Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

Zepatier (elbasvir/grazoprevir)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Based on Genotype, Treatment status, Cirrhosis status, NS5A Resistant-associated Polymorphism status, or Prior Virologic Response status

Medications	Quantity Limit
Zepatier (elbasvir/grazoprevir)	1 tablet per day

APPROVAL DURATION

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	Associated Treatment Regimen	Total Approval Duration of Zepatier
Genotype 1b (treatment-naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Zepatier	12 weeks
Genotype 1b (triple[2d] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Zepatier + RBV	12 weeks
Genotype 1a (treatment-naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis, or without cirrhosis without baseline NS5A resistant-associated polymorphism)	Zepatier	12 weeks
Genotype 1a (treatment-naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis or without cirrhosis, with baseline NS5A resistant-associated polymorphism)	Zepatier + RBV	16 weeks
Genotype 1a (triple[2d] treatment-experienced, with compensated cirrhosis or without cirrhosis, without baseline NS5A resistant-associated	Zepatier + RBV	12 weeks

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

polymorphism)		
Genotype 1a (triple[2d] treatment-experienced, with compensated cirrhosis or without cirrhosis, with baseline NS5A resistant-associated polymorphism)	Zepatier + RBV	16 weeks
Genotype 1a (post-kidney transplant, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis or without cirrhosis, without baseline NS5A resistant-associated polymorphism)	Zepatier	12 weeks
Genotype 1b or 4 (post-kidney transplant, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Zepatier	12 weeks
Genotype 3 (dual P/R[2b] treatment-experienced, with compensated cirrhosis)	Zepatier + Sovaldi	12 weeks
Genotype 4 (treatment-naïve, with compensated cirrhosis or without cirrhosis)	Zepatier	12 weeks
Genotype 4 (dual P/R[2b] treatment-experienced with virologic relapse, with compensated cirrhosis or without cirrhosis)	Zepatier	12 weeks
Genotype 4 (dual P/R[2b] treatment-experienced with on- treatment virologic failure[†], with compensated cirrhosis or without cirrhosis)	Zepatier + RBV	16 weeks

[†]The September 2017 AASLD/IDSA treatment guidance defines on-treatment virologic failure as experiencing failure to suppress or breakthrough during treatment.

APPROVAL CRITERIA

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

Requests for Zepatier (elbasvir/grazoprevir) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Documentation is provided for a diagnosis of chronic hepatitis C (CHC) infection[a], which includes genotype and a positive HCV RNA result (AASLD/IDSA 2017, CDC 2013); **AND**
III. Individual has received baseline evaluation for liver fibrosis to guide appropriate therapy; **AND**
IV. Individual does not have a short life expectancy (less than 12 months owing to non-liver related comorbid conditions) that cannot be remediated by treating HCV, by transplantation or other directed therapy (AASLD/IDSA 2017); **AND**
V. Individual has compensated[1] liver disease (with or without cirrhosis); **AND**
VI. If Genotype 1a subtype is present, a copy of the baseline NS5A resistant-associated polymorphism test result is provided;

AND
VII. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to authorized generic Epclusa (sofosbuvir/velpatasvir) OR Mavyret, unless one of the following conditions apply:

A. Individual is using in **one** of the following antiviral treatment regimens (Label/AASLD/IDSA 2019):

1. As monotherapy for **one** of the following:
   a. Individual is treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b, or Genotype 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and Y93; **AND**
   b. Individual meets one of the following criteria:
      i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
      ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
      iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR
   c. Individual is treatment-naïve, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4; **OR**

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

d. Individual is a dual P/R[2b] treatment-experienced virologic relapser, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4;
AND
e. Individual meets one of the following criteria:
   i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
   ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

f. Individual is post-kidney transplantation, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b, or Genotype 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and/or Y93, or Genotype 4; **AND**
g. Individual meets one of the following criteria:
   i. Prior trial of Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
   ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

2. In combination with ribavirin for **one** of the following:
   a. Individual is treatment-naïve, dual P/R[2b], or triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1a with a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and/or Y93; **OR**
   b. Individual is triple[2d] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis, and Genotype 1b or 1a without a baseline NS5A resistant-associated polymorphism at amino acid positions M28, Q30, L31, and Y93;
   AND
   c. Individual meets one of the following criteria:

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

d. Individual is a dual P/R[2b]treatment-experienced with prior on-treatment virologic failure, with compensated[1] cirrhosis or without cirrhosis, and Genotype 4; **AND**
e. Individual meets one of the following criteria:
   i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier; **OR**
   ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens;

OR

f. In combination with sofosbuvir for dual P/R[2b] treatment-experienced individuals, with compensated cirrhosis[1], and Genotype 3; **AND**
g. Individual meets one of the following criteria:
   i. Prior trial of authorized generic Epclusa (sofosbuvir/velpatasvir) AND Mavyret with documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier or sofosbuvir; **OR**
   ii. Individual is currently on and completing a course of therapy with Zepatier; **OR**
   iii. Individual is concurrently using an agent that cannot be substituted with another agent or temporarily discontinued and is contraindicated or not recommended for concomitant use with the preferred regimen or regimens; **OR**
   iv. Individual has had a prior trial of Mavyret with documented hypersensivity, as manifested by a severe allergic reaction to any ingredient which is not also in Zepatier or sofosbuvir, AND is not a

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

candidate for the Epclusa regimen when it contains ribavirin, due to being ribavirin ineligible (examples include individuals with hemoglobinopathies, significant cardiac disease, creatinine clearance less than 50 mL/min, documented severe allergic reaction, or pregnancy).

