

# Zepatier (elbasvir + grazoprevir)

## Summary

Zepatier is a direct-acting antiviral medication used to treat hepatitis C. It is a combination of two medications, elbasvir and grazoprevir. These two medications are co-formulated into one tablet. Zepatier is approved in Canada for the treatment of chronic hepatitis C in people over the age of 18 years with genotype 1, 3 or 4 of the hepatitis C virus. It is taken once a day with or without food, for eight, 12 or 16 weeks. Zepatier has few side effects. Common side effects are generally mild and temporary; they include tiredness and headache. Direct-acting antivirals are highly effective and cure over 95% of people with hepatitis C.

## What is Zepatier?

Zepatier is a direct-acting antiviral medication used to treat hepatitis C. It is a combination of two direct-acting antivirals: elbasvir, which is an NS5A (hepatitis C virus non-structural protein 5A) inhibitor and grazoprevir, which is a protease inhibitor.

Zepatier is approved in Canada for the treatment of chronic hepatitis C in people over the age of 18 years with genotype 1 or 4 of the hepatitis C virus. Zepatier is also approved in Canada to treat genotype 3 of the hepatitis C virus if it is used in combination with sofosbuvir (Sovaldi), another direct-acting antiviral.

## How does Zepatier work?

Zepatier directly blocks the ability of the hepatitis C virus to make copies of itself in the liver. Elbasvir works by interfering with a protein needed by the virus and grazoprevir interferes with the production of the pieces needed to build new virus particles. Together, they greatly reduce and then stop the production of new copies of the hepatitis C virus. Over time, these actions eliminate the hepatitis C virus from the body.

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## Does Zepatier cure people of hepatitis C?

Direct-acting antivirals are highly effective and cure more than 95% of people with hepatitis C. Zepatier is one of these highly effective direct-acting antiviral medications.

A cure for hepatitis C is also known as a sustained virological response (SVR). A person is cured if the hepatitis C virus is not detected in the blood 12 weeks after the end of treatment.

If a person is cured of hepatitis C, they can get hepatitis C again if they are exposed to the hepatitis C virus.

## How do people with hepatitis C use Zepatier?

Zepatier is taken as one tablet, once a day, for eight, 12 or 16 weeks. The length of treatment depends on a number of factors including the genotype of the virus, past treatment experience and the absence or presence of severe liver injury. Treatment generally lasts 12 weeks.

Each tablet is available as a fixed combination tablet containing 50 mg of elbasvir and 100 mg of grazoprevir. It can be taken with or without food.

Some people may need to take Zepatier with ribavirin, depending on their genotype and previous treatment experience. Ribavirin is another type of antiviral medication, but it is not a direct-acting antiviral. Information about ribavirin is included in a separate fact sheet.

People with genotype 3 of the virus who have never taken hepatitis C treatment take Zepatier with sofosbuvir, another direct-acting antiviral, for 12 weeks.

## How important is it to stick to treatment?

All medications work best when they are taken exactly as prescribed and directed. People taking Zepatier should take their pills every day, as prescribed by their healthcare provider. It is very important to finish the entire course of treatment.

This gives the treatment the best chance of working to cure hepatitis C.

## What can be done about missed doses?

When a person taking Zepatier misses a dose and it is within 16 hours of when it should have been taken, it is important to take the missed dose immediately or as soon as possible. If it has been more than 16 hours from when it was supposed to have been taken, that dose should be skipped and the next dose should be taken at the appropriate time. A double dose should not be taken. A person should continue their treatment until all doses have been taken.

If a person finds it difficult to stick to treatment, it is important to discuss this with their nurse or doctor. Tips for sticking to treatment can be found in CATIE's *Hepatitis C: An In-Depth Guide*.

## Warnings

### 1. Risk of hepatitis B virus reactivation in patients co-infected with hepatitis C and hepatitis B viruses

The U.S. Food and Drug Administration (FDA) recommends that all people starting hepatitis C treatment with direct-acting antiviral medications should be tested for hepatitis B before starting treatment.

There have been a small number of reports of reactivation of hepatitis B virus infection when direct-acting antivirals like Zepatier are used to treat hepatitis C infection in people who are co-infected with hepatitis B virus. Reactivation of hepatitis B virus can, in some cases, cause serious complications. People considering the use of Zepatier should speak with their doctor or nurse about their hepatitis B virus infection status.

