Government of Saskatchewan

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SASKATCHEWAN FORMULARY BULLETIN

Update to the 62nd Edition of the Saskatchewan Formulary

Related Information for Prescribers:

- Only prescribers who have completed the hepatitis C prescriber agreement and become Designated Prescribers may submit hepatitis C EDS applications for hepatitis C medications.
- Prescribers interested in becoming a Designated Prescriber can contact the Drug Plan and Extended Benefits Branch at 306-787-8744 or 1-800-667-2549 or dp.sys.support@health.gov.sk.ca to receive a copy of the prescriber agreement.
- Designated Prescribers are asked to complete the Hepatitis C therapy – EDS Application Form for each patient and return it to the Drug Plan for assessment.
- Designated Prescribers may indicate on the Hepatitis C therapy – EDS Application Form if direct observed therapy or DOT is recommended for their patient.

Updated hepatitis C Exception Drug Status (EDS) Listings effective April 1, 2017 according to the following criteria:

- **Ledipasvir/sofosbuvir, tablet, 90mg/400mg (Harvoni-GSI)**

  For use as monotherapy or as combination therapy with ribavirin for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist, or an infectious disease specialist, or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND
  - Laboratory-confirmed hepatitis C genotype 1; AND
  - Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
  - Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
    Fibrosis[2] stage less than F2 and at least one of the following:
    - Co-infection with HIV or hepatitis B virus
    - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)

- Post-organ transplant
- Extra-hepatic[3] manifestations
- Chronic kidney disease[4] stage 3, 4, or 5
- Diabetes treated with anti-diabetic drugs
- Woman of childbearing age who is planning pregnancy, or may become pregnant within the next 12 months

Treatment regimens reimbursed:

Patient Population		**Treatment Regimen and Duration**
Genotype 1	Treatment-naïve, non-cirrhotic, viral load < 6M IU/mL	8 weeks OR 12 weeks*
	Treatment-naïve, non-cirrhotic, viral load ≥ 6M IU/mL OR Treatment-naïve, cirrhotic[5] OR Treatment-experienced[1], non-cirrhotic	12 weeks
	Treatment-naïve or treatment-experienced[1] with decompensated cirrhosis[5]	12 weeks in combination with ribavirin
	Treatment-naïve or treatment-experienced[1] liver transplant recipients without cirrhosis or with compensated cirrhosis[5]	12 weeks in combination with ribavirin
	Treatment-experienced[1] , cirrhotic[5]	24 weeks

**For this population cohort, evidence has shown that the SVR rates for the 8-week and 12-week treatment regimens are similar. Treatment regimens of up to 12 weeks are recognized as a Health Canada approved treatment option. Patients may be considered for 12 weeks of coverage if they have borderline or severe fibrosis (F3-F4) or if they are co-infected with HIV.*

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis and may include combination therapy with products from different manufacturers.

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

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least three months.

[5] Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score = A (score 5-6), and decompensated cirrhosis is defined as cirrhosis with a Child Pugh Score = B or C (score 7 or above).

- **sofosbuvir, tablet, 400mg (Sovaldi-GSI)**

  For use as combination therapy with ribavirin or daclatasvir or both for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND
  - Laboratory-confirmed hepatitis C genotype 2 or 3; AND
  - Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
  - Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
    Fibrosis[2] stage less than F2 and at least one of the following:
    - Co-infection with HIV or hepatitis B virus
    - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)
    - Post-organ transplant
    - Extra-hepatic[3] manifestations
    - Chronic kidney disease[4] stage 3, 4, or 5
    - Diabetes treated with anti-diabetic drugs
    - Woman of childbearing age who is planning pregnancy or may become 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 of 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 reimbursed*:

Patient Population		**Treatment Regimen and Duration**
Genotype 2	Treatment-naïve or treatment-experienced[1]	12 weeks in combination with ribavirin

Genotype 3	Treatment-naïve or treatment-experienced[1] without cirrhosis	12 weeks in combination with daclatasvir OR 24 weeks in combination with ribavirin
	Treatment-naïve or treatment-experienced[1] with compensated or decompensated cirrhosis[5]	12 weeks in combination with daclatasvir and ribavirin OR 24 weeks in combination with ribavirin
	Treatment-naïve or treatment-experienced[1] post liver transplant	12 weeks in combination with daclatasvir and ribavirin

**Combination therapy with elbasvir/grazoprevir (Zepatier) will not be considered for funding.*

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis and may include combination therapy with products from different manufacturers.

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

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least three months.

[5] Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score = A (score 5-6), and decompensated cirrhosis is defined as cirrhosis with a Child Pugh Score = B or C (score 7 or above).

