MEDICATION POLICY

Generic Name: Elbasvir/Grazoprevir

Therapeutic Class or Brand Name: Zepatier™

Applicable Drugs (if Therapeutic Class)**:** N/A

Date of Origin: 2/13/16 **Date Last Reviewed/Revised:** 04/06/2018

GPI Code: 1235990230

Prior Authorization Criteria (may be considered medically necessary when criteria I through VIII are met):

I. Documented diagnosis of chronic hepatitis C (CHC) genotypes 1, 3, or 4 infection.

II. Documentation that patient meets ONE of the following criteria A, B, or C:

- A. Has a Metavir score of F3 (advanced fibrosis) or F4 (compensated cirrhosis).
- B. Is post-liver transplant.
- C. Has clinically severe extrahepatic manifestations of hepatitis C infection as evidenced by one of the following 1 or 2:
  1. Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (i.e. vasculitis).
  2. Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis.

III. Documentation of patient's Hepatitis C treatment history and baseline viral load.

IV. Documentation that patient has a contraindication to Mavyret™.

V. Documentation that patient meets ONE of the following criteria A or B:

- A. Patient has genotypes 1 or 4. If the patient has genotype 1a, then criterion 1 must also be met:
  1. Documentation that patient has been tested for the presence of virus with NS5A resistance-associated polymorphisms.
- B. Patient has genotype 3 AND meets criterion 1:
  1. Patient has a documented contraindication to Epclusa® and Vosevi®.

VI. Documentation that patient's hepatitis C drug therapy is prescribed as outlined in the table under Authorization in the Approval Length section

VII. Minimum age requirement: 18 years old.

VIII. Prescriber is a Gastroenterologist, Infectious Disease Specialist, or Hepatologist.

Exclusion Criteria:

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- As retreatment when there has been relapse after, or no response to, a prior treatment course with Daklinza™ (daclatasvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/sofosbuvir), Mavyret™ (glecaprevir/pibrentasvir), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir), Vosevi® (sofosbuvir/velpatasvir/voxilaprevir), or Zepatier™ (elbasvir/grazoprevir).
- Moderate or severe hepatic impairment (Child-Pugh B or C).
- Coadministration of Zepatier™ with any organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors, strong or moderate CYP3A inducers, efavirenz, or any of the drugs listed in the table below:

Drug Class	Drugs within class
Antibiotics	Nafcillin
Anticonvulsants	Carbamazepine, phenytoin
Antifungals	Ketoconazole
Antimycobacterials	Rifampin
Endothelin Antagonists	Bosentan
Herbal Products	St. John's Wort (*Hypericum perforatum*)
HIV Medications	Atazanavir, darunavir, efavirenz, elvitegravir/cobicistat/ emtricitabine/tenofovir (disoproxil fumarate or alafenamide), etravirine, lopinavir, saquinavir, tipranavir
HMG-CoA Reductase Inhibitors	Atorvastatin (if > 20 mg/day), rosuvastatin (if > 10 mg/day)
Immunosuppressants	Cyclosporine
Other NS5A inhibitors, protease inhibitors, or polymerase inhibitors used to treat chronic hepatitis C virus infection	Daklinza™ (daclatasvir), Epclusa® (sofosbuvir/velpatasvir), Harvoni® (ledipasvir/ sofosbuvir), Mavyret™ (glecaprevir/pibrentasvir), Olysio® (simeprevir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir), Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)
Wakefulness Promoting Agents	Modafinil

Other Criteria:

- N/A

Quantity/Days Supply Restrictions:

- 28 tablets per 28 days.

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Approval Length:

- **Authorization:** See table directly below.

Drug Therapy	Cirrhosis	G1a		G1b		G3		G4	
		TN	TE	TN	TE	TN	TE	TN	TE
Zepatier™	No	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
	Comp	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
Zepatier™ + RBV	No	16w[t]	12-16w[p4], 16w[t1]		12w[4]				16w[1b]
	Comp	16w[t]	12-16w[p4], 16w[t1]		12w[4]				16w[1b]
Zepatier™ + Sovaldi®	No					12w			
	Comp					12w	12w[1]		

TN = treatment naïve; TE = treatment experienced; Comp = compensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks

[t]For genotype 1a, Zepatier™ should be given alone for 12 weeks in patients without, or with ribavirin for 16 weeks in patients with, NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.
[p]Patients who have NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93 should have treatment extended to 16 weeks.
[1]For patients who have failed pegIFN/RBV.
[1a]For patients who experienced virologic relapse after prior pegIFN/RBV therapy.
[1b]For patients who experienced on-treatment virologic failure while on prior pegIFN/RBV therapy.
[4]For patients who have failed a NS3 protease inhibitor + pegIFN/RBV.

- **Re-Authorization:** N/A

Appendix:

N/A

References:

1. http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf.
2. https://pdf.hres.ca/dpd_pm/00039964.PDF.
3. http://hcvguidelines.org/full-report-view.
4. Medi-Span.

