUT**

**Febuxostat**
Brand(s): Uloric
DOSAGE FORM/ STRENGTH: 80 mg

For the treatment of patients with documented severe allopurinol hypersensitivity syndrome* where lowering uric acid is recommended by clinical practice guidelines,

OR

For the treatment of patients with recurrent gout attacks despite treatment with allopurinol at a dose of 300 mg or more per day for at least six (6) months.

* For the purpose of the criteria severe allopurinol hypersensitivity syndrome is defined as follows;

The patient has had a clear exposure to allopurinol and:

(a) at least TWO of the following major clinical criteria:
   i) worsening renal function;
   ii) acute hepatocellular injury;
Febuxostat
Brand(s): Uloric
DOSAGE FORM/ STRENGTH: 80 mg

 iii) a rash including either toxic epidermal necrolysis ("TEN"), Stevens-Johnson syndrome ("SJS"), erythema multiforme, generalised maculopapular exanthema or generalized exfoliative dermatitis ("GED");

OR

(b one of the major clinical criteria listed above in (a) and at least ONE of the following minor criteria:

(i) fever
(ii) eosinophilia
(iii) leukocytosis.

Note that an intolerance to allopurinol that does not meet the above criteria will not be eligible for reimbursement.

Duration of Approval: 1 year

Renewals will be considered in patients with objective evidence to demonstrate a benefit from treatment, documented as either a reduction in gout attacks or a reduction in uric acid levels.

Duration of Approval: 5 years
GRANULOMATOSIS WITH POLYANGIITIS OR MICROSCOPIC POLYANGIITIS

**Rituximab**
Brand(s): Rituxan

**DOSAGE FORM/ STRENGTH:** 10 mg/mL intravenous injection

For the induction of remission of severely active Granulomatosis with Polyangiitis (GPA) OR microscopic polyangiitis (MPA) as combination treatment with glucocorticoids, in patients who meet all of the following criteria:

1. The patient must have severe active disease that is life- or organ-threatening. At least one supporting laboratory and/or imaging report must be provided. The organ(s) and how the organ(s) is (are) threatened must be specified.
2. There is a positive serum assays for either proteinase 3-ANCA (anti-neutrophil cytoplasmic autoantibodies) or myeloperoxidase-ANCA. A copy of the laboratory report must be provided.
3. Cyclophosphamide cannot be used for the patient for at least ONE of the following reasons:
   i) The patient has failed a minimum of six IV pulses of cyclophosphamide; OR
   ii) The patient has failed three months of oral cyclophosphamide therapy; OR
   iii) The patient has a severe intolerance or an allergy to cyclophosphamide; OR
   iv) Cyclophosphamide is contraindicated; OR
   v) The patient has received a cumulative lifetime dose of at least 25 g of cyclophosphamide; OR
   vi) The patient wishes to preserve ovarian/testicular function for fertility.

The initial treatment would be a once weekly infusion dosed at 375 mg/m² x 4 weeks.

The physician must confirm that the treatment would not be a maintenance infusion as maintenance infusions will not be funded.

**Renewals** will be considered provided that, the patient meets the same criteria for initial approval and the request for retreatment is made no less than 6 months after the last doses of the patient’s last treatment cycle with Rituxan.

Maintenance Treatment is not funded.

First Renewal: 1 year

Subsequent Renewals after first renewal: 2 years

(Rituxan is funded for course of therapy to be given at an interval of at least 6 months only upon flare of the condition.)
HEPATOLOGY DRUGS

HEPATITIS C DRUGS

Effective with the February 2017 Formulary update, the following drugs are reimbursed on the Ontario drug benefit formulary as limited use benefits for patients with Chronic Hepatitis C Infection meeting the LU criteria:

i) Daklinza (daclatasvir) 30mg, 60mg Tab
ii) Epclusa (sofosbuvir / velpatasvir) 400mg/100mg Tab
iii) Harvoni (ledipasvir / sofosbuvir) 90mg/400mg Tab (GIL)
iv) Ibalvir (ribavirin) 200mg, 400mg, 600mg Tab
v) Sovaldi (sofosbuvir) 400mg Tab
vi) Zepatier (elbasvir / grazoprevir) 50mg/100mg Tab

The Ministry only considers funding of patient with Chronic Hepatitis C infection.

Please refer to the Limited Use Criteria in the Ontario Drug Benefit Formulary for provincial reimbursement criteria for these products which are part of Ontario’s hepatitis C framework.

Retreatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antiviral will be considered on a case-by-case basis through the Exceptional Access Program.

For consideration of retreatment the following information should be included in the request application;

- All prior hepatitis C treatments used including dates, duration of use, and treatment response (as applicable).
- Genotype information with laboratory confirmation of current infection and genotype of prior infection.
- Virologic information including details that may inform the nature of prior responses (e.g. relapse, null response, re-infection, etc)
- Fibrosis stage
- Other comorbidities
- Identifying risk factors that may have led to the treatment failure and to provide information about whether modifiable factors have been addressed.

Adefovir
Brand(s): Hepsera
DOSAGE FORM/ STRENGTH: 10 mg tablet

For the treatment of chronic hepatitis B in patients with objective evidence of lamivudine virologic* breakthrough where failure is not due to poor adherence to therapy; AND

- Liver biopsy showing Metavir stage 3 fibrosis or greater; OR
- Documented evidence of cirrhosis.
OR

- Patients with the presence of a lamivudine resistance mutation******; AND
  - Liver Biopsy showing Metavir stage 3 fibrosis or greater; OR
  - Documented evidence of cirrhosis.

**Duration of Approval:** 1 year (If Cirrhotic: Lifetime)

Duration of Approval for Renewal: 5 years

**Note:** Effective February 28, 2018, Entecavir, Lamivudine, and Tenofovir became a Limited Use Benefit on the Ontario Drug Benefit Formulary – Please refer to the formulary for the Limited Use Criteria.

**Glecaprevir/pibrentasvir**

**Brand(s):** Maviret

**DOSAGE FORM/STRENGTH:** 100 mg/40 mg tablet

For treatment-naive or treatment-experienced¹ adult patients with chronic hepatitis C (CHC) infection who meet all the following criteria:

- Treatment is prescribed by a hepatologist, gastroenterologist, or infectious disease specialist (or other physician experienced in treating a patient with chronic hepatitis C); AND
- Two laboratory confirmed quantitative HCV RNA values taken at least 6 months apart as demonstration of chronicity of infection. One level must be within the last 6 months while the first level may be at the time of the initial diagnosis; AND
- Laboratory confirmed hepatitis C genotype 1, 2, 3, 5, or 6; AND
- Laboratory confirmed severe renal impairment (estimated Glomerular Filtration Rate (eGFR) ≤ 30 mL/min/1.73m²) or end-stage renal disease on hemodialysis; AND
- Patients who have cirrhosis² must have compensated cirrhosis [Child-Turcotte-Pugh A (i.e. Scores 5 to 6)]

¹Treatment experienced for G2, G3, G5 and G6 is defined as prior treatment with regimens containing interferon, peginterferon (P), ribavirin (R), and/or sofosbuvir (PR, SOF+PR, SOF + R), but no prior treatment experience with an HCV NS3/4A protease inhibitor or NS5A inhibitor.

²Cirrhosis must be determined through a validated test (e.g. Biopsy, Fibroscan, Fibrotest)
Glecaprevir/pibrentasvir

Brand(s): Maviret

DOSAGE FORM/ STRENGTH: 100mg/ 40 mg tablet

Retreatment for failure or re-infection in patients who have received an adequate prior course of Maviret will be considered on a case-by-case basis.

Exclusion criteria:
- Hepatitis C infections from genotype 1 that are treatment-naïve
- Hepatitis C infections from genotype 4
- Patients with estimated Glomerular Filtration Rate (eGFR) > 30 mL/min/1.73m2
- In combination with other hepatitis C antiviral agents.
- Patients with decompensated cirrhosis or severe hepatic impairment (Child-Pugh C)

Dose and durations based on patient factors:
- A. Treatment naïve, non-cirrhotic genotype 2, 3, 5, or 6
  Three tablets (i.e., 300 mg/120 mg) once daily for 8 weeks.
- B. Treatment naïve, compensated cirrhosis genotype 2, 3, 5, or 6
  Three tablets (i.e., 300 mg/120 mg) once daily for 12 weeks
- C. Treatment-experienced, non-cirrhotic genotype 2, 5, or 6
  Three tablets (i.e., 300 mg/120 mg) once daily for 8 weeks
- D. Treatment-experienced, compensated cirrhosis genotype 2, 5, or 6
  Three tablets (i.e., 300 mg/120 mg) once daily for 12 weeks
- E. Treatment-experienced, non-cirrhotic or compensated cirrhosis genotype 3
  Three tablets (i.e., 300 mg/120 mg) once daily for 16 weeks
- F. Treatment-experienced non-cirrhotic or compensated cirrhosis genotype 1 with prior Harvoni and NS3/4A inhibitor-naïve.
  Three tablets (i.e., 300 mg/120 mg) once daily for 16 weeks
Interferon – alpha-2b  
Brand(s): Intron A  
DOSAGE FORM/ STRENGTH: 18 MU, 30 MU, 60 MU; 18 MU/3 mL, 10 MU/mL, 25 MU/2.5 mL vials

For the treatment of chronic hepatitis B where the patient meets the following criteria:

- Patients less than 50 years of age; AND
- 2 ALTs > 2 x ULN within the past 6 month period; AND
- HBV DNA between $1 \times 10^4$ – $1 \times 10^7$ IU/mL; AND
- Metavir stage 3 fibrosis or less (i.e. no cirrhosis)

Requests for pediatric patients will be considered case-by-case.  
Duration of Approval: HBeAg pos: 24 weeks, HBeAg neg: 48 weeks

Lamivudine  
Brand(s): Heptovir and generics  
DOSAGE FORM/ STRENGTH: 100 mg tablet

Effective February 28, 2018, Lamivudine became a Limited Use Benefit on the Ontario Drug Benefit Formulary – Please refer to the formulary for the Limited Use Criteria

Obeticholic Acid  
Brand(s): Ocaliva  
DOSAGE FORM/ STRENGTH: 5mg, 10mg tablet

Obeticholic Acid (Ocaliva) will be funded for the treatment of primary biliary cholangitis (PBC) in adult patients who meet the following criteria:

i) Diagnosis of PBC is demonstrated by antimitochondrial antibodies or a liver biopsy; AND

ii) Used in combination therapy with ursodeoxycholic acid (UDCA) in patients who have experienced an inadequate response to a minimum of twelve months of treatment with UDCA OR as monotherapy in patients who have experienced unmanageable intolerance to UDCA; AND

iii) The request is prescribed by or in consultation with a prescriber who is a gastroenterologist, hepatologist or internist with experience in the treatment of PBC. (If you are a prescriber who is not one of the specialists identified above, please submit the consultation note with the request.)
Obeticholic Acid

Brand(s): Ocaliva

DOSAGE FORM/ STRENGTH: 5mg, 10mg tablet

Note that an inadequate response is defined as a patient who has used UDCA to treat PBC for a minimum of twelve (12) months and demonstrates ANY ONE or more of the following:

a) alkaline phosphatase ≥ 1.67 x upper limit of normal
b) total bilirubin > 1 x upper limit of normal and < 2 x upper limit of normal
c) abnormal bilirubin with progressing and/or compensated cirrhosis.

(Documentation of lab work to be submitted with the request application.)

Renewals will be considered in patients who continue to benefit from treatment as evidenced by any one of the following:

(a) a reduction in the alkaline phosphatase level to less than 1.67 x upper limit of normal; and/or
(b) a 15% reduction in the alkaline phosphatase level compared with baseline values prior to initiation of treatment with obeticholic acid; and/or
(c) a normal bilirubin level.

and the patient has not developed unacceptable toxicity from treatment with obeticholic acid.

Patients not meeting the above renewal criteria may be considered on a case-by-case basis.

Exclusion Criteria (applies to both initial and renewal requests):
Pre-liver transplant patients and/or patients who have complete biliary obstruction will not be funded.

Duration of funding approval for initials: 1 year
Duration of funding approval for renewals: 1 year
| Ribavirin  |
| Brand(s): Ibavyr |
| **DOSAGE FORM/ STRENGTH:** 200 mg, 400 mg, 600 mg tablet |

The Ministry only considers funding of patient with Chronic Hepatitis C infection. Refer to the Ontario Drug Benefit Formulary for the criteria for funding as a limited use (LU) benefit.
INFLAMMATORY BOWEL DISEASES

Adalimumab
Brand(s): Humira

DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection

For the treatment of fistulising Crohn’s disease with concomitant luminal disease in patients who meet the following criteria;

- Patient with actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) AND immununosuppressive therapy (e.g. azathioprine or 6-mercaptopurine) AND
- Harvey Bradshaw Index (HBI) score ≥ 7

The dose that will be considered is Adalimumab (Humira) 160 mg at week zero, 80 mg at week two, followed by 40 mg every two weeks.

**Duration of Approval:** 3 months

**Renewal** will be considered based on the response to therapy.

The dose that will be considered on renewals is Adalimumab (Humira) 40 mg every two weeks. All requests for higher doses will not be approved.

**Duration of Approval:** 3 months to 1 year pending fistula(e) resolution

Second Renewal:

2 years for 2nd renewal of requests with complete resolution

Case-by-case duration for renewal of requests with partial resolution

Pediatric patients will be considered case-by-case.

**Treatment of moderate to severe (luminal) Crohn’s Disease** in patients who have:

- HBI (Harvey Bradshaw Index) score ≥7*; and
- Failed to respond to conventional treatment with glucocorticoids (prednisone 40mg/day or equivalent for at least 2 weeks or dose cannot be tapered to below prednisone 20 mg/day or equivalent); and
- Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months.

*Note:* Any intolerance(s) or contraindication(s) to treatment with required alternative(s) must be described in detail.
Adalimumab
Brand(s): Humira

DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection

*If the patient has HBI <7, the request will be reviewed by external medical experts when the following information is provided: bloodwork (with hematocrit, hemoglobin, C reactive protein, ESR, platelets, and ferritin levels); supporting endoscopy; details of weight loss; and a list of narcotic analgesics being used.

Pediatric patients will be considered case-by-case.

Duration of Approval: 3 months

Renewal will be considered for patients with 50% reduction in HBI from pre-treatment as well as improvement of symptoms (e.g., absence of bloody diarrhea and weight stabilization or increase) and no longer using steroids. Biochemical improvements may also be required.

The planned dosing regimen for the requested biologic should be provided.

The recommended: Adalimumab: 160mg at week 0; 80mg at week 2; followed by 40mg every two weeks

Duration of Approval: First renewal: 1 year
Second and subsequent renewals: 2 years

For the treatment of ulcerative colitis disease in adult patients who meet the following criteria:

Induction Criteria

Mild disease
a. Mayo score <6 AND
b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage

Moderate disease
a. Mayo score between 6 and 10 (inclusive); AND
b. Endoscopic* subscore of 2; AND
   c. Failed 2 weeks of oral prednisone at daily doses ≥40mg (or a 1 week course of IV equivalent) AND 3 months of
Adalimumab

Brand(s): Humira

DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection

- azathioprine (AZA)/ 6-mercaptopurine (6MP) (or where the use of immunosuppressants is contraindicated); OR
- Stabilized with 2 weeks of oral prednisone at daily dose ≥ 40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Severe disease
- Mayo score >10 AND
- Endoscopic* subscore of ≥2 AND
- Failed 2 weeks of oral prednisone at daily dose ≥ 40mg (or 1 week IV equivalent); OR
- Stabilized with 2 weeks oral prednisone ≥ 40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Initial Approval: 6 months at 160 mg initially administered at week 0, followed by 80mg at week 2, then 40 mg every other week thereafter.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment

Maintenance Criteria

After 8 weeks of Humira therapy:
- Mayo score <6 AND
- 50% reduction in prednisone from the starting dose

Approval: 6 months at 40mg every other week.

If patient is completely off steroids,
Approval: 12 months at 40 mg every other week.

Subsequent renewals:
- Mayo score <6; AND
- Must be completely off steroids

Approval: 2 years at 40mg every other week.

(Patients who remain on steroids will be considered on a case-by-case basis)

Pediatric patients will be considered case-by-case.
Infliximab
Brand(s): Remicade

DOSAGE FORM/ STRENGTH: 100mg/10mL intravenous infusion

Note that effective November 30, 2016, Inflectra (infliximab) is publicly funded for the treatment of adult patients with Inflammatory Bowel Diseases (i.e. Crohn’s Disease or Ulcerative Colitis) upon meeting the Limited Use Criteria on the Ontario Drug Benefit (ODB) formulary.

Note that effective September 27, 2018, Renflexis (infliximab) is publicly funded for the treatment of adult and pediatric patients with Inflammatory Bowel Diseases (i.e. Crohn’s Disease or Ulcerative Colitis) upon meeting the Limited Use Criteria on the ODB formulary. Requests for Renflexis for pediatric patients not meeting the LU criteria may be forwarded to EAP for case-by-case assessment.

Requests for infliximab in treatment-naïve patients with Crohn’s Disease or Ulcerative Colitis will be required to consider treatment using one of the biosimilars (Inflectra or Renflexis). Patients initiated on Remicade by the manufacturer’s patient support program after the effective date of public funding of the biosimilar infliximab products may be expected to provide ongoing access to their patient. The Ministry will only fund Remicade for patients with Crohn’s disease or Ulcerative Colitis who are treatment experienced and stabilized on the product.

Renewal of funding of patients using Remicade for the treatment of fistulizing Crohn’s Disease will be considered for patients with resolution of fistulae.

The planned dosing regimen for the requested biologic should be provided. The recommended dose for the treatment of Crohn’s Disease is 5 mg/kg/dose at 0, 2 and 6 weeks followed by 5mg/kg/dose every 8 weeks with up to 10 mg/kg/dose every 8 weeks being considered on a case-by-case basis.

Approval duration:
First renewal: 6 months to 1 year pending fistula(e) resolution
Second and subsequent renewals: 2 years with complete resolution; case-by-case duration with partial resolution

Initial induction requests for infliximab for patients with mild Ulcerative Colitis (Mayo score < 6) may be considered for Infliximab as Inflectra on a case-by-case basis through EAP but the submission must include the rationale for coverage.

Renewal requests for Maintenance therapy of Ulcerative Colitis will be considered for Remicade in patients meeting the following criteria:
**Infliximab**

**Brand(s):** Remicade

**DOSAGE FORM/ STRENGTH:** 100mg/10mL intravenous infusion

**Maintenance Criteria:**

1. After **3 loading doses of Remicade** (for example: 5mg/kg/dose at 0, 2 and 6 weeks)
   a) Mayo score<sup>1</sup> < 6 AND
   b) 50% reduction in prednisone from the starting dose

   Approved Duration: 6 months

   Approved Dosage: Up to 5 mg/kg/dose every 6 weeks will be approved by the Executive Officer

   c) If patient is completely off steroids.

   Approval Duration: 12 months

   Approved Dosage: Up to 5 mg/kg/dose every 6 weeks will be approved by the Executive Officer

2. Subsequent renewals:
   a. Mayo<sup>1</sup> score < 6; AND
   b. Must be off steroids
      (Patients who remain on steroids will be considered on a case-by-case basis)

   Approval Duration: 12 months for first renewal with subsequent renewals up to 2 years (for those off steroids)

   Approved Dosage: Up to 5 mg/kg/dose every 6 weeks will be approved by the Executive Officer

<sup>1</sup>Note that the endoscopy procedure must be done within the last year but does not have to be full endoscopy.

**Pediatric patients will be considered case-by-case.**
Golimumab
Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5mL Pre-Filled Syringe Or Auto-Injector, 100 mg/mL Pre-filled Syringe or Auto-Injector

For the treatment of ulcerative colitis disease in patients who meet the following criteria:

Induction Criteria
Mild disease
a. Mayo score <6 AND
b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage

Moderate disease
a. Mayo score between 6 and 10 (inclusive) AND
b. Endoscopic subscore of 2 AND

c. Failed 2 weeks of oral prednisone ≥40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months azathioprine(AZA)/6-mercaptopurine(6MP) (or where the use of immunosuppressants is contraindicated)

Stabilized with 2 weeks of oral prednisone ≥ 40mg

d. (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Severe disease
a. Mayo score >10 AND
b. Endoscopy subscore of ≥2 AND

c. Failed 2 weeks of oral prednisone ≥ 40mg (or 1 week IV equivalent)

OR

d. Stabilized with 2 weeks oral prednisone ≥ 40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)
Golimumab

Brand(s): Simponi

DOSAGE FORM/ STRENGTH: 50 mg/0.5mL Pre-Filled Syringe Or Auto-Injector, 100 mg/ mL  Pre-filled Syringe or Auto-Injector

Initial Approval: 6 months at 200 mg initially administered at week 0, followed by 100mg at week 2, and then 50 mg every 4 weeks thereafter. The maintenance dose of 100mg every 4 weeks can be considered at the discretion of the treating physician

Maintenance Criteria

After 4 loading doses of Simponi:

a. Mayo score <6 AND
b. 50% reduction in prednisone from the starting dose

Approval: 6 months at 50 mg or 100 mg every 4 weeks

If patient is completely off steroids.
Approval: 12 months at 50 mg or 100 mg every 4 weeks.

Subsequent renewals:

a. Mayo score <6; AND
b. Must be off steroids
(Patients who remain on steroids will be considered on a case-by-case basis)

Approval: 2 years at 50 mg or 100 mg every 4 weeks.

Duration of Approval: Renewal duration: 6 months to 1 year (Pending if patient continues on steroids.)
Second and subsequent renewal 2 years for those off steroids:
Teduglutide
Brand(s): Revestive

DOSAGE FORM/ STRENGTH: 5 mg per vial

For the ongoing treatment of patients with Short Bowel Syndrome (SBS) who meet the following criteria:

Prior to starting teduglutide (Revestive), the patient meets the following:

- Age ≥ 18 years; AND
- Has short bowel syndrome (SBS) as a result of major intestinal resection due to injury, volvulus, vascular disease, cancer, or Crohn’s Disease¹; AND
- Patient’s intestinal resection has resulted in dependency on parenteral nutrition for at least 12 months; AND
- Patient requires parenteral nutrition required at least three times weekly to meet caloric, fluid or electrolyte needs due to ongoing malabsorption; AND
- Patient’s frequency and volume of parenteral nutrition has been stable for at least one month;

Those who are initiated on teduglutide (Revestive) upon meeting the above criteria will be reimbursed for ongoing access of teduglutide (Revestive) through the Exceptional Access Program (EAP) upon meeting the below criteria;

- The patient has achieved at least a 20% reduction in Parenteral Support volume while on teduglutide (Revestive) in the 4 weeks prior to the application for funding to EAP compared to their baseline measures in the 4 weeks prior to start of teduglutide (Revestive).²

¹Case-by-case consideration will be provided for requests for patients with short bowel syndrome not due to the reasons provided.

²Parenteral support volumes measurements are to compare the 4 weeks of use prior to start of teduglutide (Revestive) with the 4 weeks of use prior to the date that EAP request for funding is provided.

Duration of approval: 12 months

Exclusion Criteria:

- Patients with active gastrointestinal malignancy OR a history of gastrointestinal malignancy in the past 5 years before start of treatment

Renewals will be considered in those who are able to demonstrate a reduction in their parenteral support volume requirements by at least 20% compared to baseline measures prior to commencing therapy with teduglutide (Revestive).
**Teduglutide**

**Brand(s): Revestive**

**DOSAGE FORM/ STRENGTH: 5 mg per vial**

Applications for renewal of reimbursement should be accompanied by a copy of the parenteral support weekly usage volumes for the 4 weeks of use prior to the date that the Ministry funding is requested.

