

## DRUGS NOT CONSIDERED FOR REIMBURSEMENT THROUGH THE ODB PROGRAM

Drug products are covered under the Ontario Drug Benefit's (ODB) Exceptional Access Program (EAP) based on recommendations and guidelines from the ministry's expert advisory committee, the Committee to Evaluate Drugs (CED). The CED makes recommendations to the Executive Officer (EO) as to whether a drug product should be listed as a Formulary benefit or whether it should be available through the EAP for those who meet specific criteria. Based on a thorough and comprehensive review, the CED may recommend that a drug product for specific indication(s) should not be listed as a Formulary benefit and should not be considered through EAP. The following document provides a summary of selected drug products that were reviewed by CED but were recommended not to be funded through the ODB formulary or the EAP. A brief summary of the rationale for the Committee's decision is provided. Where applicable, a link to more detailed information pertaining to the CED's review and subsequent decision on funding from the Executive Officer has been provided.

This document will be updated on a regular basis to include newly reviewed drugs and indications that are not recommended for funding and, on an "as needed" basis, if any changes are made to the reimbursement status of the drugs in this list. In addition, the ministry is working with the manufacturers to address concerns raised during a review and changes may be made to the recommended criteria and/or listing status.

It should be noted that there are other drugs not listed in this document at this time that may not be considered for reimbursement through the ODB Program.

DRUG NAME	BRANDS	DOSAGE FORM/ STRENGTH	RATIONALE
Alefacept	Amevive	15 mg/0.5 mL intramuscular injection	The CED noted that there are significant concerns regarding the limited efficacy, safety and cost-effectiveness data available for the use of Amevive in the treatment of moderate to severe chronic plaque psoriasis.  There are no data either comparing Amevive to relevant comparators or supporting the efficacy of Amevive in patients who are refractory to standard systemic therapies. The cost-effectiveness of Amevive has not been established. Furthermore, there is a lack of long-term safety data as a higher incidence of skin cancer and serious infections were detected with various regimens.
Atazanavir	Reyataz	300 mg Capsule	The CED noted that the 150 mg and 200 mg formulations of Reyataz are available on the Ontario Drug Benefit Formulary as general benefits and that the per mg cost of the 300 mg capsule does not offer a cost savings compared to the 150 mg or 200 mg formulation.
Butalbital and ASA and caffeine ± codeine	Fiorinal	Plain C½ C¼	The CED has indicated that there is no supportive evidence for the value of these fixed-dose combination products for the symptomatic treatment of pain such as headache, migraine and other neurological discomfort. Since the therapeutic value of butalbital, which is included in these products, has not been substantiated by objective clinical evidence, these drug combinations have no advantage over analgesics in the Ontario Drug Benefit Formulary.

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Calcium acetate	PhosLo	667 mg tablet	The CED completed two reviews of PhosLo for the treatment of hyperphosphatemia in hemodialysis patients and noted that there is no compelling evidence to support therapeutic superiority of PhosLo over standard calcium carbonate in this clinical setting. Furthermore, it was noted that PhosLo is significantly more expensive than standard calcium carbonate.
Chlorpropamide	Generic products available	100 mg and 250 mg tablet	The CED conducted a comprehensive review of the evidence related to treatments for blood glucose control to ensure that reimbursement of diabetes medications reflects current clinical knowledge and data on efficacy, safety, and cost-effectiveness. The committee has reviewed chlorpropamide for the treatment of type 2 diabetes and noted the increased risk of cardiovascular mortality with chlorpropamide, based on the UKPDS 33 study, where systolic and diastolic blood pressure were significantly higher throughout the study in patients assigned to the chlorpropamide group than any other treatment group.
Ciclopirox olamine	Stieprox	1.5% shampoo	Stieprox was reviewed for topical treatment and prophylaxis of dandruff and seborrheic dermatitis. There is little compelling evidence to support increased efficacy of Stieprox in comparison to ketoconazole shampoo (which is available to patients over-the-counter) or other formulary alternatives, including steroid creams and antifungals.
Cinacalcet	Sensipar	30 mg, 60 mg, 90 mg tablet	Sensipar was reviewed for the treatment of secondary hyperparathyroidism in patients with chronic renal disease. The CED noted that while Sensipar has been shown to impact parathyroid hormone and serum calcium levels, there is insufficient evidence to support the therapeutic efficacy of this product in achieving clinically important outcomes such as quality of life, symptomatic bone disease, hospitalizations, cardiovascular disease and mortality when compared to conventional therapy. Furthermore, the cost-effectiveness of Sensipar has not been established.  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/sensipar.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/sensipar.pdf</a>
Collagenase	Santyl	250 units/gram topical ointment	The CED has conducted several reviews of Santyl, an ointment for topical debridement that has been available in North America for over 40 years, and has noted that there is evidence that collagenase is superior to placebo and to autolysis. However, there is a lack of compelling evidence comparing the efficacy of collagenase to non-pharmacological treatments currently used for debridement. Furthermore the cost-effectiveness of Santyl therapy remains unknown.
Cyclosporine	Restasis	0.5% ophthalmic solution	The CED noted that there is a lack of robust evidence to demonstrate the efficacy of cyclosporine ophthalmic solution in the population of patients for which the manufacturer is seeking reimbursement and that currently available evidence demonstrated several methodological flaws that limit the validity and generalizability of the results. Furthermore, the cost is significantly higher than the alternative treatments available for dry eye disease.

