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.
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 C)

   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 Prezcofix),
fosamprenavir (Telzir), indinavir (Crixivan),
nelfinavir (Viracept), ritonavir (Norvir),
efavirenz (Sustiva, Stocrin and in Atripla),
etravirine (Intelence), lopinavir (in Kaletra),
saquinariv (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**

We thank Dr. Sergio Borgia, M.Sc., M.D., FRCP(C), for expert review.

**References**


**Author:** Anderson S
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.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to consult as broad a range of sources as possible. Users relying on this information do so entirely at their own risk. Neither CATIE, nor any of its partners, funders, employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE do not necessarily reflect the policies or opinions of CATIE nor the views of its partners and funders.

Permission to reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1-800-263-1638.

Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.

CATIE Ordering Centre No: ATI-50267
(aussi disponible en français, ATI-50268)

CATIE fact sheets are available for free at www.catie.ca