Boceprevir (Victrelis™)

UTILIZATION MANAGEMENT CRITERIA

**DRUG CLASS:** Protease Inhibitors

**BRAND (generic) NAMES:** Victrelis (boceprevir); 200mg strength capsule

**FDA-APPROVED INDICATIONS**

Victrelis (boceprevir) is a hepatitis C virus (HCV) NS3/4A protease inhibitor indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients (18 years of age or older) with compensated liver disease, including cirrhosis, who are previously untreated or who have failed previous interferon and ribavirin therapy, including prior null responders, partial responders, and relapsers.

Victrelis must not be used as monotherapy and should only be used in combination with peginterferon alfa and ribavirin.

The efficacy of Victrelis has not been studied in patients who have previously failed therapy with a treatment regimen that includes Victrelis or other HCV NS3/4A protease inhibitors.

**COVERAGE AUTHORIZATION CRITERIA**

**INITIAL THERAPY**

Boceprevir (Victrelis) may be eligible for coverage when the following criteria are met:

1. The patient is 18 years of age or older; **AND**
2. The patient has a diagnosis of chronic hepatitis C (CHC) infection with confirmed genotype 1; **AND**
3. The patient:
   - Has F2 or higher on the IASL, Batts-Ludwig, or Metavir fibrosis staging scales (medical record documentation required); **OR**
   - Has F3 or higher on the Ishak fibrosis staging scale (medical record documentation required); **OR**
   - Has cirrhosis secondary to CHC [Metavir F4, Ishak F5-6, or radiographic evidence of portal hypertension, esophageal varices, ascites (medical record documentation required)]; **AND**
4. The patient has contraindications to a sofosbuvir-based regimen (i.e., Sovaldi or Harvoni), in addition to Viekira Pak. Medical record documentation required; **AND**
5. The patient has compensated liver disease (Child-Pugh score <6); **AND**
6. The patient has completed, or will be completing, a 4-week “lead-in” with peginterferon alfa (i.e., Peg-Intron or Pegasys) and ribavirin prior to initiating boceprevir; **AND**
7. Boceprevir is prescribed in combination with both peginterferon alfa (Peg-Intron or Pegasys) and ribavirin; **AND**
8. The patient has not previously failed a course of therapy that included a protease inhibitor used to treat CHC (boceprevir, simeprevir, or telaprevir); **AND**
9. The patient will not be taking boceprevir in combination with other protease inhibitors used to treat CHC (i.e. simeprevir or telaprevir); **AND**
10. The patient has not attempted a previous course of therapy with a sofosbuvir-based regimen (i.e. Sovaldi, Harvoni), OR with a ombitasvir/paritaprevir/ritonavir/dasabuvir combination-based regimen (i.e., Viekira Pak); **AND**
11. Boceprevir is prescribed by or in consultation with a physician with expertise and experience in the management of infectious hepatitis; **AND**
12. The patient does not have any FDA labeled contraindications to therapy with the requested agent(s).

**APPROVAL DURATION**

Approval of boceprevir for 44 weeks (maximum FDA-labeled duration for total boceprevir therapy) will be given in patients:
- with compensated cirrhosis, OR
- with null response to prior interferon-based therapy, OR
- naïve to hepatitis C treatment and who did not achieve a decline from baseline in HCV-RNA of 0.5-log10 or more at Treatment Week 4 with peginterferon alfa plus ribavirin alone.

Approval of boceprevir for 32 weeks will be given in patients without cirrhosis who experienced partial response or relapse to prior interferon-based therapy.

Patients without cirrhosis who are naïve to treatment
- **INITIAL THERAPY**: Approval of boceprevir for 12 weeks.
- **RENEWAL EVALUATION**:
  - Patients whose HCV RNA at Treatment Week 8 is undetectable - approval of boceprevir for an additional 12 weeks
  - Patients whose HCV RNA at 8 weeks is detectable – approval of boceprevir for an additional 20 weeks.