**Discontinuation/Stopping Criteria**

Patients will not be approved for funding by the EAP if a 20% reduction in the usual average weekly volume of parenteral support solutions prior to starting therapy with Revestive has not been achieved/maintained by 52 weeks of treatment with Revestive.
Vedolizumab
Brand(s): Entyvio
DOSAGE FORM/ STRENGTH: 300 mg Injection

For the treatment of fistulising Crohn’s disease with concomitant luminal disease inpatients who meet the following criteria;

- Patient with actively draining perianal or enterocutaneous fistula(e) that have recurred or persist despite a course of appropriate antibiotic therapy (e.g. ciprofloxacin and/or metronidazole) AND immununosppressive therapy (e.g. azathioprine or 6-mercaptopurine) AND
- Harvey Bradshaw Index (HBI) score ≥ 7

Initial Approval: 6 months at 300 mg initially administered at week 0, followed by 300mg at week 2, 300mg at week 6, then 300 mg every 8 weeks thereafter.

Renewal will be considered based on the response to therapy. The dose that will be considered on renewals is Vedolizumab (Entyvio) is 300 mg every eight weeks.

Approval duration:
First renewal: 6 months to 1 year pending fistula(e) resolution
Second and subsequent renewals: 2 years with complete resolution; case-by-case duration with partial resolution

For the treatment of moderate to severe (luminal) Crohn’s Disease in patients who have:

- HBI (Harvey Bradshaw Index) score ≥7*; AND
- Failed to respond to conventional treatment with glucocorticoids (prednisone 40mg/day or equivalent for at least 2 weeks or dose cannot be tapered to below prednisone 20 mg/day or equivalent); AND
- Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months.

Note: Any intolerance(s) or contraindication(s) to treatment with required alternative(s) must be described in detail.
**Vedolizumab**

**Brand(s):** Entyvio

**DOSAGE FORM/ STRENGTH:** 300 mg Injection

*If the patient has HBI < 7, the request will be reviewed by external medical experts when the following information is provided: bloodwork (with hematocrit, hemoglobin, C reactive protein, ESR, platelets, and ferritin levels); supporting endoscopy; details of weight loss; and a list of narcotic analgesics being used.

*Initial Approval:* 6 months at 300 mg initially administered at week 0, followed by 300 mg at week 2, 300 mg at week 6, then 300 mg every 8 weeks thereafter.

**Renewal** will be considered for patients with 50% reduction in HBI from pre-treatment as well as improvement of symptoms (e.g., absence of bloody diarrhea and weight stabilization or increase) and no longer using steroids. Biochemical improvements may also be required.

**For the treatment of ulcerative colitis disease** in patients who meet the following criteria:

**Induction Criteria**

Mild disease
- a. Mayo score < 6 AND
- b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage

Moderate disease
- a. Mayo score between 6 and 10 (inclusive) AND
- b. Endoscopic* subscore of 2 AND
- c. Failed 2 weeks of oral prednisone at daily doses ≥ 40 mg (or a 1 week course of IV equivalent) and 3 months of azathioprine (AZA)/ 6-mercaptopurine (6MP) (or where the use of immunosuppressants is contraindicated)
  OR
- d. Stabilized with 2 weeks of oral prednisone at daily dose ≥ 40 mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/ 6MP (or where the use of immunosuppressants is contraindicated)
Vedolizumab

Brand(s): Entyvio

DOSAGE FORM/ STRENGTH: 300 mg Injection

Severe disease

a. Mayo score >10 AND
b. Endoscopic* subscore of ≥2 AND
c. Failed 2 weeks of oral prednisone at daily dose ≥ 40mg (or 1 week IV equivalent)

OR

Stabilized with 2 weeks oral prednisone ≥ 40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Initial Approval: 6 months at 300 mg initially administered at week 0, followed by 300mg at week 2, 300mg
at week 6, then 300 mg every 8 weeks thereafter.

*The endoscopy procedure must be done within the 12 months prior to initiation of treatment

Maintenance Criteria

After 3 loading doses of Entyvio:

a. Mayo score <6 AND
b. 50% reduction in prednisone from the starting dose

Approval: 6 months at 300 mg every 8 weeks

If patient is completely off steroids, Approval: 12 months at 300 mg every 8 weeks.

Subsequent renewals:

a. Mayo score <6; AND
b. Must be completely off steroids

Approval: 2 years at 300 mg every 8 weeks.

(Patients who remain on steroids will be considered on a case-by-case basis)
### MENTAL HEALTH TREATMENTS

#### Atomoxetine

**Brand(s):** Strattera and generics  
**DOSAGE FORM/ STRENGTH:** 10 mg, 18 mg, 25 mg, 40 mg, 60 mg Capsules  

*Note: Effective June 29, 2018, Atomoxetine is made available as a General Benefit on the Ontario Drug Benefit Formulary. Please refer to the Formulary for funded products and strengths.*

#### Buspirone

**Brand(s):** Apo-buspirone, Novo-buspirone  
**DOSAGE FORM/ STRENGTH:** 10 mg tablet  

*For the treatment of generalized anxiety disorder.* in patients who meet the following criteria;  
- Patient has had an inadequate response to a trial of a first line agent* (escitalopram, paroxetine, sertraline or venlafaxine).  
  *If the patient has experienced intolerance or has a contraindication to a first line agent, another first line agent must be tried unless the patient is concurrently taking an irreversible monoamine oxidase inhibitor (MAOI) or has a co-diagnosis of bipolar disorder.

**Duration of Approval:** 5 Years  
**Renewals** will be considered for patients who are continuing to respond to therapy.  
**Duration of Approval:** 5 Years

#### Zopiclone

**Brand(s):** Imovane + generic brands  
**DOSAGE FORM/ STRENGTH:** 5 mg, 7.5 mg tablet  

*For the treatment of insomnia* as a single hypnotic agent in patients who meet the following criteria;  
- Have failed at least two benzodiazepines; *OR*  
- Have failed or experienced intolerance to at least one benzodiazepine and one other hypnotic (i.e., amitriptyline, trazodone, etc…)

**Duration of Approval:** 2 Years  
**For the treatment of insomnia if patient has an identified psychiatric diagnosis.**  
**Renewals** will be considered in patients who are responding to therapy AND who continues to require therapy AND who are using zopiclone as a single agent.  
**Duration of Approval:** 2 Years
Zuclopenthixol Decanoate  
Brand(s): Clopixol Depot  
DOSAGE FORM/ STRENGTH: 200 mg/mL intra-muscular injection  

Zuclopenthixol Dihydrochloride  
Brand(s): Clopixol Tablet  
DOSAGE FORM/ STRENGTH: 10 mg, 25 mg tablet  
**META BOLIC/GENETIC MODIFIERS**

**Asfotase alfa**
*Brand(s): Strensiq*

**DOSAGE FORM/ STRENGTH:** 18mg/0.45mL, 28mg/0.7mL, 40mg/1mL, 80mg/0.8mL

**Initiation Criteria:**

For the treatment of perinatal/infantile, childhood, or juvenile-onset hypophosphatasia (HPP) in patients who meet the following criteria:

- Diagnosis is confirmed by genetic testing (i.e. documented tissue-nonspecific alkaline phosphatase gene mutations); AND
- Serum alkaline phosphatase (ALP) level is below the age-adjusted normal range\(^1\) using age and gender adjusted norms; AND
- Plasma pyridoxal-5-phosphate (PLP) above the upper limit of normal; AND
- Radiologically confirmed HPP-related skeletal abnormalities; AND
- Diagnosis occurred before the patient’s 12th birthday with documented onset of signs/symptoms\(^2\) of HPP prior to their 12th birthday; AND
- Patient is younger than 18 years of age at the time the treatment is initiated; AND
- Patient does not have odonto- or pseudo- HPP (i.e. craniosynostosis alone, premature loss of deciduous teeth alone and vitamin D deficiency to be ruled out); AND
- The patient’s treatment plan and goals of therapy is provided prior to the initiation of therapy; AND
- Patient is under the care of a metabolic specialist with expertise in the diagnosis and management of HPP.

Approval duration for initial requests: 6 months

**Renewal Criteria:**

Renewals of reimbursement will be considered in patients meeting the following criteria:

- Patient continues to be under the care of a metabolic specialist; AND
- Patient has demonstrated compliance to the treatment and monitoring schedule: AND
- Pre-specified goals\(^3\) based on the patient’s clinical status at initiation of treatment are met and the patient is deemed to continue to benefit from treatment. (Note: The request must include information about the treatment responses and milestones)

First renewal: 6 months
Subsequent renewals: 1 year
Asfotase alfa
Brand(s): Strensiq
DOSAGE FORM/ STRENGTH: 18mg/0.45mL, 28mg/0.7mL, 40mg/1mL, 80mg/0.8mL

Stopping Criteria:

- Discontinuation to be considered after growth is completed based on objective measure of height, weight and closure of bone growth plates as confirmed radiologically.
- Babies with perinatal/infantile HPP who fail treatment trials of 6 months
- If pre-specified goals are not met at reassessment, the treatment should not be continued.

Notes:

1. Normal range as informed by the Canadian Laboratory Initiative on Paediatric Reference Intervals (CALIPER) can be used as a reference for this information. Below upper limit of normal refers to 2 or lower standard deviations above the mean.

2. Incoming Requests should address the following;

- baseline skeletal symptoms including age and dates of for those assessments
- abnormalities of skeletal mineralization
- fracture history
- growth plate irregularities and bone and skeletal growth
- description of growth and developmental milestones
- Signs, symptoms, and history of seizures
- respiratory function including need for ventilator support
- Activity and mobility
- Laboratory markers that include vitamin D levels, calcium levels

Assessments such as the Radiographic Global Impressive of Change (RGIC) score and/or the Thacher score for evaluating rickets may be provided at baseline and at the time of renewal of coverage (as applicable) as a measure of response and benefit from therapy.

3. Specific patient treatment goals should be developed on a case-by-case basis and may include some of the following; Healing of rickets, improved bone mineralization, fewer fractures, reduced pain, improved growth, mobility, improvement in respiratory status, attainment of age-appropriate growth milestones, improvement in gait or deformities, improved quality of life measures.

Documentation of improvement from baseline is to be provided at the time of renewal.
Glycerol phenylbutyrate
Brand(s): Ravicti
DOSAGE FORM/ STRENGTH: 1.1g/mL-25mL bottle

For the management of patients with chronic urea cycle disorders (UCD) who meet all the following criteria:

- Glycerol phenylbutyrate is being used as a nitrogen binding agent; AND
- Patient has demonstrated that they cannot be managed by dietary protein restriction and/or amino acid supplementation alone\(^1\); AND
- Patient is under the care of a physician with expertise in the treatment of patients with UCD or in consultation with a physician with this expertise.

\(^1\)The initial request should include levels for blood ammonia and glutamine levels demonstrating inadequate effects of protein restriction or amino acid supplementation.

Exclusion Criteria:

- Is not used in combination with other forms of phenylbutyrate
- Will not be funded for patients who are not using a low protein diet while on treatment
- Not funded for the management of acute hyperammonemia
- Not funded for patients under 2 months of age

Recommended dose: 5 g/m\(^2\) to 12.4 g/m\(^2\) per day

Approval duration: 1 year

Renewal Criteria:

Renewals will be considered in patients who demonstrate benefit from treatment\(^2\) and who have not developed unacceptable toxicities requiring discontinuation.

\(^2\)At the time of renewal, please provide recent (within 3 months) blood ammonia and glutamine levels while on treatment and address the number and severity of hyperammonemnic events experienced while on treatment in the previous 12 months and any treatment emergent events requiring urgent care or hospitalization.

First renewal: 1 year
Subsequent renewals: 2 years
Nusinersen
Brand(s): Spinraza
DOSAGE FORM/ STRENGTH: 2.4 mg/mL – 5mL vial Pk

**Initial Criteria:**
For the treatment of Type 1 spinal muscular atrophy (SMA) in patients meeting all the following criteria,

- Provides genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation, or compound heterozygote AND two copies of the survival motor neuron 2 (SMN2) gene; AND
- Onset of clinical signs and symptoms consistent with SMA after the first week after birth and on or before 7 months of age and disease duration less than 26 weeks; AND
- Patient does not require permanent invasive ventilation; AND
- Patient is under the care of a specialist experienced in the diagnosis and management of SMA.

**Renewal Criteria:**
Renewal of funding will be considered for patients who have not demonstrated any of the Stopping/discontinuation criteria while on therapy.

**Stopping/Discontinuation Criteria for Spinraza**
(These criteria are applicable to patients funded upon meeting either initial or renewal criteria.):
An assessment of the response to therapy should be made prior to the fifth dose or every subsequent dose of Spinraza. Treatment should be discontinued upon meeting any of the following circumstances:

- Patient is not demonstrating/achieving response in motor milestones as assessed using the Hammersmith Infant Neurological Examination (HINE) Section 2
  - there is no demonstrated improvement in motor milestone function above pre-treatment scores (as assessed using the HINE Section 2); or
  - there is no demonstrated maintenance of motor milestone function (as assessed using HINE Section 2); OR
- If Permanent Invasive Ventilation (PIV)\(^1\) is required

**Exclusion criteria:**
- SMA Type 2, 3 or 4 are not funded.
- Patient with permanent invasive ventilation (PIV)\(^1\)

\(^1\)Permanent Invasive Ventilation (PIV) is defined as the use of tracheostomy and a ventilator due to progression of SMA that is not due to an identifiable and reversible cause.
Nusinersen
Brand(s): Spinraza
DOSAGE FORM/ STRENGTH: 2.4mg/mL – 5mL Vial Pk

Recommended dose:
Loading doses:
12 mg administered intrathecally on days 0, 14, 28 and 58 (Note: 4\textsuperscript{th} loading dose is administered approximately 30 days after the 3\textsuperscript{rd} loading dose)

Maintenance dose:
12 mg administered intrathecally every 4 months starting 4 months after the 4\textsuperscript{th} loading dose.

Approval duration for initial request: 8 months
Approval duration of Renewals: 1 year
Ongoing funding of sapropterin (Kuvan) will be considered through the EAP for non-pregnant patients and patients actively planning pregnancy who have a diagnosis of Phenylketonuria (PKU) and who have demonstrated a response to the initial 6 month trial of sapropterin [reimbursed through the manufacturer (see details below)] and who meet ALL of the following criteria:

1. Compliance with low protein diet, formulas, and treatment with sapropterin; AND

2. Has achieved
   a) normal sustained blood phenylalanine (Phe) levels [Greater than 120 μmol/L and less than 360 μmol/L] (At least 2 levels measured at least 1 month apart); OR
   b) sustained blood Phe reduction of at least 30% (At least 2 levels measured at least 1 month apart) compared to baseline if the Phe baseline level is less than 1200 μmol/L; OR
   c) sustained blood Phe reduction of at least 50% (At least 2 levels measured at least 1 month apart) compared to baseline if the Phe baseline level is greater than 1200 μmol/L;

AND

3. Demonstrated increase of dietary protein tolerance based on targets set between the clinician and patient; AND

4. Clinically meaningful age-appropriate improvement in:
   a) neurobehavioural or neurocognitive function or impairment for patients with such impairments as determined by peer reviewed clinically validated scales; OR
   b) demonstrated improvement in Quality of Life using peer reviewed validated scales; AND

5. Managed by a physician specialized in metabolic/biochemical diseases.

Please note that sapropterin is only considered through the EAP for responders to an initial 6 month trial period funded through the manufacturer (described in the next 2 pages). The exclusion criteria for initial funding of sapropterin also applies to funding through the EAP. (see next page)
Sapropterin
Brand(s): Kuvan

DOSAGE FORM/ STRENGTH: 100 mg tablet

Initial funding of sapropterin will be considered by the manufacturer for the management of non-pregnant patients and patients actively planning pregnancy who have a diagnosis of Phenylketonuria (PKU) and who meet ALL of the following criteria:

1. Compliance with a low protein diet and formulas.
2. Baseline blood phenylalanine (Phe) levels are greater than 360 μmol/L despite compliance with low protein diet (require at least 2 levels during 3 to 6 month time frame)
6. Ability to comply with medication regimen.
7. Managed by a physician specialized in metabolic/ biochemical diseases.

Initial funding of sapropterin will also be considered by the manufacturer for the management of pregnant patients who have a diagnosis of Phenylketonuria (PKU) and who meet ALL of the following criteria:

- Managed by a physician specialized in metabolic/ biochemical diseases.
- Baseline blood phenylalanine (Phe) levels > 360 μmol/L despite compliance with all recommendations for dietary intervention and monitoring

Funding will not be considered for patients meeting any of the following exclusion criteria:

- Known hypersensitivity to sapropterin or its excipients
- Any other contraindications
- Baseline Phe Levels less than 360 μmol/L in a non-pregnant patient
- Baseline Phe Levels less than 360 μmol/L in a pregnant patient
- Women who are nursing/breast feeding
- Patients who are not on the special diet or who are not compliant with their special diet

Note that sapropterin should be used with caution when the patient is taking medication known to inhibit folate synthesis (e.g., methotrexate) and/or has any condition that requires treatment with levodopa or any phosphodiesterase type 5 (PDE-5) inhibitor.

Additionally, consider for initial funding of sapropterin requires that the patient completes an eligibility test called the “72 hour Kuvan Challenge” described below.
Sapropterin
Brand(s): Kuvan

**DOSAGE FORM/ STRENGTH:** 100 mg tablet

**Test for Eligibility: 72 hour “Kuvan” Challenge**

- 72 hour challenge with sapropterin at 20 mg/kg/day
- Blood Phe concentrations are measured at 48 hours, 24 hours, and time “0” PRIOR TO the sapropterin dose and THEREAFTER at 4, 12, 24, 48, and 72 hours following the dose; OR as per clinic’s protocol

Note that the recommended dose of sapropterin to establish clinical benefit is 20 mg/kg/day

**Responders to the 72 hour “Kuvan” Challenge**

For Non-Pregnant patients and patients actively planning pregnancy, responders to the Kuvan challenge are those who meet the following criteria:

- Reduction in Phe blood level of at least 30% compared to baseline; AND
- Patient must have a baseline assessment of neurobehavioural or neurocognitive impairment* and quality of life assessment due to PKU after the 72 hr Kuvan challenge but before start of Kuvan therapy (this assessment does not apply to pregnant women)

Note: A baseline Phe tolerance level must be documented and Phe tolerance levels must be documented at months 1 to 2 and 4 to 6 during the initial 6 months of therapy.

* For children less than 4 years of age, clinically validated age-appropriate neurobehavioural, neurocognitive, or developmental tests may be selected at the clinician’s discretion rather than PKU specific tests

For pregnant patients and patients actively planning pregnancy, responders to the Kuvan challenge are those who meet the following criteria:

- Reduction in Phe blood level of at least 30% compared to baseline after 72 hours

Pregnant patients who meet the “responder” definition to the 72 hour Kuvan Challenge, may be eligible for Kuvan funding if the following criteria are met:

- A decrease in Phe concentration to less than 360 μmol/L is to be maintained for the duration of pregnancy to be eligible for continued funding
Sapropterin
Brand(s): Kuvan
DOSAGE FORM/ STRENGTH: 100 mg tablet

Renewals for sapropterin in pregnant patients will not be considered.

Duration of Approval: 1 year
6 months in non-pregnant and patients planning a pregnancy (Funded by the manufacturer)
Approval duration in pregnant patients: 6 months or to end of pregnancy (Funded through the manufacturer)

MIGRAINE DRUGS

Onabotulinum Toxin A
Brand(s): Botox
DOSAGE FORM/ STRENGTH: 50 U/Vial, 100 U/Vial, 200 U/vial

For the prophylaxis of headaches in adults meeting the following criteria for funding:

- Patient with chronic migraine (defined as ≥15 days per month with continuous headache lasting ≥4 hours AND at least 4 distinct headache episodes each lasting ≥4 hours); AND
- Patient has failed\(^1\) three or more prior oral prophylactic medications\(^2\); AND
- Request for Botox to treat migraine must be provided by a physician with specialty training in the management of headache. Administration should only be given by physicians with the appropriate qualifications and experience in the treatment, use, and proper administration of Botox for headaches.

\(^1\)Failure is defined as no therapeutic or unsatisfactory effect (Less than a 30% reduction in frequency of headache days) to an adequate dose and duration of 3 prophylactic therapies\(^2\) where two treatments must be of different types/classes.

Contraindication or intolerable side effects necessitating discontinuation will be considered for 1 of the 3 drugs only.

\(^2\)Prophylactic therapies to be considered include:
Onabotulinum Toxin A

Brand(s): Botox

DOSAGE FORM/ STRENGTH: 50 U/Vial, 100 U/Vial, 200 U/vial

- Beta blockers
- Tricyclic antidepressants
- Verapamil or flunarizine
- Sodium valproate (or divalproex sodium)
- Topiramate
- Gabapentin

Requests should contain the following information:
- Objective measure of baseline headache days and response to other prophylactic medications (i.e. headache diary)
- List of previously tried prophylactic medications, including doses and duration as well as why they were discontinued
- Confirmation of specialty training in the management of headache.

Dosing: As per product monograph

Notes regarding continued therapy with “Botox”:

i) Patients who have not obtained an adequate treatment response after 2 treatment cycles should be discontinued from further therapy.

ii) Patients who obtain an adequate response and who transition from chronic migraine to episodic migraine should be discontinued from therapy within 3 months of that transition.

An adequate treatment response is defined as a ≥ 50% reduction in frequency of headache days per month

**Duration of Approval:** 1 year

**Renewal criteria:**

- Objective evidence (i.e. headache diary) that the patient has obtained an adequate treatment response defined as a ≥ 50% reduction in frequency of headache days per month; AND
- Confirmation that the patient has not transitioned from chronic migraine to episodic migraine. Therapy will be reimbursed for a maximum of 3 months after transition from chronic migraine to episodic migraine.
- Consideration will be given for renewals in patients who had an initial adequate response to Botox, discontinued therapy and subsequently transitioned back to chronic migraine status.

**Duration of Approval:** 1 year
Almotriptan
Brand(s): Axert
DOSAGE FORM/ STRENGTH: 6 mg, 12.5 mg tablet

Naratriptan
Brand(s): Amerge
DOSAGE FORM/ STRENGTH: 1 mg, 2.5 mg tablet

Rizatriptan
Brand(s): Maxalt, Maxalt RPD
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet and wafer

Sumatriptan
Brand(s): Imitrex
DOSAGE FORM/ STRENGTH: 50 mg, 100 mg tablet

For the treatment of migraines with or without aura in patients who failed adequate trials of other medications for migraines (e.g. acetaminophen, NSAIDs) and where the following information is provided:

- Details of migraine prophylactic regimens (e.g. amitriptyline, beta-blockers) tried or rationale why they are inappropriate; and
- The number of attacks, duration, and severity of migraines.

Duration of Approval: 5 years

Renewal requests may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.

Warning: The frequent use of triptans (i.e. more than three days per week for longer than three months at a time) may predispose a patient to developing triptan-induced chronic daily headaches.
### Sumatriptan

**Brand(s):** Imitrex Injection  
**DOSAGE FORM/ STRENGTH:** 12 mg/mL subcutaneous injection  
**Brand(s):** Imitrex Nasal Spray  
**DOSAGE FORM/ STRENGTH:** 5 mg/dose and 20 mg/dose nasal spray

For the treatment of migraines with or without aura in patients who failed adequate trials of other medications for migraines (e.g. acetaminophen, NSAIDs) and has documented intolerance* to an oral triptan. The following information must also be provided:

- Details of migraine prophylactic regimens (e.g. amitriptyline, beta-blockers) tried or rationale why they are inappropriate; and
- The number of attacks, duration, and severity of migraines.

* The nature of intolerance or why oral sumatriptan cannot be used must be specified.

Duration of Approval: 5 years

**Renewal** requests for sumatriptan may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.

*Warning: The frequent use of triptans (i.e. more than three days per week for longer than three months at a time) may predispose a patient to developing triptan-induced chronic daily headaches.*

### Zolmitriptan

**Brand(s):** Zomig  
**DOSAGE FORM/ STRENGTH:** 2.5 mg tablet  
**Brand(s):** Zomig Rapimelt  
**DOSAGE FORM/ STRENGTH:** 2.5 mg dispersible tablet

For the treatment of migraines with or without aura in patients who have failed an adequate trial of or experienced intolerance to all other oral triptans considered under the Exceptional Access Program.

