## Protease Inhibitors for Hepatitis C

### Covered Medications
- Boceprevir (Victrelis™)
- Telaprevir (Incivek™)

### What they do and how they are used
- Victorlis and Incivek are indicated for combination therapy with peginterferon alfa and ribavirin for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease, including cirrhosis, who are treatment-naïve or who have previously been treated with interferon-based treatment.
- Victorlis and Incivek are protease inhibitors, which work by binding to the virus and preventing it from multiplying.
- According to the U.S. Centers for Disease Control and Prevention, about 3.2 million people in the United States have chronic hepatitis C, a viral disease that causes inflammation of the liver that can lead to diminished liver function or liver failure. Most people with hepatitis have no symptoms of the disease until liver damage occurs, which may take several years.
- The dose of Incivek for ALL patients is 750 mg (two 375-mg tablets) taken orally three times a day (7-9 hours apart), with food, for 12 weeks, in combination with peginterferon alfa and ribavirin.
- The dose of Victorlis is 800 mg (four 200-mg capsules) three times daily (every 7-9 hours) with food. The patient should receive 4 weeks of peginterferon alfa and ribavirin followed by 24, 32 or 44 weeks of Victorlis in combination with peginterferon alfa and ribavirin.
- The total duration of therapy for boceprevir is determined based upon whether a patient has previously been treated with interferon-based treatment AND their response to therapy.
- **Treatment naïve patients** who have an undetectable hepatitis C viral load (HCV-RNA) at Treatment Week 8 (that is, and early responder, after 4 weeks of boceprevir) AND undetectable at TW24 may discontinue all three medications at TW 28. Those who do not achieve undetectable levels until TW24 should receive 32 weeks of boceprevir.
- Further, if at TW 4, the patient achieves less than 0.5-log10 decrease in HCV-RNA, the patient can be classified as poorly interferon responsive and is predicted to have a lower likelihood of achieving sustained virological response (SVR). Therefore, therapy with boceprevir should be continued for up to 44 weeks.
- It is recommended that patients with cirrhosis, regardless of whether or not they have been previously treated, continue boceprevir for up to 44 weeks.
- Patients who have been previously treated with an interferon product and are eligible for a triple-medication regimen with peginterferon alfa, ribavirin, and a protease inhibitor fall into three categories:
  - **Relapsers** are defined as patients who achieved an end-of-treatment response (undetectable HCV RNA at the end of treatment) but subsequently relapsed and did not achieve a SVR.
  - **Partial responders** are patients who achieved a decrease in HCV RNA of greater than or equal to 2-log10 by week 12, but never achieved SVR.
  - **Non-responders or Null responders** are patients who failed to achieve a decline of 2-log10 HCV RNA after 12 weeks of treatment or who never achieved undetectable HCV RNA during treatment of a minimum duration of 24 weeks.
- Relapsers and partial responders should receive 32 weeks of boceprevir while therapy in null responders should continue for up to 44 weeks.
- **Futility rules** to determine when to stop therapy are part of the response-guided therapy recommendations in labeling to help prescribers predict whether continuing the three-drug regimen will be beneficial for the patient.
- Patients with inadequate viral response are unlikely to achieve sustained virologic response (SVR), and may develop treatment-emergent resistance substitutions:
  - For Victorlis - If the patient has hepatitis C virus (HCV) RNA results greater than or equal to 100 IU/mL at treatment week 12 or confirmed detectable HCV RNA at treatment week 24, then the three-drug regimen, boceprevir, peginterferon alfa and ribavirin, should be discontinued.
  - For Incivek – If the patient has HCV RNA results greater than or equal to 1000 IU/mL at either treatment week 4 or treatment week 12, then the three-drug regimen should be discontinued. If the patient has confirmed detectable HCV RNA levels at treatment week 24, peginterferon alfa and ribavirin therapy should be discontinued.
Rationale for coverage authorization
To reduce exposure to cost associated with use for conditions for which effectiveness is not known (for example, genotypes other than viral genotype 1, patients with decompensated liver disease) and to limit exposure to longer durations of therapy.

<table>
<thead>
<tr>
<th>Drug</th>
<th>AWP per tablet</th>
<th>AWP per day</th>
<th>AWP per month</th>
<th>AWP per course of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incivek 375 mg</td>
<td>$117</td>
<td>$702</td>
<td>$19,680</td>
<td>$59,040 per 12 weeks</td>
</tr>
<tr>
<td>Victrelis 200 mg</td>
<td>$16</td>
<td>$189</td>
<td>$5,300</td>
<td>$42,400 per 32 weeks $58,200 per 44 weeks</td>
</tr>
</tbody>
</table>

Benefit design
- Coverage is determined through prior authorization for every claim AND
- Coverage is provided for a quantity sufficient for one course of therapy for Chronic Hepatitis C

Coverage authorization criteria
Coverage is provided in accord with the following criteria:

1. Coverage is provided for the treatment of genotype 1 chronic hepatitis C as indicated by a quantifiable hepatitis C viral level
2. Coverage is provided when boceprevir OR telaprevir is used in combination with a peginterferon alfa product and ribavirin
3. Coverage is not provided:
   - For use in patients infected with genotypes other than viral genotype 1
   - For use in patients with decompensated liver disease
   - For use in patients who have previously failed either boceprevir or telaprevir due to lack of efficacy

Covered quantity and duration:
Boceprevir – Coverage is provided for a quantity not to exceed 2400 mg per day (administered as four 200 mg capsules three times per day).

Coverage is provided for up to 32 weeks (8 months). Note: the first four weeks of therapy is comprised of standard of care peginterferon alfa and ribavirin followed by the addition of boceprevir.

OR

For past null responders or treatment-naïve poor responders or patients with compensated cirrhosis, coverage is provided for up to 44 weeks (11 months). Note: null responders are patients who have not achieved a 2-\( \log_{10} \) or more decrease by week 12 or 0.5 \( \log_{10} \) or more decrease by week 4 in HCV RNA from baseline. Poor responders are patients who have not achieved a 0.5 \( \log_{10} \) or more decrease by week 4 in HCV RNA from baseline.

Coverage of boceprevir beyond 44 weeks is not provided.

Telaprevir – Coverage is provided for quantity not to exceed 2250 mg per day (administered as two 375 mg tablets three times per day).

Coverage is provided for up to 12 weeks (3 months). Note: telaprevir is initiated with standard of care peginterferon alfa and ribavirin.

Coverage for an additional or longer course of therapy with telaprevir is not provided.
<table>
<thead>
<tr>
<th>References</th>
</tr>
</thead>
</table>