**CONTRAINDICATIONS:**
All contraindications to peginterferon alfa and ribavirin also apply since Victrelis must be administered with peginterferon alfa and ribavirin.
- Because ribavirin may cause birth defects and fetal death, boceprevir in combination with peginterferon alfa and ribavirin is contraindicated in pregnant women and in men whose female partners are pregnant.
- Coadministration with drugs that are highly dependent on CYP3A4/5 for clearance, and for which elevated plasma concentrations are associated with serious and/or life-threatening events.
- Potent CYP3A4/5 inducers where significantly reduced boceprevir plasma concentrations may be associated with reduced efficacy.

**WARNINGS AND PRECAUTIONS:**

*Use of Victrelis with Ribavirin and Peginterferon alfa:*

- **Ribavirin** may cause birth defects and fetal death; avoid pregnancy in female patients and female partners of male patients. Patients must have a negative pregnancy test prior to therapy; use two or more forms of contraception, and have monthly pregnancy tests.
- **Anemia** - The addition of Victrelis to peginterferon alfa and ribavirin is associated with an additional decrease in hemoglobin concentrations compared with peginterferon alfa and ribavirin alone.
- **Neutropenia** - The addition of Victrelis to peginterferon alfa and ribavirin may result in worsening of neutropenia associated with peginterferon alfa and ribavirin therapy alone.

**DOSAGE AND ADMINISTRATION:**

*Victrelis/Peginterferon Alfa/Ribavirin Combination Treatment*

Victrelis must be administered in combination with peginterferon alfa and ribavirin. The dose of Victrelis is 800 mg (four 200-mg capsules) three times daily (every 7-9 hours) with food [a meal or light snack] (see Table 1).

The following dosing recommendations differ for some subgroups from the dosing studied in the Phase 3 trials. Response-Guided Therapy (RGT) is recommended for most individuals, but longer dosing is recommended in targeted subgroups (e.g., patients with cirrhosis).

*Victrelis Combination Therapy: Patients Without Cirrhosis Who Are Previously Untreated or Who Are Previous Partial Responders or Relapsers to Interferon and Ribavirin therapy*

- Initiate therapy with peginterferon alfa and ribavirin for 4 weeks (Treatment Weeks 1-4).
- Add Victrelis 800 mg (four 200-mg capsules) orally three times daily (every 7-9 hours) to peginterferon alfa and ribavirin regimen after 4 weeks of treatment. Based on the patient's HCV-RNA levels at Treatment Week (TW) 8, TW12 and TW24, use the following Response-Guided Therapy (RGT) guidelines to determine duration of treatment (see Table 1).
Table 1: Duration of Therapy Using Response-Guided Therapy (RGT) Guidelines in Patients Without Cirrhosis Who Are Previously Untreated or Who Are Previous Partial Responders or Relapsers to Interferon and Ribavirin Therapy

<table>
<thead>
<tr>
<th>ASSESSMENT* (HCV-RNA Results**)</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At Treatment Week 8</strong></td>
<td><strong>At Treatment Week 24</strong></td>
</tr>
<tr>
<td>Previously Untreated Patients</td>
<td></td>
</tr>
<tr>
<td>Undetectable</td>
<td>Undetectable</td>
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<tr>
<td>Detectable</td>
<td>Undetectable</td>
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<tr>
<td>Previous Partial Responders or Relapsers</td>
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<tr>
<td>Undetectable</td>
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<td>Detectable</td>
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</table>

*TREATMENT FUTILITY
If the patient has HCV-RNA results greater than or equal to 100 IU/mL at TW12, then discontinue three medicine regimen. If the patient has confirmed, detectable HCV-RNA at TW24, then discontinue three medicine regimen.

**In clinical trials, HCV-RNA in plasma was measured using a Roche COBAS® TaqMan® assay with a lower limit of quantification of 25 IU/mL and a limit of detection of 9.3 IU/mL.