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<table>
<tr><td colspan="2">Historical Tracking Of Changes Made To Policy</td></tr>
<tr><td>4/6/2018</td><td>No changes</td></tr>
<tr><td>10/17/2017</td><td>
1. Added “Documentation that patient has a contraindication to Mavyret™” under Prior Authorization Criteria.
2. Changed “V. B. 1. Patient has a documented contraindication to Epclusa®” to “V. B. 1. Patient has a documented contraindication to Epclusa® and Vosevi®” under Prior Authorization Criteria.
3. Added “Mavyret™ (glecaprevir/pibrentasvir)” and “Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)” to list of drugs following the statement “As retreatment when there has been relapse after, or no response to, a prior treatment course with…” under Exclusion Criteria.
4. Added “Mavyret™ (glecaprevir/pibrentasvir)” and “Vosevi® (sofosbuvir/velpatasvir/voxilaprevir)” and removed “Sovaldi® (sofosbuvir)” under Exclusion Criteria to table under “Coadministration of Zepatier™ with…”, line entitled “Other NS5A inhibitors, protease inhibitors, or polymerase inhibitors used to treat chronic hepatitis C virus infection”.
5. Changed table below Authorization under Approval Length from (change made highlighted in yellow):
<table>
<tr><th>Drug Therapy</th><th>Cirrhosis</th><th colspan="2">G1a</th><th colspan="2">G1b</th><th colspan="2">G3</th><th colspan="2">G4</th></tr>
<tr><td></td><td></td><td>TN</td><td>TE</td><td>TN</td><td>TE</td><td>TN</td><td>TE</td><td>TN</td><td>TE</td></tr>
<tr><td rowspan="2">Zepatier™</td><td>No</td><td>12w[t]</td><td>12w[t1]</td><td>12w</td><td>12w[1]</td><td></td><td></td><td>12w</td><td>12w[1a]</td></tr>
<tr><td>Comp</td><td>12w[t]</td><td>12w[t1]</td><td>12w</td><td>12w[1]</td><td></td><td></td><td>12w</td><td>12w[1a]</td></tr>
<tr><td rowspan="2">Zepatier™ + RBV</td><td>No</td><td>16w[t]</td><td>12-16w[p4], 16w[t1]</td><td></td><td>12w[4]</td><td></td><td></td><td></td><td>16w[1b]</td></tr>
<tr><td>Comp</td><td>16w[t]</td><td>12-16w[p4], 16w[t1]</td><td></td><td>12w[4]</td><td></td><td></td><td></td><td>16w[1b]</td></tr>
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<tr><td>Comp</td><td></td><td></td><td></td><td></td><td>12w</td><td></td><td></td><td></td></tr>
</table>
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<tr><td>Comp</td><td></td><td></td><td></td><td></td><td>12w</td><td>12w[1]</td><td></td><td></td></tr>
</table>
6. Updated “http://www.merck.ca/assets/en/pdf/products/ZEPATIER-PM_E.pdf” to “https://pdf.hres.ca/dpd_pm/00039964.PDF” under References.
</td></tr>
<tr><td>7/30/2016</td><td>
1. Changed “Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir /dasabuvir)” to “Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir)” in list of drugs following the statement “As retreatment when there has been relapse after, or no response to, a prior treatment course with…” under Exclusion Criteria.
2. Changed “Viekira Pak™ (ombitasvir, paritaprevir, and ritonavir/ dasabuvir)” to “Viekira Pak™/XR™
</td></tr>
</table>

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(dasabuvir, ombitasvir, paritaprevir, ritonavir)" **under Exclusion Criteria** to table under "Coadministration of Zepatier™ with…", line entitled "Other NS5A inhibitors, protease inhibitors, or polymerase inhibitors used to treat chronic hepatitis C virus infection".

7/20/2016

1. **Changed** "IV. If the patient has genotype 1a, then criterion A must also be met: A. Documentation that patient has been tested for the presence of virus with NS5A resistance-associated polymorphisms" **to** "IV. Documentation that patient meets ONE of the following criteria A or B: A. Patient has genotypes 1 or 4. If the patient has genotype 1a, then criterion 1 must also be met: 1. Documentation that patient has been tested for the presence of virus with NS5A resistance-associated polymorphisms; B. Patient has genotype 3 AND meets criterion 1: 1. Patient has a documented contraindication to Epclusa®" **under Prior Authorization Criteria**.
2. **Added** "Epclusa® (sofosbuvir/velpatasvir)" **under Exclusion Criteria** to: 1) List of drugs following the statement "As retreatment when there has been relapse after, or no response to, a prior treatment course with…; 2) table under "Coadministration of Zepatier™ with…", line entitled "Other NS5A inhibitors, protease inhibitors, or polymerase inhibitors used to treat chronic hepatitis C virus infection".
3. **Changed table below Authorization under Approval Length from (changes made highlighted in yellow):**

Drug Therapy	Cirrhosis	Authorization Duration							
		G1a		G1b		G3		G4	
		TN	TE	TN	TE	TN	TE	TN	TE
Zepatier™	No	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
	Comp	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
Zepatier™ + RBV	No	16w[t]	12w[t5], 16w[t5]		12w[5]				16w[1b]
	Comp	16w[t]	12w[t4], 16w[t5]		12w[4]				16w[1b]
Zepatier™ + Sovaldi®	No					12w			
	Comp					12w			

