

Zepatier (elbasvir + grazoprevir)

Summary

Zepatier is a treatment for hepatitis C. It is approved in Canada for the treatment of people with genotype 1, 3 or 4 hepatitis C virus. Zepatier contains two drugs in one tablet: elbasvir and grazoprevir. It is taken once a day with or without food. Zepatier appears to have few side effects. Common side effects are generally mild and temporary and include fatigue and headache. Hepatitis C treatment can cure a person from hepatitis C. However, a person could become infected again.

What is Zepatier?

Zepatier is a medication used to treat hepatitis C.

How does Zepatier work?

Hepatitis C virus is a disease that can injure the liver. A virus is a very tiny germ that makes copies of itself to survive by a process called replication. The hepatitis C virus has at least seven different strains, which are also known as genotypes.

Zepatier is a direct-acting antiviral (DAA) medication. DAAs are a group of medications that directly block the ability of the hepatitis C virus to make copies of itself.

Zepatier is a combination of two DAAs. One is grazoprevir, which is a protease inhibitor, and the other is elbasvir, which is an NS5A inhibitor. Grazoprevir interferes with the production of the pieces needed to build new virus particles, stopping the production of new hepatitis C virus. Elbasvir works by interfering with a protein needed to complete the hepatitis C virus life cycle in the liver cell.

Treatment with DAAs can usually cure a person from hepatitis C infection and can lessen the likelihood of further health issues, such as liver failure and liver cancer. However, a person could get infected again. For more information on preventing hepatitis from passing from person to person, see Prevention and Harm Reduction.

FACT SHEET

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How do people use Zepatier?

Zepatier is taken as one tablet once a day. Zepatier can be taken with or without food.

Zepatier is approved for people over the age of 18 with genotype 1 or 4 hepatitis C virus. Some people may also be prescribed ribavirin along with Zepatier.

Zepatier in combination with sofosbuvir (Sovaldi) is approved for treating people with genotype 3 hepatitis C virus.

How long is treatment?

In most cases, the duration of treatment with Zepatier is based on pre-existing liver injury and, to some degree, on a person's genotype and past treatment experience.

The following group would take Zepatier for eight weeks without ribavirin:

- Genotype 1b who have never been treated (treatment-naïve) without severe liver damage (cirrhosis)

The following groups would take Zepatier for 12 weeks without ribavirin:

- genotype 1 or 4 who are treatment-naïve
- genotype 1 or 4 who have previously taken peg-interferon + ribavirin but relapsed (relapse is when the virus becomes undetectable during treatment but returns after treatment)
- genotype 1 who have previously taken a protease inhibitor, such as telaprevir (Incivek), boceprevir (Victrelis) or simeprevir (Galexos), but relapsed
- genotype 1b who have previously taken peg-interferon + ribavirin +/- a protease inhibitor but did not complete treatment because hepatitis C virus levels remained persistently high

The following groups would take treatment for 16 weeks with ribavirin:

- genotype 1a who have previously taken peg-interferon + ribavirin +/- a protease inhibitor but stopped treatment because of persistently high hepatitis C virus levels
- genotype 4 who have previously taken peg-interferon + ribavirin but stopped treatment because of persistently high hepatitis C virus levels

Genotype 3

People with genotype 3 virus who are treatment-naïve would take Zepatier with sofosbuvir for 12 weeks. Zepatier is *not* approved in Canada for people with genotype 3 virus who previously took treatment but were not cured.

Sticking to treatment

All medications work best when they are taken exactly as prescribed and directed. This means taking the medications in the right amount and at the right time for the entire length of time that your treatment lasts. Skipping doses or stopping treatment altogether means that the treatment may not work and the chance of being cured is lower.

With some hepatitis C medications, there is a chance that the virus can become resistant to the medication if it is not taken as directed. In this case, the medication will not be effective against the virus and cannot be used to treat the infection. (See the "Resistance" section to learn about the potential for resistance to Zepatier.)

What can you do if you forget to take your medication?

If you miss taking a dose of Zepatier and it has been less than 16 hours since you were

supposed to take it, take it as soon as possible. If it has been more than 16 hours from when you were supposed to take it, wait and take the next tablet at your regular time. Do not take a double dose.

If you find that you are not able to take your medication as prescribed and directed, talk to your nurse or doctor right away. You can also check out the section “Tips for staying on track with treatment” in CATIE’s *Hepatitis C: An in-depth guide* at www.catie.ca.

How likely is a cure from treatment that includes Zepatier?

Hepatitis C treatment can cure a person from hepatitis C virus.

In clinical trials of Zepatier, in most cases the cure rates were above 90%. Cure rates can be affected by various factors, such as alcohol use, not taking the medication as prescribed, and, in rare cases, if the virus is resistant to the medications in Zepatier. Talk to your doctor about the likelihood of a cure for you.

Sometimes in real life the cure rates can be lower than in clinical trials.

A cure for hepatitis C is also known as a sustained virological response (SVR). This is when the hepatitis C virus is no longer detected in the blood 12 or 24 weeks after treatment ends.

