

Frequently Asked Questions for Health Care Providers: Hepatitis C Drug Products

1. What hepatitis C drug products are being funded?

Effective **February 28, 2017**, the following hepatitis C drug products will be added to the Ontario Drug Benefit (ODB) Program for eligible ODB recipients for the treatment of hepatitis C as Limited Use (LU) benefits:

- Harvoni (ledipasvir/sofosbuvir)
- Sovaldi (sofosbuvir)
- Epclusa (sofosbuvir/velpatasvir)
- Zepatier (elbasvir/grazoprevir)
- Daklinza (daclatasvir)
- Sunvepra (asunaprevir)
- Ibavyr (ribavirin)

2. What are the Limited Use (LU) criteria for these Hepatitis C drug products?

The specific LU criteria and approved regimens differ for individual drug products. The following summary is provided for your information but health care providers are advised to refer to the Ontario Drug Benefit Program's e-formulary for specific criteria related to each hepatitis C drug product.

Health care professionals are advised to refer to the product monograph and prescribing guidelines for appropriate use of the drug product, including use in special populations.

Harvoni (ledipasvir – sofosbuvir)

For treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C genotype 1; 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
- Fibrosis² stage of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 (Metavir scale or equivalent) and at least one of the following;

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Post organ transplant (may include liver and/or non-liver organ transplant)
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs
- Woman of childbearing age who is planning to get pregnant within the next 12 months

Treatment regimens for Harvoni (ledipasvir-sofosbuvir):

1. Treatment-naïve, non-cirrhotic, recent quantitative hepatitis C viral load < 6 M IU/mL
Approved duration: 8 weeks
2. Treatment-naïve, non-cirrhotic, viral load ≥ 6 M IU/mL; or treatment-naïve, cirrhotic⁵; or treatment-experienced¹ non-cirrhotic
Approved duration: 12 weeks
3. Treatment-experienced, cirrhotic
Approved duration: 24 weeks
4. Treatment-naïve and treatment-experienced¹ liver transplant recipients without cirrhosis, or with compensated cirrhosis⁵
Approved regimen: 12 weeks in combination with Ribavirin (RBV)

5. Treatment-naïve and treatment-experienced¹ with decompensated cirrhosis⁵

Approved regimen: 12 weeks in combination with Ribavirin (RBV)

Notes:

1. Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.
2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.
4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) < 60 mL/min/1.73 m² for ≥3 months. (Please refer to the product monograph for *Harvoni* in patients with severe renal impairment.)
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A [i.e. Score 5 to 6]) and decompensated cirrhosis (Child-Turcotte-Pugh B or C [i.e. Score 7 or above])
6. 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.

Sovaldi (Sofosbuvir)

In combination with ribavirin or daclatasvir or both for treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C genotype 2 or genotype 3; 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
- Fibrosis² stage of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 (Metavir scale or equivalent) and at least one of the following:

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Post organ transplant (may include liver and/or non-liver organ transplant)
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs
- Woman of childbearing age who is planning to get pregnant within the next 12 months

For patients who meet the eligibility criteria for sofosbuvir (Sovaldi), clinicians are encouraged to choose sofosbuvir/velpatasvir (Epclusa) or sofosbuvir in combination with daclatasvir (Daklinza) as one of the preferred therapeutic options over sofosbuvir with ribavirin regimens for treatment genotype 2 or 3 patients only. This recommendation is based on evidence that Epclusa or Daklinza in combination with sofosbuvir offers advantages in some patient populations, including potentially higher SVR rates and a shorter course of therapy for genotype 3 infections.

Treatment regimens for Sovaldi (Sofosbuvir) for genotype 2:

1. Treatment-naïve or treatment-experienced¹ genotype 2:
Approved regimen: 12 weeks in combination with Ribavirin (RBV)

Treatment regimens for Sovaldi (Sofosbuvir) for genotype 3:

1. Treatment-naïve or treatment-experienced¹ adult patients without cirrhosis
Approved regimens:
12 weeks with daclatasvir (Daklinza) OR
24 weeks in combination with Ribavirin (RBV)
2. Treatment-naïve or treatment-experienced¹ adult patients with compensated or decompensated cirrhosis.
Approved regimens:
12 weeks with Daclatasvir (Daklinza) and Ribavirin OR
24 weeks in combination with Ribavirin (RBV)

3. Treatment-naïve or treatment-experienced¹ adult patients post-liver transplant:

Approved regimen:

12 weeks with Daclatasvir (Daklinza) and Ribavirin (RBV) OR

24 weeks in combination with Ribavirin (RBV)

Notes:

1. Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.
2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.
4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥3 month. (Please refer to the prescribing information for *Sovaldi* in patients with severe renal impairment.)
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A [i.e. Score 5 to 6]) and decompensated cirrhosis (Child-Turcotte-Pugh B or C [i.e. Score 7 or above])
6. Combination therapy with Zepatier (elbasvir/grazoprevir) will not be considered for funding.
7. 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.