Duration of Approvals: 5 years

**Renewal** requests may be considered for patients who continue to benefit from treatment. The physician must provide the frequency of triptan use.
MULTIPLE SCLEROSIS DRUGS

Alemtuzumab
Brand(s): Lemtrada

DOSAGE FORM/ STRENGTH: 12 mg/ 1.2 mL Solution for IV infusion

For the treatment of Relapsing–Remitting Multiple Sclerosis (RRMS) as monotherapy in patients who meet all of the following criteria:

- The patient’s physician provides documentation setting out the details of the patient’s most recent neurological examination (which must have been conducted within ninety [90] days of the request, including a description of any recent attacks, the dates of attacks, and neurological findings); AND
- Patient has failed to respond\(^1\) to full and adequate courses of at least ONE of the following therapies: interferon, glatiramer acetate, dimethyl fumarate, or teriflunomide or has had a documented intolerance or contraindication to TWO or more of the listed therapies; AND
- Patient has experienced one (1) or more clinically disabling relapses in the previous year; AND
- Patient has had a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e. 3 or more new lesions) OR at least one gadolinium-enhancing lesion;
- Patient is being followed by a neurologist experienced in the management of relapsing–remitting multiple sclerosis (RRMS); AND
- The patient has a current Expanded Disability Status Scale (EDSS) score less than or equal to 5.0.

\(^1\) “Failed to respond to full and adequate courses” of certain therapies means that the patient has received a trial of at least 6 months of interferon, glatiramer acetate, dimethyl fumarate therapy, or teriflunomide; AND has experienced at least one disabling relapse (attack) while on such therapy.

Exclusion Criteria: No reimbursement if the patient satisfies any of the following exclusion criteria:

- the patient is receiving combination therapy of Lemtrada with other disease modifying therapies, such as Aubagio, Avonex, Betaseron, Copaxone/Glatect, Extavia, Rebif, Extavia, Tysabri, Gilenya and Tecfidera; OR
- the patient has an EDSS score greater than 5.0; OR
- the patient is younger than 18 years old.

Dosage: 12 mg per day for two treatment courses.
**Alemtuzumab**

Brand(s): Lemtrada

**DOSAGE FORM/ STRENGTH:** 12 mg/ 1.2 mL Solution for IV infusion

Initial course: 12 mg per day for 5 consecutive days (60mg total dose). Second course: 12 mg per day for 3 consecutive days (36mg total dose) administered 12 months after the initial treatment course.

Retreatment beyond two cycles (eight vials) may be considered.

**Note:** MRI reports are NOT mandatory to submit with the initial request.

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**Dimethyl fumarate**

Brand(s): Tecfidera

**DOSAGE FORM/ STRENGTH:** 120 mg delayed-release capsule

*For the treatment of Relapsing–Remitting Multiple Sclerosis (RRMS)* in patients who meet all of the following criteria:

- The patient’s physician provides documentation setting out the details of the patient’s most recent neurological examination (which must have been conducted within ninety [90] days of the request, including a description of any recent attacks, the dates of attacks, and neurological findings).
- Patient has had one (1) or more clinical relapses in the previous year.
- The drug is requested by and followed by a neurologist experienced in the management of RRMS.
- The patient has a recent Expanded Disability Status Scale (EDSS) score ≤ 5.

Dosage: Initial: 120 mg twice daily

Maintenance: 240 mg twice daily

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**Renewal** requests will be considered. Renewals for Tecfidera can be submitted through the Telephone Request Service.

The date and details of the most recent neurological examination and EDSS scores must be provided (exam must have occurred within the last ninety [90] days); **AND**

- The patient must be stable or experienced no more than one clinical relapse* in the past year; **AND**
- The patient has a recent EDSS score ≤ 5.

Dosage: 120 mg twice daily.

Maintenance: 240 mg twice daily
Dimethyl fumarate
Brand(s): Tecfidera
DOSAGE FORM/ STRENGTH: 120 mg delayed-release capsule

Duration of Approval: 1 year

*Renewal requests where patients have experienced more than one (1) clinical relapse in the past year are to be externally reviewed.

As applicable, please also include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the patient was examined, or an MS consult note as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years
Second and subsequent renewals: 5 years

Fingolimod
Brand(s): Gilenya
DOSAGE FORM/ STRENGTH: 0.5 mg capsule

As monotherapy for the treatment of patients with Relapsing Remitting Multiple Sclerosis (RRMS) who meet all of the following criteria:

- The patient’s physician provides documentation setting out the details of the patient’s most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attack(s), the date(s) of the attack(s), and the neurological findings; AND
- Failure to respond to full and adequate courses¹ of at least one of interferon OR glatiramer acetate OR dimethyl fumarate; OR teriflunomide OR documented intolerance or contraindication to 2 of the above listed therapies; AND
- Experienced one or more clinically disabling relapses in the previous year; AND
- Has had a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e. 3 or more new lesions) OR at least one gadolinium-enhancing lesion.
- Is being followed by a neurologist experienced in the management of RRMS.
- Has a current EDSS of less than or equal to 5.5 (i.e. patients must be able to ambulate at least 100 meters without assistance).
Fingolimod
Brand(s): Gilenya
DOSAGE FORM/ STRENGTH: 0.5 mg capsule

Exclusion Criteria (Patients meeting any of the following exclusion criteria will not be funded):

- Patient’s receiving combination therapy of Gilenya with other disease modifying therapies (e.g. Aubagio, Avonex, Betaseron, Copaxone/Glatect, Extavia, Rebif, Extavia, Tysabri, and Tecfidera).
- Patients with EDSS greater than 5.5
- Patients who have had a heart attack or stroke in the last 6 months of the funding request, history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure.
- Patients younger than 18 years of age.
- Patients requesting Gilenya due to needle phobia or preference for oral therapy over injection who do not have a clinical contraindication to interferon or glatiramer therapy.
- Skin reactions at the site of injection do NOT qualify as a contraindication to interferon or glatiramer therapy.

Dosage: 0.5 mg once daily

Failure to respond to full and adequate courses: defined as having received a trial of at least 6 months of interferon or glatiramer or dimethyl fumarate therapy or teriflunomide AND experienced at least one disabling relapse (attack) while on interferon or glatiramer or dimethyl fumarate or teriflunomide.

MRI reports do NOT need to be submitted with the initial request.

Duration of Approval: 1 year

Renewals are considered. Renewals can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy.

Physicians must provide the following information:

- Documentation providing the date and details of the Patient’s most recent neurological examination and EDSS scores (exam must have occurred within the last ninety (90) days); AND
- Evidence that the patient is stable and has experienced no more than one (1) disabling attack/relapse in the past year. (Note: If the Patient has had more than one attack/relapse, the request will be sent for external review. Please include details of the attack(s) including the dates on which they occurred); AND
- A recent Expanded Disability Status Scale (EDSS) that is less than or equal to 5.5 (Note: Requests with an EDSS greater than 5.5 will not be funded).

Dosage: 0.5 mg once daily.

Duration of Approval: First Renewal: 2 years
Second and subsequent renewals: 5 years
Glatiramer acetate
Brand(s): Copaxone

DOSAGE FORM/ STRENGTH: 20 mg/mL pre-filled syringe for subcutaneous injection

*Effective September 27, 2018, Glatiramer as Copaxone for the treatment of Relapsed Refractory Multiple Sclerosis (RRMS)/ Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) will only be considered for funding for existing EAP renewals. All EAP requests for patients treatment-naive to Copaxone should consider Glatiramer as Glatect upon meeting Limited Use Criteria on the Ontario Drug Benefit Formulary effective on September 27, 2018.*

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see criteria in next section. Also, note that patients who are treatment naïve to Copaxone should refer to the formulary for consideration of Glatect.

For CDMS: Copaxone requests for patients with CDMS will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days); and
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year; and
- EDSS score ≤ 5.

**Duration of Approval:** 1 year

**Renewal**

requests for Copaxone can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient’s most recent EDSS score.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

**Duration of Approval:** First Renewal: 2 years

Second and subsequent renewals: 5 years
Interferon beta-1a
Brand(s): Avonex PS, Avonex Pen
DOSAGE FORM/ STRENGTH: 30 mcg/ 0.5mL prefilled syringe for intramuscular injection, 30 mcg single-use prefilled autoinjector

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see CIS criteria in next section).

For CDMS: Avonex requests for patients with CDMS will be reviewed by external medical experts when the following information is provided:

- Details of the most recent neurological examination within the last ninety (90) days, including a description of any recent attacks (date and neurological findings)
- The patient has experienced at least two clinical attacks including one clinical attack within the past year
- MRI findings as applicable
- The patient’s EDSS is less than or equal to 6.0

Renewal requests for Avonex can be submitted through the Telephone Request Service. Avonex renewals will be considered for patients who have benefited from therapy. Patients must be stable (i.e. no relapses or attacks during the last year) and the patient’s EDSS must be less than or equal to 6.0

The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient's most recent EDSS score.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.
Interferon beta-1a
Brand(s): Rebif

DOSAGE FORM/ STRENGTH: 22 mcg and 44 mcg prefilled syringe for subcutaneous injection, 66 mcg/ml and 132 mcg/ml pre-filled cartridge

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see CIS criteria in next section).

For CDMS: Rebif requests for patients with CDMS will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days); and
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year; and
- EDSS score ≤ 6.

Duration of Approval: 1 year

Renewal requests for Rebif can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6. The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient’s most recent EDSS score.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

Duration of Approval: First Renewal: 2 years

Second and subsequent renewals: 5 years
For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see criteria in next section)

For CDMS: Betaseron requests for patients will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days);
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year;
- EDSS score ≤ 6.

**Duration of Approval:** 1 year

**Renewal** requests for Betaseron can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days);
- The patient’s most recent EDSS score.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

**Duration of Approval:** First Renewal: 2 years

**Second and subsequent renewals:** 5 years
Interferon beta-1b
Brand(s): Extavia

**DOSAGE FORM/ STRENGTH:** 0.3 mg/vial subcutaneous injection

For the treatment of Clinically Definite Multiple Sclerosis (CDMS) or Clinically Isolated Syndrome (CIS) (see criteria in next section).

For **CDMS:** Extavia requests for patients will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination (within the last 90 days) AND
- Dates and details (e.g., neurological findings) of at least two clinical attacks, including one clinical attack within the past year AND
- EDSS score ≤ 6.

**Duration of Approval:** 1 year

**Renewal** requests for Extavia can be submitted through the Telephone Request Service and will be considered for patients who have benefited from therapy and have an EDSS score ≤ 6.

The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient’s most recent EDSS score.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

**Duration of Approval:** 2 years
Second and subsequent renewals: 5 years
Natalizumab
Brand(s): Tysabri
DOSAGE FORM/ STRENGTH: 300 mg/15 mL concentrate for solution for intravenous infusion

Initial Request:
As monotherapy for the treatment of Rapidly Evolving Severe Relapsing-Remitting Multiple Sclerosis (RES-RRMS) for the patient who meets all the following:

a) The patient’s physician provides documentation setting out the details of the patient’s most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attacks, including the corresponding dates, and the neurological findings; AND

b) Has been diagnosed with MS; AND

c) Is 18 to 65 years of age; AND

d) Has a current EDSS of less than or equal to 5.0; AND

e) Has had ONE of the following types of relapses in the past year:
   - The occurrence of one relapse with partial recovery during the past year AND has at least ONE gadolinium-enhancing lesion on brain MRI, OR significant increase in T2 lesion load compared to a previous MRI (i.e. 3 or more new lesions); OR
   - The occurrence of two or more relapses with partial recovery during the past year; OR
   - The occurrence of two or more relapses with complete recovery during the past year AND has at least ONE gadolinium-enhancing lesion on brain MRI, OR significant increase in T2 lesion load compared to a previous MRI;

(f) has failed to respond to full and adequate courses\(^1\) of at least one of interferon OR glatiramer acetate OR dimethyl fumarate; OR teriflunomide OR documented intolerance or contraindication to 2 of the 3 therapies. (Note that needle phobia is not acceptable.)

(g) is being followed by a neurologist experienced in the management of RRMS

(h) details of past treatment, including dates and Patient response;
Natalizumab
Brand(s): Tysabri
DOSAGE FORM/ STRENGTH: 300 mg/15 mL concentrate for solution for intravenous infusion

Failure to respond to a full and adequate course: defined as a trial of at least 6 months of interferon or glatiramer therapy or dimethyl fumarate AND experienced at least one disabling relapse (attack) while on interferon or glatiramer or dimethyl fumarate.

MRI reports do NOT need to be submitted with the initial request.

Duration of Approval: 1 year

Renewals will be considered for requests meeting the following;

(a) Documentation providing the date and details of the patient’s most recent neurological examination and EDSS scores (exam must have occurred within the last ninety (90) days); AND

(b) Evidence that the Patient is stable and has experienced no more than one (1) disabling attack/relapse in the past year (Note: if the Patient has had more than one attack/relapse, the request will be sent for external review); AND

(c) A recent Expanded Disability Status Scale (EDSS) that is less than or equal to 5.0 (Note that the request will be rejected if the EDSS is greater than 5.0).

Duration of Approval: First Renewal: 2 years
Second and subsequent renewals: 5 years
Modafanil
Brand(s): Alertec
DOSAGE FORM/ STRENGTH: 100 mg tablet

For the treatment of fatigue in patients with multiple sclerosis who have demonstrated a lack of response to or an inability to tolerate amantadine.

Note: See additional indications and criteria under “CNS” drugs

Duration of Approval: Lifetime

Peginterferon beta-1a
Brand(s): Plegridy
DOSAGE FORM/ STRENGTH: 125mcg/0.5mL, 94mcg/0.5mL Injection, Starter Pack: 63mcg/0.5mL, 94mcg/0.5mL

For the treatment of Clinically Definite Multiple Sclerosis (CDMS)/ Relapsing remitting multiple sclerosis (RRMS) in patients meeting the following criteria:

Plegridy requests will be reviewed by external medical experts when the following information is provided:

- Details of the most recent neurological examination within the last ninety (90) days, including a description of any recent attacks (date and neurological findings)
- The patient has experienced at least two clinical attacks in his or her lifetime, including one clinical attack within the past 12 months preceding the EAP request;
- MRI findings as applicable
- The patient’s EDSS is less than or equal to 6.0

Duration of Approval: 1 year

Renewal requests for Plegridy can be submitted through the Telephone Request Service. Plegridy renewals will be considered for patients who have benefited from therapy. Patients must be stable (i.e. no relapses or attacks during the last year) and the patient’s EDSS must be less than or equal to 6.0

The physician must provide the following information:

- Description of the patient’s clinical course in the last year, including details of all attacks;
- Date and details of the most recent neurological examination (within the last 90 days); and
- The patient’s most recent EDSS score.
### Peginterferon beta-1a

**Brand(s):** Plegridy  
**DOSAGE FORM/ STRENGTH:** 125mcg/0.5mL, 94mcg/0.5mL Injection, Starter Pack: 63mcg/0.5mL, 94mcg/0.5mL

*Renewal* requests where patients have experienced more than one (1) clinical relapse in the past year will be considered on a case-by-case basis through an external review.

As applicable, include information regarding the requesting physician’s specialty (e.g. is the physician a neurologist or a physician with specialized experience with multiple sclerosis (MS), the name of the MS clinic where the neurologist is based, or an MS consult note supporting the diagnosis as this information may reduce the turnaround times for assessment.

**Duration of Approval:**  
First Renewal: 2 years  
Second and subsequent renewals: 5 years

### Teriflunomide

**Brand(s):** Aubagio  
**DOSAGE FORM/ STRENGTH:** 14 mg tablet

**For the treatment of relapsing-remitting multiple sclerosis (RRMS)** in patients who meet the following criteria;

i) the physician making the request on behalf of the patient is a neurologist who is experienced in the management of RRMS; AND  
ii) the physician provides documentation of the patient’s most recent neurological examination which must have been conducted within ninety (90) days preceding the submission of the EAP request. This must include a description and dates of any recent attacks and other pertinent neurological findings; AND  
iii) the patient’s diagnosis is confirmed to be RRMS; AND  
x) the patient has experienced one or more clinical attacks/relapses in the year preceding the request; AND  
xi) the patient has a recent Expanded Disability Status Scale (EDSS) score that is equal to or less than 5.0 prior to starting therapy with teriflunomide.

Dosage: 14 mg once daily

**Duration of Approval:** 1 year
Renewals for the funding of teriflunomide will be considered in patients who meet the following criteria;

i) the physician provides documentation of the date and details of the patient’s most recent neurological examination and EDSS scores (the examination must have occurred within the last ninety [90] days preceding the submission of the renewal request); AND

ii) the physician confirms that the Patient is stable and has experienced no more than one (1) clinical relapse in the past year¹; AND

iii) the patient’s most recent EDSS score while on teriflunomide is less than or equal to 5.0.

¹Renewal requests where the patient has experienced more than 1 clinical relapse in the past year will be considered on a case-by-case basis with the assistance of external medical consultants.

Dosage: 14 mg once daily.

Duration of Approval 2 years
CLINICALLY ISOLATED SYNDROME DRUGS

**Glatiramer acetate**
Brand(s): Copaxone
**DOSAGE FORM/ STRENGTH:** 20 mg/mL pre-filled syringe for subcutaneous injection

**Interferon beta-1a**
Brand(s): Avonex PS, Avonex Pen
**DOSAGE FORM/ STRENGTH:** 30 mcg/0.5mL prefilled syringe for intramuscular injection, 30 mcg single-use prefilled autoinjector
Brand(s): Rebif
**DOSAGE FORM/ STRENGTH:** 22 mcg and 44 mcg prefilled syringe for subcutaneous injection, 66 mcg/ml and 132 mcg/ml pre-filled cartridge

**Interferon beta-1b**
Brand(s): Betaseron
**DOSAGE FORM/ STRENGTH:** 0.3 mg/vial subcutaneous injection
Brand(s): Extavia
**DOSAGE FORM/ STRENGTH:** 0.3 mg/vial subcutaneous injection

*For the treatment of Clinically Isolated Syndrome (CIS):* requests for patients who have experienced a single demyelinating event will be reviewed by external medical experts when the following information is provided:

- Date and details of the most recent neurological examination which must have been conducted within the last ninety days of the request;
- The patient’s EDSS is less than or equal to 6.0 (please provide EDSS score); AND
- The patient’s clinically isolated syndrome occurred within the last twelve months.

**Duration of Approval:** 1 year

**Renewal** requests will be assessed according to the following criteria:

- the requesting physician provides the date and details of the patient’s most recent neurological examination and EDSS scores;
- the patient’s neurological examination occurred within that last ninety days;
- the patient is stable (i.e. no relapses or attacks during the last year) and
- the patient’s EDSS is less than or equal to 6.0
OCULAR TREATMENTS

Mycophenolate Mofetil
Brand(s): Cellcept and generics

DOSAGE FORM/ STRENGTH: 250 mg capsules, 500 mg tablets, 200mg/mL oral suspension

For the treatment of non-infectious ocular inflammation (e.g., uveitis, scleritis and ocular mucous membrane pemphigoid) in patients meeting the following criteria;

- Experienced failure, intolerance, or contraindication to at least one Formulary immunosuppressant; OR
- First-line use for the treatment of severe non-infectious ocular inflammation
- Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

Duration of Approval: 1 year

Renewals will be considered for requests where consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met.

Duration of Approvals: 2 years

Infliximab
Brand(s): Remicade

DOSAGE FORM/ STRENGTH: 100 mg/10 mL Injection for intravenous infusion

For the treatment of severe non-infectious ocular inflammatory disease (OID) in patients meeting one of the following criteria;

- Experienced failure, intolerance, or contraindication to oral corticosteroid (or topical corticosteroid for anterior uveitis) and failure or intolerance to at least one immunosuppressive therapy; OR
- For the treatment of chronic Juvenile Idiopathic Arthritis (JIA)-associated uveitis after failure or intolerance to a first-line immunosuppressive agent; OR
- For patients who have immediately vision-threatening OID and do not meet the above criteria, where consultation notes/letter from an ophthalmologist expert specializing in OIDs (who may be the requesting physician) confirm the severity of the patient’s condition and indicate detailed rationale for an immediate biologic therapy (e.g. ocular inflammation associated with Behcet’s disease; severe non-necrotizing scleritis; necrotizing scleritis; etc.); AND
**Infliximab**

**Brand(s):** Remicade

**DOSAGE FORM/ STRENGTH:** 100 mg/10 mL Injection for intravenous infusion

- Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

**Approved Dose:** Infliximab 5-10 mg/kg IV at weeks 0, 2, 6 and maintenance every 4-8 weeks

**Duration of Approval:** 1 year

**Renewals** will be considered for requests where consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met.

**Duration of Approval:** 2 years

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**Adalimumab**

**Brand(s):** Humira

**DOSAGE FORM/ STRENGTH:** 40 mg per 0.8 mL Injection

- For the treatment of severe non-infectious ocular inflammatory disease (OID) in patients meeting one of the following criteria:
  - Experienced failure, intolerance, or contraindication to oral corticosteroid (or topical corticosteroid for anterior uveitis) and failure or intolerance to at least one immunosuppressive therapy; OR
  - For the treatment of chronic Juvenile Idiopathic Arthritis (JIA)-associated uveitis after failure or intolerance to a first-line immunosuppressive agent; OR
  - For patients who have immediately vision-threatening OID and do not meet the above criteria, where consultation notes/letter from an ophthalmologist expert specializing in OIDs (who may be the requesting physician) confirm the severity of the patient’s condition and indicate detailed rationale for an immediate biologic therapy (e.g. ocular inflammation associated with Behcet’s disease; severe non-necrotizing scleritis; necrotizing scleritis; etc.); AND
  - Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

**Approved Dose:** Adalimumab 40 mg subcutaneous every 1 to 2 weeks.

**Duration of Approval:** 1 year

**Renewals** will be considered for requests where consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met.

**Duration of Approval:** 2 years
Rituximab
Brand(s): Rituxan
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

For the treatment of severe non-infectious ocular inflammatory disease (OID) in patients failed or did not tolerate treatment with infliximab or adalimumab; OR has contraindication to anti-TNF therapy AND who meet one of the following criteria;

- Experienced failure, intolerance, or contraindication to oral corticosteroid (or topical corticosteroid for anterior uveitis) and failure or intolerance to at least one immunosuppressive therapy; OR
- For the treatment of chronic Juvenile Idiopathic Arthritis (JIA)-associated uveitis after failure or intolerance to a first-line immunosuppressive agent; OR
- For patients who have immediately vision-threatening OID and do not meet the above criteria, where consultation notes/letter from an ophthalmologist expert specializing in OIDs (who may be the requesting physician) confirm the severity of the patient’s condition and indicate detailed rationale for an immediate biologic therapy (e.g. ocular inflammation associated with Behcet’s disease; severe non-necrotizing scleritis; necrotizing scleritis; etc.); AND
- Patient must be followed by a uveitis specialist, a retina specialist familiar with ocular inflammatory diseases, or a pediatric ophthalmologist.

Approved Dose: Rituximab up to 1000 mg IV per infusion at days 1 & 15 and 3\textsuperscript{rd} infusion at 6-12 months.

Note that maintenance rituximab infusions are not funded.

Duration of Approval: 1 year

Renewals will be considered for requests where;

- Consultation notes or a letter is provided by the requesting physician to confirm that treatment has resulted in improvement/stability of vision and other treatment goals (e.g., remission from/control of ocular inflammation) have been met; AND

Patients must also have demonstrated subsequent deterioration of symptoms, at least 6 months from the last dose of rituximab.

Duration of Approval: 2 years
Reimbursement criteria for Zytiga in patients who have not trialed docetaxel.

For the treatment of metastatic castrate-resistant prostate cancer (mCRPC) in patients who meet the following criteria:

- Zytiga is being used in combination with prednisone; AND
- The patient is asymptomatic or mildly symptomatic after failure of androgen deprivation therapy; AND
- The patient has an ECOG* ≤ 1; AND
- The patient must not meet any of the exclusion criteria stated below.