DRUG NAME	BRANDS	DOSAGE FORM/ STRENGTH	RATIONALE
Desogestrel and ethinyl estradiol	Linessa	21-day and 28-day packs	The CED noted that Linessa provides no advantage in terms of efficacy, safety, or tolerability to justify its price premium over oral contraceptives listed in the current Formulary.  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/desogestrel.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/desogestrel.pdf</a>
Desvenlafaxine extended release	Pristiq	50 mg and 100 mg tablet	The CED noted the lack of evidence in terms of a head-to-head randomized, controlled trial to demonstrate that desvenlafaxine is at least non-inferior to venlafaxine or any other active comparator at Health Canada approved dosing. Furthermore, there is a price premium that has not been adequately justified as there are many effective anti-depressants on the formulary that are available at a lower cost. Additionally, there are no therapeutic gaps.
Diclofenac sodium	Pennsaid	1.5% topical solution	Pennsaid was reviewed in the treatment of symptoms associated with osteoarthritis of the knee. The CED noted that there is a lack of evidence to demonstrate that Pennsaid provides superior therapeutic efficacy, safety, or cost-effectiveness over currently available alternatives listed on the Formulary.
Donepezil	Aricept RDT	5 mg and 10 mg orally disintegrating tablet	Aricept film-coated tablets are currently listed on the Formulary as a Limited Use (LU) benefit for the symptomatic treatment of patients with mild and moderate dementia of the Alzheimer's type. The CED noted that Alzheimer's patients with severe disease are most likely to have difficulty swallowing and may therefore benefit from Aricept RDT. However, the manufacturer has never made a submission to the Ministry for the use of Aricept RDT in the treatment of severe Alzheimer's disease.  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/donepezil.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/donepezil.pdf</a>
Doxycycline hyclate	Periostat	20mg capsule	The CED noted that although this product has been shown to have efficacy in the treatment of periodontal disease, the manufacturer was unable to demonstrate cost-effectiveness given the significant cost premium over viable clinical alternatives currently available (eg. generic doxycycline).
Dronedarone	Multaq	400 mg tablet	The CED noted that available evidence suggests dronedarone is not superior to amiodarone, which is the current standard of care. The committee also expressed concerns of the safety profile of this agent. Furthermore dronedarone is more costly and the price premium is not justified.

