Treatment of Hepatitis C with simeprevir (Olysio®) PLUS sofosbuvir (Sovaldi®)

Archived Medical Policy

Archived medical policies are no longer subject to periodic review, are maintained for reference, and may be returned to active status if the need is identified.

Policy # 00457
Original Effective Date: 11/21/2014
Archived 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 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 ombitasvir, paritaprevir, ritonavir, and dasabuvir (Viekira Pak®)† is addressed separately in medical policy 00462.

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.

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.
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Based on review of available data, the Company may consider combination therapy with simeprevir (Olysio) PLUS sofosbuvir (Sovaldi) for the treatment of chronic hepatitis C virus (HCV) to be **eligible for coverage**.

Patient Selection Criteria

Based on review of available data, the Company may consider combination therapy with simeprevir (Olysio) PLUS sofosbuvir (Sovaldi) when ALL of the following criteria (I, II, III, IV, V, VI, and VII) are met:

I. 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**

II. Patient has a diagnosis of chronic hepatitis C virus (HCV), genotype 1; AND

III. Patient does NOT have decompensated cirrhosis; AND

IV. Patient has NOT been treated with a sofosbuvir containing regimen (ie, Sovaldi, Harvoni) in the past; AND

V. Patient has NOT been treated with a hepatitis C virus (HCV) NS3/4A protease inhibitor containing regimen in the past (ie Olysio, Incivek, Victrelis, Viekira Pak); AND

VI. The combination of simeprevir (Olysio) PLUS sofosbuvir (Sovaldi) is NOT used in combination with pegylated interferon; AND

VII. Patient meets the following definitions and adheres to the timeframes for treatment:

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Length of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naïve patients WITHOUT cirrhosis AND treatment experienced patients WITHOUT cirrhosis</td>
<td>12 weeks of Olysio PLUS Solvaldi</td>
</tr>
<tr>
<td>Treatment naïve patients WITH cirrhosis AND treatment experienced patients WITH cirrhosis</td>
<td>24 weeks of Olysio PLUS Solvaldi</td>
</tr>
</tbody>
</table>

Table Definitions:

Treatment **experienced**: defined as prior relapsers, prior partial responders, and prior null responders who failed prior interferon based therapy.

Cirrhosis:

- Metavir Stage 4; or
- Ishak score of 5 or 6; or
- FibroTest/FibroSure score greater than 0.75; or
- APRI of greater than 2; or
- FibroScan results greater than 12.5kPA
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When Services Are Considered Not Medically Necessary

Based on review on available data, the Company considers the use of combination therapy with simeprevir (Olysio) PLUS sofosbuvir (Sovaldi) WITHOUT 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.**

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 combination therapy with simeprevir (Olysio) PLUS sofosbuvir (Sovaldi) when patient selection criteria are NOT met (with the exception of the criterion denoted above as not medically necessary**) to be investigational.*

Background/Overview

Olysio is a HCV NS3/4A protease inhibitor indicated for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen. Olysio’s efficacy has been established in combination with pegylated interferon alfa and ribavirin in genotype 1 infected patients with compensated liver disease (including cirrhosis). It’s efficacy in combination with Sovaldi has also been recently established. Therefore, Olysio was also approved for use in combination with Sovaldi in genotype 1 patients. Olysio must not be used as monotherapy. It is recommended that patients with HCV genotype 1a infections with the Q80K mutation be given an alternative therapy. The Q80K mutation is likely overcome by the use of combination therapy with Sovaldi, so this is not a requirement for those patients using combination therapy with Sovaldi.

Sovaldi is a HCV nucleotide analog NS5B polymerase inhibitor indicated for the treatment of CHC infection as a component of a combination antiviral treatment regimen. Sovaldi’s efficacy has been established in subjects with HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection. Sovaldi should be used in combination with ribavirin or in combination with pegylated interferon and ribavirin, depending on the patient scenario. The manufacturer of Sovaldi did not seek an additional indication for use with Olysio, and therefore the label is unlikely to change.

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. Another recently released drug, Sovaldi (sofosbuvir), 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. With the addition of these new drugs, the majority of SVRs are in the 90% range. Harvoni was recently launched, with desirable SVRs as well, and is an interferon and ribavirin free regimen. Recently the use of Olysio in combination with Sovaldi was approved by the FDA. Even though this combination is mentioned in treatment guidelines, its use will be limited due to the availability of Harvoni, which is an interferon and ribavirin free regimen as well. Harvoni is less costly than using combination therapy with Olysio and Sovaldi. 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 (addressed in policy 00462). Drugs and treatment regimens used for CHC will be part of an ever evolving landscape over the next few years.

This combination (Olysio PLUS Sovaldi) has been integrated into the American Association for the Study of Liver Diseases (AASLD) 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)
Olysio was approved in November of 2013 and is indicated for the treatment of CHC genotype 1 infections in select patient populations as part of a combination antiviral treatment regimen. Janssen gained an
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additional indication in November 2014 for use along with Sovaldi for the treatment of patients with HCV genotype 1. Sovaldi was approved in December of 2013 and is indicated for the treatment of CHC genotype 1-4 as a component of a combination antiviral treatment regimen.

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 medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The COSMOS trial was a phase II trial that evaluated the safety and efficacy of 12 or 24 weeks of Olysio in combination with Sovaldi with or without ribavirin in patients with HCV genotype 1 infection. There were 2 cohorts. The first cohort included those that were prior null responders with a Metavir score of F0-F2. The second cohort included subjects that were treatment naïve or null responders with Metavir scores of F3-F4 and compensated liver disease. The overall SVR12 in those receiving 12 weeks of Olysio PLUS Sovaldi with F0-F3 was 95% (61/64). The overall SVR12 in those patients with F4 receiving 24 weeks of therapy was 96% (22/23).

References

Policy History
Original Effective Date: 11/21/2014
11/06/2014 Medical Policy Committee review
02/05/2015 Medical Policy Committee review
02/18/2015 Medical Policy Implementation Committee approval. Removed any mention of F3/F4. Updated background info. Clarified that patient should NOT have decompensated cirrhosis.
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. Recommend archiving policy.
02/15/2017 Medical Policy Implementation Committee approval. Archived.
Next Scheduled Review Date: 02/15/2017
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*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 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
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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