*ECOG = Eastern Cooperative Oncology Group Status

(Please provide clinical information as objective evidence that the above criteria are met (e.g. castrate testosterone level, prostate surface antigen levels, evidence of metastatic disease such as presence and location of lesions, surgical procedures related to the condition, and name(s), date, duration of androgen deprivation therapy used details of the response to therapy, labwork or clinical confirmation to support that the patient does not meet any of the exclusion criteria.)

Approved dosage: 1000 mg once daily will be funded until there is evidence of disease progression.

Duration of Approval: 1 year

Renewals will be considered in patients with evidence of not having had disease progression while on Zytiga therapy.

Exclusion Criteria:

Funding for Zytiga will NOT be approved in patients who meet any ONE (or more) of the following exclusion criteria:
Abiraterone
Brand(s): Zytiga

DOSAGE FORM/ STRENGTH: 250 mg, 500 mg tablet

- the Patient has viral hepatitis or chronic liver disease; OR
- the Patient has clinically significant heart disease; OR
- Zytiga is being prescribed for combination use with Jevtana or Xtandi for mCRPC; OR
- The patient has received prior chemotherapy for mCRPC.

Reimbursement criteria for Zytiga in patients who are requesting Zytiga after a trial of docetaxel.

For the treatment of metastatic castrate-resistant prostate cancer (mCRPC) in patients who meet the following criteria:

- Zytiga is being used in combination with prednisone; AND
- The patient’s cancer has progressed after having received prior docetaxel containing therapy; AND
- The patient has ECOG* ≤ 2.
- Patients must not meet ANY of the exclusion criteria for funding stated below.

*ECOG = Eastern Cooperative Oncology Group Status

Requests for patients who initiated Jevtana (cabazitaxel) or Xtandi (enzalutamide) therapy within the three (3) months preceding the EAP request for Zytiga and who have not had disease progression, will be considered on a case-by-case basis.

Approved dosage: 1000 mg once daily will be funded until there is evidence of disease progression.

Renewals will be considered in patients with evidence of not having had disease progression while on Zytiga therapy.

Exclusion Criteria:

Funding for Zytiga will NOT be approved in patients who meet any ONE (or more) of the following exclusion criteria:

- the Patient has viral hepatitis or chronic liver disease; OR
- the Patient has clinically significant heart disease; OR
- Zytiga is being prescribed for combination use with Jevtana or Xtandi for mCRPC; OR
- the Patient has already used Zytiga in the pre-docetaxel setting.

Duration of Approval: 1 year
Afatinib
Brand(s): Giotrif
DOSAGE FORM/ STRENGTH: 20 mg, 30 mg, 40 mg tablet

Initial requests:

For the treatment of patients with advanced or metastatic non-small cell lung cancer (NSCLC) who meet the following criteria:

- Afatanib is being used as first line therapy; AND
- Afatanib is being used as monotherapy; AND
- Patient’s cancer is EGFR positive

Dose: 40 mg orally once daily

Exclusion Criteria:

- Patients with EGFR wild-type, negative, or unknown mutation.
- Afatinib will not be considered for funding in patients who have progressed on a prior EGFR TKI targeted therapy.
- Not funded for 2\textsuperscript{nd} or 3\textsuperscript{rd} line or maintenance NSCLC.

Notes:

- Patients should be assessed for disease status at least every two months. Afatinib may be continued until evidence of disease progression or development of unacceptable toxicity requiring discontinuation of afatinib.
- Patients who receive afatinib 1\textsuperscript{st} line are NOT eligible for erlotinib in the 2\textsuperscript{nd} or 3\textsuperscript{rd} line or maintenance NSCLC setting.
- Requests for afatinib for patients who have initiated another EGFR TKI therapy (i.e. Iressa [gefitinib]) in the first line setting and who have not had disease progression will be considered on a case-by-case basis.

Renewal requests will be considered based on the following:

Afatinib 40 mg once daily may be continued until evidence of disease progression or development of unacceptable toxicity at which point the drug should be discontinued. Patients should have their disease status assessed at least every two months.

Exclusion Criteria:

- Patients with EGFR wild-type, negative, or unknown mutation.
- Afatinib will not be considered for funding in patients who have progressed on a prior EGFR TKI targeted therapy. Not funded for 2\textsuperscript{nd} or 3\textsuperscript{rd} line or maintenance NSCLC.
Axitinib
Brand(s): Inlyta
DOSAGE FORM/ STRENGTH: 1 mg, 5 mg tablet

For the treatment of metastatic renal carcinoma (MRCC) of clear cell histology in patients meeting the following criteria:

- Axitinib is being used as second-line therapy after failure of prior systemic therapy with a tyrosine kinase inhibitor (i.e. one of sunitinib, pazopanib, or sorafenib)

  OR

- Axitinib is being used as a second line treatment switch for patients who do not have disease progression, but are unable to tolerate ongoing use of an effective dose of second line therapy with everolimus.

(Note: Patients are only eligible for either axitinib or everolimus or nivolumab in the second line setting)

Exclusions:

- Axitinib will not be funded if used in the third-line setting or later

Dosage: The usual starting dose is 5 mg twice a day.

(Dose titration based on individual response and tolerability will be funded.)

Approval duration: 1 year

Renewals will be considered for those who have demonstrated benefit from Inlyta therapy and are expected to continue to benefit do so.

Duration of Approval: 1 year
Bosutinib
Brand(s): Bosulif
DOSAGE FORM/ STRENGTH: 100 mg, 500 mg tablet

Chronic phase chronic myelogenous leukemia (CML):

i) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase with documented resistance/disease progression to 2 (two) prior oral tyrosine kinase inhibitors (TKI) (imatinib, dasatinib or nilotinib), where bosutinib would be the third or fourth line TKI; OR

ii) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase with documented intolerance to 1 (one) prior oral TKI (imatinib, dasatinib or nilotinib) where subsequent treatment with an alternative oral TKI (imatinib, dasatinib or nilotinib) is not clinically appropriate. Dosing recommendation: 500 mg per day.

Renewals will be considered upon confirmation from the clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so.

Dosing recommendation: 500 mg per day.

Accelerated Phase CML:

i) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase with documented resistance/disease progression to 2 (Two) prior oral TKIs (imatinib, dasatinib or nilotinib), where bosutinib would be the third or fourth line TKI; OR

ii) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase with documented resistance/disease progression to 2 (Two) prior oral TKIs (imatinib, dasatinib or nilotinib), where bosutinib would be the third or fourth line TKI; OR
Bosutinib

Brand(s): Bosulif

DOSAGE FORM/ STRENGTH: 100 mg, 500 mg tablet

iii) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase with documented intolerance to 1(One) prior oral TKI (imatinib, dasatinib or nilotinib) where subsequent treatment with an alternative oral TKI (imatinib, dasatinib or nilotinib) is not clinically appropriate.

Dosing recommendation: 500 mg per day.

Duration of Approval: 1 year

Renewals will be considered upon confirmation from the clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so.

Dosing recommendation: 500 mg per day.

Duration of Approval: 1 year

Blast Phase CML:

i) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase with documented resistance/disease progression to 2 prior oral TKIs (imatinib or dasatinib), where bosutinib would be the third or fourth line TKI; OR

ii) For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase with documented intolerance to 1 (ONE) prior oral TKI (imatinib or dasatinib) where subsequent treatment with an alternative oral TKI (imatinib or dasatinib) is not clinically appropriate.

Dosing recommendation: 500 mg per day.

Duration of Approval: 1 year

Renewal criteria: Confirmation from the clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so

Dosing recommendation: 500 mg per day.

Duration of Approval: 1 year
Ceritinib
Brand(s): Zykadia
DOSAGE FORM/ STRENGTH: 150mg capsule

Initial Criteria:

For the treatment of anaplastic lymphoma kinase (“ALK”) – positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients meeting ALL the following criteria;

- Patient is using ceritinib as monotherapy; AND
- Ceritinib is being used as second line therapy in patients who have experienced disease progression to crizotinib OR in patients who have experienced intolerance to crizotinib.

Exclusion criteria:

- Ceritinib will not be funded if the patient has experienced disease progression while on an ALK inhibitor other than crizotinib.
- Ceritinib will not be funded beyond third line therapy.

1Time-limited funding will be considered case-by-case in patients with ALK-positive NSCLC who have progressed on chemotherapy and crizotinib OR crizotinib and an immune checkpoint inhibitor commenced prior to the public funding of ceritinib.

2Include details of the intolerance including the grade of toxicity and reasons why crizotinib was not able to be used, particularly in situations where a toxicity was deemed to be grade 1 or 2.

Recommended dose: 750 mg daily

Renewal Criteria:

Ongoing funding will be considered in patients who have not experienced disease progression or unacceptable toxicities to treatment with ceritinib.

Approval duration of initial and renewal requests: 1 year
Reimbursement as **first-line therapy**\(^1\) to treat patients with advanced non-small cell lung cancer (NSCLC) who meet the following criteria:

i) ALK-positive  
ii) ECOG* performance status ≤ 2  

*ECOG = Eastern Cooperative Oncology Group Status

**Renewals** will be considered for patients who have not experienced disease progression as stated by the physician.

Reimbursement as **second-line therapy**\(^1\) to treat patients with advanced non-small cell lung cancer (NSCLC) who meet the following criteria:

i) ALK-positive  
ii) ECOG* performance status ≤ 2  

*ECOG = Eastern Cooperative Oncology Group Status

**Duration of Approval: 1 year**

**Renewals** will be considered for patients who have not experienced disease progression as stated by the physician.

Dosing: 250 mg orally twice a day.

\(^1\)Exclusion Criteria: Patients who have progressed during or following first-line therapy with crizotinib are not eligible to receive crizotinib as a second-line therapy.
Dabrafenib
Brand(s): Tafinlar
DOSAGE FORM/ STRENGTH: 50 mg, 75 mg capsule

Initial requests:
For the mutation-targeted treatment of patients with BRAF V600 mutation-positive unresectable melanoma or metastatic melanoma meeting the following criteria:

- As first-line monotherapy; OR
- As first-line combination therapy with trametinib; OR
- As second-line monotherapy in which the disease has progressed after receiving treatment in the first line setting; OR
- As second-line combination therapy with trametinib in which the disease has progressed after receiving treatment in the first line setting; AND
- If brain metastases are present, they should be asymptomatic or stable

Recommended Dose as Monotherapy:
150 mg twice until disease progression or development of unacceptable toxicity requiring discontinuation of dabrafenib.

Recommended Dose as combination dual therapy with trametinib:
Dabrafenib 150 mg twice daily and trametinib 2 mg once daily until disease progression or development of unacceptable toxicity requiring discontinuation.

Renewal requests:
Therapy as monotherapy OR as combination dual therapy (as above) may be continued until evidence of disease progression\(^1\) or development of unacceptable toxicity requiring discontinuation.

\(^1\) Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months.

Case by case:
Requests in patients who have initiated another single-agent BRAF or MEK inhibitor therapy will be considered on a case-by-case basis ONLY IF there has been no disease progression.

Exclusion Criteria:
- BRAF V600 negative, or wild type tumors, or unknown status will not be funded
- Dabrafenib therapy (as monotherapy or in combination with trametinib) will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.
Dasatinib
Brand(s): Sprycel
DOSAGE FORM/ STRENGTH: 20 mg, 50 mg, 70 mg, 100 mg tablet

For the treatment of Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in the chronic phase.

Dosing recommendation: 100 mg per day.

Renewals will be considered for patients who have experienced hematologic and/or cytogenic response and is expected to continue to do so.

Duration of Approval: 1 Year

Exclusion criteria:

Combination treatment with any two or more of the oral tyrosine-kinase inhibitors (TKI) (i.e. imatinib, nilotinib or dasatinib) will not be funded.

¹Note: Funding is only considered for any two oral TKIs* per patient in a lifetime for chronic phase CML (*TKIs: imatinib, nilotinib, or dasatinib). If a patient develops grade 3 or grade 4 toxicity on one of the listed TKI’s within 3 months of initiating therapy, funding for a third oral TKI will be allowed.

For the treatment of patients with accelerated phase or blast phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with documented resistance¹ or intolerance² (as defined below) to imatinib therapy

Dosing recommendation: 140 mg per day.

Definitions of resistance and intolerance:

¹Imatinib resistance is defined as primary or acquired resistance to imatinib at doses of at least 600 mg/day or through a mutational analysis report.

²Intolerance to imatinib (at any dose) is defined as persistent grade 3 or grade 4 toxicity requiring discontinuation of therapy.

Renewals will be considered for patients who have experienced hematologic and/or cytogenic response and are expected to continue to do so.

Duration of Approval: 1 Year
Dasatinib
Brand(s): Sprycel
DOSAGE FORM/ STRENGTH: 20 mg, 50 mg, 70 mg, 100 mg tablet

Exclusion criteria:
- Combination treatment with any 2 or more of the oral TKIs (i.e. imatinib, nilotinib or dasatinib) will not be funded.
- Dasatinib is not funded as a sequential third line therapy in patients who experience primary or acquired resistance (not including mutational resistance) to nilotinib.

For the treatment of Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in patients meeting the following criteria:
  i) An adult patient with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL); AND
  ii) Patient’s disease is resistant\(^1\) to imatinib-containing chemotherapy (patient must have tried 600 mg/day); O
  iii) Patient has experienced intolerance\(^2\) to imatinib therapy.

\(^1\)Imatinib resistance is defined as primary or acquired resistance to imatinib at doses of at least 600 mg/day or through a mutational analysis report.
\(^2\)Intolerance to imatinib (at any dose) is defined as the patient has experienced persistent grade 3 or grade 4 toxicity requiring discontinuation of therapy.

Renewals will be considered after confirmation from the patient’s physician that the patient has benefited or continues to benefit from therapy with Sprycel and is expected to continue to do so.

Duration of Approval: 1 Year

Reimbursement of dasatinib for children with acute lymphoblastic leukemia will be considered on a case-by-case basis.
Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/ STRENGTH: 40 mg capsule

Reimbursement criteria for Xtandi in patients who have not received prior chemotherapy:

For the treatment of metastatic castrate-resistant prostate cancer (mCRPC) in patients who meet the following criteria:

- The patient is asymptomatic or mildly symptomatic after failure of androgen deprivation therapy; **and**
- The patient has an ECOG* ≤ 1; **and**
- The patient must not meet any of the exclusion criteria\(^1\) stated below.

\(^*\)ECOG = Eastern Cooperative Oncology Group Status

\(^1\) Exclusion Criteria:

Xtandi will NOT be approved for funding in patients who meet any ONE (or more) of the following exclusion criteria:

- The patient has risk factors for seizures;
- The patient is using Xtandi in combination with Zytiga (abiraterone) for metastatic castration-resistant prostate cancer;
- The patient has used and experienced disease progression on Zytiga; **or**
- The patient has received prior chemotherapy for mCRPC.

Renewal of funding requests for Xtandi in patients who initiated Zytiga therapy and who have not had disease progression while on Zytiga will be considered on a case-by-case basis.

Duration of Approval: 1 Year

Reimbursement criteria for Xtandi in patients in the post-docetaxel setting:

For the treatment of metastatic castration resistant prostate cancer in patients who meet the following criteria;

- Xtandi is being used in patients who have progressed on docetaxel-based chemotherapy; **and**
- Patient has an ECOG* ≤ 2 (prior to the start of Xtandi therapy).

\(^*\)ECOG = Eastern Cooperative Oncology Group Status
Enzalutamide
Brand(s): Xtandi
DOSAGE FORM/ STRENGTH: 40 mg capsule

Requests for Xtandi for patients who meet the above criteria and who have initiated therapy with Jevtana or Zytiga (abiraterone) during the three months prior to the request for reimbursement of Xtandi and who have not had disease progression will be considered.

Note: Xtandi will only be considered as an alternative to Zytiga (abiraterone) for patients in the post-docetaxel setting but will not be considered as an add-on therapy to Zytiga (abiraterone) treatment.

Exclusion criteria:
Xtandi will not be funded in patients who meet any ONE (or more) of the following exclusion criteria;

- Patient has risk factors for seizures;
  - Patient is using Xtandi in combination with Jevtana (cabazitaxel) or Zytiga (abiraterone) for metastatic castration-resistant prostate cancer;

Patient’s requesting Xtandi for 1st line metastatic castration-resistant prostate cancer, refer to criteria in pre-docetaxel / pre-chemotherapy setting above.

Renewal of funding requests will be considered in patients who have not experienced disease progression while on Xtandi.

Duration of Approval: 1 Year
Erlotinib
Brand(s): Tarceva
DOSAGE FORM/ STRENGTH: 25 mg, 100 mg, 150 mg tablet

For the treatment of clinically documented incurable progressive non-small cell lung cancer (NSCLC) where:

- Erlotinib is used as monotherapy for the 2nd- or 3rd-line treatment after failure of prior chemotherapy (any regimen) in patients 70 years of age or older.
- Erlotinib is used as monotherapy for the 2nd- or 3rd-line treatment of patients with clinically documented incurable progressive non-small cell lung cancer (NSCLC) despite prior chemotherapy including both docetaxel and a platinum-based treatment (i.e. cisplatin or carboplatin).
- Erlotinib is used as monotherapy for the 3rd-line treatment of patients with clinically documented incurable progressive non-small cell lung cancer (NSCLC) despite prior chemotherapy including both a platinum-based therapy (i.e. cisplatin or carboplatin) AND either pemetrexed or topotecan.
- Erlotinib is used as monotherapy for 2nd line treatment of NSCLC after 1st line platinum-based therapy, where no other chemotherapy will be given and erlotinib is used as the last treatment for the patient

Patients should be assessed for disease status at least every two months. Erlotinib should be discontinued if there is evidence of disease progression.

Note that erlotinib is not indicated and therefore, is not considered for reimbursement as 1st line therapy in treatment of NSCLC.

Requests for 2nd-line and 3rd-line use of erlotinib in patients 70 years of age or older and have not received treatment with either platinum-based combinations will be considered on a case-by-case basis.

Approved dosage: 150 mg/day

Duration of Approval: 6 Months

Renewal will be considered for patients who respond to therapy with no evidence of disease progression. Patients should be assessed for disease status at least every two months. Erlotinib should be discontinued if there is evidence of disease progression.

Duration of Approval: 6 Months
**Everolimus**
**Brand(s):** Afinitor

**DOSAGE FORM/ STRENGTH:** 2.5 mg, 5 mg, 10 mg tablet

**For the treatment of metastatic renal cell carcinoma (mRCC) as second or third line therapy in patients previously treated for mRCC with a funded tyrosine kinase inhibitor (TKI).**

Exclusion criteria: Use in the 4th line setting or later in the treatment course of their disease

Dosage: 10 mg daily

**Renewal** will be considered for those who have demonstrated benefit from Afinitor therapy (i.e. no disease progression) and is expected to continue to do so.

1Funded TKIs include sunitinib (Sutent), sorafenib (Nexavar), and pazopanib (Votrient). The criteria are derived from the review of everolimus for provincial funding for the treatment of MRCC at the time of the original review. Drugs that may have been used as standard treatment in first line may have included interferon and temserolimus. Everolimus is currently not funded after progression on axitinib (Inlyta) or nivolumab.

**For the treatment of patients who have progressive, unresectable, well or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors (pNET).**

Patient must have an ECOG* ≤ 2 (prior to the start of Afinitor therapy).

*ECOG = Eastern Cooperative Oncology Group Status

Exclusion criteria: the patient’s disease progressed while taking sunitinib (Sutent) to treat pNET.

Dosage: 10 mg daily

**Duration of Approval:** 1 year

**Renewal** will be considered for those who have benefited from Afinitor therapy (i.e. no disease progression) and is expected to continue to do so.

Reimbursement of Afinitor will be considered until disease progression occurs on Afinitor.

**Duration of Approval:** 1 year
Everolimus
Brand(s): Afinitor
DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of unresectable, locally advanced or metastatic, well-differentiated non-functional neuroendocrine tumours (NETs) of gastrointestinal or lung origin (GIL) in adult patients meeting the following criteria:

- Documented radiological disease progression within six months; AND
- Good performance status (ECOG 0-2).

Treatment should continue until confirmed disease progression or unacceptable toxicity.

Renewals will be considered where the patient’s physician has confirmed that the Patient has benefited or continues to benefit from therapy with Afinitor as evidenced by no disease progression, and that they are expected to continue to do so.

For the treatment of postmenopausal women with hormone-receptor positive, HER2 negative advanced breast cancer meeting the following criteria:

- Afinitor is to be used in combination with exemestane; AND
- Patient must have an ECOG* ≤ 2 after recurrence or progression following a non-steroidal aromatase inhibitor (NSAI).
*ECOG = Eastern Cooperative Oncology Group Status

Dosage: 10 mg daily (dose titration is allowed).

Duration of Approval: 1 year

Renewals will be considered for patients who have benefited or continues to benefit from therapy with Afinitor and is expected to continue to do so.

Duration of Approval: 1 year
Everolimus

Brand(s): Afinitor

DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of renal angiomyolipoma (AML) associated with tuberous sclerosis complex (TSC) in patients who meet all the following conditions:

(i) Presence of coalescent or multifocal AMLs in either one or both kidneys; AND
(ii) AML progression despite previous embolization and/or surgery; AND
(iii) Further embolization and/or surgery is not recommended due to a documented clinical reason (Note: The physician must submit a clinical note with the request outlining/detailing why invasive therapy cannot be considered);

The approved dosage: 10 mg orally once daily.

Duration of Approval: 1 year
Case-by-Case consideration will be considered in patients who have never been treated with invasive procedures such as embolization and/or surgery. The physician must provide detailed clinical rationale (e.g., from clinical consultation notes) as to why embolization and/or nephrectomy would be medically contraindicated for the patient.

Renewals will be considered in patients with the following documented benefits from therapy;
No AML progression (i.e. no significant new lesions and increase in kidney volume, as well as no significant AML related bleeding);

AND
  • There is a reduction in volume of AMLs identified prior to treatment with the everolimus.

Duration of Approval: 2 years
Everolimus

Brand(s): Afinitor

DOSAGE FORM/ STRENGTH: 2.5 mg, 5 mg, 10 mg tablet

For the treatment of Subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) for whom surgical resection cannot be considered* for reasons such as:

- Location, size, and/or distribution of tumour(s); OR
- SEGA progression despite previous surgical interventions; OR
- Neurocognitive problems/ other complications secondary to previous surgical interventions.
- *Requests must provide details/ consultation notes outlining why the patient cannot be considered for surgical treatment.

Duration of Approval: 1 year

Renewals will be considered in patients with the following documented benefits from therapy:

- Stabilization of SEGA progression (based on assessment of SEGA volume and/or appearance of new lesions); AND
- Improvement of symptoms (e.g., reduced seizure frequency and decreased need for neurosurgical intervention).

Duration of Approval: 2 years
Gefitinib
Brand(s): Iressa and generics
DOSAGE FORM/ STRENGTH: 250 mg tablet

For the first line, monotherapy treatment of locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) in patients who have activating mutations of epidermal growth factor receptor-tyrosine kinase (EGFR-TK).
(i.e. Patients who are EGFR Positive)

The patient is to be assessed for disease status at least every two months and treatment will be discontinued if there is evidence of disease progression.

Dose Reimbursed: 250 mg orally once daily.

**Duration of Approval:** 6 months

Iressa will not be granted funding in the following circumstances;
Patients with EGFR wild-type mutation (i.e. negative for mutation);
Patients with EGFR unknown mutation;
2\textsuperscript{nd} or 3\textsuperscript{rd} line or maintenance NSCLC; or
Patients with unknown EGFR status who start their first chemotherapy while waiting for EGFR testing, then are found/confirmed to be EGFR positive, should continue with the current therapy and will not be eligible for gefitinib (Iressa) in this setting.
Patients who receive gefitinib (Iressa) first line are not eligible for erlotinib in the second- or third-line in the setting of maintenance therapy of NSCLC.