DRUG NAME	BRANDS	DOSAGE FORM/ STRENGTH	RATIONALE
Eletriptan	Relpax	20mg and 40mg tablet	The CED noted that there is a lack of compelling evidence demonstrating that Relpax is therapeutically superior to the other "triptans" that are currently considered for reimbursement via the EAP mechanism (i.e., sumatriptan, almotriptan, naratriptan, and rizatriptan). The cost-effectiveness of Relpax compared to the other triptans has not been clearly established. Additionally, the committee noted that eletriptan, unlike other drugs in this class, is primarily metabolized by the cytochrome P450 (CYP3A4) pathway, thus increasing its potential to cause drug interactions and adverse effects.
Enalapril maleate/ hydrochlorothiazide	Vaseretic	10mg/25mg tablet	The CED noted that there is no published evidence demonstrating that this product is more effective than other ACE inhibitor/thiazide diuretic combination products already listed on the Formulary. It was further noted that Vaseretic is also more expensive than the other formulary products and the sum of the individual single ingredient products (enalapril and hydrochlorothiazide).
Erythromycin and benzoyl peroxide	Benzamycin	3% erythromycin and 5% benzoyl peroxide topical gel	The CED noted that there is no objective evidence demonstrating that Benzamycin is more effective than current formulary alternatives.
Esomeprazole	Nexium	20 mg and 40 mg tablet	The CED noted that there is no compelling evidence demonstrating that Nexium is more effective than the proton-pump inhibitors (PPIs) listed on the Formulary. Several PPIs are listed in the Formulary as Limited Use benefits, and Pariet (rabeprazole) 10mg and 20mg are listed as general benefits.
Etonogestrel and ethinyl estradiol	NuvaRing	Contraceptive vaginal ring	The CED noted there is no significant clinical benefit of NuvaRing versus oral contraceptives. The clinical evidence does not demonstrate any significant differences in the pregnancy rates, rates of adverse events or compliance rates of NuvaRing over oral contraceptives. In addition, Depo-Provera, which is available on the current Formulary as General Benefit, and intrauterine devices (IUD) are available alternatives for patients who are unable to use formulary oral contraceptives. The price premium of NuvaRing over these formulary alternatives has not been justified.
Fentanyl	Duragesic 12	12.5 mcg/hr transdermal patch	The CED noted that Duragesic 12 patches were proportionately more expensive than the higher dose preparations of fentanyl transdermal patches which are currently listed as Limited Use (LU) benefits on the Formulary.  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/fentanyl.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/fentanyl.pdf</a>
Fluticasone propionate	Cutivate	0.05% cream	The CED noted that, in light of the lack of therapeutic or economic advantage compared with other agents in its class, Cutivate has not been shown to provide any additional value to patient care. Also, several other alternatives are available on the formulary.

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Fulvestrant	Faslodex	50 mg/mL prefilled syringe for intramuscular injection	The CED has completed a review of fulvestrant (Faslodex) for the treatment of metastatic breast cancer. In their review, the CED has noted that the current evidence for use of fulvestrant is second- or third-line therapy to anastrozole or exemestane for locally advanced or metastatic hormone receptor positive breast cancer in post-menopausal women. However, there is a lack of evidence demonstrating the use of fulvestrant would delay the need for intravenous chemotherapy and palliative care. As such, the Executive Officer has made the decision to not fund fulvestrant.
Gatifloxacin	Zymar	0.3% ophthalmic solution	The CED noted that in comparative trials, gatifloxacin was not shown to be superior to ofloxacin for the treatment of bacterial conjunctivitis. It was also noted that, since gatifloxacin is dosed every two hours for the first two days of therapy, the risk for patient non-compliance may compromise efficacy. Moreover, it appears that gatifloxacin has a similar side effect profile to ofloxacin. Lastly, gatifloxacin is significantly more expensive than other formulary alternatives with no added therapeutic benefit for this price premium.
Glimepiride	Amaryl	1 mg, 2 mg, and 4 mg tablet	The CED noted that there is insufficient evidence to demonstrate a therapeutic advantage for Amaryl over other oral anti-diabetic agents currently listed on the Formulary. In addition, it was noted that Amaryl is more costly than other alternatives.
Idoxuridine	Herplex D	0.1% topical liquid	The CED has noted that Herplex D appears to have minimal effect in recurrent or primary herpes simplex virus (HSV) on duration of symptoms, new lesion formation, healing time, or risk of subsequent recurrence. It may be associated with complications such as local burning, generalized contact dermatitis, and vulvar carcinoma in situ.
Levonorgestrel and ethinyl estradiol	Seasonale	0.15 mg/0.03 mg tablet	The CED has completed a review of Seasonale for use as a long-term oral contraceptive. While the CED noted that Seasonale is equally efficacious to other oral contraceptives, the CED did note that Seasonale was not associated with increased safety, increased compliance, or improved quality of life versus comparators. In addition, it was noted that there are less costly contraceptives currently on the Formulary. In view of the above, the price premium of Seasonale is not justified.  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/seasonale.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/seasonale.pdf</a>
Levothyroxine sodium	Synthroid	0.137 mg	The CED has reviewed Synthroid 0.137mg tablets and the committee noted that the proposed price for the 0.137mg tablet is significantly higher than other strengths of the same medication. This would translate into a significant overall cost increase when compared to the use of the 0.15mg and 0.125mg tablets alternated daily. Therefore, there appears to be little rationale to justify the significant cost difference.