### 2. Breastfeeding/Chestfeeding

People with infants who are taking Zepatier should not breastfeed or chestfeed their children. It is not known whether the medication is present in human milk.

### 3. People under the age of 18 years

The safety and effectiveness of treatment with Zepatier for people under the age of 18 years has not been determined.

### 4. Special populations

People with any of the following conditions should speak with their doctor or nurse about the most appropriate hepatitis C treatment options for them:

- liver problems other than hepatitis C
- co-infection with hepatitis B
- co-infection with HIV
- pregnancy or planning to have a baby while on treatment for hepatitis C
- severe liver injury such as Child–Pugh B or C cirrhosis
- awaiting a liver transplant or a liver transplant recipient
- severe kidney injury or on dialysis

Zepatier is generally safe and highly effective. Anyone who is considering treatment with Zepatier should discuss all of their medical conditions with their doctor or nurse.

### Side effects

The most common side effects of Zepatier are:

- fatigue (extreme tiredness)
- headache

In most cases these side effects are mild or moderate and gradually resolve. Headache and fatigue occurred with similar frequency among people taking Zepatier and among people taking placebo in double-blinded clinical trials.

### Drug interactions

Some prescription drugs, over-the-counter drugs, herbs, supplements and other drugs (both legal and illegal) can interfere with the absorption

and/or the effectiveness of Zepatier. This is called a drug interaction.

Some drugs taken for other conditions can interact with Zepatier by increasing or decreasing the level of one or both drugs in the body. Increased levels can lead to new or more severe side effects. Decreased levels may mean that the drug won't be as effective.

It is important that people discuss all medications, supplements, herbs and other drugs (both legal and illegal) they are taking with their doctor, nurse or pharmacist. If a person has more than one doctor or pharmacist, it is possible for drug interactions to get missed. Using the same pharmacy for all prescriptions can be helpful.

This fact sheet is not comprehensive and lists only some of the potential and actual drug interactions with Zepatier. Speak with a pharmacist to find out more about drug interactions with Zepatier.

The following medications are contraindicated (should not be used) with Zepatier:

- the tuberculosis medication rifampin (Rifadin, Rofact)
- HIV medications that contain atazanavir (Reyataz), darunavir (Prezista, and in Prezcofix), lopinavir (in Kaletra), saquinavir (Invirase), tipranavir (Aptivus) and efavirenz (Sustiva, and in Atripla)
- the immune-suppressant medication cyclosporine (Neoral, Sandimmune IV)
- the anti-seizure medications carbamazepine (Tegretol) and phenytoin (Dilantin)
- any medicinal herbs, especially St. John's wort (*Hypericum perforatum*), which is an herb used to treat depression, or hyperforin or hypericin, which are active ingredients in St. John's wort

The manufacturer does not recommend taking Zepatier with the following medications:

- oral medicines to treat fungal infection, such as ketoconazole
- medicines for the lung problem pulmonary hypertension, such as bosentan (Tracleer)

- HIV treatments with a fixed-dose combination of elvitegravir, cobicistat, emtricitabine and tenofovir disoproxil fumarate or alafenamide (Genvoya, Stribild)
- HIV medications that contain etravirine (Intelence)
- medicines to promote wakefulness, such as modafinil (Alertec)

When Zepatier is taken with the following medications, it could potentially cause significant drug interactions:

- the immune-suppressant medication tacrolimus (Prograf, Advagraf, Protopic)
- the cholesterol-lowering medications atorvastatin (Lipitor), rosuvastatin (Crestor), fluvastatin (Lescol), lovastatin and simvastatin (Zocor)
- the cancer medicine sunitinib (Sutent)
- vitamin K antagonist medications that reduce clotting, such as warfarin (Coumadin)
- medicines to treat diabetes

## Availability

Zepatier, manufactured by Merck, has been approved by Health Canada and is available in Canada. Pharmacists are a good source of information about public and private health insurance coverage for Zepatier.

CATIE's online module "Federal, Provincial and Territorial Drug Access Programs" also contains information about Canadian drug coverage.

## Acknowledgement

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## Reference

Merck. Zepatier (Elbasvir/Grazoprevir). *Product monograph*. March 17, 2021.

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## Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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