Requests for gefitinib for patients who have initiated another EGFR TKI therapy (i.e. Afatanib [Giotrif]) in the first line setting and who have not had disease progression will be considered on a case-by-case basis.

**Renewal** will be considered for patients until there is any evidence of disease progression, at which point, treatment with gefitinib (Iressa) must be discontinued. Patients must have their disease status assessed at least every two months.

Dose Reimbursed: 250 mg orally once daily.

**Duration of Approval:** 6 months
Ibrutinib
Brand(s): Imbruvica
DOSAGE FORM/ STRENGTH: 140 mg capsule

For the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) who meet the following criteria;

i) Patient has received at least one prior therapy to treat CLL/SLL; AND
ii) Patient’s prescriber has deemed that it would be inappropriate for the patient to receive treatment or retreatment with a fludarabine-based regimen.

Duration of Approval: 1 Year

Exclusion criteria:
Patients whose disease has progressed on idelalisib therapy in the relapsed setting are not eligible to receive iburitinib.

Renewals will be considered for patients who have not experienced disease progression while on ibrutinib (Imbruvica) therapy.

Duration of Approval: 1 Year

Initial criteria for Treatment naïve patients with high risk CLL/SLL (First-line therapy):

For patients with previously untreated chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) who present with one of the following cytogenic markers:

- chromosome 17p deletion; OR
- TP 53 mutation; OR
- unmutated immunoglobulin heavy chain variable region (IgHV)

Renewal criteria: Patient has experienced no disease progression while on Imbruvica therapy.
Initial and renewal approval period: 1 year.

Initial criteria for Relapsed or Refractory Mantle cell lymphoma:
For patients with relapsed or refractory mantle cell lymphoma who have received at least one prior therapy.

Renewals will be considered if patient has experienced no disease progression while on Imbruvica therapy.
Initial and renewal approval period: 1 year.
Idelalisib
Brand(s): Zydelig
DOSAGE FORM/ STRENGTH: 100 mg, 150 mg Tablets

For the treatment of patients with relapsed chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) in combination with Rituximab.

Exclusion criteria:
Patients whose disease has progressed on ibrutinib therapy in the relapsed setting are not eligible to receive idelalisib.

Note: Patients who have experienced intolerance but not disease progression to ibrutinib in the relapsed setting may switch to idelalisib. Documentation on the nature of the intolerance is required.

Renewals will be considered for patient who has not experienced disease progression while on idelalisib (Zydelig) therapy.

Funded Dose:
Idelalisib will be funded in combination with up to 8 cycles of rituximab at the recommended dose of 150 mg orally twice daily and will continue following the completion of the rituximab portion of the regimen.

Imatinib
Brand(s): Gleevec + generics (see below for billing information)
DOSAGE FORM/ STRENGTH: 100 mg tablet, 400 mg tablet

For the treatment of Metastatic Gastrointestinal Stromal Tumours (GIST) in patients with a tumour deemed to be NOT surgically resectable (metastatic or recurrent)

Duration of Approval: 1 Year

Renewal will be considered for patients with GIST who have benefited from or continues to benefit from therapy with Gleevec and is expected to continue to do so.

Duration of Approval: 1 Year
Imatinib

Brand(s): Gleevec + generics (see below for billing information)

DOSAGE FORM/ STRENGTH: 100 mg tablet, 400 mg tablet

For the Adjuvant treatment of Gastrointestinal Stromal Tumours (GIST) in patients who meet the following criteria:

- Patients are at intermediate to high risk of recurrence following complete resection (using Miettinen relapse risk criteria, risk ≥ 20%) or has had tumor rupture before surgery or at surgery; AND
- The pathology has been confirmed with c-kit positivity.

Note that the dosing regimen covered is no more than 400 mg daily.

Duration of Approval: 3 Years

Renewals will NOT be considered for patients receiving Gleevec for Adjuvant GIST. (i.e. Funding for adjuvant GIST is approved for up to 3 years. Longer coverage durations are not considered.)

For the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL)

Duration of Approval: 1 Year

Renewal will be considered for patients receiving Gleevec for Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL) who demonstrate a hematologic or cytogenetic response to therapy.

Duration of Approval: 1 Year

As of June 15, 2013, EAP approval letters will indicate PINs to be used for billing purposes. The PINs will allow the full price of each product to be submitted for reimbursement of EAP approved requests. Pharmacists should refer to the respective product monograph(s) for prescribing information and approved indications.

<table>
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<th>Drug Product</th>
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Lapatinib
Brand(s): Tykerb
DOSAGE FORM/ STRENGTH: 250 mg tablet

For the second-line treatment of HER2-positive metastatic breast cancer when used in combination with chemotherapy after previous exposure to trastuzumab-based treatments.

For the treatment of HER-2 positive metastatic breast cancer when used in combination with chemotherapy after use of trastuzumab in patients who have an adverse drug reaction or contraindication to trastuzumab therapy.

Lapatinib will not be considered in patients who meet the following exclusions:

- Lapatinib (Tykerb) will not be funded in combination with trastuzumab (Herceptin) for second-line HER-2 positive metastatic breast cancer.
- Patients who have progressed while on trastuzumab (Herceptin) for second-line treatment of HER-2 positive metastatic breast cancer, will not be eligible for funding of lapatinib (Tykerb).
- Lapatinib (Tykerb) will not be funded in the adjuvant setting.

Dosing schedule:

1250 mg (5 tablets) once daily in combination with capecitabine for days 1 to 14 (in a 21 day cycle) until disease progression, unacceptable toxicity, or withdrawal of consent.

Note: Funding of second-line lapatinib for HER-2 positive metastatic breast cancer will be discontinued upon evidence of disease progression

Duration of Approval: 6 Months

Renewal will be considered for lapatinib until there is evidence of disease progression at which point the drug should be discontinued.

Duration of Approval: 6 Months
Lenalidomide
Brand(s): Revlimid
DOSAGE FORM/ STRENGTH: 2.5mg, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg capsule

For the treatment of anemia due to myelodysplastic syndrome (MDS) for patients who meet all the following clinical criteria;

- Demonstrated diagnosis of MDS on bone marrow aspiration; AND
- Presence of del[5q] documented by standard cytogenetic or fluorescence in situ hybridization; AND
- International Prognostic Scoring System (IPSS) risk category low or intermediate-1; AND
- Transfusion-dependent symptomatic anemia.

Duration of Approval: 6 Months

Renewal will be considered for patients who are transfusion-dependent and who have demonstrated at least a fifty percent (50%) reduction in transfusion requirements.

Duration of Approval: Up to 1 Year

Note: Patients with anemia due to MDS who are not transfusion-dependent will be assessed on a case-by-case basis.

- Physicians submitting initial requests for non-transfusion-dependent patients must provide clinical evidence of symptomatic anemia affecting the patient’s quality of life and the rationale for why transfusions are not being used.
- Renewal requests for non-transfusion-dependent patients will be considered on a case-by-case basis. In such cases, the requesting physician will be required to provide the patient’s serial clinical blood culture (CBC) pre- and post-lenalidomide therapy in addition to any other objective evidence of the patient’s response to lenalidomide therapy.

For the treatment of multiple myeloma in combination with dexamethasone for patients who are not candidates for autologous stem cell transplant for patients meeting one of the following scenarios;

- As first line treatment; OR
- Refractory to or has relapsed after the conclusion of initial or subsequent treatments and who are suitable for further chemotherapy; OR
- Have completed at least one full treatment regimen as initial therapy and has demonstrated intolerance(s) to their current chemotherapy.

Duration of Approval: 1 Year
Lenalidomide

Brand(s): Revlimid

**DOSAGE FORM/ STRENGTH:** 2.5mg, 5 mg, 10 mg, 15 mg, 25 mg capsule

Renewals will be considered for those who continue to respond to therapy.

**Duration of Approval:** 1 Year

**Exclusion Criteria:**

Patients with multiple myeloma who are not candidates for autologous stem cell transplantation and whose disease has progressed following a treatment regimen with first line lenalidomide are not eligible to receive lenalidomide in the relapsed/refractory setting.

For the maintenance treatment of patients with newly diagnosed multiple myeloma following autologous stem-cell transplantation who have stable or improved disease, and with no evidence of disease progression.

**Recommended Dosage:**

Initial dose of 10 mg daily. Dose adjustments of 5 mg to 15 mg may be necessary based on individual patient characteristics and responses to lenalidomide.

**Duration of Approval:** 1 Year

Renewals will be considered for patients with no evidence of disease progression or development of unacceptable toxicity to lenalidomide requiring discontinuation of therapy.

**Duration of Approval:** 1 Year

**Lenalidomide Combinations funded with an injectable anticancer drug through the New Drug Funding Program (NDFP).**

Lenalidomide will be considered for funding in a triple combination with Carfilzomib (Kyprolis®) lenalidomide and dexamethasone for relapsed multiple myeloma in patients meeting the funding criteria for Carfilzomib through the New Drug Funding Program (NDFP). Please refer to the Cancer Care Ontario website for the full Carfilzomib funding criteria.

b) Eligibility Criteria:

• Carfilzomib is used in combination with lenalidomide and dexamethasone for patients with multiple myeloma who have received at least one prior treatment.

• Treatment should be in patients who have good performance status and are deemed to have adequate renal function.
### Lenalidomide

**Brand(s):** Revlimid  
**DOSAGE FORM/ STRENGTH:** 2.5mg, 5 mg, 10 mg, 15 mg, 25 mg capsule

All of the following criteria must be met:
- The patient did not progress during treatment with bortezomib
- If previously treated with lenalidomide, the patient did not discontinue lenalidomide due to adverse events and/or did not experience disease progression during the first 3 months of treatment
- If the patient was most recently treated with lenalidomide, the patient disease has not progressed at any time during treatment

### Lenvatinib

**Brand(s):** Lenvima  
**DOSAGE FORM/ STRENGTH:** 4 mg, 10 mg capsules (packaged as 8mg, 10mg, 14mg, 18 mg, 20 mg, and 24 mg daily dose cartons.

For the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid cancer (DTC) who meet ALL the following criteria:

- Papillary or Follicular subtypes of DTC that are histologically or cytologically confirmed; AND
- Thyroid cancer is refractory or resistant to radioactive iodine; AND
- DTC shows evidence of disease progression within the past 13 months; AND
- Patient has good performance status with ECOG less than or equal to 2; AND
- Lenvatinib is being used as monotherapy

**Exclusion criteria:**
- Patients with anaplastic or medullary thyroid cancer
- Patients who have received more than one prior therapy with a tyrosine kinase inhibitor.

**Duration of Approval:** 1 Year

**Renewal** of funding will be considered until a patient progresses on treatment or develops unacceptable toxicity to lenvatinib.

**Duration of Approval:** 1 Year
Midostaurin
Brand(s): Rydapt
DOSAGE FORM/ STRENGTH: 25 mg capsule

For the treatment of adult patients diagnosed with FMS-like tyrosine kinase 3 (FLT3)-mutated acute myeloid leukemia (AML) who meet ALL the following criteria:

- FLT3 mutation is confirmed by an approved test; AND
- Midostaurin is used as first-line\(^1\) for FLT3-mutated AML; AND
- Midostaurin is used in combination with standard induction chemotherapy with cytarabine and daunorubicin followed by standard consolidation chemotherapy with cytarabine OR any 7+3 induction regimen containing idarubicin followed by standard consolidation chemotherapy with cytarabine.

Exclusion criteria:
Midostaurin will not be funded in the following situations:

- As maintenance therapy for AML;
- Patients who have developed therapy-related AML after radiation therapy or chemotherapy for another cancer or disorder;
- Patients receiving other induction chemotherapy regimens aside from those mentioned in the eligibility criteria or upon finishing the consolidation phase of treatment;
- Patients undergoing re-induction and/or re-consolidation.

Recommended Dose(s):
Induction dose: Midostaurin 50 mg twice daily on Days 8 to 21 with each cycle of induction cytarabine and daunorubicin.

A maximum of 2 induction cycles may be funded. (Note: EAP only considers funding of outpatient midostaurin usage.)*

Consolidation phase: Midostaurin 50 mg twice daily on days 8 to 21 of each cycle of consolidation with cytarabine.

A maximum of 4 consolidation cycles may be funded by EAP (for cycles administered as an outpatient)*.

Up to 2 cycles of induction and 4 cycles of consolidation may be funded in accordance with patient response to therapy.*
**Midostaurin**

**Brand(s):** Rydapt

**DOSAGE FORM/ STRENGTH:** 25 mg capsule

**Approval duration:** Up to 6 months (maximum of 2 cycles of induction and 4 cycles of consolidation)

*For a short-term, time limited period, the Ministry will consider requests from prescribers who wish to add midostaurin to their patients’ current regimens that have been initiated prior to the provincial funding of midostaurin. To be considered, patients must currently be on standard induction and consolidation chemotherapy, and have not experienced disease progression or unacceptable intolerance during the first-line treatment with the standard chemotherapies being used.*

*EAP will provide coverage for midostaurin administered in the outpatient setting (e.g., consolidation cycles). Those responding to induction therapy may require ongoing access to midostaurin for the consolidation phase of treatment upon discharge from the hospital.*

**Nilotinib**

**Brand(s):** Tasigna

**DOSAGE FORM/ STRENGTH:** 150 mg, 200 mg capsule

For the treatment of patients with chronic phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML).

*Note: Ministry will only fund any TWO of the oral Tyrosine Kinase inhibitors (TKIs) * used for chronic phase CML per patient in a lifetime. (* TKIs: imatinib, nilotinib, or dasatinib)*

*If the patient develops grade 3 or 4 toxicity on one of the above TKI’s within 3 months of initiating therapy, access to a 3rd oral TKI will be funded for that patient.*

Approved dose: 300 mg twice daily but not exceeding 800 mg/day

**Duration of Approval:** 1 Year
Nilotinib

Brand(s): Tasigna

DOSAGE FORM/ STRENGTH: 150 mg, 200 mg capsule

For the treatment of patients with accelerated phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) with documented intolerance\(^1\) or resistance\(^2\) to imatinib therapy.

\(^1\) Intolerance to imatinib at any dose occurs where the Patient has experienced persistent grade 3 or grade 4 toxicity requiring discontinuation of imatinib therapy; or

\(^2\) Imatinib resistance occurs where the Patient has primary or acquired resistance to imatinib at doses of at least 600mg/day or via a mutational analysis report.

Exclusion Criteria – Patients with the following exclusion criteria will not be funded:

- blast phase CML;
  - a. for Ph+ acute lymphocytic leukemia (ALL);
  - b. combination treatment with any two or more oral TKIS’s (imatinib, nilotinib, or dasatinib) will not be funded
  - c. For accelerated phase CML, nilotinib is not funded as a sequential third line therapy in patients who experience primary or acquired resistance (not including mutational resistance) to dasatinib.
    Approved dosage: Up to 800 mg/day but doses above 800 mg per day will not be considered

Renewals are considered for patients who experience hematologic and/or cytogenic response to therapy, is expected to continue to do benefit from therapy with Tasigna.

Duration of Approval: 1 Year
Olaparib
Brand(s): Lynparza

DOSAGE FORM/ STRENGTH: 50mg capsules (Restricted access for patients already using capsules), 100mg tablets, 150mg tablets

For the maintenance treatment of platinum-sensitive\(^1\), relapsed, BRCA-mutated, high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer in adult patients who meet ALL the following criteria;

i) Has documented mutation in BRCA1 or BRCA2 genes (germline or somatic detected by an approved testing method); AND

ii) Patient has received at least two previous lines of platinum-based chemotherapy in which platinum sensitive disease\(^1\) is demonstrated with one completed treatment course and there is radiologic response (complete or partial) to their most recently completed course of platinum-based chemotherapy\(^2\) in which at least 4 cycles of treatment has been completed prior to initiating olaparib; AND

iii) Olaparib is being used as monotherapy for maintenance treatment; AND

iv) Olaparib is started within 8 weeks\(^3\) of their final dose of platinum-based chemotherapy\(^2\); AND

v) Patient has good performance status.

Renewal Criteria:
Ongoing funding will be considered in patients until disease progression or development of unacceptable toxicity to olaparib.

Exclusion Criteria:
- Patients who have not demonstrated platinum-sensitive disease\(^1\) will not be funded.
- Olaparib is not funded when used as combination with chemotherapy.
- Olaparib is not funded as first-line therapy.

\(^1\)Platinum-sensitive disease is defined as disease progression/recurrence/relapse occurring at least 6 months following completion of a platinum-based chemotherapy in which an initial response had been demonstrated.

\(^2\)Patients who are unable to use a platinum-based chemotherapy after having demonstrated platinum-sensitive disease to an earlier line of treatment may be considered on a case-by-case basis if they have received at least 4 cycles of a non-platinum treatment, submit documentation for clinically relevant allergies or intolerance to platinum treatment, and meet all other aspects of the above criteria.

\(^3\)Patients not meeting this criteria component due to extenuating circumstances may be considered on a case-by-case basis if they have no evidence of disease progression, provide information to explain why treatment could not be started within 8 weeks, and meet all other aspects of the above criteria.

Recommended dose:
400 mg twice daily if using olaparib capsules
300 mg twice daily if using olaparib tablets
(It should be noted that the capsules and tablets are not bioequivalent)
Osimertinib
Brand(s): Tagrisso
DOSAGE FORM/ STRENGTH: 40mg, 80mg tablets

For the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) in a patient who meets the following criteria:

- has a documented Epidermal Growth Factor Receptor (EGFR) T790M resistance mutation detected by an approved testing method; AND
- has experienced disease progression during or following treatment with a first- or second-generation EGFR tyrosine kinase inhibitor (TKI) therapy (i.e., afatinib, gefitinib or erlotinib); AND
- has a good performance status; AND
- osimertinib is being used second line\(^1,2\) as monotherapy

\(^1\)Time-limited consideration will be provided for patients with EGFR T790M mutation-positive NSCLC who have progressed on EGFR TKI therapy and who are currently on or have recently completed treatment with chemotherapy or an immune checkpoint inhibitor prior to the public funding of osimertinib.

\(^2\)Patients with de novo EGFR 790M mutations may be considered case-by-case.

Renewal of treatment will be considered in patients who continue to derive treatment benefit from osimertinib. (i.e. until clinically meaningful progression occurs.)

Recommended dose: 80mg per day orally.

(It should be noted that since the 40mg and 80mg tablets are the same cost, 40mg tablets will be reimbursed upon request for patients who require dose adjustments in accordance with the Tagrisso product monograph.)

Duration of Approval for Initial and Renewal requests: 1 year
Palbociclib
Brand(s): Ibrance
DOSAGE FORM/ STRENGTH: 75 mg, 100 mg, 125 mg tablet

For the treatment of post-menopausal women with estrogen receptor (ER) – positive, human epidermal growth factor receptor 2 (HER 2)-negative unresectable locally advanced breast cancer or metastatic breast cancer in patients who meet the following criteria:

- Palbociclib is used in combination with an aromatase inhibitor (i.e. letrozole, anastrozole, or exemestane)\(^1\); AND
- The combination is being used as first line treatment\(^2\) of unresectable locally advanced or metastatic disease; AND
- Patient has good performance status (ECOG 0 to 2); AND
- Patient does not have active or uncontrolled metastases to the central nervous system; AND
- For patients who received anastrozole or letrozole in the neoadjuvant or adjuvant setting, a minimum disease free interval of twelve (12) months after stopping therapy is required for Palbociclib eligibility. (Note: There is no time restriction for patients who relapse after receiving tamoxifen or exemestane in the neoadjuvant or adjuvant setting.)

\(^1\) Other combinations with palbociclib will not be considered.

\(^2\) Patient must not have progressed on a prior systemic treatment (e.g. hormonal, chemotherapy, or immunotherapy) for their locally advanced or metastatic disease.

Renewals will be considered in patients who have not demonstrated evidence of disease progression or development of unacceptable toxicity requiring discontinuation while on palbociclib.

Exclusion Criteria (applies to initial and renewal requests):

- Patients whose disease was resistant\(^3\) to a non-steroidal aromatase inhibitor therapy (letrozole or anastrozole) used in the neoadjuvant or adjuvant setting.
- Patients using palbociclib as second-line or beyond.
- Patients with active or uncontrolled metastases to the central nervous system.
- Patients whose disease progressed while treated with Afinito (in combination with exemestane)

\(^3\) Resistance is defined as disease progression occurred during treatment or within 12 months after stopping of the aromatase inhibitor in the neoadjuvant or adjuvant setting.
**Palbociclib**

**Brand(s): Ibrance**

**DOSAGE FORM/ STRENGTH:** 75 mg, 100 mg, 125 mg tablet

**Dosing:**

Palbociclib (Ibrance) 125mg orally once daily for 21 consecutive days, followed by 7 days off treatment. In combination with continuous daily aromatase inhibitor.

**Approval duration:** 1 year for initial requests and 1 year for renewal requests

**Notes:**

- Funding will be considered for patients who missed the opportunity to use Ibrance in the advanced setting in patients started on monotherapy with an aromatase inhibitor (AI) (e.g. letrozole, anastrozole, exemestane) as first line treatment of post-menopausal ER-positive, HER2-negative (ER+/HER2-) advanced breast cancer AND who have not received any prior systemic treatment for metastatic disease AND who have no disease progression with current AI therapy AND who meet the disease-free time requirement if anastrozole or letrozole was used previously in the adjuvant or neoadjuvant setting.

- Public funding will be considered for only one of Ibrance (in combination with an aromatase inhibitor) OR Afinitor (in combination with exemestane); no public funding for sequential treatment e.g. Afinitor then Ibrance (or vice versa)

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**Pazopanib**

**Brand(s): Votrient**

**DOSAGE FORM/ STRENGTH:** 200 mg tablet

**For first-line treatment of advanced or metastatic renal cell carcinoma of clear cell histology in patients with good performance status**

(ECOG* ≤ 1)

ECOG = Eastern Cooperative Oncology Group Performance Status

The approved dosage is 800 mg once daily.

**Duration of Approval:** 1 year

**Renewals** will be considered for patients who have benefited from therapy (i.e. no disease progression) and are expected to continue to do so. Exclusion criteria: Funding for Votrient will not be approved for patients who demonstrate disease progression while on sunitinib, sorafenib, temsirolimus, everolimus or other drugs approved for treatment of metastatic renal cell carcinoma.

**Duration of Approval:** 1 year
For the treatment of patients with relapsed and/or refractory multiple myeloma (MM) who meet the following criteria;

i) Patient has failed lenalidomide\(^1\); AND

ii) Patient has previously failed\(^2\) OR may have a contraindication OR demonstrated an intolerance\(^3\) to bortezomib; AND

iii) Patient has demonstrated disease progression following the last treatment\(^4\) used for MM.

\(^1\) Failure to lenalidomide may include failure to treatment received during the maintenance setting.

\(^2\) Failure to bortezomib can include patients who have received a course of bortezomib during which there was no disease progression, however, at the time of relapse of the patient’s MM, the patient is no longer eligible for retreatment with bortezomib.

\(^3\) Details of the patient’s intolerance(s) to bortezomib must be provided on the funding application to EAP.

\(^4\) The patient’s last treatment may be a regimen other than one containing lenalidomide or bortezomib.

**Duration of Approval:** 1 year

**Renewals** will be considered for patients who continue to respond to therapy (i.e. is not refractory and has not relapsed).

**Duration of Approval:** 1 year
Ponatinib  
Brand(s): Iclusig  
DOSAGE FORM/ STRENGTH: 15 mg, 45 mg tablets

**Chronic Phase CML:**

a. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in chronic phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib, dasatinib or nilotinib), where ponatinib would be the third or fourth line TKI.

**Duration of Approval:** 1 year

**Accelerated Phase CML:**

a. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in accelerated phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib, dasatinib or nilotinib), where ponatinib would be the third or fourth line TKI.

