Treatment of Hepatitis C with ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak™/Viekira XR™)

Policy # 00462
Original Effective Date: 02/18/2015
Current Effective Date: 02/15/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Treatment of Hepatitis C with Triple Therapy (Ribavirin Plus Pegylated Interferon Alfa Plus Telaprevir [Incivek®] or Boceprevir [Victrelis®])‡ is addressed separately in medical policy 00373.

Note: Treatment of Hepatitis C with Dual Therapy (Ribavirin Plus Pegylated Interferon Alfa) is addressed separately in medical policy 00374.

Note: Pegylated Interferons (Pegasys®, PegIntron®)‡ for Other (Non-Hepatitis C) Uses is addressed separately in medical policy 00375.

Note: Treatment of Hepatitis C with a simeprevir (Olysio®)‡ Based Regimen is addressed separately in archived medical policy 00396.

Note: Treatment of Hepatitis C with a sofosbuvir (Sovaldi®)‡ Based Regimen is addressed separately in medical policy 00397.

Note: Treatment of Hepatitis C with sofosbuvir/ledipasvir (Harvoni®)‡ is addressed separately in medical policy 00455.

Note: Treatment of Hepatitis C with simeprevir (Olysio®)‡ PLUS sofosbuvir (Sovaldi®)‡ is addressed separately in archived medical policy 00457.

Note: Treatment of Hepatitis C with daclatasvir (Daklinza™)‡ and sofosbuvir (Sovaldi®)‡ is addressed separately in medical policy 00479.

Note: Treatment of Hepatitis C with ombitasvir, paritaprevir, and ritonavir (Technivie®)‡ is addressed separately in medical policy 00478.

Note: Treatment of Hepatitis C with elbasvir and grazoprevir (Zepater™)‡ is addressed separately in medical policy 00509.

Note: Treatment of Hepatitis C with sofosbuvir and velpatasvir (Epclusa®)‡ is addressed separately in medical policy 00514.
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When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Chronic Hepatitis C Virus
Based on review of available data, the Company may consider ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak™/Viekira XR™) for the treatment of individuals with chronic hepatitis C virus (HCV) to be eligible for coverage.

Patient Selection Criteria
Based on review of available data, the Company may consider ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak/Viekira XR) when ALL of the following criteria (I, II, III, IV, V, VI, and VII) are met:

I. Patient has a diagnosis of chronic hepatitis C virus (HCV) genotype 1; AND
II. Patient does NOT have decompensated cirrhosis; AND
III. Patient has NOT received prior therapy with a protease inhibitor (eg Olysio, Incivek, Victrelis); AND
IV. Patient has NOT received prior therapy with a sofosbuvir containing regimen (eg Sovaldi, Harvoni, Epclusa); AND
V. Patient will take Viekira Pak/Viekira XR with or without ribavirin as noted below in the chart; AND
VI. There is clinical evidence or patient history that suggests the use of sofosbuvir/ledipasvir (Harvoni) will be ineffective or will cause an adverse reaction to the patient; AND
   Note that failure to meet this criterion, which is an additional company requirement, will result in a denial of not medically necessary**
VII. Patient meets the following definitions and adheres to the timeframes for treatment:

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Drugs</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a with OUT cirrhosis</td>
<td>Viekira Pak/Viekira XR only</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a with cirrhosis (treatment naïve, prior relapser, prior partial responder)</td>
<td>Viekira Pak/Viekira XR PLUS ribavirin</td>
<td>12 weeks**</td>
</tr>
<tr>
<td>Genotype 1a with cirrhosis (prior null responder)</td>
<td>Viekira Pak/Viekira XR PLUS ribavirin</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 1b, without cirrhosis</td>
<td>Viekira Pak/Viekira XR only</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1b with cirrhosis</td>
<td>Viekira Pak PLUS ribavirin OR Viekira XR only</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1 liver transplant recipient with normal hepatic function and mild fibrosis (Metavir ≤2)</td>
<td>Viekira Pak/Viekira XR PLUS ribavirin</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>
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**This will be denied as not medically necessary if 24 weeks is requested. See package insert for more info.**

**Chart Definitions**

**Cirrhotic:**
- Metavir Stage 4; or
- Ishak score of 5 or 6; or
- FibroTest/FibroSure score of more than 0.75; or
- APRI of greater than 2; or
- FibroScan results greater than 12.5kPA

**When Services Are Considered Not Medically Necessary**

Based on review of available data, the Company considers the use of ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak/Viekira XR) in the absence of clinical evidence or patient history that suggests the use of sofosbuvir/ledipasvir (Harvoni) will be ineffective or will cause an adverse reaction to the patient to be **not medically necessary.**