Warnings

1. Breastfeeding/nursing

People with infants who are taking Zepatier should not breastfeed or nurse their children.

2. Combination therapy

If Zepatier is combined with sofosbuvir or ribavirin, all of the warnings that apply to sofosbuvir and ribavirin also apply in these cases. For more information on sofosbuvir and ribavirin, see the sofosbuvir and ribavirin factsheets.

3. Hepatitis B

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

This is because if someone has hepatitis C and hepatitis B and is not receiving treatment for hepatitis B, treatment with DAAs could reactivate hepatitis B during or after treatment. For more information about being tested for hepatitis B, speak to your doctor or nurse.

4. Special populations

Zepatier is not recommended if you have one or more of the following issues:

- you are pregnant
- you have severe liver injury (class Child-Pugh B or C¹)

Speak to your doctor about the most appropriate treatment options if you have one or more of the following issues:

- you are under the age of 18
- you have genotype 2, 3, 5 or 6 hepatitis C virus
- you are co-infected with hepatitis B

People who are over the age of 65

In clinical trials, participants over the age of 65 had no differences in efficacy or safety compared to participants under the age of 65.

People who are co-infected with HIV

The efficacy and safety of Zepatier has been established in the following groups of people who are co-infected with HIV:

- genotype 1 virus who have not been treated before
- genotype 1 virus who are treatment experienced
- genotype 4 virus who have not been treated before
- genotype 4 virus who are treatment experienced

1. Child-Pugh Class A, B and C are measurements of cirrhosis. Child-Pugh B and C are more severe forms of cirrhosis.

People with severe kidney disease

The safety and efficacy of Zepatier has been demonstrated in people with severe kidney disease who have genotype 1 virus. In people with severe kidney disease, including people on hemodialysis, it is recommended to take Zepatier without ribavirin.

Side effects

The most common side effects of Zepatier are:

- fatigue
- headache

In most cases these side effects are mild or moderate.

Drug interactions

Always consult your doctor and pharmacist about all of the prescription and non-prescription drugs you are taking, including methadone or other opiate substitution therapies, herbs, supplements and street drugs.

Drug interactions occur when one medication affects how another is absorbed, used or flushed out of the body. Some drugs can interact with Zepatier, 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.

When Zepatier is taken with the following medications it could potentially cause significant drug interactions. This is not a complete list of possible drug interactions with Zepatier:

- antibiotics for tuberculosis (TB) – rifampin
- antiseizure drugs – carbamazepine, phenytoin
- herbs – St. John's wort (or its extracts hypericin and hyperforin)
- HIV medications – atazanavir (Reyataz), darunavir (Prezista and in PrezcoBix), fosamprenavir (Telzir), indinavir (Crixivan), nelfinavir (Viracept), ritonavir (Norvir), efavirenz (Sustiva, Stocrin and in Atripla), etravirine (Intelence), lopinavir (in Kaletra),

saquinavir (Invirase), tipranavir (Aptivus), Stribild or Genvoya

- transplant drugs – cyclosporine (Neoral, Sandimmune), tacrolimus (Advagraf, Prograf)
- medicine for the lung problem pulmonary hypertension, such as bosentan (Tracleer)
- oral medicine to treat fungal infection, such as ketoconazole
- medicine to lower cholesterol, such as atorvastatin (Lipitor), lovastatin, rosuvastatin (Crestor), simvastatin, fluvastatin
- medicine to promote wakefulness, such as modafinil

Talk to your nurse, doctor and pharmacist if you are taking any of these medicines. One way to manage drug interactions is to make sure that your doctor and pharmacist know about *everything* you are taking, including prescription drugs, over-the-counter drugs, street drugs, herbal medications, supplements or anything else. If you have more than one doctor or pharmacist, it is possible for drug interactions to get missed. If more than one doctor is writing prescriptions for you, let each one know about everything you are taking.

If possible, use the same pharmacy for all your prescriptions.

Drug resistance

Drug resistance develops when a virus mutates, or changes. This usually means changes happen to its genetic material during the process of making copies of the hepatitis C virus. Some mutations of the virus may be able to resist hepatitis C medications. When this happens, the medication becomes less effective or stops working. Resistance to Zepatier can develop when a person does not take their medication as prescribed and directed or if the virus they have contained these mutations at the time of infection.

In clinical trials, it was rare for people to develop resistance to Zepatier. However, it is still important for people taking Zepatier to take it exactly as prescribed. If you skip or miss doses, Zepatier could potentially fall to low levels in your body. This can

allow the hepatitis C virus to mutate and become able to resist the effect of treatment.

If you have questions about drug resistance talk to your doctor.

Availability

Zepatier, manufactured by Merck, has been approved by Health Canada and is available in Canada. Your nurse, doctor or pharmacist can tell you more about availability and coverage of Zepatier in your region.

CATIE's online Treatment coverage in your region section of *Hepatitis C: An in-depth guide* on www.catie.ca contains information about provincial and territorial drug coverage.

Acknowledgment

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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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