TN = treatment naïve; TE = treatment experienced; Comp = compensated;
RBV = ribavirin; pegIFN = peginterferon; w = weeks
[t]For genotype 1a, Zepatier™ should be given alone for 12 weeks in patients without, or with ribavirin for 16 weeks in patients with, NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.
[1]For patients who have failed pegIFN/RBV.
[1a]For patients who experienced virologic relapse after prior pegIFN/RBV therapy.
[1b]For patients who experienced on-treatment virologic failure while on prior pegIFN/RBV therapy.
[4]For patients who have failed a NS3 protease inhibitor + pegIFN/RBV.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.

to:

Drug Therapy	Cirrhosis	G1a		G1b		G3		G4	
		TN	TE	TN	TE	TN	TE	TN	TE
Zepatier™	No	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
	Comp	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
Zepatier™ +	No	16w[t]	12-16w[p4],		12w[4]				16w[1b]

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RBV			16w[t1]						
	Comp	16w[t]	12-16w[p4], 16w[t1]		12w[4]				16w[1b]
Zepatier™ + Sovaldi®	No					12w			
	Comp					12w			

TN = treatment naïve; TE = treatment experienced; Comp = compensated; RBV = ribavirin; pegIFN = peginterferon; w = weeks

[t]For genotype 1a, Zepatier™ should be given alone for 12 weeks in patients without, or with ribavirin for 16 weeks in patients with, NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.

[P]Patients who have NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93 should have treatment extended to 16 weeks.

[1]For patients who have failed pegIFN/RBV.

[1a]For patients who experienced virologic relapse after prior pegIFN/RBV therapy.

[1b]For patients who experienced on-treatment virologic failure while on prior pegIFN/RBV therapy.

[4]For patients who have failed a NS3 protease inhibitor + pegIFN/RBV.

[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.

3/21/2016

1. **Changed** "member" **to** "patient" **throughout policy**.
2. **Changed** "V. If the member has genotype 3, then both of criteria A AND B must also be met: A. Member is treatment-naïve; B. Member has documented intolerance or contraindication to peginterferon" **to** "V. Documentation that patient's hepatitis C drug therapy is prescribed as outlined in the table under Authorization in the Approval Length section" **under Prior Authorization Criteria**.
3. **Changed table following Authorization under Approval Length from:**

Patient Characteristics		**Authorization Information**	
Genotype, Other Features	**Hepatitis Treatment History**	**Treatment**	**Authorization Duration**
1a, without baseline NS5A polymorphisms[*], with or without cirrhosis	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin)*	Zepatier™	**12 weeks**
1a, without baseline NS5A polymorphisms[*], with or without cirrhosis	Treatment-experienced *(failed peginterferon + ribavirin + HCV NS3/4A protease inhibitor[^])*	Zepatier™ + ribavirin	**12 weeks**
1a, with baseline NS5A polymorphisms[*], with or without cirrhosis	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin)*	Zepatier™ + ribavirin	**16 weeks**
1b, with or without cirrhosis	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin)*	Zepatier™	**12 weeks**
1b, with or without cirrhosis	Treatment-experienced *(failed peginterferon +*	Zepatier™ + ribavirin	**12 weeks**

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	ribavirin + HCV NS3/4A protease inhibitor^)		
3, with or without cirrhosis	Treatment-naïve	Zepatier™ + Sovaldi®	**12 weeks**
4, with or without cirrhosis	Treatment-naïve	Zepatier™	**12 weeks**
4, with or without cirrhosis	Treatment-experienced *(failed peginterferon + ribavirin)*	Zepatier™ + ribavirin	**16 weeks**

*NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.
^Boceprevir, simeprevir, or telaprevir.

to:

Drug Therapy	**Cirrhosis**	**Authorization Duration**							
		G1a		**G1b**		**G3**		**G4**	
		TN	**TE**	**TN**	**TE**	**TN**	**TE**	**TN**	**TE**
Zepatier™	No	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
	Comp	12w[t]	12w[t1]	12w	12w[1]			12w	12w[1a]
Zepatier™ + RBV	No	16w[t]	12w[t5], 16w[t5]		12w[5]				16w[1b]
	Comp	16w[t]	12w[t4], 16w[t5]		12w[4]				16w[1b]
Zepatier™ + Sovaldi®	No					12w			
	Comp					12w			

TN = treatment naïve; TE = treatment experienced; Comp = compensated;
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[t]For genotype 1a, Zepatier™ should be given alone for 12 weeks in patients without, or with ribavirin for 16 weeks in patients with, NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.
[1]For patients who have failed pegIFN/RBV.
[1a]For patients who experienced virologic relapse after prior pegIFN/RBV therapy.
[1b]For patients who experienced on-treatment virologic failure while on prior pegIFN/RBV therapy.
[4]For patients who have failed a NS3 protease inhibitor + pegIFN/RBV.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.