HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VICTRELIS safely and effectively. See full prescribing information for VICTRELIS.

VICTRELIS® (boceprevir) capsules, for oral use
Initial U.S. Approval: 2011

---------- RECENT MAJOR CHANGES ----------
Contraindications (4) 01/2017

----------INDICATIONS AND USAGE----------
VICTRELIS 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 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. (1)

- VICTRELIS must not be used as a monotherapy and should only be used in combination with peginterferon alfa and ribavirin. (1)
- 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. (1)

---------- DOSAGE AND ADMINISTRATION ----------
- 800 mg administered orally three times daily (every 7 to 9 hours) with food (a meal or light snack). (2)
- VICTRELIS must be administered in combination with peginterferon alfa and ribavirin. Initiate therapy with peginterferon alfa and ribavirin for 4 weeks, then add VICTRELIS to peginterferon alfa and ribavirin regimen. The duration of treatment is based on viral response, prior response status and presence of cirrhosis. (2)
- Refer to the prescribing information for peginterferon alfa and ribavirin for specific dosing instructions. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Capsules: 200 mg (3)

----------CONTRAINDICATIONS----------
- **All contraindications to peginterferon alfa and ribavirin also apply since VICTRELIS must be administered with peginterferon alfa and ribavirin. (4)**
- 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. (4)
- Contraindicated in patients with a history of a hypersensitivity reaction to boceprevir. (4)
- 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 is contraindicated. (4)
- Coadministration with potent CYP3A4/5 inducers where significantly reduced boceprevir plasma concentrations may be associated with reduced efficacy is contraindicated. (4)

----------WARNINGS AND PRECAUTIONS----------
Use of VICTRELIS with Ribavirin and Peginterferon alfa:
- **Embryofetal Toxicity (Use 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. (5.1)
- 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. (5.2)
- Neutropenia - The addition of VICTRELIS to peginterferon alfa and ribavirin may result in worsening of neutropenia associated with peginterferon alfa and ribavirin therapy alone. (5.3)
- Hypersensitivity – Serious acute hypersensitivity reactions (e.g., urticaria, angioedema) have been observed during combination therapy with VICTRELIS, peginterferon alfa and ribavirin. (5.5)

----------ADVERSE REACTIONS----------
The most commonly reported adverse reactions (greater than 35% of subjects) in clinical trials in adult subjects receiving the combination of VICTRELIS with PegIntron and REBETOL were fatigue, anemia, nausea, headache and dysgeusia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- VICTRELIS is a strong inhibitor of CYP3A4/5 and is partly metabolized by CYP3A4/5. The potential for drug-drug interactions must be considered prior to and during therapy. (4, 7, 12.3)

----------USE IN SPECIFIC POPULATIONS----------
- Safety and efficacy have not been studied in the following populations:
  - Patients with decompensated cirrhosis (8.7); and
  - Organ transplant recipients (8.8)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 01/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VICTRELIS® (boceprevir) is indicated for the treatment of chronic hepatitis C genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients 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 *[see Clinical Studies (14)].*

The following points should be considered when initiating VICTRELIS for treatment of chronic hepatitis C infection:

- 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.
- Poorly interferon responsive patients who were treated with VICTRELIS in combination with peginterferon alfa and ribavirin have a lower likelihood of achieving a sustained virologic response (SVR), and a higher rate of detection of resistance-associated substitutions upon treatment failure, compared to patients with a greater response to peginterferon alfa and ribavirin *[see Microbiology (12.4) and Clinical Studies (14)].*

2 DOSAGE AND ADMINISTRATION

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 to 9 hours) with food [a meal or light snack] (see Table 1). Refer to the prescribing information for peginterferon alfa and ribavirin for instructions on dosing.

The following dosing recommendations differ for some subgroups from the dosing studied in the Phase 3 trials *[see Clinical Studies (14)]*. Response-Guided Therapy (RGT) is recommended for most individuals, but longer dosing is recommended in targeted subgroups (e.g., patients with cirrhosis).