**Duration of Approval:** 1 year

**Blast Phase CML:**

a. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in blast phase with documented resistance/disease progression or intolerance to at least 2 prior oral TKIs (imatinib and dasatinib), where ponatinib would be the third or fourth line TKI.


**Ponatinib**

Brand(s): Iclusig  
DOSAGE FORM/ STRENGTH: 15 mg, 45 mg tablets

**For Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL):**

a. For the treatment of patients with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL) and documented T315i mutation; OR

b. For the treatment of patients with Philadelphia chromosome positive acute lymphoblastic leukemia (Ph +ALL) with documented resistance/disease progression or intolerance to imatinib and dasatinib, where ponatinib would be the third line TKI.

**Renewals** will be considered upon confirmation from the clinician that the patient has experienced hematologic and/or cytogenic response and is expected to continue to do so.

**Duration of Approval:** 1 year

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**Regorafenib**

Brand(s): Stivarga  
DOSAGE FORM/ STRENGTH: 40 mg tablets

**For the treatment of metastatic and/or unresectable gastrointestinal stromal tumors (GIST) in patients who have had disease progression on, or intolerance to, imatinib and sunitinib**  
Dosage: 160 mg once daily for 3 weeks followed by 1 week of no therapy to comprise a cycle of 4 weeks.

**Duration of Approval:** 6 Months

Reimbursement of Stivarga will be considered as long as benefit is observed or until unacceptable toxicity occurs.

**Renewals** will be considered in patients who continue to derive benefit from therapy.

**Duration of Approval:** 6 Months
Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10mg, 15 mg, 20 mg tablets

For the treatment of intermediate to high risk symptomatic Myelofibrosis (MF) in patients meeting the following criteria;

i)  MF is assessed using the Dynamic International Prognostic Scoring System (DIPSS) Plus; or the patient has symptomatic splenomegaly
ii)  Patient has an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 3
iii)  Patient is previously untreated or refractory to other treatment

Dosing regimen: 5 mg to 25 mg twice a day

Duration of Approval: 1 Year

Initial Renewals are considered for patients who:

- Have confirmation of either a reduction in spleen size or documented improvement of disease symptoms within 6 months of initiating therapy with Jakavi.

Second and subsequent Renewals are considered for patients who continue to benefit from therapy with Jakavi.

For the treatment of patients with polycythemia vera who meet the following criteria:

i)  Demonstrated resistance or demonstrated intolerance to hydroxyurea (HU); AND
ii)  Have a good performance status (ECOG ≤ 3)

Resistance to Hydroxyurea as defined by:

- Patient continues to require phlebotomy to keep hematocrit (HCT) at less than 45%; OR
- Patient demonstrates uncontrolled myeloproliferation (i.e. platelet count > 400 x 10^9/L and white blood cell count > 10 x 10^9/L); OR
- Symptomatic splenomegaly Intolerance to Hydroxyurea as defined:
  After any dose of hydroxyurea, patient demonstrates one of the following:
- Absolute neutrophil count < 1 x 10^9/L or platelet < 100 x 10^9/L or hemoglobin < 100 g/L at the lowest dose of HU required to achieve a response; OR
- Presence of leg ulcers or other unacceptable HU-related grade 3 or 4 non-hematological toxicities (eg. Mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis, fever); OR
Ruxolitinib
Brand(s): Jakavi
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg, 15 mg, 20 mg tablets

- If patient demonstrates non-hematological grade 2 toxicities for at least one week: 
  OR
- If toxicity requires permanent discontinuation of HU, interruption of HU until resolution of toxicity, or requiring hospitalization as a result of HU toxicity.

Renewal:

Patient continues to respond\(^3\) to treatment and has not experienced disease progression.

\(^3\)Response defined by any one or more of the following;
- Hematocrit <45% without phlebotomy; AND/OR
- Platelet count ≤ 400 x 10\(^9\)/L; AND/OR
- White blood cell count ≤ 10 x 10\(^9\)/L; AND/OR
- non-palpable spleen
Sorafenib
Brand(s): Nexavar
DOSAGE FORM/ STRENGTH: 200 mg tablet

For the treatment of metastatic renal cell carcinoma (MRCC) as second-line treatment for patients who have:

- Histologically confirmed metastatic clear-cell renal-cell carcinoma; and
- Experienced disease progression after prior cytokine therapy within the previous 8 months; and
- A performance status of 0 or 1 on the basis of the Eastern Cooperative Oncology Group criteria; and
- Intermediate-risk or low-risk status, according to the Memorial Sloan-Kettering Cancer Center (MSKCC) prognostic score.

Duration of Approval: 1 year

Renewals will be considered with confirmation from the physician that the patient has benefited from therapy and is expected to continue to do so.

For the treatment of advanced hepatocellular carcinoma (HCC) in patients who have:

- Child-Pugh Class A disease; and
- ECOG* status 0, 1 or 2; and
- Either progressed on transarterial chemoembolization (TACE) or are not suitable for the TACE procedure (where detailed rationale is provided).

Duration of Approval: 3 months

*ECOG = Eastern Cooperative Oncology Group Performance Status

Renewal will be considered for patients with documentation of radiography and/or scan results indicating no diseases progression.
Sunitinib
Brand(s): Sutent

DOSAGE FORM/ STRENGTH: 12.5 mg, 25 mg, 50 mg capsule

For the treatment of gastrointestinal stromal tumour (GIST) in patients with unresectable or metastatic/recurrent GIST where one of the following conditions is met:

- Early progression (within 6 months) while on imatinib; OR
- Progression following treatment with optimum (escalated) doses of imatinib (800mg per day); OR
- Intolerance* to imatinib (where detailed description of intolerance is provided).

*Definition of intolerance to imatinib – patient has experienced persistent grade 3 toxicity requiring discontinuation of therapy.

Duration of Approval: 6 months
Renewal will be considered for patients who are stable (no disease progression) and not experiencing intolerance to sunitinib therapy.

Note: Approval will be granted at a dose of 50mg per day (4 weeks on, 2 weeks off).

For the treatment of metastatic renal cell carcinoma (MRCC):

- First-line therapy for patients with MSK Prognostic Score of Favourable Risk or an Intermediate Risk OR
- Second-line therapy for patients where:
  - The disease is of clear cell histology AND
  - Documented failure to first-line cytokine-based therapy.

Duration of Approval: 1 year
Renewal will be considered for patients with documentation of radiography and/or scan results indicating no disease progression.

Duration of Approval: 1 year
Note: The prescribed dosage should be 50 mg daily for four (4) weeks, followed by two (2) weeks off the Drug Product, in repeated six (6) week cycles.

For the treatment of progressive, unresectable, well-differentiated or moderately differentiated, locally advanced or metastatic pancreatic neuroendocrine tumors (“pNET”) with good performance status (ECOG ≤ 2), until disease progression.

Exclusion criteria: Sutent will not be approved for second-line sequential therapy after everolimus failure in the first-line setting.

Dosing: 37.5 mg daily
Thalidomide
Brand(s): Thalomid
DOSAGE FORM/ STRENGTH: 50 mg capsule, 100 mg capsule, 200 mg capsule

For the treatment of Multiple Myeloma in patients 65 years of age or older meeting the following criteria:

- Thalidomide is being used in combination with melphalan and prednisone; AND
- The patient has not previously received other treatments\(^1\) for multiple myeloma; AND
- The patient is deemed to be unsuitable for stem cell transplantation; AND

\(^1\)Exception is for those meeting bortezomib criteria as described below.

It should be noted that funding of thalidomide will be considered on a case-by-case basis for patients who have developed severe (grade III/IV) thrombocytopenia during the first 1 to 2 cycles of treatment with bortezomib and who have not experienced disease progression on bortezomib.

Duration of Approval: A maximum of 12 six-week cycles

Exclusion criteria:

Funding will not be considered for patients who are using thalidomide as second-line treatment of multiple myeloma.

Trametinib
Brand(s): Mekinist
DOSAGE FORM/ STRENGTH: 0.5 mg, 2 mg tablet

Initial requests:

For the mutation-targeted treatment of patients with BRAF V600 mutation-positive unresectable melanoma or metastatic melanoma meeting the following criteria:

- As first-line monotherapy; OR
- As first-line combination therapy with dabrafenib; OR
- As second-line monotherapy in which the disease has progressed after receiving treatment in the first line setting; OR
- As second-line combination therapy with dabrafenib in which the disease has progressed after receiving treatment in the first line setting; AND
- If brain metastases are present, they should be asymptomatic or stable
**Trametinib**

**Brand(s): Mekinist**

**DOSAGE FORM/STRENGTH: 0.5 mg, 2 mg tablet**

Recommended Dose as Monotherapy:

2 mg once daily until disease progression or development of unacceptable toxicity requiring discontinuation of trametinib

Recommended Dose as combination dual therapy with Dabrafenib:

Trametinib 2 mg once daily and Dabrabenib 150 mg twice daily, until disease progression or development of unacceptable toxicity requiring discontinuation.

**Duration of Approval:** 6 months (Patients should have their disease status assessed at least every 3 months)

Renewal requests:

Therapy as monotherapy OR as combination dual therapy (as above) may be continued until evidence of disease progression\(^1\) or development of unacceptable toxicity requiring discontinuation.

\(^1\) Letter from physician outlining radiological and clinical benefit requiring continuation of the drug and verification of no disease progression must be submitted.

Approval duration (both initial and renewal requests): 6 months (patients should have their disease status assessed at least every 6 months)

**Duration of Approval:** 6 months (Patients should have their disease status assessed at least every 3 months)

Case by case:

Requests in patients who have initiated another single-agent BRAF or MEK inhibitor therapy will be considered on a case-by-case basis ONLY IF there has been no disease progression.

**Exclusion Criteria:**

- BRAF V600 negative, or wild type tumors, or unknown status will not be funded
- Trametinib therapy (as monotherapy or in combination with dabrafenib) will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.
Vandetanib
Brand(s): Caprelsa
DOSAGE FORM/ STRENGTH: 100 mg, 300mg tablet

Caprelsa (Vandetanib) is funded for the treatment of symptomatic and/or progressive medullary thyroid cancer (MTC) in patients who meet the following criteria:

(a) Patient has unresectable locally advanced or metastatic disease; AND  
(b) Vandetanib is being used as monotherapy for MTC; AND  
(c) ECOG less than or equal to 2; AND  
(d) Prescribed by or in consultation with an oncologist or internist experienced with the treatment of MTC.

Exclusion Criteria:

(a) Patients with QT interval prolongation/abnormalities (e.g. QTc that is unmeasurable or greater than or the same as 480ms) or who are taking medications that prolong QT interval prolongation.  
(b) Patients with indolent, asymptomatic, or slowly progressive disease.  
(c) Vandetanib is not funded as combination therapy

Renewal Criteria:  
Renewal of funding will be provided until disease progression or development of unacceptable toxicity.  
1As confirmed by radiological reports.  
2Patients with an ECOG greater than 2 will be considered case-by-case upon submission of information regarding the risk of toxicity.  
3At the time of renewal, prescriber should address whether there have been any significant cardiac events or concerns regarding cardiovascular toxicities.

Duration of approval for initial and renewal criteria: 1 year

Note: Prescribers and dispensing pharmacies are presumed to be in compliance with the requirements of the Caprelsa Restricted Distribution Program which is administered through the manufacturer.
Vemurafenib
Brand(s): Zelboraf
DOSAGE FORM/ STRENGTH: 240 mg tablet

Vemurafenib is funded when used as monotherapy for the 1st line treatment of patients with BRAF V600 mutation-positive unresectable stage III or IV melanoma or metastatic disease.

The recommended dose for vemurafenib in the 1st line setting is 960 mg twice daily until disease progression or development of unacceptable toxicity requiring discontinuation of vemurafenib.

Exclusion Criteria

- Vemurafenib is not funded in patients with BRAF V600 negative mutation
- Vemurafenib is not funded in patients with wild type tumours;
- Vemurafenib is not funded in patients with unknown mutational status
- Vemurafenib will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.

Duration of Approval: 6 months

Renewals will be considered for requests where the patient’s physician provides documentation outlining;

- the radiological and clinical benefit requiring continuation of the patient on vemurafenib;
  AND
- verifying that there has been no disease progression or development of unacceptable toxicity in the patient.

Duration of Approval: 6 months

Vemurafenib is funded when used as monotherapy in the 2nd line treatment of patients with BRAF V600 mutation-positive unresectable stage III or IV melanoma or metastatic disease which has progressed after receiving treatment in the 1st line setting.

The recommended dose for vemurafenib in the 2nd line setting is 960 mg twice daily until disease progression or development of unacceptable toxicity requiring discontinuation of vemurafenib.

Duration of Approval: 6 months
Vemurafenib
Brand(s): Zelboraf
DOSAGE FORM/ STRENGTH: 240 mg tablet

Exclusion Criteria
- Vemurafenib is not funded in patients with BRAF V600 negative mutation.
- Vemurafenib is not funded in patients with wild type tumours;
- Vemurafenib is not funded in patients with unknown mutational status
- Vemurafenib will not be considered for funding in patients who have progressed on a prior BRAF inhibitor therapy used as monotherapy or in combination.

Requests for Zelboraf for patients who have initiated another BRAF therapy [i.e. Mekinist (trametinib), Tafinlar (dabrafenib)] and who have not had disease progression will be considered on a case-by-case basis.

Renewals will be considered for requests where the patient’s physician provides documentation outlining;
- the radiological and clinical benefit requiring continuation of the patient on vemurafenib; AND
- verifying that there has been no disease progression or development of unacceptable toxicity in the patient.

Duration of Approval: 6 months

Vismodegib
Brand(s): Erivedge
DOSAGE FORM/ STRENGTH: 150 mg tablet

For the treatment of metastatic basal cell carcinoma (BCC) or locally advanced BCC (including patients with basal cell nevus syndrome, i.e. Gorlin syndrome) in patients who meet the following criteria;
- Patient must have measurable metastatic disease or locally advanced disease; AND
- Patient’s disease must be considered inoperable or inappropriate for surgery; AND
- Patient’s disease must be considered inappropriate for radiotherapy; AND
- Patient is 18 years or age or older; AND
- Patient has an ECOG ≤ 2

Dose: 150 mg orally once daily taken until disease progression or unacceptable toxicity.
Requests must include the following information:
Duration of Approval: 1 Year
Vismodegib
Brand(s): Erivedge
DOSAGE FORM/ STRENGTH: 150 mg tablet

Physicians must provide rationale for why surgery AND radiation cannot be considered

- The request must include a surgical consult note that provides a preoperative/surgical evaluation why surgery is not appropriate for the patient; AND
- A consult note as to why radiation therapy is not appropriate for the patient; AND
- Both of the above evaluations must come from a physician who is not the requesting physician; AND
- The request must include confirmation that the patient has been discussed at a multi-disciplinary cancer conference (MCC) or equivalent.

1Considered inoperable or inappropriate for surgery for at least ONE of the following reasons:

- Technically not possible to perform surgery due to size/location/invasiveness of BCC (either lesion too large or can be several small lesions making surgery not feasible); OR
- Recurrence of BCC after two or more surgical procedures and curative resection unlikely; OR
- Substantial deformity and/or morbidity anticipated from surgery.

2Considered inappropriate for radiation for at least ONE of the following reasons:

- Contraindication to radiation (e.g. Gorlin syndrome); OR
- Prior radiation to lesion; OR
- Suboptimal outcomes expected due to size/location/invasiveness of BCC.

Note: Patient preference for oral therapy will not be considered

Renewals will be considered where the physician has confirmed that the patient has not experienced disease progression while on Erivedge therapy.

Duration of Approval: 1 Year
Aprepitant
Brand(s): Emend
DOSAGE FORM/ STRENGTH: 80 mg, 125 mg capsule, Tri-pack

Effective September 25, 2014, Emend transitioned to the ODB formulary for reimbursement in patients who meet the Limited Use criteria. Dosage regimens not meeting the LU criteria may be submitted to the EAP for consideration of reimbursement.

Denosumab
Brand(s): Xgeva
DOSAGE FORM/ STRENGTH: 120 mg per vial for subcutaneous injection

For the treatment of bony metastases in patients with hormone refractory prostate cancer.

Xgeva is considered through CCO for those receiving prostate cancer treatment from a cancer clinic.

Hormone refractory prostate cancer is determined using the following criteria:
   i) Patient has an elevated PSA level or evidence of progressive bony disease\(^1\), despite castrate serum testosterone levels (Less than 1.7 nmol/L or less than 50 ng/dL\(^2\)).

\(^1\) Progressive bony disease is defined as progressive changes in radionucleotide bone scan or clinical signs of disease progression, such as pathologic fracture or increasing bone pain.

\(^2\) Note: Patients who have undergone orchidectomy do not need to provide a serum testosterone level in the request submission.

Approved Dosing. 120 mg subcutaneously every four (4) weeks

Duration of Approval: 1 Year

Renewals will be considered for patient responding to treatment with Xgeva and who still requires treatment.

Duration of Approval: 1 Year
Filgrastim [Granulocyte colony stimulating factor (G-CSF)]
Brand(s): Neupogen
DOSAGE FORM/ STRENGTH: 300 mcg/mL, 480 mcg /1.6 mL

Effective August 30, 2017, Exceptional Access Program (EAP) requests for Neupogen (filgrastim) will no longer be accepted for any indication.

Patients who have an existing EAP approval for Neupogen can continue to receive Neupogen for the duration of the EAP approval period.

Neupogen and Grastofil are not interchangeable products. As of August 30, 2017, new prescriptions for filgrastim for ODB eligible patients will be dispensed Grastofil, unless it specifies Neupogen with the appropriate LU code. Refer to the Ministry’s e-formulary for a listing of Limited Use (LU) criteria for Neupogen.

Effective December 22, 2016, the subsequent entry biologic (SEB) filgrastim as Grastofil® is funded under the Ontario Drug Benefit (ODB) Program as a general benefit (GB).

Please refer to the e-formulary for funded strengths.

Zoledronic Acid
Brand(s): Zometa Concentrate
DOSAGE FORM/ STRENGTH: 4 mg/ 5 mL Vial

Zoledronic acid as Zometa Concentrate will only be considered for the treatment of bony metastases in those with hormone refractory prostate cancer as well as other cancers through the Exceptional Access Program (EAP) in those receiving outpatient care who do not meet the criteria of Cancer Care Ontario (CCO).

Zometa is considered through CCO for those receiving prostate cancer treatment from a cancer clinic.

Duration of Approval: 6 Months

For the treatment of bony metastases for patients with hormone refractory prostate cancer as determined by an elevated PSA level, or evidence of progressive bony disease¹, despite castrate serum testosterone levels (<50 ng/dL).

¹Progressive bony disease should be demonstrated by: progressive changes in radionucleotide bone scan or clinical signs of disease progression (e.g., via radionucleotide scanning, pathologic fracture or increasing bone pain).

Requests for patients who have undergone orchidectomy do not need to provide a serum testosterone level.
Zoledronic Acid

Brand(s): Zometa Concentrate

DOSAGE FORM/STRENGTH: 4 mg/5 mL Vial

- For the prevention of skeletal related events in patients who have not experienced previous skeletal related events\(^2\) and who have bony metastases secondary to:
  - solid tumours (e.g. renal, small cell lung, pancreatic cancers) who have good performance status\(^3\) OR
  - breast cancer or multiple myeloma who are intolerant to pamidronate.

\(^2\)A skeletal related event is defined as: pathologic fracture, spinal cord compression, radiation therapy to bone or surgery to bone.

\(^3\)Good performance status is defined as patients that are ambulatory, capable of self care and up and about more than 50 per cent of waking hours.

- For the treatment of patients with symptoms due to bony metastases secondary to breast cancer or multiple myeloma who have failed or are intolerant to pamidronate.

- Consideration for patients who are symptomatic due to bony metastases secondary to other types of solid tumours or cancers will be considered on a case-by-case basis. The physician is asked to include information describing the patient’s bone pain and use of other therapies including the use of bisphosphonates. The use of other non-pharmacologic treatment modalities such as surgery or radiation that have been tried should be provided in the request.

Duration of Approval: 6 Months

Renewals will be considered for patients who are responding to therapy and is still deemed to require treatment.

Duration of Approval: 6 Months
OSTEOPOROSIS

Teriparatide
Brand(s): Forteo
DOSAGE FORM/ STRENGTH: 250 mcg/mL - 3 mL prefilled pen, 250 mcg/mL 2.4 mL prefilled pen

For the treatment of osteoporosis in patients who meet the following criteria;

- 65 years of age or older who are mobile; **AND**
- Patient is at high risk of fragility fractures*; **AND**
- Patient who has osteonecrosis of the jaw due to an anti-resorptive agent **OR** who has atypical femur fracture due to an anti-resorptive agent. (Note: One of the two conditions must be present.)

*High risk for fragility fractures is defined as :

- A bone mineral density (BMD) T-score less than or equal to -3; **AND**
- Prior fragility fracture

Note: Requesting physicians must include a copy of the BMD report with the EAP request

Requests meeting criteria will be funded for 24 months. It should be noted that renewals are NOT considered.

(As noted in the product monograph, the maximum life time exposure to an individual patient is 24 months)

1\(^{\text{nd}}\) No other contraindications to anti-resorptive therapies will be considered for funding.

**Duration of Approval:** Total approval duration of 24 months will be provided. Renewals are not considered.
Cannabidiol and delta-9-tetrahydro-cannabinol
Brand(s): Sativex
DOSAGE FORM/ STRENGTH: 25 mg/27 mg per mL buccal spray

For the treatment of **neuropathic pain related to multiple sclerosis** in patients who have:

- Ineffective response or intolerable side effects / contraindications to adequate trials* of a tricyclic antidepressant and gabapentin and pregabalin; and
- Ineffective response or intolerable side effects / contraindications to adequate trials* of Cesamet (nabilone) and Marinol (delta-9-tetrahydrocannabinol); and
- No contraindications to Sativex therapy.

* Adequate trial is defined as 2 months unless intolerable side effect(s) occur.

**Duration of Approval**: 1 Year

Note: Side effects and contraindications must be described in detail. Side effects should be deemed serious by the physician such that no further therapy with the agent would be warranted.

**Renewal** will be considered for patients responding to Sativex therapy as demonstrated by decreased pain and other pain-related symptoms; no initiation of new analgesics; and no increase in doses of any analgesics.

**Duration of Approval**: Renewal is lifetime.

Sativex is also reimbursed for the treatment of refractory pain in palliative cancer patients according to specified criteria.

**Duration of Approval**: 6 Months
Methadone
Brand(s): Metadol
DOSAGE FORM/ STRENGTH: 1 mg, 5 mg, 10 mg, 25 mg tablets, 1 mg/mL oral solution, 10 mg/mL oral concentrate solution

For the treatment of cancer and non-cancer pain in patients who cannot tolerate, or have failed treatment with a listed long-acting opioid.

The CED noted that there is a potential for drug interactions with the use of methadone resulting from inhibition of drug metabolism (via CYP 3A4 inhibition; e.g. QT prolongation with certain antibiotics). The requesting physician is asked to ensure that this issue is addressed with the patient.

Duration of Approval 1 Year

Renewals will be considered on a case-by-case basis.

For renewals, the requesting physician is asked to provide details of the patient’s clinical response to therapy and additional information pertaining to the current medications and addition or stoppage of other pain medications in the prior year of methadone use. Please specify the dosages and dosing frequency of current medications and provide reasons for any changes in the medication regimen.

Oxycodone Controlled Release Tablet
Brand(s): OxyNeo
DOSAGE FORM/ STRENGTH: 10 mg CR, 15 mg CR, 20 mg CR, 30 mg CR, 40 mg CR

For the treatment of chronic pain in patients who have experienced intolerance or have failed an adequate trial (for example, three months) of at least one other listed long-acting opioid product.

Note: Physicians should consider best practice guidelines for the safe and effective use of opioids in chronic non-cancer pain, such as the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain.

Please include the following information in your request:

iv) The diagnosis for which the pain management is required must be documented.

v) All concomitant pain medication therapy must be documented.

vi) Other medications with potential for abuse or interaction with opioid therapy should be documented.