Based on review of available data, the Company considers the use of ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak/Viekira XR) for a genotype 1a, cirrhotic patient that is treatment naïve, a prior relapser, or a prior partial responder for more than 12 weeks of treatment to be **not medically necessary.**

**When Services Are Considered Investigational**

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak/Viekira XR) for the treatment of individuals with chronic hepatitis C virus (HCV) when patient selection criteria are not met (with the exception of those denoted in the patient selection criteria above as **not medically necessary**) to be investigational.*

**Background/Overview**

Viekira Pak and Viekira XR contain 4 ingredients. Ombitasvir is a HCV NS5A inhibitor, paritaprevir is a hepatitis C virus NS3/4A protease inhibitor, ritonavir is a CYP3A inhibitor, and dasabuvir is a HCV non-nucleoside NS5B palm polymerase inhibitor. Viekira Pak/ Viekira XR are both indicated for the treatment of patients with genotype 1 chronic HCV infection, including those with compensated cirrhosis. This product also carries an indication for HIV/HCV co-infection. Viekira Pak and Viekira XR need to be used in combination with ribavirin in most of its indications.

**Hepatitis C**

Hepatitis C is the most common blood borne pathogen. In the US, there are approximately 3.2 million people chronically infected with hepatitis C. Hepatitis C, a single-stranded ribonucleic acid (RNA) virus, is genetically complex with several recognized genotypes. Genotypes 1, 2, and 3 are the most frequently
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encountered genotypes worldwide. Type 1a is most frequently found in Northern Europe and North America, while 1b is most common in Japan and Southern and Eastern Europe.

Up until the last few years, Interferon alfa has been considered the only effective treatment of hepatitis C. A total of 40% of patients will show an initial response to interferon alfa, but most patients relapse soon after stopping treatment. Ribavirin (Rebetron®), a synthetic nucleoside analogue with antiviral activity, has also been investigated as a treatment of hepatitis C. Up until a few years ago, pegylated interferon alfa (Pegasys and Pegintron) and ribavirin were the standard treatment in patients with non-genotype 1 infections. The addition of the pegylated moiety improved the pharmacokinetic profile of the drug as well as doubled sustained virologic response (SVR) rates. The standard has since evolved into Sovaldi plus ribavirin for genotype 2 and 3 patients. The approval of hepatitis C protease inhibitors such as Victrelis and Incivek improved the arsenal of treatment options for those patients with hepatitis C genotype 1. These protease inhibitors were used in combination with pegylated interferon alfa and ribavirin for a variety of timeframes depending on the patient’s hepatitis C treatment status. Over the past few years, these drugs have fallen out of favor for the treatment of genotype 1 patients. The latest addition to the protease inhibitor family of medications is simeprevir (Olysio). Olysio is indicated for use in combination with pegylated interferon and ribavirin in genotype 1 patients. Sofosbuvir (Sovaldi) is actually part of a new class of medications in which it is the first approved drug of its kind. Sovaldi is a nucleotide analog NS5B polymerase inhibitor indicated for use in patients with genotypes 1-4 chronic HCV. It is approved for use in combination with pegylated interferon and ribavirin or with ribavirin alone in some situations. Harvoni (combination of sofosbuvir/ledipasvir) was recently launched, with desirable SVRs as well. With the addition of these new drugs, the majority of SVRs are in the 90% range. Recently the use of Olysio in combination with Sovaldi was approved by the U.S. Food and Drug Administration (FDA) (addressed in policy 00457). In late 2014, Viekira Pak was launched as well for the treatment of patients with genotype 1 chronic hepatitis C. Viekira Pak contains ritonavir along with a HCV NS5A inhibitor, a NS3/4A protease inhibitor, and a NS5B palm polymerase inhibitor. In mid-2016 an extended release version of Viekira was approved (Viekira XR). Zepatier, a new product from Merck was also recently approved for the treatment of genotype 1 HCV. Meanwhile, a pangenotypic product by Gilead was approved as well for genotypes 1-6 (Epclusa). Drugs and treatment regimens used for CHC will be part of an ever evolving landscape over the next few years.

Viekira Pak and Viekira XR have been integrated into the AASLD (American Association for the Study of Liver Diseases) guidelines in various scenarios for the treatment of HCV, however it should be noted that these guidelines are receiving constant updates as new products are approved.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
Viekira Pak was approved in late 2014 for the treatment of patients with genotype 1 chronic hepatitis C virus infection, including those with compensated cirrhosis. Viekira XR was approved in mid-2016 for the same indication.

