

# Boceprevir (*Victrelis*)

**Discontinued.** This treatment has been discontinued.

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## Drug Summary

Boceprevir is a first-generation hepatitis C protease inhibitor that played a valuable role in treatment of patients with genotype 1 infection during the years 2011, 2012, and 2013. With the availability of multiple, new direct-acting antiviral agents that are far superior to boceprevir, Merck has made the decision to discontinue the manufacturing of boceprevir. The relevance of boceprevir is now historical, but prior treatment failure with a boceprevir-based regimen may have resulted in development of resistance-associated variants.

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## Adverse Effects

The most common adverse effects reported with boceprevir are anemia, decreased neutrophil count, dysgeusia (alteration in taste), and vomiting. Rare cases of severe hypersensitivity reaction have been reported in patients taking boceprevir in combination with peginterferon and ribavirin. Boceprevir is classified as pregnancy category B.

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## Class and Mechanism

Boceprevir (*Victrelis*) is a NS3/4A protease inhibitor. Specifically, boceprevir inhibits the proteolytic cleavage of the HCV encoded polyprotein, an essential step in the viral life cycle for the production of mature forms of the viral proteins NS4A, NS4B, NS5A, and NS5B.

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## Manufacturer for United States

Boceprevir (*Victrelis*) is no longer manufactured in the United States. Boceprevir (*Victrelis*) ([Figure 1](#)) was previously manufactured by Merck & Co. Boceprevir was developed at Schering-Plough, which merged with Merck & Co. in 2009.

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## FDA Status

On May 13, 2011, Boceprevir was approved by the FDA for treatment of chronic hepatitis C in adults in combination with peginterferon-alpha and ribavirin. Boceprevir (*Victrelis*) is no longer manufactured in the United States.

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## Indications

The following list summarizes the key points related to boceprevir indications.

- Boceprevir is approved for use in combination with peginterferon and ribavirin to treat adults with genotype 1 chronic hepatitis C infection and compensated liver disease.
  - Boceprevir is approved for hepatitis C treatment-naïve patients and in patients with prior interferon-based treatment, including null responders, partial responders, and relapsers.
  - Boceprevir should never be used as monotherapy due to the rapid development of resistance when used alone.
  - A high percentage of treatment-experienced patients who had a prior null response do not obtain an SVR when treated with a boceprevir-based regimen.
  - The efficacy of boceprevir in patients who have previously failed a regimen that included a protease inhibitor is unknown.
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## Dosing

Boceprevir was manufactured as 200 mg capsules ([Figure 2](#)). The recommended dose for boceprevir is 800 mg orally three times daily (every 7 to 9 hours) with food (a meal or light snack) in combination with peginterferon and ribavirin. No dose adjustment is recommended with any degree of renal or hepatic impairment.

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## Clinical Use

Boceprevir is given with peginterferon and ribavirin. The treatment regimen consists of an initial 4 weeks of only peginterferon plus ribavirin. After this 4-week lead-in treatment, boceprevir is added to the peginterferon and ribavirin, with the total treatment duration dependent on the patient's virologic response to therapy, prior response status, and presence or absence of cirrhosis.

- For previously untreated patients who have an undetectable HCV RNA at weeks 8 and 24, continue the three medications to treatment week 28 (total duration of boceprevir 24 weeks and peginterferon plus ribavirin 28 weeks).
- For previously untreated patients with a detectable HCV RNA at week 8 and nondetectable HCV RNA at week 24, continue all three medications to week 36 and then peginterferon and ribavirin should be continued for an additional 12 weeks (total duration of boceprevir 32 weeks and peginterferon plus ribavirin for 48 weeks).
- For treatment-experienced patients who were previous partial responders or relapsers, if the HCV RNA is undetectable at weeks 8 and 24, continue the three medications to treatment week 36 (total duration of boceprevir 32 weeks and peginterferon ribavirin 36 weeks).
- For previously treated patients who are previous partial responders or relapsers, if the HCV RNA is detectable at week 8 and nondetectable at week 24, all three medications should be continued to week 36 and then peginterferon and ribavirin should be continued for an additional 12 weeks (total duration of boceprevir 32 weeks and peginterferon plus ribavirin 48 weeks).
- Previously treated patients who were previous null responders should continue all three medications to week 48 (total duration of boceprevir 44 weeks and peginterferon plus ribavirin 48 weeks).
- Patients with cirrhosis (treatment-naïve or treatment experienced) should continue all three medications to week 48 (total duration of boceprevir 44 weeks and peginterferon ribavirin 48 weeks).
- Therapy should be discontinued if: (a) the patient has an HCV RNA level greater than 100 IU/mL at treatment week 4 or 12, or (b) the patient has a confirmed detectable HCV RNA level at treatment week 24.

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## Cost and Medication Access

Boceprevir (*Victrelis*) is no longer manufactured in the United States.

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## Resistance

Among patients on a boceprevir-based regimen, resistance to boceprevir develops in more than 50% who do not achieve a SVR; the development of specific mutations and the impact of these mutations varies depending on whether the patient has genotype 1a or 1b HCV.

- In clinical trials, the most common treatment-associated resistance mutations to develop in patients with genotype 1a were V36M, T54S, and R155K.
- In vitro studies with genotype 1a have shown the following impact on boceprevir activity: (a) more than 10-fold reduced activity with the R155T and A156S mutations, (b) a 2- to 6-fold reduced activity with V36A/L/M, Q41R, T54A/S, V55A, R155K and V158I mutations, and (c) more than 10-fold reduced sensitivity with the double amino acid substitutions V55A+I170V, T54S+R155K, R155K+D168N, R155T+D168N and V36M+R155K.

- In clinical trials, the most common treatment-associated resistance mutations to develop in patients with genotype 1b were T54A, T54S, V55A, A156S, and V170A.
- In vitro studies with genotype 1b have shown the following impact on boceprevir activity: (a) more than 10-fold reduced activity with A156S/T/V, V170A and V36M+R155K mutations and (b) a 2- to 8-fold reduced activity with V36A/M, Q41R, F43S, T54A/G/S, V55A/I, R155K, V158I, V170M and M175L mutations.

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## Key Drug Interactions

Boceprevir metabolism occurs primarily through aldo-ketoreductase and partly via CYP3A4/5. In addition, boceprevir is a substrate for p-glycoprotein. Levels of boceprevir do not significantly change with concomitant administration of aldo-ketoreductase inhibitors. Significant interactions can occur with boceprevir and other drugs that are primarily metabolized via CYP3A4/5. Use of boceprevir is contraindicated with a number of medications that are either potent CYP3A4/5 inducers or medications that are highly dependent on CYP3A4/5 for clearance. See the [Boceprevir \(Victrelis\) full Prescribing Information](#) for a detailed description of drug interactions with boceprevir.

For complete information on boceprevir-related drug interactions, see the [Drug Interactions section in the Boceprevir \(Victrelis\) Prescribing Information](#).

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## Full Prescribing Information

[Boceprevir \(Victrelis\) Full Prescribing Information](#). Note that Boceprevir (Victrelis) is no longer manufactured in the United States.

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## Figures

[Figure 1. Boceprevir \(Victrelis\) Packaging](#)

Photo: Andrew Karpenko, University of Washington

[Figure 2. Boceprevir \(Victrelis\) Capsules](#)

Photo: Andrew Karpenko, University of Washington