2.1 VICTRELIS/Peginterferon alfa/Ribavirin Combination Therapy: Patients Without Cirrhosis Who Are Previously Untreated or Who Previously Failed 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 to 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 guidelines to determine duration of treatment (see Table 1).

Table 1
Duration of Therapy in Patients Without Cirrhosis Who Are Previously Untreated or Who Previously Failed Interferon and Ribavirin Therapy

	ASSESSMENT* (HCV-RNA Results†)		RECOMMENDATION
	At Treatment Week 8	At Treatment Week 24	
Previously Untreated Patients	Not Detected	Not Detected	Complete three-medicine regimen at TW28.
	Detected	Not Detected	1. Continue all three medicines and finish through TW36; and then 2. Administer peginterferon alfa and ribavirin and finish through TW48.
Previous Partial Responders or Relapsers‡	Not Detected	Not Detected	Complete three-medicine regimen at TW36.
	Detected	Not Detected	1. Continue all three medicines and finish through TW36; and then 2. Administer peginterferon alfa and ribavirin and finish through TW48.
Previous Null Responders‡	Detected or Not Detected	Not Detected	Continue all three medicines and finish through TW48.

***TREATMENT FUTILITY**
If the patient has HCV-RNA results greater than or equal to 1000 IU/mL at TW8, then discontinue three-medicine regimen.
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.

†"Not Detected" refers to HCV-RNA assay results reported as "Target Not Detected" or "HCV-RNA Not Detected". 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. See Warnings and Precautions (5.7) for a description of HCV-RNA assay recommendations.
‡ *See Clinical Studies (14)* for definitions of previous response to interferon and ribavirin therapy.

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 to 9 hours) in combination with peginterferon alfa and ribavirin in order to maximize rates of SVR.

2.2 VICTRELIS/Peginterferon alfa/Ribavirin Combination Therapy: Patients with Cirrhosis

Prior to initiating therapy in patients with compensated cirrhosis, see Use in Specific Populations (8.7) for additional information.

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 to 9 hours) in combination with peginterferon alfa and ribavirin.

2.3 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 prescribing information for peginterferon alfa and ribavirin 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. If peginterferon alfa or ribavirin is permanently discontinued, VICTRELIS must also be discontinued.

2.4 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 1000 IU per mL at TW8; or 2) HCV-RNA levels of greater than or equal to 100 IU per mL at TW12; or 3) confirmed detectable HCV-RNA levels at TW24.

3 DOSAGE FORMS AND STRENGTHS

VICTRELIS 200 mg Capsules, red-colored cap with the Merck logo printed in yellow ink, and a yellow-colored body with “314” printed in red ink.

4 CONTRAINDICATIONS

Contraindications to peginterferon alfa and ribavirin also apply to VICTRELIS combination treatment. Refer to the respective prescribing information for a list of the contraindications for peginterferon alfa and ribavirin.

VICTRELIS in combination with peginterferon alfa and ribavirin is contraindicated in:

- Pregnant women and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)]*.
- Patients with a history of a hypersensitivity reaction to boceprevir *[see Warnings and Precautions (5.5)].*

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, including those in Table 2, is contraindicated *[see Drug Interactions (7)].*

Coadministration with potent CYP3A4/5 inducers, where significantly reduced boceprevir plasma concentrations may be associated with reduced efficacy, including those in Table 2, is contraindicated *[see Drug Interactions (7)]*.

Table 2
Drugs that are contraindicated with VICTRELIS

Drug Class	Drugs Within Class that are Contraindicated With VICTRELIS	Clinical Comments
Alpha 1-Adrenoreceptor antagonists	Alfuzosin, doxazosin, silodosin, tamsulosin	Potential for alpha 1-adrenoreceptor antagonist-associated adverse events, such as hypotension and priapism
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin	May lead to loss of virologic response to VICTRELIS
Antimycobacterial Agents	Rifampin	May lead to loss of virologic response to VICTRELIS.
Antipsychotics	Lurasidone Pimozide	Potential for serious and/or life-threatening reactions. Potential for cardiac arrhythmias.

Ergot Derivatives	Dihydroergotamine, ergonovine, ergotamine, methylergonovine	Potential for acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues.
GI Motility Agent	Cisapride	Potential for cardiac arrhythmias.
Herbal Products	St. John's wort (*Hypericum perforatum*)	May lead to loss of virologic response to VICTRELIS.
HMG-CoA Reductase Inhibitors	Lovastatin, simvastatin	Potential for myopathy, including rhabdomyolysis.
Oral Contraceptives	Drospirenone	Potential for hyperkalemia.
PDE5 enzyme Inhibitor	REVATIO® (sildenafil) or ADCIRCA® (tadalafil) when used for the treatment of pulmonary arterial hypertension*	Potential for PDE5 inhibitor-associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope.
Sedative/Hypnotics	Triazolam; orally administered midazolam†	Prolonged or increased sedation or respiratory depression.

* See *Drug Interactions, Table 5* for coadministration of sildenafil and tadalafil when dosed for erectile dysfunction.
† See *Drug Interactions, Table 5* for parenterally administered midazolam.

5 WARNINGS AND PRECAUTIONS

5.1 Embryofetal Toxicity (Use with Ribavirin and Peginterferon Alfa)

Ribavirin may cause birth defects and/or death of the exposed fetus. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin therapy should not be started unless a report of a negative pregnancy test has been obtained immediately prior to initiation of therapy. Refer to the prescribing information for ribavirin for additional information.

Women of childbearing potential and men must use at least two forms of effective contraception during treatment and for at least 6 months after treatment has concluded. One of these forms of contraception can be a combined oral contraceptive product containing at least 1 mg of norethindrone. Oral contraceptives containing lower doses of norethindrone and other forms of hormonal contraception have not been studied or are contraindicated. Routine monthly pregnancy tests must be performed during this time *[see Contraindications (4) and Drug Interactions (7)]*.

5.2 Anemia (Use with Ribavirin and Peginterferon Alfa)

Anemia has been reported with peginterferon alfa and ribavirin therapy. The addition of VICTRELIS to peginterferon alfa and ribavirin is associated with an additional decrease in hemoglobin concentrations. Complete blood counts (with white blood cell differential counts) should be obtained pretreatment, and at Treatment Weeks 2, 4, 8, and 12, and should be monitored closely at other time points, as clinically appropriate. If hemoglobin is less than 10 g per dL, a decrease in dosage of ribavirin is recommended; and if hemoglobin is less than 8.5 g per dL, discontinuation of ribavirin is recommended *[see Adverse Reactions (6.1) and Clinical Studies (14)]*. If ribavirin is permanently discontinued for management of anemia, then peginterferon alfa and VICTRELIS must also be discontinued *[see Dosage and Administration (2.3)]*.

Refer to the prescribing information for ribavirin for additional information regarding dose reduction and/or discontinuation.

In clinical trials with VICTRELIS, the proportion of subjects who experienced hemoglobin values less than 10 g per dL and less than 8.5 g per dL was higher in subjects treated with the combination of VICTRELIS with PegIntron®/REBETOL® than in those treated with PegIntron/REBETOL alone (see Table 4). With the interventions used for anemia management in the clinical trials, the average additional decrease of hemoglobin was approximately 1 g per dL.

In clinical trials, the median time to onset of hemoglobin less than 10 g per dL from the initiation of therapy was similar among subjects treated with the combination of VICTRELIS and PegIntron/REBETOL (71 days with a range of 15-337 days), compared to those who received PegIntron/REBETOL (71 days with a range of 8-337 days). Certain adverse reactions consistent with symptoms of anemia, such as dyspnea, exertional dyspnea, dizziness and syncope were reported more frequently in subjects who received the combination of VICTRELIS with PegIntron/REBETOL than in those treated with PegIntron/REBETOL alone *[see Adverse Reactions (6.1)]*.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.