New hepatitis C Exception Drug Status (EDS) listings effective April 1, 2017 according to the following criteria:

- **asunaprevir, softgel, 100mg (Sunvepra-BMY)**

  For use as combination therapy with daclatasvir for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND
  - Laboratory-confirmed hepatitis C genotype 1b; AND
  - Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
  - Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
    Fibrosis[2] stage less than F2 and at least one of the following:
    - Co-infection with HIV or hepatitis B virus
    - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)
    - Post-organ transplant
    - Extra-hepatic[3] manifestations
    - Chronic kidney disease[4] stage 3, 4, or 5
    - Diabetes treated with anti-diabetic drugs
    - Woman of childbearing age who is planning pregnancy, or may become pregnant within the next 12 months

Treatment regimens reimbursed:

Patient Population		Treatment Regimen and Duration
Genotype 1b	Treatment-naïve or treatment-experienced[1] with or without compensated cirrhosis[5]	24 weeks in combination with daclatasvir

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis, and may include combination therapy with products from different manufacturers.

[1] Treatment-experienced is defined as those who have failed prior therapy with an interferon-based regimen,.

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least three months.

[5] Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score = A (score 5-6), and decompensated cirrhosis is defined as cirrhosis with a Child Pugh Score = B or C (score 7 or above).

- **daclatasvir, tablet, 30mg, 60mg (Daklinza-BMY)**

  For use as combination therapy with asunaprevir or sofosbuvir for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND

- Laboratory-confirmed hepatitis C genotype 1b or 3; AND
- Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
- Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
  Fibrosis[2] stage less than F2 and at least one of the following:
  - Co-infection with HIV or hepatitis B virus
  - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)
  - Post-organ transplant
  - Extra-hepatic[3] manifestations
  - Chronic kidney disease[4] stage 3, 4, or 5
  - Diabetes treated with anti-diabetic drugs
  - Woman of childbearing age who is planning pregnancy, or may become pregnant within the next 12 months

Treatment regimens reimbursed:

Patient Population		**Treatment Regimen and Duration**
Genotype 1b	Treatment-naïve or treatment-experienced[1] with or without compensated cirrhosis[5]	24 weeks in combination with asunaprevir
Genotype 3	Treatment-naïve or treatment-experienced[1] without cirrhosis	12 weeks in combination with sofosbuvir
	Treatment-naïve or treatment-experienced[1] with compensated or decompensated cirrhosis[5]	12 weeks in combination with sofosbuvir and ribavirin
	Treatment-naïve or treatment-experienced[1] post-liver transplant	12 weeks in combination with sofosbuvir and ribavirin

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis, and may include combination therapy with products from different manufacturers.

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

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least 3 months.

[5] Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score = A (score 5-6), and decompensated cirrhosis is defined as cirrhosis with a Child Pugh Score = B or C (score 7 or above).

- **sofosbuvir/velpatasvir, 400mg/100mg tablet (Epclusa-GSI)**

  For use as monotherapy or combination with ribavirin for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND
  - Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6, or mixed genotypes; AND
  - Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
  - Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
    Fibrosis[2] stage less than F2 and at least one of the following:
    - Co-infection with HIV or hepatitis B virus
    - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)
    - Post-organ transplant
    - Extra-hepatic[3] manifestations
    - Chronic kidney disease[4] stage 3, 4, or 5
    - Diabetes treated with anti-diabetic drugs
    - Woman of childbearing age who is planning pregnancy, or may become pregnant within the next 12 months

Treatment regimens reimbursed:

Patient Population		**Treatment Regimen and Duration**
All HCV genotypes	Treatment-naïve or treatment-experienced[1] without cirrhosis, or with compensated cirrhosis[5]	12 weeks
	Treatment-naïve or treatment-experienced[1] with decompensated cirrhosis[5]	12 weeks in combination with ribavirin

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis and may include combination therapy with products from different manufacturers.

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

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least three months.

[5] Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score = A (score 5-6), and decompensated cirrhosis is defined as cirrhosis with a Child Pugh Score = B or C (score 7 or above).

- **elbasvir/grazoprevir, tablet, 50mg/100mg (Zepatier-MRK)**

  For use as monotherapy or combination therapy with ribavirin for treatment-naïve or treatment-experienced[1] adult patients with chronic hepatitis C infection according to the following criteria:
  - Treatment is prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan; AND
  - Laboratory-confirmed hepatitis C genotype 1 or 4; AND
  - Laboratory-confirmed quantitative HCV RNA value within the last six months; AND
  - Fibrosis[2] stage of F2 or greater (Metavir scale or equivalent), OR
    Fibrosis[2] stage less than F2 and at least one of the following:
    - Co-infection with HIV or hepatitis B virus
    - Co-existent liver disease with diagnostic evidence of fatty liver disease (e.g. non-alcoholic steatohepatitis)
    - Extra-hepatic[3] manifestations
    - Chronic kidney disease[4] stage 3, 4, or 5
    - Diabetes treated with anti-diabetic drugs
    - Woman of childbearing age who is planning pregnancy, or may become pregnant within the next 12 months