Response-Guided Therapy was not studied in subjects who had less than a 2-log10 HCV-RNA decline by treatment week 12 during prior therapy with peginterferon alfa and ribavirin. If considered for treatment, these subjects should receive 4 weeks of peginterferon alfa and ribavirin followed by 44 weeks of Victrelis 800 mg orally three times daily (every 7-9 hours) in combination with peginterferon alfa and ribavirin. In addition, consideration should be given to treating previously untreated patients who are poorly interferon responsive (as determined at TW4) with 4 weeks peginterferon alfa and ribavirin followed by 44 weeks of Victrelis 800 mg orally three times daily (every 7-9 hours) in combination with peginterferon alfa and ribavirin in order to maximize rates of SVR.

Victrelis Combination Therapy: Patients with Cirrhosis
Patients with compensated cirrhosis should receive 4 weeks peginterferon alfa and ribavirin followed by 44 weeks Victrelis 800 mg (four 200-mg capsules) three times daily (every 7-9 hours) in combination with peginterferon alfa and ribavirin.
Dose Modification

- Dose reduction of Victrelis is not recommended.
- If a patient has a serious adverse reaction potentially related to peginterferon alfa and/or ribavirin, the peginterferon alfa and/or ribavirin dose should be reduced or discontinued. Refer to the peginterferon alfa and ribavirin Package Inserts for additional information about how to reduce and/or discontinue the peginterferon alfa and/or ribavirin dose. Victrelis must not be administered in the absence of peginterferon alfa and ribavirin.

Discontinuation of Dosing Based on Treatment Futility
Discontinuation of therapy is recommended in all patients with 1) HCV-RNA levels of greater than or equal to 100 IU/mL at TW12; or 2) confirmed detectable HCV-RNA levels at TW24.

Table 2
Drugs that are contraindicated with Victrelis
(Drugs that are highly dependent on CYP3A4/5 for clearance, and for which elevated plasma concentrations are associated with serious and/or life-threatening events, and potent CYP3A4/5 inducers where significantly reduced boceprevir plasma concentrations may be associated with reduced efficacy)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drugs Within Class that are Contraindicated With Victrelis</th>
<th>Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha 1-Adrenergic antagonist</td>
<td>Alfuzosin</td>
<td>Increased alfuzosin concentrations can result in Hypotension</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine, phenobarbital, phenytoin</td>
<td>May lead to loss of virologic response to Victrelis</td>
</tr>
<tr>
<td>Antimycobacterial</td>
<td>Rifampin</td>
<td>May lead to loss of virologic response to Victrelis</td>
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<tr>
<td>Ergot Derivatives</td>
<td>Dihydroergotamine, ergonovine, ergotamine, methylergonovine</td>
<td>Potential for acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues</td>
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<tr>
<td>GI Motility Agent Cisapride Potential for cardiac arrhythmias.</td>
<td>Cisapride</td>
<td>Potential for cardiac arrhythmias</td>
</tr>
<tr>
<td>Herbal Products</td>
<td>St. John’s Wort (hypericum perforatum)</td>
<td>May lead to loss of virologic response to Victrelis</td>
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<tr>
<td>HMG-CoA Reductase Inhibitors</td>
<td>Lovastatin, simvastatin</td>
<td>Potential for myopathy, including rhabdomyolysis</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td>Drospirenone</td>
<td>Potential for hyperkalemia</td>
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<tr>
<td>PDE5 enzyme Inhibitor</td>
<td>REVATIO® (sildenafil) or ADCIRCA® (tadalafil) when used for the treatment of pulmonary arterial hypertension*</td>
<td>Potential for PDE5 inhibitor-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope</td>
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<tr>
<td>Neuroleptic</td>
<td>Pimozide</td>
<td>Potential for cardiac arrhythmias</td>
</tr>
<tr>
<td>Sedative/Hypnotics</td>
<td>Triazolam; orally administered Midazolam*</td>
<td>Prolonged or increased sedation or respiratory depression</td>
</tr>
</tbody>
</table>

*See Victrelis product labeling for information on the coadministration of sildenafil and tadalafil when dosed for erectile dysfunction, and for information on parenterally administered midazolam.

REFERENCES: