Ombitasvir+paritaprevir+ritonavir + dasabuvir Agents

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Based on Genotype, Treatment status, or Cirrhosis status

Medication	Quantity Limit
Viekira Pak (ombitasvir + paritaprevir + ritonavir + dasabuvir)	4 tablets per day
Viekira XR (ombitasvir + paritaprevir + ritonavir + dasabuvir)	3 tablets per day

APPROVAL DURATION

Genotype and Status (HCV mono-infected or HCV/HIV-1 co-infected[a])	Associated Treatment Regimens	Total Approval Duration of ombitasvir + paritaprevir + ritonavir + dasabuvir agents (Viekira Pak, Viekira XR)
Genotype 1b (treatment naïve or dual P/R[2b] treatment-experienced, with compensated cirrhosis or without cirrhosis)	Viekira Pak Viekira XR	12 weeks
Genotype 1a, unknown Genotype 1 subtype, or mixed Genotype 1 subtypes (treatment naïve or dual P/R[2b] treatment-experienced, without cirrhosis)	Viekira Pak+ ribavirin Viekira XR + ribavirin	12 weeks

APPROVAL CRITERIA

Requests for ombitasvir + paritaprevir + ritonavir + dasabuvir (Viekira Pak, Viekira XR) 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, a reactive HCV antibody, and a subsequent positive HCV RNA result to confirm diagnosis (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. Individuals who abuse alcohol or intravenous drugs must be enrolled in a substance abuse program; **AND**

VI. Individual has Genotype 1 and compensated liver disease[1] (with or without cirrhosis);

AND

VII. Individual is using with **one** of the following antiviral treatment regimens (AASLD/IDSA 2017):

A. As monotherapy for individuals with Genotype 1b, treatment-naïve or dual P/R[2b] treatment-experienced, with compensated[1] cirrhosis or without cirrhosis; **AND**

B. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to Mavyret; **OR**

1. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
2. Documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient in Mavyret which is not also in Viekira Pak/Viekira XR; **OR**
3. 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. In combination with ribavirin for the following:

1. Individual with Genotype 1a or mixed/unknown Genotype1, treatment-naïve or dual P/R[2] treatment-experienced;
   AND
2. Individual has had a prior trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response to Mavyret; **OR**
   a. Individual is currently on and completing a course of therapy with the requested regimen; **OR**
   b. Documented hypersensitivity, as manifested by a severe allergic reaction to any ingredient in Mavyret which is not also in Viekira Pak/Viekira XR; **OR**
   c. 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;

Ombitasvir + paritaprevir + ritonavir + dasabuvir (Viekira Pak, Viekira XR) may **not** be approved for the following:

I. Individual has decompensated[1] cirrhosis; **OR**

II. Individual is requesting in concurrent therapy with contraindicated or not recommended agents, such as but not limited to the following: Strong cytochrome (CYP) 2C8 inhibitors [such as but not limited to, gemfibrozil, ritonavir-boosted atazanavir], strong CYP 2C8

inducers (such as but not limited to, carbamazepine, phenobarbital, rifampin, rifabutin, rifapentine), moderate or strong CYP 3A4 inducers (such as but not limited to, phenytoin, St. Johns' Wort, efavirenz-based regimens, agents highly dependent on CYP3A clearance (substrates) [such as but not limited to, dronedarone, amiodarone, flecainide, propafenone, quinidine, ranolazine, lurasidone, cisapride, alfuzosin, colchicine, ergot derivatives, ethinyl estradiol-containing agents, lovastatin, simvastatin, pimozide, Revatio, triazolam, oral midazolam, darunavir, lopinavir/ritonavir, rilpivirine-based regimens, voriconazole, salmeterol], atorvastatin, everolimus, sirolimus, tacrolimus, tipranavir/ritonavir, etravirine, nevirapine or cobicistat-containing regimens; **OR**

III. Individual is using in combination with a regimen containing another NS3/4A[2c] protease inhibitor; **OR**

IV. Individual is using in combination with a regimen containing another nucleotide NS5B polymerase inhibitor (such as sofosbuvir) or another non-nucleoside NS5B polymerase inhibitor (such as dasabuvir); **OR**

V. Individual is using in combination with a regimen containing another NS5A[2a] inhibitor; **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 NS3/4A[2c] protease inhibitor, NS5A[2a] inhibitor, or NS5B polymerase inhibitor (such as sofosbuvir or dasabuvir).

Notes:

[a]Per label, ombitasvir/paritaprevir/ritonavir + dasabuvir agents (Viekira Pak, Viekira XR) may be used in individuals co-infected with HIV-1. Individuals co-infected with HCV/HIV-1 treated with Viekira Pak/Viekira XR should also be on a suppressive antiretroviral drug regimen to reduce the risk of HIV-1 protease inhibitor drug resistance.

1. **Compensated Liver Disease**:
   According to the American Association for the Study of Liver Diseases (AASLD/IDSA2017), 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.

   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)**:

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.

Key References:

American Association for the Study of Liver Diseases and the Infectious Disease Society of America, in collaboration with the International Antiviral Society-USA. Recommendations for testing, managing and treating hepatitis C. Available at http://www.hcvguidelines.org/. Published on: January 29, 2014. Updated on: September 21, 2017. Accessed on: January 25, 2018.

Centers for Disease Control and Prevention. Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians. *MMWR*. 2013; 62(18):362-365. Available from: https://www.cdc.gov/mmwr/pdf/wk/mm6218.pdf. Accessed on: December 27, 2017.

DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed on: January 25, 2018.

European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C 2016. *J Hepatol*. 2017; 66(1):153-194. Available from: http://www.journal-of-hepatology.eu/article/S0168-8278(16)30489-5/pdf. Accessed on: December 27, 2017.

U.S. Food & Drug Administration. Drugs@FDA: FDA Approved Drug Products (Package inserts). Available from: http://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed on: January 25, 2018.

U.S. Department of Health and Human Services AIDSinfo treatment guidelines. Concomitant use of selected antiretroviral drugs and hepatitis C virus direct-acting antiviral drugs for treatment of HCV in adults with HIV. Available at https://aidsinfo.nih.gov/guidelines/htmltables/1/5536. Accessed on: December 27, 2017.

DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.

Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

PL Detail-Document, Cytochrome P450 Drug Interactions. Pharmacist's Letter/Prescriber's Letter. May 2016.

PL Detail-Document, OATP Drug Interactions. Pharmacist's Letter/Prescriber's Letter. March 2014.

PL Detail-Document, P-glycoprotein Drug Interactions. Pharmacist's Letter/Prescriber's Letter. April 2016.