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Loteprednol	Lotemax	0.5% ophthalmic solution	The CED acknowledged that loteprednol has been shown to have similar efficacy compared to other ophthalmic corticosteroids. However, as there are several ophthalmic corticosteroids already listed on the Formulary, there is no therapeutic gap that is specifically addressed by loteprednol.
Memantine	Ebixa	10 mg tablet	The CED completed a review of Ebixa for the symptomatic treatment of patients with moderate to severe dementia of the Alzheimer's type. It was noted that the evidence currently available fails to establish clinically significant benefits from the use of Ebixa; and there were no demonstrated differences in rates of hospitalization or institutionalization with Ebixa in randomized clinical trials. In addition, the Committee also noted that there are safety concerns regarding the use of Ebixa, as described in the product's monograph.
Methyl aminolevulinate	Metvix	168 mg/g topical cream	The CED noted that Metvix appears to be as effective as cryotherapy, simple excision surgery, or imiquimod for the treatment of primary superficial basal cell carcinoma. The cream must be used in combination with photodynamic therapy (PDT). Several disadvantages were further noted including access to a dermatologist with the special lamp required for this treatment and there were concerns that this would likely incur additional costs for the photodynamic sessions. In addition, the Committee noted that, given some of the limitations identified in the pharmacoeconomic analysis, a cost savings of this treatment over available therapies is unlikely to be realized.
Methylnaltrexone bromide	Relistor	20 mg/mL subcutaneous injection	The CED raised concerns about the clinical relevance of study outcomes provided in the trials submitted by the manufacturer. It was further noted that data is lacking to examine the cost-effectiveness of Relistor in patients who have failed all other alternatives.
Moxifloxacin	Vigamox	0.5% ophthalmic solution	The CED noted that the majority of cases of acute bacterial conjunctivitis resolve spontaneously within 5 days regardless of therapy. It was further noted that current published medical literature did not demonstrate that Vigamox was superior to ciprofloxacin or ofloxacin eye drops, yet was significantly more expensive. The physician is reminded that ofloxacin eye drops are currently listed on the Formulary as a Limited Use (LU) benefit.
Nateglinide	Starlix	60 mg and 120 mg tablet	The CED found that current head to head comparisons between nateglinide and other antidiabetic agents indicate a decreased efficacy compared to glyburide in lowering fasting plasma glucose and is similar in cost to other alternatives such as repaglinide (Gluconorm).
Omalizumab	Xolair	150 mg subcutaneous injection	The CED noted that while there are several upcoming trials that might help to provide additional information to support the efficacy of omalizumab, there remains a lack of evidence to demonstrate the efficacy of omalizumab on other clinically meaningful outcomes such as hospitalizations or emergency department visits. In addition, the Committee noted that there are several limitations in the manufacturer's pharmacoeconomic analysis to substantiate the product's cost-effectiveness.

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Oxybutynin chloride	Ditropan XL	5 mg and 10 mg extended release tablet	A review of the available clinical data demonstrated that Ditropan XL has similar efficacy and adverse effect profiles to regular oxybutynin which is a formulary benefit. Specifically, it was noted that there is a lack of supportive evidence demonstrating that Ditropan XL is better tolerated than regular oxybutynin. The CED is of the opinion that Ditropan XL does not provide an advantage over existing listed formulary alternatives.
	Uromax	10 mg and 15 mg controlled release tablet	The CED noted that there is no convincing evidence to demonstrate that Uromax is therapeutically superior to immediate release (IR) oxybutynin or provides an improved adverse event profile to justify the price premium. It was also noted that the clinical evidence does not demonstrate any significant differences in quality of life between IR oxybutynin and Uromax.
Oxycodone	OxyContin	5 mg slow release tablet	The CED completed multiple reviews of OxyContin 5mg tablets and noted that even in patients who are very sensitive to opioids, the 5mg tablet does not appear to afford a therapeutic advantage over other multiple short-acting and long-acting opioid analgesics currently available on the Formulary. Moreover, it was noted that the price of the 5mg tablet is proportionately more expensive than other OxyContin tablets currently listed on the Formulary (10mg, 20mg, 40mg, and 80mg).  For more information, please go to: <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/oxycodone.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/oxycodone.pdf</a>
Pegaptanib	Macugen	0.3 mg/90 µL intravitreal injection	The CED completed a review of Macugen for the treatment of wet form age-related macular degeneration (AMD). While Macugen has been shown to impact visual acuity, there is insufficient evidence to support the therapeutic efficacy of this product in achieving clinically important outcomes such as quality of life when compared to a sham procedure. In addition, the committee has noted that there are concerns surrounding ophthalmic related adverse events with the use of Macugen and complications related to the intravitreal injection such as endophthalmitis, traumatic cataract, and retinal detachment. Furthermore, the cost-effectiveness of Macugen has not been clearly established.
Pegfilgrastim	Neulasta	10 mg/mL subcutaneous injection	The CED noted that pegfilgrastim is therapeutically equivalent to filgrastim (Neupogen). The Committee also noted that, based on Ontario Drug Benefit utilization data, pegfilgrastim does not provide value-for-money compared to filgrastim.
Pramipexole	Mirapex	0.5 mg tablet	Mirapex 0.25mg, 1mg and 1.5mg strengths are currently listed as General Benefits on the Formulary. The CED noted that the price of the 0.5mg tablet is similar to the price of the 1.0mg tablet and that the 1.0mg tablet is scored and can be split into halves. It was further noted that the 0.5mg tablet is approximately double the price of the 0.25mg tablet. Given the strengths available on the formulary, the CED concluded that there is no cost advantage in reimbursing Mirapex 0.5mg tablets.

DRUG NAME	BRANDS	DOSAGE FORM/ STRENGTH	RATIONALE
Ramipril	Altace	15 mg capsule	<p>The CED noted that multiple strengths of generic ramipril are currently listed as General Benefits in the Formulary. In addition, it was noted that there is no evidence of clinical need or economic advantage to support the inclusion of Altace 15mg in the formulary.</p> <p>For more information, please go to:  <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/ramipril.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/ramipril.pdf</a></p>
Ramipril and felodipine	Altace Plus Felodipine	2.5 mg/2.5 mg and 5mg/5mg tablet	<p>The CED reviewed Altace Plus Felodipine for the treatment of mild to moderate essential hypertension in patients for whom combination therapy is appropriate. The Committee determined that there was no compelling evidence demonstrating superior clinical efficacy, improved compliance or an improved safety profile with the fixed dose combination versus administration of the single agent components together. Moreover, the Committee noted that there is no cost-effective advantage of the fixed-dose combination over the combined use of the individual components. Lastly, the use of individual products allows for the ability to titrate and offers improved flexibility in dosing.</p> <p>For more information, please go to:  <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/ramipril_felodipine.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/ramipril_felodipine.pdf</a></p>
Risedronate	Actonel 75	75 mg tablet	<p>The CED reviewed the pertinent literature for the use of Actonel 75 mg in the prevention and treatment of osteoporosis and noted that there is no evidence that Actonel 75 mg is more efficacious than currently available Formulary alternatives. A clinical study comparing Actonel 75 mg twice monthly to Actonel 5 mg once daily found the two agents demonstrated similar efficacy and adverse event profiles. There is no published data supporting improved compliance with the 75 mg dosage and there is lack of evidence comparing Actonel 75 mg to other agents such as alendronate. Therefore, a clinically relevant comparison with formulary agents is not available.</p>
Risedronate and calcium carbonate	Actonel Plus Calcium	35 mg risedronate sodium and 1250 mg calcium carbonate	<p>This is a combination/compliance package that contains one tablet of risedronate sodium 35mg and six tablets of calcium carbonate 1250mg. The CED noted that there is a lack of evidence to support therapeutic advantage of Actonel Plus Calcium over existing bisphosphonate alternatives on the formulary. It was also noted that Actonel Plus Calcium is significantly more expensive than formulary bisphosphonate alternatives. Furthermore, Actonel is currently listed on the Formulary as General Benefit.</p> <p>For more information, please go to:  <a href="http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/risedronate.pdf">http://www.health.gov.on.ca/english/providers/program/drugs/ced/pdf/risedronate.pdf</a></p>

