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News and information on viral hepatitis in Europe

Hepatitis C treatment factsheet
Boceprevir *(Victrelis)*

Boceprevir (brand name *Victrelis*) is a new medication used to treat hepatitis C. It was approved in Europe in July 2011 for treatment of adults with genotype 1 chronic hepatitis C in combination with pegylated interferon and ribavirin.

Overall, boceprevir triple therapy cures about two-thirds of people who take it, but it works better for some groups than others. Successful treatment reduces the risk of long-term complications of hepatitis C such as liver cancer or needing a liver transplant.

Boceprevir is no longer available in the United States. Boceprevir is still licensed in the European Union but is no longer recommended as an appropriate treatment for hepatitis C by the European Association for the Study of the Liver, owing to a higher rate of side-effects and a lower cure rate when compared to newer interferon-free treatments licensed since 2014.

How does boceprevir work?

Boceprevir is one of the new direct-acting antiviral drugs that target different steps of the hepatitis C virus (HCV) lifecycle. It is an HCV protease inhibitor, meaning it blocks the protease enzyme which the virus must use to reproduce. Boceprevir must be used with two older drugs: pegylated interferon, which stimulates the body's own immune response against the virus, and ribavirin, which improves the effectiveness of interferon.

Who can use boceprevir?

Boceprevir is indicated for use by adults with chronic hepatitis C, meaning infection lasting more than six months. It is approved for people with HCV genotype 1, which is the most common type in Europe and considered the hardest to treat. It is not approved and should not be used to treat other HCV genotypes.

Boceprevir can be used by people being treated for hepatitis C for the first time (known as 'treatment-naive') and for retreatment of people who were not cured with previous interferon-based therapy.

Boceprevir has also been tested in people with HIV and HCV co-infection. Response rates and side-effects are similar to those of HIV-negative people. However, boceprevir should not be used with certain HIV medications due to drug interactions. People with HIV and HCV co-infection who want to take boceprevir should do so under the care of a doctor who has experience treating both infections.

Boceprevir can be used by people with all stages of compensated liver disease including cirrhosis, but it works better for people with less advanced liver damage. Also, people with cirrhosis who take boceprevir may experience more serious side-effects. Boceprevir triple therapy can be dangerous and therefore should not be used by people with decompensated liver disease, or liver failure.

How is boceprevir taken?

Boceprevir is taken as four capsules three times daily with a light meal or snack. It must be used with weekly pegylated interferon injections and twice-daily ribavirin pills. Boceprevir is not effective if taken alone, and this can lead to drug resistance.

Treatment starts with a 'lead-in' period of pegylated interferon and ribavirin taken alone for 4 weeks. Then boceprevir plus pegylated interferon and ribavirin are taken together as triple therapy for 24 to 44 additional weeks. Some people will then continue on pegylated interferon/ribavirin alone for several more weeks. Treatment duration will depend on early response, previous treatment history and extent of liver damage. This is known as 'response-guided therapy'.

How effective is boceprevir?

Boceprevir works better for some people than for others. Several factors predict how well someone will respond. Boceprevir is only approved for genotype 1 hepatitis C. It is not effective for other genotypes including 2, 3 or 4. Different direct-acting antivirals work better against these other genotypes.

One of the most important factors is previous treatment history. People who are new to treatment, and those who relapsed after finishing previous treatment, have the best chance of being cured with boceprevir. Boceprevir triple therapy does not work as well for people who had only a partial response or no response to prior interferon treatment.

- **Sustained responder:** a person who was successfully treated and cured of hepatitis C.
- **Relapser:** a person who reached undetectable HCV viral load with previous interferon-based therapy, but relapsed, or saw the virus return, after finishing treatment.
- **Partial responder:** a person who had some decrease in HCV viral load with previous treatment, but did not reach an undetectable level.

- **Null responder:** a person who had little or no decrease in HCV viral load with previous treatment.

People with less advanced liver damage respond better to treatment. People with cirrhosis are less likely to be cured with boceprevir triple therapy and they may have more problems with drug side-effects.

Because they are more difficult to treat, previous null responders and people with cirrhosis should receive boceprevir triple therapy for a full 44 weeks if they can tolerate the side-effects.

Boceprevir treatment response

People who experience a rapid drop in HCV viral load soon after starting treatment are more likely to be cured. Undetectable viral load at week 8 and week 24 of boceprevir triple therapy is a good predictor of who will be cured. This will make some patients eligible for shorter treatment. But people who do not respond well after the first 12 or 24 weeks should stop treatment, as it is unlikely to work if continued longer.

People with sustained virological response, who still have undetectable viral load at 12 or 24 weeks after finishing treatment (known as 'SVR12' or 'SVR24'), are considered cured.

A clinical study called SPRINT-2 tested boceprevir triple therapy in previously untreated patients. Up to 66% of people who took boceprevir were cured, compared with 38% of those who took only pegylated interferon and ribavirin.

Another study called RESPOND-2 tested boceprevir triple therapy in previously treated people. Up to 75% of prior relapsers who took boceprevir were cured, compared with 29% who took only pegylated interferon and ribavirin. The boceprevir sustained response rate was lower for previous partial responders (up to 52%). This trial did not include previous null responders, but another study showed they had a cure rate of about 40%.

Boceprevir has also been tested in people with HIV and HCV coinfection, showing response rates and side-effects similar to those of people with hepatitis C alone. In one study, 61% of previously untreated patients with co-infection who took boceprevir triple therapy were cured, compared with 27% who took only pegylated interferon and ribavirin.

Boceprevir's effectiveness in 'real world' use is somewhat lower than cure rates seen in clinical trials, in part because patients may be sicker or have other conditions that can make treatment more complicated.

Boceprevir triple therapy has been tested in people with advanced liver disease, including people who are awaiting or have received liver transplants. Sustained response rates are higher than those of pegylated interferon/ribavirin alone, but people with advanced disease often have trouble tolerating treatment side-effects.

What are the side-effects of boceprevir?

Boceprevir causes some side-effects of its own, but many symptoms in people taking triple therapy are due to pegylated interferon or ribavirin. The most common side-effects of boceprevir are anaemia (low haemoglobin level), nausea, fatigue, headache and unusual taste sensations (known as 'dysgeusia'). Anaemia is the most likely serious side-effect. Some people also develop neutropenia (low white blood cell count).

Side-effects of interferon include headache, fatigue, muscle and joint aches and depression. Ribavirin also causes anaemia, which can be worse when combined with boceprevir. Ribavirin can cause birth defects and should not be used by pregnant women or their male partners.

Does boceprevir interact with other drugs?

Boceprevir can interact with other drugs that are processed by the same enzymes in the liver. These include some antiretroviral drugs for HIV, heart disease drugs and psychiatric medications. Sometimes drug doses can be adjusted to overcome these interactions, but some medications should not be used together with boceprevir. Information about specific drug interactions is available online at **www.hep-druginteractions.org**.

How can I get boceprevir?

Boceprevir is available by prescription in European Union countries to treat genotype 1 hepatitis C. Ask your GP or liver specialist if boceprevir combination therapy may be a good option.

When to start treatment will depend on a number of factors, including severity of liver damage (as determined by *FibroScan* or a liver biopsy). People with mild liver disease may be able to wait, and new more effective and better-tolerated hepatitis C medications that can be used without interferon are coming soon. However, the decision to wait must take into account how fast your liver disease might progress – which is hard to predict – and how soon new treatments will be approved in your country.

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