Duration of Approval: 1 Year
Oxycodone Controlled Release Tablet
Brand(s): OxyNeo
DOSAGE FORM/ STRENGTH: 10 mg CR, 15 mg CR, 20 mg CR, 30 mg CR, 40 mg CR

Renewals will be considered if treatment continues to be appropriate for the management of the patient’s chronic pain. Please include the following information on your renewal request:

Duration of Approval: 1 Year

i) All concomitant pain medication therapy must be documented.

ii) Other medications with potential for abuse or interaction with opioid therapy should be documented.

Note: OxyNEO 60mg and 80mg tablets are not funded.

Note: Physicians registered on the Ontario Medical Association’s Palliative Care Facilitated Access List can access OxyNeo for chronic pain management of their palliative care patient for an initial duration of one year without approval through the Exceptional Access Program.
Levodopa 20 mg/mL and Carbidopa 5 mg/mL Intestinal gel
Brand(s): Duodopa
DOSAGE FORM/ STRENGTH: Intestinal Gel containing Levodopa 20 mg/mL – Carbidopa 5 mg/mL (100 mL cassette)

For the treatment of Parkinson's disease in patients who meet the following criteria;

- Experiences at least 25% of the waking day in the off state; **AND**
- Has severe disability while in the off-state as assessed by a Movement Disorder Specialist; **AND**
- Has received an adequate trial of maximally tolerated doses of levodopa, with demonstrated clinical response; **AND**
- Has failed adequate trials of other adjunctive medications (entacapone, dopamine agonists, monoamine oxidase-B [MAO-B] inhibitors) if not contraindicated. Note that if a contraindication is deemed to be applicable to the patient, the requesting physician must state the contraindication and provide the rationale why it is considered a contraindication for the patient).

Clinical details pertaining to the severity of the patient’s disability while in the off-state as well as a complete history of all previous and current medications (e.g., name, start date and duration of therapy, doses used, side effects, and response) must be included.

Requests for treatment initiation will be limited to the physicians practicing in the following specialized movement disorder clinics: Ottawa, London, Toronto Western, Kingston, Baycrest and Hamilton.

**Exclusion criteria** (Patients who meet the following criteria will NOT be considered):

- Patients who have a contraindication to insertion of a percutaneous endoscopic gastrostomy (PEG) tube
- Severe psychosis or dementia

**Duration of Approval:** 1 Year

**Renewals** will be considered in patients who continue to benefit from treatment. The patient should continue to demonstrate a significant reduction in the time spent in the off state and an improvement in the severity of the disability in the off state.

**Duration of Approval:** 1 Year
Rasagiline
Brand(s): Azilect
DOSAGE FORM/ STRENGTH: 0.5 mg, 1 mg tablet

For the treatment of patients with Parkinson’s disease who experience about 25% of the waking day in the off-state despite maximally tolerated doses of levodopa.

**Duration of Approval:** 5 Years (Both Initial and Renewals)
PSORIATIC ARTHRITIS TREATMENTS

Adalimumab
Brand(s): Humira
DOSAGE FORM/ STRENGTH: 40 mg/0.8 mL prefilled syringe and 40mg/0.8mL prefilled pen for subcutaneous injection

Certolizumab
Brand(s): Cimzia
DOSAGE FORM/ STRENGTH: 200 mg/mL prefilled syringe

Etanercept
Brand(s): Enbrel
DOSAGE FORM/ STRENGTH: 25 mg/vial and 50 mg prefilled syringe for subcutaneous injection

Golimumab
Brand(s): Simponi
DOSAGE FORM/ STRENGTH: 50 mg/0.5 ml prefilled syringe and autoinjector

Secukinumab
Brand(s): Cosentyx
DOSAGE FORM/ STRENGTH: 150 mg/mL prefilled syringe and 150 mg/mL prefilled pen

For the treatment of psoriatic arthritis in patients who have:

Severe active disease (≥ 5 swollen joints and radiographic evidence of psoriatic arthritis) despite treatment with methotrexate (20mg/week) for at least 3 months and one of leflunomide (20mg/day) or sulfasalazine (1g twice daily) for at least 3 months.

If the patient has documented contraindications or intolerances to methotrexate, then only one of leflunomide (20 mg/day) or sulfasalazine (1 g twice daily) for at least 3 months is required. Details of contraindications and intolerances must also be provided.

Duration of Approval: 1 Year
Renewal will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Duration of Approval 1 Year

The planned dosing regimen for the requested biologic should be provided. The recommended doses for the treatment of psoriatic arthritis are as follows:

- Adalimumab 40mg every two weeks
- Certolizumab 400 mg at week 0, 2, 4 then maintenance doses of 200 mg every 2 weeks or 400 mg every 4 weeks
- Etanercept 25mg twice weekly or 50mg once weekly
- Golimumab 50mg once a month
- Secukinumab 150mg sc at weeks 0, 1, 2, and 3 followed by monthly maintenance dosing starting at week 4. If a patient is an anti-TNFalpha inadequate responder and continues to have active psoriatic arthritis, consider using the 300 mg sc dose. For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis (i.e. 300 mg sc at weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at week 4)

Duration of Approval: Second and subsequent renewals are 2 years
**PULMONARY ARTERIAL HYPERTENSION**

**Drugs for Pulmonary Arterial Hypertension (PAH) under EAP**

i) Phosphodiesterase (PDE)-5 inhibitor: sildenafil (Revatio), tadalafil (Adcirca)

ii) Endothelin receptor antagonists (ERAs): ambrisentan (Volibris), bosentan (Tracleer)

iii) Prostanoids: epoprostenol (Flolan, Caripul), treprostinil (Remodulin), selexipag (Uptravi)

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<tr>
<th><strong>Sildenafil</strong></th>
<th>Brand(s): Revatio</th>
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<td><strong>DOSAGE FORM/ STRENGTH:</strong> 20 mg tablet</td>
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<tr>
<th><strong>Tadalafil</strong></th>
<th>Brand(s): Adcirca</th>
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<td><strong>DOSAGE FORM/ STRENGTH:</strong> 20 mg tablet</td>
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All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**  
  Hamilton Health Sciences – General Hospital

- **The Firestone Institute Pulmonary Hypertension Program**  
  St. Joseph's Healthcare Hamilton and McMaster University

- **Pulmonary Hypertension Clinic**  
  Hotel Dieu Hospital/Kingston General Hospital

- **Pulmonary Hypertension Program**  
  London Health Science Centre – Victoria Hospital

- **Ottawa Pulmonary Hypertension Clinic**  
  University of Ottawa Heart Institute and the Ottawa Hospital

- **University Health Network Pulmonary Hypertension Program**  
  Toronto General Hospital
**Sildenafil**  
Brand(s): Revatio  
DOSAGE FORM/ STRENGTH: 20 mg tablet  

**Tadalafil**  
Brand(s): Adcirca  
DOSAGE FORM/ STRENGTH: 20 mg tablet  

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;  
Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis.

i) **Sildenafil (Revatio, generics), Tadalafil (Adcirca, generics)**

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of \( \geq 25 \) mmHg at rest AND normal pulmonary capillary wedge pressure (PCWP) \( \leq 15 \) mmHg on right heart catheterization\(^1\); AND

- The drug request meets one of the following circumstances of use:
  
  o Drug is being used as monotherapy in a patient with WHO-functional class II (Note that a PDE-5 inhibitor must be used as first line monotherapy for WHO-FC II (unless contraindicated or demonstrated intolerance), III, or IV; OR

  o Drug is being used as sequential dual therapy in combination with a funded ERA (i.e. ambrisentan, bosentan) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient who has had an inadequate response with monotherapy (i.e., failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure); OR

  o Drug is being used as up-front dual therapy in combination with a funded ERA (i.e. ambrisentan, bosentan) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient with advanced disease (i.e. WHO-functional class III or IV, 6MWD <380 metres; OR evidence of RV failure.)

\(^1\) Note: Left ventricular end-diastolic pressure \( \leq 15 \) mmHg is also acceptable.
All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital

- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph’s Healthcare Hamilton and McMaster University

- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital

- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital

- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital

- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;

Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of \( \geq 25 \text{ mmHg} \) at rest AND normal pulmonary capillary wedge pressure (PCWP) \( \leq 15 \text{ mmHg} \) on right heart catheterization\(^1\); AND

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\(^1\) Pulmonary hypertension: WHO Group 1 PAH.
Ambrisentan
Brand(s): Volibris
DOSAGE FORM/ STRENGTH: 5 mg, 10 mg tablet

Bosentan
Brand(s): Tracleer, Generics (Co-, Mylan-, PMS-, Sandoz-)
DOSAGE FORM/ STRENGTH: 62.5 mg, 125 mg tablet

- The drug request meets one of the following circumstances of use:
  - Drug is being used as monotherapy in a patient with WHO-functional class III or IV; OR
  - Drug is being used as monotherapy in a patient with WHO-functional class II who has contraindication or has intolerance to a PDE-5 inhibitor; OR
  - Drug is being used as sequential dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient who has had an inadequate response with monotherapy (i.e., failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure); OR
  - Drug is being used as up-front dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or a funded prostanoid (i.e. epoprostenol, treprostinil) in a patient with advanced disease (i.e. WHO-functional class III or IV; OR 6MWD <380 metres; OR evidence of RV failure.)

1 Note: Left ventricular end-diastolic pressure ≤ 15 mmHg is also acceptable.
Treprostinil  
Brand(s): Remodulin  
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials  

Epoprostenol  
Brand(s): Flolan  
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial  

Epoprostenol  
Brand(s): Caripul  
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial  

All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.  

- **Pulmonary Hypertension Centre**  
  Hamilton Health Sciences – General Hospital  

- **The Firestone Institute Pulmonary Hypertension Program**  
  St. Joseph’s Healthcare Hamilton and McMaster University  

- **Pulmonary Hypertension Clinic**  
  Hotel Dieu Hospital/Kingston General Hospital  

- **Pulmonary Hypertension Program**  
  London Health Science Centre – Victoria Hospital  

- **Ottawa Pulmonary Hypertension Clinic**  
  University of Ottawa Heart Institute and the Ottawa Hospital  

- **University Health Network Pulmonary Hypertension Program**  
  Toronto General Hospital  

Requests from other physicians/centres must include a recent (less than or equal to 3 months old) consult note/recommendation from a recognized PAH referral centre that supports the request;  

Out-of-province referral centre consults (e.g., from Winnipeg for patients in Northern Ontario) will also be considered on a case-by-case basis.
Treprostinil
Brand(s): Remodulin
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials

Epoprostenol
Brand(s): Flolan
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial

Epoprostenol
Brand(s): Caripul
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial

Epoprostenol (Flolan, Caripul), Treprostinil (Remodulin)

Initial Criteria:

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria;

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of $\geq 25$ mmHg at rest AND normal pulmonary capillary wedge pressure (PCWP) $\leq 15$ mmHg on right heart catheterization\(^1\); AND

- The drug request meets one of the following circumstances of use:
  - Drug is being used as monotherapy in a patient with WHO-functional class III or IV; OR
  - Drug is being used as sequential dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or with a funded ERA (i.e. ambrisentan, bosentan) in a patient who fails to meet treatment targets (i.e. failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure) with monotherapy; OR
  - Drug is being used as up-front dual therapy in combination with a funded PDE-5 (i.e. sildenafil, tadalafil) or with a funded ERA (i.e. ambrisentan, bosentan) in a patient with advanced disease (i.e. WHO-functional class III or IV; OR 6MWD <380 metres; OR evidence of RV failure.)

\(^1\) Note: Left ventricular end-diastolic pressure $\leq 15$ mmHg is also acceptable.
Treprostinil
Brand(s): Remodulin
DOSAGE FORM/ STRENGTH: 1 mg/mL, 2.5 mg/mL, 5 mg/mL and 10 mg/mL vials

Epoprostenol
Brand(s): Flolan
DOSAGE FORM/ STRENGTH: 0.5 mg and 1mg vial

Epoprostenol
Brand(s): Caripul
DOSAGE FORM/ STRENGTH: 0.5 mg and 1.5 mg vial

For all funded PAH Drugs, case-by-case consideration may be provided for the following:

- Requests for triple therapy (Including patients awaiting lung transplant.)
- Patients who may have mixed co-morbidities that include ILD, COPD or LV failure. (i.e. patients with mixed WHO Group 1 and Group 3 pulmonary hypertension OR mixed WHO Group 1 and Group 2 pulmonary hypertension)

Exclusion Criteria:
Combinations of drugs targeting similar pathways will not be funded. (i.e. combination regimen may only include one agent from each drug class -- phosphodiesterase type 5 [PDE-5] inhibitors, endothelin receptor antagonists (ERA), and/or prostanoids)

Renewal criteria for funded PAH Drugs:
Renewals will be provided for patients who remain under the care of a physician from a recognized PAH Centre (see list above) and who continue to benefit from therapy.

Approval Durations:
Duration of Approval for Initial Requests: 1 year
Duration on triple therapy regimens awaiting lung transplantation: 1 year
Duration of first renewal: 1 Year
Duration of subsequent renewals: 5 Years
Selexipag
Brand(s): Uptravi
DOSAGE FORM/ STRENGTH: 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg Tablets

All requests (initial, renewal, monotherapy, combination therapy) for a PAH drug must come from one of the following recognized PAH referral centres.

- **Pulmonary Hypertension Centre**
  Hamilton Health Sciences – General Hospital

- **The Firestone Institute Pulmonary Hypertension Program**
  St. Joseph’s Healthcare Hamilton and McMaster University

- **Pulmonary Hypertension Clinic**
  Hotel Dieu Hospital/Kingston General Hospital

- **Pulmonary Hypertension Program**
  London Health Science Centre – Victoria Hospital

- **Ottawa Pulmonary Hypertension Clinic**
  University of Ottawa Heart Institute and the Ottawa Hospital

- **University Health Network Pulmonary Hypertension Program**
  Toronto General Hospital

**Initial Criteria:**

For the treatment of patients with pulmonary arterial hypertension (PAH) [WHO Group 1 Pulmonary hypertension] who meet all the following criteria:

- PAH defined as a resting mean pulmonary artery pressure (mPAP) of ≥ 25 mmHg at rest AND normal pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg on right heart catheterization\(^1\); AND

- Patient with World Health Organization (WHO) functional class II to IV; AND

- Selexipag is being used in a patient experiencing inadequate control\(^2\) with a Phosphodiesterase (PDE)-5 inhibitor (i.e. tadalafil or sildenafil) AND an endothelin receptor antagonist (ERA) (i.e. bosentan or ambrisentan).

**Notes:**

1. Left ventricular end-diastolic pressure ≤ 15 mmHg is also acceptable.
2. Unable to meet treatment targets (i.e. failure to achieve WHO-FC I or II; or 6MWD >440 metres; or no/mild RV failure)
Selexipag
Brand(s): Uptravi
DOSAGE FORM/ STRENGTH: 200mcg, 400mcg, 600mcg, 800mcg, 1000mcg, 1200mcg, 1400mcg, 1600mcg Tablets

Case-by-case consideration may be provided for the following:

- Requests for Selexipag in patients who demonstrate intolerance or have a contraindication to either PDE-5 inhibitors (i.e. both sildenafil and tadalafil) or ERAs (i.e. both bosentan and ambrisentan)
- Patients who may have mixed co-morbidities that include ILD, COPD or LV failure. (i.e. patients with mixed WHO Group 1 and Group 3 pulmonary hypertension OR mixed WHO Group 1 and Group 2 pulmonary hypertension)

Exclusion Criteria:
Combination therapy with prostacyclin or prostacyclin analog therapies and Selexipag will not be covered.

Renewal criteria:
Renewals will be provided for patients who remain under the care of a physician from a recognized PAH Centre (see list above) and who continue to benefit from therapy.

Approval Durations:
Duration of Approval for Initial Requests: 1 year
Duration on triple therapy regimens awaiting lung transplantation: 1 year
Duration of first renewal: 1 Year
Duration of subsequent renewals: 5 Years
For the treatment of chronic thromboembolic pulmonary hypertension (CTEPH) in patients who meet the following criteria;

- the physician making the request is a clinician with experience in the diagnosis and treatment of CTEPH; AND
- the patient is diagnosed with inoperable CTEPH (World Health Organization [WHO] Group 4); OR persistent or recurrent CTEPH after surgical treatment in adult patients (18 years of age or older) with WHO Functional Class (FC) II or III pulmonary hypertension.

1 Request should come from a clinician from a Pulmonary Hypertension referral centre (See Pulmonary Arterial Hypertension referral clinics above).

Duration of Approval: 1 Year

Renewal of funding will be considered for patients who continue to respond to therapy with riociguat. When submitting a request for renewal of funding, the physician should submit clinical information to support that the patient is deriving benefit from the treatment compared to before they started the treatment. The physician should provide confirmation of improvement of any ONE or more reasonable clinical parameters which supports the response of the patient’s CTEPH to riociguat.

Duration of Approval: 1 Year

Requests for subsequent funding renewals (i.e. beyond the first two years of treatment) will be considered when a physician provides written confirmation that the patient continues to respond to therapy with riociguat. The physician should provide confirmation of improvement of any ONE or more reasonable clinical parameters which supports the response of the patient’s CTEPH to riociguat compared to baseline or that supports that the patient’s condition is stable while on riociguat.

Duration of Approval: Subsequent Renewals - 5 Years
Ivacaftor
Brand(s): Kalydeco
DOSAGE FORM/ STRENGTH: 150 mg tablets

For the treatment of cystic fibrosis in patients who meet the following criteria:

- Age 6 years and older; AND
- Patient has documented G551D mutation in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene.

Initial renewal criteria:

Duration of Approval: 1 Year
Renewals will be considered in patients with documented response to treatment (after at least 6 months of therapy), as evidenced by the following:

In cases where the patient’s sweat chloride levels prior to commencing therapy were above 60 mmol/litre:

i) the Patient’s sweat chloride level fell below 60 mmol/litre; OR
ii) the Patient’s sweat chloride level is 30% lower than the level reported in a previous test;

In cases where the patient’s sweat chloride levels prior to commencing therapy were below 60 mmol/litre:

i) the patient’s sweat chloride level is 30% lower than the level reported in a previous test; OR
ii) the patient demonstrates a sustained absolute improvement in FEV1 of at least 5% when compared to the FEV1 test conducted prior to the commencement of therapy.

Subsequent renewal criteria after the patient has met the initial renewal criteria:
The Patient is continuing to benefit from therapy with Kalydeco.

1It should be noted that, while baseline sweat chloride levels and FEV1 are not required to meet initial approval criteria for Kalydeco, these parameters may be used to evaluate the effect of Kalydeco upon renewal of the request. It is important that the physician measures baseline sweat chloride levels and FEV1 and provides this information upon renewal to avoid delays in the assessment of the renewal funding decision as these measurements may be required to evaluate renewal requests.

Duration of Approval: 1 Year
**Nintedanib**  
**Brand(s): Ofev**  
**DOSAGE FORM/ STRENGTH: 100 mg, 150 mg capsules**

**Initial approval criteria:**  
For the treatment of adult patients with a diagnosis of **mild to moderate idiopathic pulmonary fibrosis (IPF):**

- Diagnosis confirmed by a respirologist and a high-resolution CT scan.  
- All other causes of restrictive lung disease (e.g. collagen vascular disorder or hypersensitivity pneumonitis) should be excluded.  
- Mild to moderate IPF is defined as forced vital capacity (FVC) greater than or equal to 50% of predicted.  
- Patient is under the care of a physician with experience in IPF.

Initial approval period: 7 months (allow 4 weeks for repeat pulmonary function tests)

**Initial renewal criteria (at 6 months):**  
Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% from initiation of therapy until renewal (initial 6 month treatment period). If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.  

Initial Renewal Duration: 6 Months

**Second and subsequent renewals (at 12 months and thereafter):**

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% within any 12 month period. If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 12 months

**Documentation/information required:**

- *If high-resolution CT scan is not available, lung biopsy may be provided to support the diagnosis of IPF as applicable and available*

- *Full pulmonary function test results.*

Second Renewal Duration: 12 Months

**Exclusion Criteria:**

Combination use of Ofev (nintedanib) and Esbriet (pirfenidone) will not be funded.
Pirfenidone
Brand(s): Esbriet
DOSAGE FORM/ STRENGTH: 267 mg capsule, 267 mg tablet, 801 mg tablet

Initial approval criteria:
For the treatment of adult patients with a diagnosis of **mild to moderate idiopathic pulmonary fibrosis (IPF):**

- Diagnosis confirmed by a respirologist and a high-resolution CT scan.
- All other causes of restrictive lung disease (e.g. collagen vascular disorder or hypersensitivity pneumonitis) should be excluded.
- Mild to moderate IPF is defined as forced vital capacity (FVC) greater than or equal to 50% of predicted.
- Patient is under the care of a physician with experience in IPF.

Initial approval period: 7 months (allow 4 weeks for repeat pulmonary function tests)

Initial renewal criteria (at 6 months):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% from initiation of therapy until renewal (initial 6 month treatment period). If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 6 months

Second and subsequent renewals (at 12 months and thereafter):

Patients must NOT demonstrate progression of disease defined as an absolute decline in percent predicted FVC of ≥10% within any 12 month period. If a patient has experienced progression as defined above, then the results should be validated with a confirmatory pulmonary function test conducted 4 weeks later.

Approval period: 12 months

Documentation/information required:

- If high-resolution CT scan is not available, lung biopsy may be provided to support the diagnosis of IPF as applicable and available
- Full pulmonary function test results.

Exclusion Criteria:
Combination use of Esbriet (pirfenidone) and Ofev (nintedanib) will not be funded.
Abatacept
Brand(s): Orencia

DOSAGE FORM/ STRENGTH: 250 mg/15 mL vial

For the treatment of polyarticular-course juvenile idiopathic arthritis in patients meeting the following criteria;

- Patient has active disease (a minimum of 3 (three) swollen joints and a total of 5 active joints); AND
- Patient has had an inadequate response to a three month course of methotrexate administered subcutaneously at a dosage of at least 15 mg/m² per week for at least 3 months. If the patient is unable to tolerate or has a contraindication to subcutaneous methotrexate the nature of the intolerance or contraindication must be described in detail.; AND
- Patient has had an inadequate response to a three month course of etanercept (Enbrel) OR adalimumab (Humira) OR tocilizumab (Actemra). If the patient is unable to tolerate or has a contraindication to etanercept OR adalimumab OR tocilizumab (Actemra), the nature of the intolerance or contraindication must be described in detail.

Duration of Approval: 1 Year

Renewals will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count. For renewals beyond the second year, objective evidence of preservation of treatment effect should be provided. (i.e. the current joint count should be compared to the count prior to initiating treatment with the biologic agent)

Duration of Approval: 1 Year
### Etanercept
**Brand(s):** Enbrel*  
**DOSAGE FORM/ STRENGTH:** 25 mg/vial, 50 mg prefilled syringe for subcutaneous injection

### Adalimumab
**Brand(s):** Humira  
**DOSAGE FORM/ STRENGTH:** 40 mg/0.8mL prefilled syringe and 40 mg/0.8mL prefilled pen for subcutaneous injection

### Tociluzumab
**Brand(s):** Actemra  
**DOSAGE FORM/ STRENGTH:** 80 mg/4 mL Vial, 200 mg/10 mL Vial, 400 mg/20 mL Vial

*Effective December 21, 2017 etanercept as Erelzi for the treatment of polyarticular juvenile idiopathic arthritis (pJIA), ankylosing spondylitis (AS), and rheumatoid arthritis (RA), and will be considered as Limited Use on the ODB Formulary.*

It should be noted that etanercept as Enbrel will continue to be considered for renewals of requests for pJIA in those who have an existing EAP funding approval prior to the availability of Erelzi on the ODB formulary. Additionally, Enbrel will continue to be reimbursed for patients with pJIA who are unable to use Erelzi to accommodate weight-based dosing. For example, the available formats of Erelzi do not have graduated markings on the syringe or pen to enable a more accurate measurement of drug doses that are less than 50 mg or less than 25 mg.