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Rivastigmine	Exelon Patch 5 Exelon Patch 10	4.6 mg/24 hours and 9.5 mg/24 hours transdermal patch	In the review, the CED noted that there is a small clinical effect for rivastigmine patch versus placebo and no evidence that the patch is more effective than the oral capsules and oral liquid. Furthermore, there is no comparative data for the patch versus other acetylcholine esterase inhibitors. As rivastigmine is indicated only in the treatment of mild to moderate Alzheimer's disease, the CED has expressed concerns of misuse in the treatment of severe Alzheimer's disease.
Rosiglitazone and metformin	Avandamet	1 mg/500 mg, 2 mg/1000 mg, 2 mg/500 mg, 4 mg/1000 mg, 2 mg/500 mg tablet	Avandamet is a combination product containing both rosiglitazone and metformin. The CED noted that there is a lack of clinical evidence to support the therapeutic advantage of fixed-dose combinations. Furthermore, it was noted that the cost of the combination product is not significantly lower than that of the sum of the two single ingredient products at the most commonly prescribed doses.
Sapropterin	Kuvan	100 mg tablet	The CED noted that there is lack of evidence to demonstrate clinically relevant efficacy. Furthermore the price premium of sapropterin is not justified.
Saxagliptin	Onglyza	5 mg tablet	The CED commented that there remain no trials showing clinically important outcomes with saxagliptin and that such studies are ongoing. Given that there is already a DPP-4 inhibitor listed on the Formulary at a lower effective price, there is no therapeutic gap or cost reason to list saxagliptin at this time.
Sitagliptin/metformin	Janumet	50 mg/500 mg 50 mg/850 mg 50 mg/1000 mg	Overall, the CED noted the lack of evidence comparing the fixed-dose combination tablet with its individual components to justify the price premium.
Sodium oxybate	Xyrem	500 mg/mL oral solution	The CED raised concerns around the short-term duration of the submitted trials, the high attrition rates, and the lack of long-term data. Furthermore, it was noted that cost-effectiveness has not been demonstrated.
Sodium Thiosulfate		25% - 0.25 g/mL vials for injection	The CED noted that there is a lack of randomized controlled trials to support the efficacy of sodium thiosulfate in the treatment of calciphylaxis. In addition, the true benefits of sodium thiosulfate are difficult to ascertain since many of the case reports included a number of interventions that may have contributed to the overall effect observed. Furthermore, the cost of sodium thiosulfate is significant and there is no justification for the price premium.

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Solifenacin	Vesicare	5mg and 10mg tablet	The CED found no clinically significant benefits for Vesicare over existing formulary alternatives for the treatment of overactive bladder in adults with symptoms of urge urinary incontinence, urinary urgency, and urinary frequency. It was also noted that there is a lack of evidence assessing the efficacy and safety of Vesicare beyond twelve weeks of use. In addition, the CED expressed concern regarding the potential for this medication to cause serious adverse effects in the elderly, particularly delirium.
Somatropin	Saizen	6 mg cartridge 12 mg cartridge 20 mg cartridge Injection solution	The CED that the data presented did not adequately demonstrate the benefits of these new formats of Saizen. Formats of Saizen that do not require reconstitution are already currently funded by the OPDP. Furthermore, there is no therapeutic gap as there are many growth hormone products currently reimbursed under OPDP.
Telbivudine	Sebivo	600 mg tablet	The CED raised concerns around the lack of evidence supporting clinically relevant outcomes within clinical trials. It was also noted that the true cost-effectiveness of this product is questionable.
Telithromycin	Ketek	400mg tablet	The CED indicated that there is insufficient evidence to demonstrate that this product has any therapeutic advantages over other less expensive formulary alternatives, including macrolide antibiotics. In addition, the Committee has noted that there are safety concerns regarding potential drug interactions involving drug metabolism by the CYP450-3A4 pathway; and, the side effect profile includes vision disturbances which are not part of the profile associated with the macrolide antibiotics currently listed as formulary benefits.
Tolbutamide	Generic products available	500mg tablet	Due to the increased risk of cardiovascular mortality with tolbutamide compared to other equally effective formulary alternatives, the CED recommended that tolbutamide no longer be reimbursed under the Ontario Drug Benefit Program. The CED conducted a comprehensive review of the evidence related to treatments for blood glucose control to ensure that reimbursement of diabetes medications reflects current clinical knowledge and data on efficacy, safety, and cost-effectiveness. The committee reviewed the use of tolbutamide for the treatment of type 2 diabetes and noted that this agent has been associated with an increased risk of cardiovascular mortality.
Teriparatide	Forteo	250µG/mL subcutaneous injection	The CED completed multiple reviews of Forteo for the treatment of osteoporosis. Given the large cost differential between teriparatide and anti-resorptive therapies and the current clinical information available, it was felt that teriparatide has not been shown to be cost-effective for the first-line treatment of osteoporosis. In addition, the CED is unaware of any evidence to support Forteo's efficacy for patients who continue to fracture despite adequate anti-resorptive therapy. It was felt that this evidence was required to determine whether a switch to teriparatide would offer any advantage over continued bisphosphonate treatment in these patients.