  Treatment regimens reimbursed*:

Patient Population		**Treatment Regimen and Duration**
Genotype 1	Treatment-naïve without cirrhosis, or with compensated cirrhosis[5]	12 weeks**
	Treatment-experienced[1] relapsers without cirrhosis, or with compensated cirrhosis[5]	12 weeks
	Treatment-experienced[1] genotype 1b with null response, partial response, virologic breakthrough or rebound, or intolerance to prior treatment	12 weeks
	Treatment-experienced[1] genotype 1a with null response, partial response, virologic breakthrough or rebound, or intolerance to prior treatment	16 weeks in combination with ribavirin

Genotype 4	Treatment-naïve without cirrhosis, or with compensated cirrhosis[5]	12 weeks
	Treatment-experienced[1] relapsers without cirrhosis, or with compensated cirrhosis[5]	12 weeks
	Treatment-experienced[1] with null response, partial response, virologic breakthrough or rebound, or intolerance to prior treatment	16 weeks in combination with ribavirin

**Combination therapy with sofosbuvir (Sovaldi) will not be considered for funding for any genotypes.*

***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.*

Note: 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.

Exceptional case-by-case consideration: Retreatment for direct-acting antiviral failures may be considered on a case-by-case basis, and may include combination therapy with products from different manufacturers.

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

[2] Acceptable methods for measuring fibrosis score include: liver biopsy, transient elastography (FibroScan®), FibroTest and serum biomarker panels (e.g. AST-to-Platelet Ratio Index (APRI) or Fibrosis-4 (FIB-4) score).

[3] Extra-hepatic manifestation may include: symptomatic vasculitis associated with HCV-related mixed cryoglobulinemia, HCV immune complex-related nephropathy and non-Hodgkin B cell lymphoma, porphyria cutanea tarda, lichen planus, and glomerulonephritis.

[4] As defined by National Kidney Foundation Kidney Disease Outcomes Quality Initiative, chronic kidney disease stages 3, 4, or 5 include patients with glomerular filtration rate less than 60 mL/min/1.73m^2 for at least three months.

[5] Treatment may be considered for patients with compensated cirrhosis, defined as cirrhosis with a Child Pugh Score = A (score 5-6).

Updated Exception Drug Status (EDS) Criteria for Holkira-Pak:

- **ombitasvir/paritaprevir/ritonavir and dasabuvir, tablet, 12.5mg/75mg/50mg and 250mg (Holkira Pak-ABV)**

  This medication will only be considered for patients in whom the other listed oral hepatitis C treatment alternatives are not appropriate. Requests for this medication should provide details of why the listed alternatives are not appropriate as well as indicating how the patient meets the medical criteria below.

  For treatment-naïve and treatment-experienced adult patients with chronic hepatitis C genotype 1 infection, with compensated liver disease, (including compensated cirrhosis)[1] according to the following criteria:

  - Prescribed by a hepatologist, gastroenterologist or an infectious disease specialist or other physician experienced in treating hepatitis C as determined by the Drug Plan
  - Lab-confirmed hepatitis C genotype 1, subtype 1a and 1b required
  - Patient has a quantitative HCV RNA value within the last 6 months
  - Fibrosis stage F2 or greater (Metavir scale or equivalent)

  Duration of therapy reimbursed:

Genotype 1 Patient Population	**Duration of therapy**
Treatment naïve and experienced Genotype 1b, non-cirrhotic	12 weeks
Treatment naïve and experienced Genotype 1a, non-cirrhotic	12 weeks in combination with RBV
Treatment naïve and experienced Genotype1b, cirrhotic	12 weeks in combination with RBV
Treatment naïve and experienced (prior relapsers and prior partial responders) Genotype 1a, cirrhotic	12 weeks in combination with RBV
Treatment experienced Genotype 1a, with cirrhosis, and who have had a previous null response to pegIFN and RBV	24 weeks in combination with RBV

Exclusion criteria:

- Patients currently being treated with another HCV antiviral agent
- Patients who have received a previous trial of Holkira Pak (re-treatment requests will **NOT** be considered)
- Decompensated patients
- No funding for other Genotypes except as noted in the above funding criteria for Genotype 1
- Patients who have received previous NS3/4A protease inhibitor-based regimens (i.e. boceprevir, telaprevir, and simeprevir-based regimens)
- Patients who have received previous sofosbuvir-based regimens (i.e. including ledispasvir/sofosbuvir)

NOTES:

1. Compensated cirrhosis is defined as cirrhosis with a Child Pugh Score =A (5-6).
2. Treatment experienced patients are defined as those who have previously been treated with PegINF/RBV and did NOT receive adequate response.
3. HIV-HCV co-infected patients with Genotype 1 may be considered as per criteria listed above.

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