**For the first-line treatment of polyarticular-course juvenile idiopathic arthritis in patients** meeting the following criteria:

- Patient has active disease (≥ 3 swollen joints and ≥ 5 active joints) despite a trial of optimal dose of subcutaneously administered methotrexate (i.e. 15 mg/m² per week) for at least 3 months. If the patient is unable to tolerate or has a contraindication to subcutaneous methotrexate, the nature of the intolerance or contraindication must be described in detail.

**Duration of Approval:** 1 Year  
**Renewal** will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.  
**Duration of Approval:** 1 Year
<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand(s)</th>
<th>DOSAGE FORM/ STRENGTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>Enbrel*</td>
<td>25 mg/vial, 50 mg prefilled syringe for subcutaneous injection</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Humira</td>
<td>40 mg/0.8mL prefilled syringe and 40 mg/0.8mL prefilled pen for subcutaneous injection</td>
</tr>
<tr>
<td>Tociluzumab</td>
<td>Actemra</td>
<td>80 mg/4 mL Vial, 200 mg/10 mL Vial, 400 mg/20 mL Vial</td>
</tr>
</tbody>
</table>

**Dosing for Etanercept (Enbrel):**

The planned dosing regimen should be provided. The maximum recommended dose is 50mg once weekly.

**Recommended Dosing for Adalimumab (Humira):**

- a) 24 mg/m² (maximum 40 mg) every two weeks; OR
- b) 20 mg every 2 weeks, if the Patient weighs less than 30 kg; OR
- c) 40 mg every 2 weeks, if the Patient weighs more than 30 kg.

**Recommended dosing for tociluzumab (Actemra):**

- (a) 10 mg/kg every 4 weeks, if the Patient weighs less than 30kg; OR
- (b) 8 mg/kg every 4 weeks, if the Patient weighs more than or equal to 30kg.
Infliximab
Brand(s): Remicade
DOSAGE FORM/ STRENGTH: 100 mg/vial

For the treatment of polyarticular-course juvenile idiopathic arthritis in patients meeting the following criteria:

- Patient has active disease (a minimum of 3 (three) swollen joints and a total of 5 active joints); AND
- Patient has had an inadequate response to a three month course of methotrexate administered subcutaneously at a dosage of at least 15 mg/m$^2$ per week for at least 3 months. If the patient is unable to tolerate or has a contraindication to subcutaneous methotrexate the nature of the intolerance or contraindication must be described in detail.; AND
- Patient has had an inadequate response to a three month course of etanercept (Enbrel) OR adalimumab (Humira). If the patient is unable to tolerate or has a contraindication to etanercept OR adalimumab, the nature of the intolerance or contraindication must be described in detail.

Infliximab dosing:
Up to 6 mg/kg/dose at weeks 0, 2, and 6, followed by maintenance of up to 6 mg/kg/dose every 8 weeks.

Duration of Approval: 1 Year

Renewals will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count. For renewals beyond the second year, objective evidence of preservation of treatment effect should be provided (i.e the current joint count should be compared to the count prior to initiating treatment with the biologic agent).

Duration of Approval: 1 Year

Initial and Renewal requests that do not meet the stated criteria will undergo external review.
### RHEUMATOID ARTHRITIS

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Brand(s)</th>
<th>DOSAGE FORM/ STRENGTH:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>Humira</td>
<td>40 mg/0.8mL prefilled syringe and 40 mg/0.8mL prefilled pen for subcutaneous injection</td>
</tr>
<tr>
<td>Anakinra</td>
<td>Kineret</td>
<td>100 mg /0.67 mL subcutaneous injection</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>Cimzia</td>
<td>200 mg/mL prefilled syringe</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Enbrel</td>
<td>25 mg/vial and 50mg prefilled syringe for subcutaneous injection</td>
</tr>
<tr>
<td>Golimumumab</td>
<td>Simponi</td>
<td>50 mg/0.5 mL prefilled syringe and autoinjector</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Remicade</td>
<td>100 mg/10 mL intravenous infusion</td>
</tr>
</tbody>
</table>

*Bio similars on the formulary as Limited Use Benefits:*

**Effective February 25, 2016,** Infliximab as Remicade for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis will only be considered for funding for existing EAP renewals. Infliximab as Inflectra or Renflexis (Effective September 27, 2018) can be considered through Limited Use criteria on the Ontario Drug Benefit Formulary.

**Effective July 31, 2017,** etanercept as Enbrel for the treatment of ankylosing spondylitis (AS) and rheumatoid arthritis (RA) will only be considered for funding for existing EAP renewals. Etanercept as Brenzys can be considered through Limited Use criteria on the Ontario Drug Benefit Formulary.
Effective December 21, 2017 etanercept as Erelzi for the treatment of ankylosing spondylitis (AS), rheumatoid arthritis (RA), and polyarticular juvenile idiopathic arthritis (pJIA) will only be considered for funding for existing EAP renewals. Etanercept as Brenzys can be considered through Limited Use criteria on the Ontario Drug Benefit Formulary.

For the treatment of rheumatoid arthritis in patients who have:

- Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or, anti-CCP positive, and/or radiographic evidence of rheumatoid arthritis) despite the optimal use of various formulary disease-modifying anti-rheumatic drugs (DMARDs)*.

*Optimal use of DMARDs include:

- Methotrexate (20 mg/week) for at least 3 months and leflunomide (20 mg/day) for at least 3 months in addition to an adequate trial (3 months) of at least one combination of DMARDs; or
- Methotrexate (20 mg/week) for at least 3 months and leflunomide in combination with methotrexate for at least 3 months.
- If the patient could not receive adequate trial(s) of methotrexate and/or leflunomide due to contraindication(s) or intolerance(s), the nature of contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale why other DMARDs cannot be considered.

**OR**

- Methotrexate (20mg/week), sulfasalazine (2 GM/day) and hydroxychloroquine (400mg/day)* for at least 3 months. If the patient could not receive an adequate trial of methotrexate, sulfasalazine and hydroxychloroquine due to intolerance, then the above DMARD trial criteria must be met.

Hydroxychloroquine is based by weight up to 400 mg per day

**Duration of Approval:** 1 Year

**Renewal** will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The planned dosing regimen for the requested biologic should be provided. The recommended doses for the treatment of rheumatoid arthritis are as follows:

- Adalimumab 40mg every two weeks
- Anakinra 100mg per day
- Certolizumab pegol 400mg at 0, 2 and 4 weeks followed by maintenance therapy of 200 mg every 2 weeks. For maintenance dosing, 400mg every 4 weeks may be considered
- Etanercept 25mg twice weekly or 50mg once weekly
- Golimumab 50mg once a month
Infliximab 3mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of 3mg/kg/dose every 8 weeks up to a maximum of six maintenance doses per year

(Note that effective December 22, 2016, Tofacitinib (Xeljanz) 5mg is available on the ODB Formulary in patients meeting the Limited Use criteria)

Duration of Approval: First Renewal – 1 Year, Subsequent Renewals – 5 Years

Rituximab
Brand(s): Rituxan
DOSAGE FORM/ STRENGTH: 10 mg/mL intravenous injection

First course of Rituxan for the treatment of rheumatoid arthritis in adult patients with:
Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or radiographic evidence of rheumatoid arthritis); AND
• Failure to respond to optimal use of DMARDs or documented intolerance or contraindications to DMARDs (per current EAP reimbursement criteria for anti-TNF agents); AND
• Failure to respond to, or the patient has intolerance or contraindications to, an adequate trial of at least ONE anti-TNF agent (e.g., adalimumab, etanercept, infliximab, golimumab, certolizumab pegol)

Initial approval: One year: One course of treatment is 1000 mg followed two weeks later by the second 1000mg dose. Two courses will be approved each year (courses should be at least 6 months apart with second course being given only AFTER loss of effect as noted in the re-treatment guidelines below). Second course is not approved for “maintenance” therapy.

Renewal criteria: A joint count at 3-4 months indicating at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints, should be recorded to indicate a response, and then re-treatment can be given after an interval of at least 6 months AND after a loss of effect. Details of all courses given and the subsequent response should be provided in the renewal request.

Renewal approval: 1 year (2 courses). One course of treatment is 1000 mg followed two weeks later by the second 1000mg dose. Repeated courses are not approved for maintenance therapy.

Note: Rituximab should not be used concomitantly with other anti-TNF agents.

More information describing one of the Committee to Evaluate Drugs’ review of rituximab can be found on the Ministry website.
Abatacept
Brand(s): Orencia

DOSAGE FORM/ STRENGTH: 250 mg/15 mL intravenous injection, 125 mg/mL pre-filled syringe for subcutaneous injection

For the treatment of adult patients with severe active rheumatoid arthritis who meet the following criteria:

The Patient has severe active disease as demonstrated by:
- ≥ 5 swollen joints; AND
- rheumatoid factor positive; AND/OR
- having radiographic evidence of rheumatoid arthritis

Despite the optimal* use of various disease-modifying anti-rheumatic drugs (“DMARDs”).

*For the purpose of the criteria, the optimal use of DMARDs is defined as;
- use of methotrexate (dosed at 20 mg per week) for at least 3 months; AND
- use of leflunomide (dosed at 20 mg per day) for at least 3 months; AND
- an adequate trial (3 months) of at least one combination of DMARDs;
  OR
- use of methotrexate (dosed at 20 mg per week) for at least 3 months; AND
- leflunomide in combination with methotrexate for at least 3 months.

Note: If the patient cannot be treated with adequate trial(s) of methotrexate and/or leflunomide due to contraindication(s) or intolerance(s), the nature of the contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale why other DMARDs cannot be considered.

For patients who have failed treatment with an anti-TNF therapy due to lack of efficacy or toxicity, prescribers should consider use of a biologic with a different mechanism of action.

Approved Dosing:

IV use: The initial dose is administered at 0, 2, and 4 weeks then every 4 weeks thereafter. Note that funding for higher doses will not be considered.

<table>
<thead>
<tr>
<th>Body weight of patient</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60 kg</td>
<td>500 mg</td>
</tr>
<tr>
<td>60-100 kg</td>
<td>750 mg</td>
</tr>
<tr>
<td>&gt;100 kg</td>
<td>1 gram</td>
</tr>
</tbody>
</table>
Abatacept
Brand(s): Orencia
DOSAGE FORM/ STRENGTH: 250 mg/15 mL intravenous injection, 125 mg/mL pre-filled syringe for subcutaneous injection

SC use: 125 mg SC weekly. Note that an IV loading dose of 750 mg may be given prior to initiating the weekly SC dosing. (Please refer to the Orencia product monograph for further details.)

Duration of Approval: First Renewal – 1 Year, Subsequent Renewals – 5 Years

Renewals will be considered in patients with objective evidence of at least a twenty percent (20%) reduction in swollen joint count and a minimum of improvement in two (2) swollen joints over the previous year.

For renewals beyond the second year, objective evidence of the preservation of treatment effect must be provided by the requesting physician.

Tocilizumab
Brand(s): Actemra
DOSAGE FORM/ STRENGTH: 80 mg / 4 mL Vial, 200 mg / 10 mL Vial, 400 mg / 20 mL Vial, 162 mg/0.9 mL solution for injection

For the treatment of rheumatoid arthritis in adult patients with;

- Severe active disease (≥ 5 swollen joints and rheumatoid factor positive and/or anti-CCP positive and/or has radiographic evidence of rheumatoid arthritis); \( \text{AND} \)

- Failure to respond to optimal use\(^1\) of DMARDs or with documented intolerance to DMARDs (per current EAP reimbursement criteria for anti-TNF agents).

Optimal use of DMARDs (hydroxychloroquine, methotrexate, sulfasalazine, leflunomide, cyclosporine, azathioprine, penicillamine, chloroquine and gold compounds) defined as:

- Methotrexate (20 mg/week) for at least 3 months \( \text{AND} \)
leflunomide (20 mg/day) for at least 3 months, in addition to an adequate trial (3 months) of at least one combination of DMARDs; \( \text{OR} \)
Tocilizumab

Brand(s): Actemra

DOSAGE FORM/ STRENGTH: 80 mg / 4 mL Vial, 200 mg / 10 mL Vial, 400 mg / 20 mL Vial, 162 mg/0.9 mL solution for injection

- Methotrexate (20 mg/week) for at least 3 months AND leflunomide in combination with methotrexate for at least 3 months; OR

¹Note: If the patient could not receive adequate trial(s) of methotrexate and/or leflunomide due to contraindication(s) or intolerance(s), the nature of the contraindication(s) or intolerance(s) must be provided along with details of trials of other DMARDs or clear rationale as to why other DMARDs cannot be considered.

- Methotrexate (20 mg/week), sulfasalazine (2 G/day) and hydroxychloroquine (400 mg/day)² for at least 3 months. If the patient could not receive an adequate trial of methotrexate, sulfasalazine and hydroxychloroquine due to intolerance, then the above DMARD trial criteria must be met.

²Hydroxychloroquine is based by weight up to 400 mg per day

The requesting physician is required to provide the planned dosing regimen on the request.

The following are the recommended doses for tocilizumab (Actemra) IV and SC for rheumatoid arthritis:

**IV recommended dose:**

- Approval for 4mg/kg/dose once every 4 weeks followed by an increase to 8mg/kg/dose based on clinical response; even for individuals whose body weight is more than 100kg, doses exceeding 800mg per infusion are not recommended

**SC recommended dose:**

For patients < 100 kg weight, starting dose of 162 mg every other week, followed by an increase to every week based on clinical response. For patients at or above 100 kg weight, 162 mg every week.

**Duration of Approval:** 1 Year

**Renewal** will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 joints over the previous year.

For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

**Duration of Approval:** First Renewal – 1 Year, Subsequent Renewals – 5 Years
SUBSTANCE DEPENDENCE

Acamprosate Calcium
Brand(s): Campral
DOSAGE FORM/ STRENGTH: 333 mg tablet

Note: Effective June 29, 2018, Acamprosate is made available as a Limited Use drug on the Ontario Drug Benefit Formulary.

Methadone Compounded Solution
Brand(s):
DOSAGE FORM/ STRENGTH:

Effective September 1, 2014
Reimbursement of Compounded Methadone solution for the treatment of opioid dependence will be considered for patients who meet the following criteria;

Patient has demonstrated that they have experienced a true allergy to both commercially available Methadose formulations (i.e., Methadose 10 mg/mL oral cherry flavoured concentrate AND Methadose 10 mg/mL dye-free, sugar-free, unflavoured oral concentrate).

The request must be accompanied by a completed Health Canada adverse drug reaction form (Canada Vigilance Adverse Reaction Reporting Form) and include a detailed description of the allergic reaction to each Methadose product, a description of the circumstances in which the reactions occurred, and demonstration that the allergy is unlikely to be related to any diluent in which Methadose was mixed, but rather, that it was caused by the excipients within the Methadose formulation.

Naltrexone
Brand(s): Revia
DOSAGE FORM/ STRENGTH: 50 mg tablet

Note: Effective June 29, 2018, Naltrexone is made available as a Limited Use drug on the Ontario Drug Benefit Formulary.
**SYSTEMIC JUVENILE IDEOPATHIC ARTHRITIS**

**Anakinra**
Brand(s): Kineret

**DOSAGE FORM/ STRENGTH:** 100mg/0.67mL pre-filled syringe

For the treatment of systemic juvenile idiopathic arthritis in patients who meet the following criteria:

- Patient must have a diagnosis of sJIA with fever (>38 degrees Celsius) for at least 2 weeks AND at least ONE of the following:
  - rash of systemic JIA
  - serositis (e.g. pericarditis, pleuritis, or peritonitis)
  - lymphadenopathy (e.g. cervical, axillary, inguinal)
  - hepatomegaly
  - splenomegaly

- The physician making the request has ruled out other potential etiologies (e.g. malignancies, serious clinical infections, and other inflammatory or connective tissue diseases); AND

- Age of disease onset is younger than 16 years of age. (Note: the physician must specify age of disease onset in the request); AND

- Systemic corticosteroids cannot be used for at least ONE of the following reasons (please specify name and current dose of corticosteroid, if applicable):
  - The patient is unresponsive and/or refractory to systemic corticosteroids; OR
  - The patient has experienced a systemic reaction (e.g. fever, rash of sJIA, serositis, lymphadenopathy, hepatomegaly or splenomegaly) while on tapering doses of systemic corticosteroids (i.e. the patient is corticosteroid dependent); OR
  - The patient has experienced an adverse drug reaction to a systemic corticosteroid; OR
  - The use of systemic corticosteroids is contraindicated in this patient.

Note: The following requests will undergo external review on a case-by-case basis:

- Patients with Macrophage Activation Syndrome
- Patients who meet initial sJIA criteria and are currently 16 years of age or older
- Patients who meet initial sJIA criteria and are requesting higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)

Dosing: 1-2 mg/kg subcutaneously once daily.
Anakinra

Brand(s): Kineret

DOSAGE FORM/ STRENGTH: 100mg/0.67mL pre-filled syringe

Duration of Approval: 1 Year

Renewal will be considered for patients demonstrating at least a 50% reduction in corticosteroid dose (unless contraindicated, not tolerated, unresponsive or refractory at the time of initial request) and no evidence of active systemic disease. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The following renewal requests will undergo external review:

- Evidence of active systemic disease
- Requests for higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)
- Patient is currently 16 years of age or older

Duration of Approval: 1 Year

Tocilizumab

Brand(s): Actemra

DOSAGE FORM/ STRENGTH: 80 mg / 4 mL, 200 mg / 10 mL, 400 mg / 20 mL

For the treatment of systemic juvenile idiopathic arthritis in patients who meet the following criteria;

- Patient must have a diagnosis of sJIA with fever (>38 degrees Celsius) for at least 2 weeks AND at least ONE of the following:
  - rash of systemic JIA
  - serositis (e.g. pericarditis, pleuritis, or peritonitis)
  - lymphadenopathy (e.g. cervical, axillary, inguinal)
  - hepatomegaly
  - splenomegaly

- The physician has ruled out other potential etiologies (e.g. malignancies, serious clinical infections, and other inflammatory or connective tissue diseases); AND
- Age of disease onset is younger than 16 years of age. (Note: the physician must specify age of disease onset in the request); AND
- Systemic corticosteroids cannot be used for at least ONE of the following reasons (please specify name and current dose of corticosteroid, if applicable):
**Tocilizumab**

**Brand(s): Actemra**

**DOSAGE FORM/ STRENGTH:** 80 mg / 4 mL, 200 mg / 10 mL, 400 mg / 20 mL

- The patient is unresponsive and/or refractory to systemic corticosteroids; OR
- The patient has experienced a systemic reaction (e.g. fever, rash of sJIA, serositis, lymphadenopathy, hepatomegaly or splenomegaly) while on tapering doses of systemic corticosteroids (i.e. the patient is corticosteroid dependent); OR
- The patient has experienced an adverse drug reaction to a systemic corticosteroid; OR
- The use of systemic corticosteroids is contraindicated in this patient.

Note: The following requests will undergo external review on a case-by-case basis:
- Patients with Macrophage Activation Syndrome
- Patients who meet initial sJIA criteria and are currently 16 years of age or older
- Patients who meet initial sJIA criteria and are requesting higher dosing regimens
  (Please provide rationale for the higher dosing regimen with your request)

**Dosing:** For those less than 30 kg, 12 mg/kg IV every 2 weeks

For those greater than or the same as 30 kg 8 mg/kg IV every 2 weeks

**Duration of Approval:** 1 Year

Note: Recommended maximum adult dose is 800mg.

**Renewal** will be considered for patients demonstrating at least a 50% reduction in corticosteroid dose (unless contraindicated, not tolerated, unresponsive or refractory at the time of initial request) and no evidence of active systemic disease. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

The following renewal requests will undergo external review:
- Evidence of active systemic disease
- Requests for higher dosing regimens (Please provide rationale for the higher dosing regimen with your request)

Patient is currently 16 years of age or older

**Duration of Approval:** 1 Year
# JUVENILE SPONDYLOARTHRITIS OR ENTHESIS-RELATED ARTHRITIS

**Etanercept**  
Brand(s): Enbrel  
**DOSAGE FORM/ STRENGTH:** 25mg/vial, 50 mg prefilled syringe for subcutaneous injection  

**Infliximab**  
Brand(s): Remicade  
**DOSAGE FORM/ STRENGTH:** 100 mg/vial

For the treatment of juvenile spondyloarthritis (JSpA) or enthesitis-related arthritis (ERA) in patients who meet the following criteria for either axial or peripheral disease:

### Axial Disease

- Age of disease onset ≤ 16 years; AND
- Low back pain and stiffness for > 3 months that improve with exercise and not relieved by rest; AND
- Failure to respond to or documented intolerance to adequate trials of 2 non-steroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks each; AND
- BASDAI score of ≥ 4 after at least 4 weeks of standard NSAID therapy; AND
- Radiographic evidence of severe active disease by X-ray, CT scan or MRI *

*The details of radiographic reports for severe active disease must provide the following:
- X-ray or CT scan report stating the presence of “SI joint fusion” or “SI joint erosion” OR
- MRI report stating the presence of “inflammation” or “edema” or “erosion” of the SI joint.

Actual radiographic reports must be submitted with the request. If the radiographic reports do not specify the above findings, the request will be reviewed by external medical experts. The radiographic interpretation report from the radiologist or rheumatologist may be submitted along with radiographic report.

The planned dosing regimen for the requested biologic should be provided. The recommended dose for the treatment of JSpA/ERA is as follows:

- Etanercept 0.4mg/kg (max 25 mg) twice weekly or 0.8mg/kg (max 50 mg) once weekly
Etanercept  
Brand(s): Enbrel  
DOSAGE FORM/ STRENGTH: 25mg/vial, 50 mg prefilled syringe for subcutaneous injection  

Infliximab  
Brand(s): Remicade  
DOSAGE FORM/ STRENGTH: 100 mg/vial

- Infliximab: 5mg/kg/dose at 0, 2 and 6 weeks followed by maintenance therapy of up to 5mg/kg/dose every 6-8 weeks

Higher dosing will undergo external review.

Duration of Approval: 1 Year

Renewal will be considered for patients with objective evidence of at least a 50% reduction in BASDAI score or ≥ 2 absolute point reduction in BASDAI score. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Peripheral Disease
- Age of disease onset ≤ 16 years; and  
- Patients must have a minimum of 3 (three) swollen joints and 5 (five) active joints; and  
- Evidence of enthesitis in at least 2 locations; and  
- Failure to respond to or documented intolerance to trials of 2 non-steroidal anti-inflammatory drugs (NSAIDs) for at least 4 weeks each AND at least one of either sulfasalazine (50 mg/kg/day-maximum 2 grams per day) or methotrexate (15mg/m² per week subcutaneously-maximum 25 mg per week) for 3 months.

Renewal will be considered for patients with objective evidence of at least a 20% reduction in swollen joint count and a minimum of improvement in 2 swollen joints over the previous year. There should also be an improvement in number of enthesitis sites. For renewals beyond the second year, objective evidence of preservation of treatment effect must be provided.

Requests that do not meet these criteria will undergo external review.

Duration of Approval: 1 Year
SPASTICITY TREATMENTS

**Tizanidine**
Brand(s): Zanaflex
DOSAGE FORM/ STRENGTH: 4 mg tablet

For the treatment of spasticity in patients who have failed and/or cannot tolerate at least two of the following available alternatives: baclofen, diazepam and dantrolene.
- Submission must describe the intolerance experienced.

**Duration of Approval:** Lifetime

URINARY ANTISPASMODICS

**Oxybutynin Transdermal System**
Brand(s): Oxytrol
DOSAGE FORM/ STRENGTH: 36 mg transdermal patch (3.9 mg/day system)

The treatment of urinary frequency, urgency or urge incontinence in patients who are unable to take oral treatments (e.g. inability to swallow or who are unable to absorb (e.g. short gut syndrome)).

Adverse effects to oral therapy (e.g. dizziness) are not acceptable.

**Duration of Approval:** 5 Years