Epclusa (sofosbuvir – velpatasvir)

For treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes; 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
- Fibrosis² stage of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 and at least one of the following:

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Post organ transplant (may include liver and non-liver)
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs
- Woman of childbearing age who is planning to get pregnant within the next 12 months

Treatment regimens for Eplclusa (sofosbuvir-velpatasvir):

1. Treatment-naïve or treatment-experienced¹ non-cirrhotic or compensated cirrhosis⁵
Approved duration: 12 weeks
2. Treatment-naïve or treatment-experienced¹ patients with decompensated cirrhosis⁵
Approved regimen: 12 weeks in combination with Ribavirin (RBV)

Notes:

1. Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.
2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.

4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥ 3 month. (Please refer to the prescribing information for *Epclusa* in patients with severe renal disease.)
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A [i.e. Score 5 to 6]) and decompensated cirrhosis (Child-Turcotte-Pugh B or C [i.e. Score 7 or above])
6. 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.

Zepatier (elbasvir – grazoprevir)

For treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C genotype 1 or genotype 4; 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
- Fibrosis² stage of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 and at least one of the following poor prognostic factors:

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs
- Woman of childbearing age who is planning to get pregnant within the next 12 months

Treatment regimens for Zepatier (elbasvir-grazoprevir) for genotype 1:

1. Treatment-naïve¹ with or without compensated cirrhosis⁵

Approved duration: 12 weeks

Note: As approved by Health Canada, **8 weeks** may be considered in treatment-naïve genotype 1b patients without significant fibrosis or cirrhosis as determined by liver biopsy (i.e., Metavir F0-F2) or by non-invasive tests.

2. Treatment-experienced¹ genotype 1b patients and genotype 1a relapsers, with or without compensated cirrhosis⁵

Approved duration: 12 weeks

3. Treatment-experienced¹ genotype 1a who have had on-treatment virologic failures⁶

Approved regimen: 16 weeks in combination with Ribavirin (RBV)

Treatment regimens for Zepatier (elbasvir-grazoprevir) for genotype 4:

1. Treatment-naïve patients with or without compensated cirrhosis⁵

Approved duration: 12 weeks

2. Treatment-experienced¹ relapsers with or without compensated cirrhosis⁵

Approved duration: 12 weeks

3. Treatment-experienced¹ genotype 4 who have had on-treatment virologic failures⁶

Approved regimen: 16 weeks in combination with Ribavirin (RBV)

Notes:

1. Treatment-experienced for patients with *genotype 1* is defined as patients who have been previously treated with a pegylated interferon + ribavirin regimen or a protease inhibitor + pegylated interferon + ribavirin regimen and have not experienced adequate response.

Treatment-experienced for patients with *genotype 4* is defined as patients who have been previously treated with a pegylated interferon + ribavirin regimen and have not experienced adequate response.

2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.

4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥ 3 month. (Please refer to the prescribing information for *Zepatier* in patients with severe renal disease.)
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A) [i.e. Score 5-6]).
6. On-treatment virologic failures are patients who have had a null response, partial response, virologic breakthrough or rebound, or intolerance to prior treatment.
7. Combination therapy with Sovaldi (sofosbuvir) will not be considered for funding for any genotypes.
8. 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.

Sunvepra (asunaprevir)

For use as combination treatment with daclatasivir (Daklinza) for treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C infection with genotype 1b; AND
- Two laboratory confirmed quantitative HCV RNA values taken at least 6 months apart as confirmation of chronicity of infection. One value must be within the last 6 months while the first level may be at the time of the initial diagnosis; AND
- Fibrosis stage² of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 and at least one of the following:

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Post organ transplant (may include liver and/or non-liver organ transplant)
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by the National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs

- Woman of childbearing age who is planning to get pregnant within the next 12 months

Treatment regimens for Sunvepra (asunaprevir) for genotype 1b:

Treatment-naïve or treatment-experienced¹ adult patients, with or without compensated cirrhosis⁵

Approval regimen: 24 weeks in combination with daclatasvir (Daklinza)

Notes:

1. Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.
2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.
4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥3 months.
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A) (Score 5 to 6)
6. 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.