Zepatier (elbasvir/grazoprevir) may not be approved for the following:

I. Individual has decompensated[1] cirrhosis, or any history or prior hepatic decompensation; **OR**
II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, including but not limited to the following: strong cytochrome (CYP) 3A4 inducers (including but not limited to, efavirenz, phenytoin, phenobarbital, carbamazepine, St John's Wort, rifampin, rifabutin, rifapentine), organic anion transporting peptide (OATP) 1B1/1B3 inhibitors (including but not limited to, atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine, eltrombopag, ritonavir-containing regimens), cobicistat-containing regimens, nevirapine, nafcillin, etravirine, modafinil, bosentan, oral ketoconazole; **OR**
III. Individual is using in combination with a regiment containing another NS3/4A[2c] protease inhibitor; **OR**
IV. Individual is using in combination with a regimen containing another NS5A[2a] inhibitor; **OR**
V. Individual is using in combination with a regimen containing a NS5B polymerase inhibitor other than sofosbuvir (such as dasabuvir); **OR**
VI. Individual is requesting the regimen for re-treatment and either failed to achieve a SVR (defined as a lower limit HCV RNA of 25 IU/mL) or relapsed after achieving a SVR during a prior successfully completed treatment regimen consisting of a NS5B polymerase inhibitor (such as dasabuvir or sofosbuvir) or an NS5A[2a] inhibitor.

Notes:

[a]Per label and AASLD/IDSA treatment guidance, Zepatier (grazoprevir/elbasvir) may be used in individuals who are co-infected with human immunodeficiency virus-1 (HIV-1).

1. **Compensated Liver Disease**:
   According to the American Association for the Study of Liver Diseases (AASLD/IDSA 2017), the specific criteria for compensated liver disease include all of the following: a total bilirubin; serum albumin; prothrombin time/INR; presence of ascites; and presence of hepatic encephalopathy. However, these criteria do not establish a comprehensive definition of compensated liver disease. The AASLD guidance refers to compensated liver disease as Class A based on the Child Pugh-Turcotte (CPT) classification scoring system.

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

Moderate to Severe (Decompensated) Liver Disease:
The AASLD guidance refers to decompensated (moderate to severe) liver disease as Class B or C based on the Child-Pugh Turcotte (CPT) classification scoring system.

Child Pugh Classification (AASLD/IDSA 2017)

Parameters			
Points Assigned	1 point	2 points	3 points
Total Bilirubin (µmol/L)	<34	34-50	>50
Serum Albumin (g/L)	>35	28-35	<28
Prothrombin time/INR	<1.7	1.71-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic Encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

Child Pugh Score Interpretation (AASLD/IDSA 2017)

Class A	5-6 points	Well compensated liver disease
Class B	7-9 points	Significant functional compromise (moderate hepatic impairment)
Class C	10-15 points	Uncompensated liver disease (severe hepatic impairment)

2. Past Treatment Exposure Definitions (AASLD/IDSA 2017):
    a. NS5A Inhibitor: includes daclatasvir, ledipasvir, elbasvir, ombitasvir, pibrentasvir, or velpatasvir-containing regimens
    b. P/R: includes peginterferon (or non-pegylated interferon) ± ribavirin
    c. NS3/4A Protease Inhibitor: includes simeprevir, grazoprevir, paritaprevir, glecaprevir, and voxilaprevir-containing regimens
    d. Triple therapy: includes NS3 protease inhibitor (simeprevir, boceprevir or telaprevir) plus peginterferon and ribavirin
    e. Direct Acting Antiviral (DAA): includes NS5A inhibitors, NS3/4A protease inhibitors, and NS5B polymerase inhibitors (sofosbuvir, dasabuvir)

3. Chronic Kidney Disease (CKD) Definitions (AASLD/IDSA 2017):
   Severe CKD (Stage 4): eGFR 15-29 mL/min
   End-Stage CKD (Stage 5): eGFR < 15 mL/min

4. **Metavir Scoring Systems for Fibrosis Staging (AASLD 2009):**

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	NA	NA	X	NA	X	X	NA

Stage (F)	
0	No fibrosis
1	Periportal fibrotic expansion
2	Periportal septae 1 (septum)
3	Porto-central septae
4	Cirrhosis

5. Hepatitis C virus (HCV) direct acting antiviral (DAA) agents have a black box warning for risk of hepatitis B virus (HBV) reactivation in individuals with HCV-HBV co-infection. Individuals should be tested for evidence of current or prior HBV infection prior to initiation of DAA therapy. HBV reactivation has been reported in HCV/HBV co-infected individuals currently taking or previously completed DAA therapy and not concomitantly receiving HBV antiviral therapy. Some cases of HBV reactivation have led to fulminant hepatitis, hepatic failure, and death. Individuals should be monitored for hepatitis flare or HBV reactivation during and following HCV DAA therapy. Individuals should be appropriately managed for HBV infection as indicated.

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