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:** 7/30/16

GPI Code: 1235990230

Prior Authorization Criteria (may be considered medically necessary when criteria I through VII 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 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®.

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

VI. Minimum age requirement: 18 years old.

VII. 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), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir), 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), Olysio® (simeprevir), Sovaldi® (sofosbuvir), Technivie™ (ombitasvir, paritaprevir, and ritonavir), Viekira Pak™/XR™ (dasabuvir, ombitasvir, paritaprevir, ritonavir)
Wakefulness Promoting Agents	Modafinil

Other Criteria:

- N/A

Quantity/Days Supply Restrictions:

- 28 tablets per 28 days.

Approval Length:

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

Disclaimer: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgment in providing the most appropriate care for their patients.

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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			

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. http://www.merck.ca/assets/en/pdf/products/ZEPATIER-PM_E.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>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™ (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”.</td></tr>
<tr><td>7/20/2016</td><td>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):
<table>
<tr><th rowspan="2">Drug Therapy</th><th rowspan="2">Cirrhosis</th><th colspan="8">Authorization Duration</th></tr>
<tr><th colspan="2">G1a</th><th colspan="2">G1b</th><th colspan="2">G3</th><th colspan="2">G4</th></tr>
<tr><th></th><th></th><th>TN</th><th>TE</th><th>TN</th><th>TE</th><th>TN</th><th>TE</th><th>TN</th><th>TE</th></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>12w[t5], 16w[t5]</td><td></td><td>12w[5]</td><td></td><td></td><td></td><td>16w[1b]</td></tr>
<tr><td>Comp</td><td>16w[t]</td><td>12w[t4], 16w[t5]</td><td></td><td>12w[4]</td><td></td><td></td><td></td><td>16w[1b]</td></tr>
<tr><td rowspan="2">Zepatier™ + Sovaldi®</td><td>No</td><td></td><td></td><td></td><td></td><td>12w</td><td></td><td></td><td></td></tr>
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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:</td></tr>
</table>

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Historical Tracking Of Changes Made To Policy

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]
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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			

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

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[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**

Historical Tracking Of Changes Made To Policy

1b, with or without cirrhosis	Treatment-naïve/ Treatment-experienced *(failed peginterferon + ribavirin)*	Zepatier™	**12 weeks**
1b, with or without cirrhosis	Treatment-experienced *(failed peginterferon + ribavirin + HCV NS3/4A protease inhibitor^)*	Zepatier™ + ribavirin	**12 weeks**
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]
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[4]For patients who have failed a NS3 protease inhibitor + pegIFN/RBV.
[5]For patients who have failed pegIFN/RBV +/- a NS3 protease inhibitor.