Daklinza (daclatasvir)

For use as combination therapy with asunaprevir (Sunvepra) or Sofosbuvir (Sovaldi) for treatment naïve or treatment-experienced¹ adult patients with chronic hepatitis C 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
- Laboratory confirmed hepatitis C infection with genotype 1b or genotype 3; AND
- Two laboratory confirmed quantitative HCV RNA values taken at least 6 months apart as confirmation of chronicity of infection. One value must be within the last 6 months while the first level may be at the time of the initial diagnosis; AND

- Fibrosis stage² of F2 or greater (Metavir scale or equivalent)

OR

Fibrosis stage less than F2 and at least one of the following;

- Co-infection with human immunodeficiency virus (HIV) or hepatitis B virus
- Co-existent liver disease with diagnostic evidence of fatty liver disease (Example: non-alcoholic steatohepatitis [NASH])
- Post organ transplant (may include liver and/or non-liver organ transplant)
- Extra-hepatic³ manifestations
- Chronic kidney disease⁴ stage 3, 4 or 5 as defined by the National Kidney Foundation Kidney Disease outcomes Quality Initiative (K/DOQI)
- Diabetes receiving treatment with anti-diabetic drugs
- Woman of childbearing age who is planning to get pregnant within the next 12 months

Treatment regimens for daclatasvir (Daklinza) for genotype 1b:

Treatment-naive or treatment-experienced¹ adult patients, with or without compensated cirrhosis⁵

Approved regimen: 24 weeks in combination with a asunaprevir (Sunvepra)

Treatment regimens for daclatasvir (Daklinza) for genotype 3:

1. Treatment-naive or treatment-experienced¹ adult patients without cirrhosis

Approved regimen: 12 weeks in combination with Sofosbuvir

2. Treatment-naive or treatment-experienced¹ adult patients with compensated or decompensated cirrhosis.

Approved regimen: 12 weeks in combination with Sofosbuvir and Ribavirin (RBV)

3. Treatment-naive or treatment-experienced¹ adult patients post-liver transplant:

Approved regimen: 12 weeks in combination with Sofosbuvir and Ribavirin (RBV)

Notes:

1. Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing an HCV protease inhibitor.

2. Acceptable methods for the measurement of fibrosis score include liver biopsy, transient elastography (FibroScan®), fibrotest, serum biomarker panels (such as AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score) either alone or in combination.
3. Extra-hepatic manifestation include but not limited to: symptomatic vasculitis associated with HCV-related mixed cryoglobulinaemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, Lichen planus, and glomerulonephritis.
4. Chronic kidney disease stage 3, 4 or 5 to include patients with glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥3 months.
5. Treatment may be considered for patients with compensated cirrhosis (Child-Turcotte-Pugh A [i.e. Score 5 to 6]) and decompensated cirrhosis (Child-Turcotte-Pugh B or C [i.e. Score 7 or above])
6. 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.

Ribavirin (Ibavyr)

For use within a Ministry-approved and funded combination therapy regimen for the treatment of chronic hepatitis C according to specific eligibility criteria.

The regimen for the use of ribavirin must comply with the criteria for funding of the hepatitis C regimen in which it is being administered and the requesting physician is a hepatologist, gastroenterologist or an infectious disease specialist, or otherwise experienced in treating hepatitis C.

3. Is funding available for patients who have experienced failure or re-infection after a prior course of direct-acting antiviral therapy?

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 (EAP).

4. Will there be consideration of prior funded products such as simeprevir (Galexos), pegylated interferon and ribavirin, or ombitasvir/paritaprevir/ritonavir (Holkira) through the Exceptional Access Program?

The reimbursed products and regimens represent very effective therapies that provide the best value for the treatment of hepatitis C.

All interferon-based treatments for the treatment of hepatitis C will no longer be available on the Canadian market by the fall of 2017, and as such, previously funded treatment regimens for hepatitis C that include interferon injections will no longer be funded. This includes sovaldi triple therapy regimens and Galexos triple therapy regimens for genotype 1 infection. Additionally, Holkira will continue to be considered on a case-by-case basis through the Exceptional Access Program in circumstances where formulary funded alternatives are deemed to be inappropriate.

5. What should I do if my patient has started on a regimen that was approved through the EAP?

Requests that have an existing approval from the EAP will continue to be funded until the end of the approval duration.

Health care providers should ensure that patients continue to use the approved regimen to completion. Note that requests for retreatment will require an application to the EAP for consideration on a case-by-case basis.

6. When will treatment criteria be expanded for all fibrosis scores?

The criteria for coverage of hepatitis C treatments is being expanded in a phased approach. Coverage will be further extended to all patients regardless of severity of disease or genotype within the next 12 months.

7. How should pharmacies submit claims for hepatitis C drug products?

Pharmacies should submit claims using the drug identification number (DIN) of the product and the appropriate Reason for Use code.

If appropriate, please refer to the additional ministry materials on claim submission located on the EO Communications webpage at:

www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/notices/exec_office_20151113.pdf

www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/notices/fq_exec_office_20151113_1.pdf

For pharmacies:

Please call ODB Pharmacy Help Desk at: 1-800-668-6641

For all other Health Care Providers and the Public:

Please call ServiceOntario, InfoLine at 1-866-532-3161 TTY 1-800-387-5559. In Toronto, TTY 416-327-4282.