Clinical Policy: Elbasvir/Grazoprevir (Zepatier)

Reference Number: PA.CP.PHAR.275
Effective Date: 001/18
Last Review Date: 09/17 Revision Log

Description
Grazoprevir/elbasvir (Zepatier®) is a fixed-dose combination product containing elbasvir, a hepatitis C virus (HCV) NS5A inhibitor, and grazoprevir, an HCV NS3/4A protease inhibitor.

FDA-Approved Indication
Zepatier is indicated for treatment of chronic HCV genotype 1 or 4 infection in adults. Zepatier is indicated for use with ribavirin in certain patient populations.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness ® that Zepatier is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

A. Chronic Hepatitis C Infection (must meet all)**:**
1. Age ≥ 18 years;
2. Diagnosis of chronic hepatitis C virus (HCV) infection as evidenced by detectable HCV RNA (ribonucleic acid) levels;
3. Confirmed HCV genotype is 1 or 4;
4. If actively abusing alcohol or IV drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse and an offer of a referral for substance use disorder treatment.
5. Has all of the following:
   a. Documented quantitative HCV RNA at baseline that was tested within the past 3 months.
   b. Dose not have a life expectancy of less than 12 months due to non-liver-related comorbid conditions.
   c. Has correct or addressed the causes of non-adherence to a previously prescribed Hepatitis C treatment regimen if the recipient has a history of failed treatment due to non-adherence.
   d. Had all potential drug interactions addressed by the prescriber
6. Prescribed regimen is consistent with an FDA or AASLD-IDSA recommended regimen (*see Section V Dosage and Administration for reference)*;*)*;
7. Has a documented commitment to adherence with the planned course of treatment
   a. ;
8. If member is without cirrhosis or with compensated cirrhosis (Child-Pugh A): contraindication or intolerance to Mavyret;
9. If prescribed with ribavirin (RBV), at the time of request, member is not pregnant;
10. Has documented completion of

a. Hepatitis B immunization series or Hepatitis B screening (sAb/sAg and cAb/cAg) and
b. If there is detectable HBV DNA, will be treated for Hepatitis B or if negative for hepatitis BsAb, is being vaccinated against Hepatitis B. and
c. Has a documented HIV screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay: Is being treated for HIV or is not being treated for HIV and the medical record documents the rationale for not being treated

11. If cirrhosis is present, confirmation of Child-Pugh A status;
12. Dose does not exceed elbasvir/grazoprevir 50 mg/100 mg (1 tablet) per day.

Approval duration: Up to 16 weeks

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

B. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

*** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria ***

A. Chronic Hepatitis C Infection (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Dose does not exceed elbasvir/grazoprevir 50 mg/100 mg (1 tablet) per day.

Approval duration: up to a total of 16 weeks*

*(*Approved duration should be consistent with a regimen in Section V Dosage and Administration)*

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices

Appendix A: Abbreviation Key

ALT: alanine aminotransferase
APRI: AST to platelet ratio
AASLD: American Association for the Study of Liver Diseases
CTP: Child Turcotte Pugh
DAA: direct acting antiviral
FDA: Food and Drug Administration
FIB-4: Fibrosis-4 index
HBV: hepatitis B virus
RBV: ribavirin
HCC: hepatocellular carcinoma
HCV: hepatitis C virus
IDSA: Infectious Diseases Society of America
MRE: magnetic resonance elastography
NS3/4A, NS5A/B: nonstructural protein
Peg-IFN: pegylated interferon
PI: protease inhibitor
ULN: upper limit of normal

Appendix B: Direct-Acting Antivirals (DAAs) for Treatment of HCV Infection

Brand Name	Drug Class				
	NS5A Inhibitor	Nucleotide Analog NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Palm Polymerase Inhibitor	NS3/4A Protease Inhibitor (PI)**	CYP3A Inhibitor
Daklinza	Daclatasvir				
Epclusa*	Velpatasvir	Sofosbuvir			
Harvoni*	Ledipasvir	Sofosbuvir			
Olysio				Simeprevir	
Sovaldi		Sofosbuvir			
Technivie*	Ombitasvir			Paritaprevir	Ritonavir
Viekira XR/PAK*	Ombitasvir		Dasabuvir	Paritaprevir	Ritonavir
Zepatier*	Elbasvir			Grazoprevir	

*Combination drugs
**Additional PIs no longer recommended: Victrelis (boceprevir), Incivek (telaprevir)

V. Dosage and Administration

A. **AASLD/IDSA treatment guidelines for chronic hepatitis C infection are updated at irregular intervals; refer to the most updated AASLD/IDSA guideline for most accurate treatment regimen.*

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naïve or PegIFN/RBVexperienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet PO QD for 12 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2 https://www.hcvguidelines.org/

Indication	Dosing Regimen	Maximum Dose	Reference
Genotype 1a: Treatment-naïve or PegIFN/RBV experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet PO QD plus weight-based RBV for 16 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)
Genotype 1b: Treatment-naïve or PegIFN/RBV experienced	One tablet PO QD for 12 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)
Genotype 1a or 1b: PegIFN/RBV/PI*-experienced with or without compensated cirrhosis without baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet PO QD plus weight-based RBV for 12 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)
Genotype 1a or 1b: PegIFN/RBV/NS3 PI*ǂ-experienced with or without compensated cirrhosis with baseline NS5A polymorphisms at amino acid positions 28, 30, 31, or 93	One tablet PO QD plus weight-based RBV for 16 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) ǂ AASLD-IDSA (updated 04/17)
Genotype 4: Treatment-naïve with or without compensated cirrhosis	One tablet PO QD for 12 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)
Genotype 4: PegIFN/RBV-experienced with or without compensated cirrhosis with virologic relapse without prior on-treatment virologic failure	One tablet PO QD for 12 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	AASLD-IDSA (updated 04/17)
Genotype 4: PegIFN/RBV-experienced with or without compensated cirrhosis with virologic relapse with prior on-treatment virologic failure	One tablet PO QD plus weight-based RBV for 16 weeks	Zepatier (grazoprevir 100 mg /elbasvir 50mg): 1 tablet per day	1) FDA-approved labeling 2) AASLD-IDSA (updated 04/17)

**AASLD/IDSA treatment guidelines for chronic hepatitis C infection are updated at irregular intervals; refer to the most updated AASLD/IDSA guideline for most accurate treatment regimen.*

ǂ *Off-label, AASLD-IDSA guideline-supported dosing regimen*

VI. Product Availability

Tablets: grazoprevir 100 mg/elbasvir 50 mg

VII. References

1. Zepatier Prescribing Information. Whitehouse Station, NJ: Merck and Company, Inc.; February 2017. Available at http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf. Accessed May 11, 2017.
2. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). Recommendations for testing, managing, and treating hepatitis C. April 2017. Available at http://www.hcvguidelines.org. Accessed May 11, 2017.
3. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. Curr Gastroenterol Rep. 2014; 16(372): 1-7. DOI 10.1007/s11894-014-0372-6.
4. Halfon P, Bourliere M, Deydier R, et al. Independent prospective multicenter validation of biochemical markers (Fibrotest–Actitest) for the prediction of liver fibrosis and activity in patients with chronic hepatitis C: The Fibropaca study. Am J Gastroenterol. 2006; 101: 547-555. DOI: 10.1111/j.1572-0241.2006.0411.x
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