Rationale/Source
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of
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The efficacy and safety of Viekira Pak was evaluated in six randomized, multicenter, clinical trials in 2,308 subjects with genotype 1 chronic HCV infection.

**Subjects with Chronic HCV GT1a Infection without Cirrhosis**
Subjects with chronic hepatitis C virus genotype 1a infection without cirrhosis were treated with Viekira Pak with ribavirin for 12 weeks in SAPPHIRE-I and -II and in PEARL-IV. The overall SVR12 in SAPPHIRE-I was 96%, PEARL-IV was 97% and SAPPHIRE-II was 96%.

**Subjects with Chronic HCV GT1b Infection without Cirrhosis**
Subjects with chronic HCV genotype 1b infection without cirrhosis were treated with Viekira Pak with or without ribavirin for 12 weeks in PEARL-II and –III. The SVR rate for HCV genotype 1b infected subjects without cirrhosis treated with Viekira Pak without RBV for 12 weeks in PEARL-II and PEARL-III was 100%.

**Subjects with Chronic HCV GT1a or GT1b Infection with Cirrhosis**
TURQUOISE-II was an open-label trial that enrolled 380 chronic HCV genotype 1a and 1b-infected subjects with cirrhosis and mild hepatic impairment (Child-Pugh A) who were either treatment-naïve or did not achieve SVR with prior treatment with peginterferon/ribavirin. Subjects were randomized to receive Viekira Pak in combination with ribavirin for either 12 or 24 weeks of treatment. The overall SVR in those patients with genotype 1b was 99% in the 12 week group. The overall SVR in patients with genotype 1a was 95% in the 24 week treatment group vs. 89% in the 12 week treatment group. If the treatment experienced patients are broken out and examined, there was a 100%SVR in the partial responders for 12 weeks of treatment (11/11), 93% in the relapsers (14/15), and 80% in the null responders (40/50). In the 24 week group, the partial responders had a 100% SVR (10/10), the relapsers had a 100% SVR (13/13), and the null responders had a 93% SVR (39/42). This data shows that the 24 week regimen is more appropriate than the 12 week regimen for those with genotype 1a and cirrhosis that were prior null responders. Based on the 12 week data, the package insert states that 12 weeks may be considered based on prior treatment history.

**Select Liver Transplant Recipients OR HIV/HCV Co-infection**
Viekira Pak with ribavirin was administered for 24 weeks to 34 chronic HCV genotype 1-infected liver transplant recipients who were at least 12 months post transplantation at enrollment with normal hepatic function and mild fibrosis (Metavir fibrosis score F2 or lower). The initial dose of ribavirin was left to the discretion of the investigator with 600 to 800 mg per day being the most frequently selected dose range at initiation of Viekira Pak and at the end of treatment. Of the 34 subjects (29 with genotype 1a infection and 5 with genotype 1b infection) enrolled, (97%) achieved SVR12 (97% in subjects with GT1a infection and 100% of subjects with GT1b infection). One subject with HCV GT1a infection relapsed post-treatment.

In an open-label clinical trial 63 subjects with chronic HCV genotype 1 infection co-infected with HIV-1 were treated for 12 or 24 weeks with Viekira Pak in combination with ribavirin. Subjects were on a stable HIV-1...
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Antiretroviral therapy (ART) regimen that included tenofovir disoproxil fumarate plus emtricitabine or lamivudine, administered with ritonavir boosted atazanavir or raltegravir. The SVR12 rates were 91% (51/56) for subjects with genotype 1a infection and 100% (7/7) for those with genotype 1b infection. Of the 5 subjects who were non-responders, 1 experienced virologic breakthrough, 1 discontinued treatment, 1 experienced relapse and 2 subjects had evidence of HCV re-infection post-treatment. One subject had confirmed HIV-1 RNA >400 copies/mL during the post-treatment period. This subject had no evidence of resistance to the ART regimen. No subjects switched their ART regimen due to loss of plasma HIV-1 RNA suppression.

References

Policy History
Original Effective Date:  02/18/2015
Current Effective Date:  02/15/2017
02/05/2015  Medical Policy Committee review
02/18/2015  Medical Policy Implementation Committee approval. New policy.
02/04/2016  Medical Policy Committee review
02/17/2016  Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/02/2017  Medical Policy Committee review
02/15/2017  Medical Policy Implementation Committee approval. Integrated the new dosage form (Viekira XR) into the medical policy.
Next Scheduled Review Date:  02/2018

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:
A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

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C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease. For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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