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Testosterone	Androderm	24.3 mg transdermal patch	The CED noted that there is a lack of evidence demonstrating dose proportional bioequivalence between the 24.3mg patch and the 12.2mg patch formulation, which is currently available as a Limited Use (LU) benefit on the Formulary.
Tramadol	Ralivia	100 mg, 200 mg, and 300 mg extended release tablet	The CED has reviewed Ralivia and noted that there is no evidence that tramadol offers a therapeutic advantage over existing formulary alternatives. The majority of clinical studies compared Ralivia to placebo and there is minimal data comparing the drug to long-acting narcotics. Therefore, a clinically relevant comparison with many formulary alternatives is not available.
	Tridural	100 mg, 200 mg, and 300 mg extended release tablet	The CED has reviewed Tridural and noted that there is no evidence that tramadol offers a therapeutic advantage over existing formulary alternatives. Clinical trials with tramadol are of short-duration and there's concern with lack of long-term safety data as patients with chronic pain would be taking it indefinitely. Tridural has not been shown to be more efficacious or safer than alternative analgesics to justify its price premium.
	Zytram XL	150 mg, 200 mg, 300 mg, and 400 mg controlled release tablet	The CED noted that there is no evidence that tramadol offers a therapeutic advantage over formulary alternatives, including a codeine/acetaminophen combination and nonsteroidal anti-inflammatory drugs (NSAIDs). Zytram XL was not compared to long-acting narcotics in clinical trials and therefore a clinically relevant comparison with many formulary long-acting narcotic alternatives is not available. Furthermore, there is a lack of clinical safety and efficacy data to support the long-term use of Zytram XL beyond 28 days.
Tropium chloride	Sanctura XR	60 mg extended release capsule	The CED felt that there was no clear advantage of tropium XR over currently funded anticholinergics. As well the advantages have not been proven in good-quality clinical trials and remain theoretical. In addition, cost savings may be negated with the availability of generic tolterodine.
Valsartan	Diovan	40 mg tablet	<p>The CED has reviewed Diovan 40mg tablets to be used as an initial dosing regimen for the reduction of cardiovascular mortality in patients with signs and symptoms of left ventricular dysfunction in conjunction with acute myocardial infarction, when the use of an angiotensin converting enzyme (ACE) inhibitor is not appropriate. The Committee determined that there is no compelling evidence from clinical trials demonstrating clinical superiority of Diovan versus an ACE inhibitor for this indication. Moreover, the Committee noted that there is no cost-effective advantage for Diovan 40mg tablets over alternative formulary agents.</p> <p>Please note that Diovan 80mg, 160mg, and 320mg as well as Diovan-HCT 80mg/12.5mg, 160mg/12.5mg, and 150mg/25mg are listed on the Formulary as General Benefit.</p>

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Verapamil and trandolapril	Tarka	2/240 mg and 4/240 mg tablet	The CED noted that it offers no additional therapeutic value over available Formulary alternatives for the treatment of hypertension. There were no studies that demonstrate benefit in outcomes (i.e. mortality and cardiovascular events) from treatment with Tarka. Both verapamil and trandolapril are currently listed on the Formulary as single agents. Furthermore, there are other more appropriate combination products available on the market that are less expensive than Tarka.