

Holkira Pak (dasabuvir + ombitasvir/ paritaprevir/ ritonavir)

Summary

Holkira Pak is a medication used to treat Hep C. Holkira Pak is a combination of dasabuvir, ombitasvir and paritaprevir boosted with ritonavir. Ombitasvir, paritaprevir and ritonavir are co-formulated into one tablet that is taken once per day. Dasabuvir is a separate tablet that is taken twice per day. Holkira Pak may be prescribed with ribavirin. Holkira Pak appears to have few side effects. Common side effects are generally mild and include fatigue, headache, weakness and nausea. Hep C treatment can cure a person from Hep C. However, a person could become infected again.

What is Holkira Pak?

Holkira Pak is a medication used to treat hepatitis C (Hep C).

How does Holkira Pak work?

Hep C is a disease of the liver that is caused by a virus. A virus is a very tiny germ that infects a cell and causes the cell to make copies of the virus in a process called replication. The Hep C virus has at least six different strains, which are also known as genotypes.

Holkira Pak is a direct-acting antiviral (DAA) medication. DAAs are a group of medications that directly attack the ability of a specific virus, such as hepatitis C, to make copies of itself.

FACT SHEET

Published
2017

CONTACT US

by telephone
1-800-263-1638
416-203-7122

by fax
416-203-8284

by e-mail
info@catie.ca

by mail
555 Richmond Street West
Suite 505, Box 1104
Toronto ON M5V 3B1

Holkira Pak is a combination of three DAAs:

- paritaprevir – a protease inhibitor that is boosted with ritonavir
- ombitasvir – an NS5A inhibitor
- dasabuvir – an NS5B inhibitor

Paritaprevir works by interfering with the production of the pieces needed to build new virus particles. Ombitasvir works by interfering with a protein needed to make new copies of Hep C virus. Dasabuvir works by inserting itself into the virus so other pieces of the Hep C virus cannot attach to it. These medications work together to stop new viruses from being made.

Hep C treatment can cure a person from Hep C. However, being cured of Hep C does not protect you from being reinfected in the future.

How do people use Holkira Pak?

Holkira Pak is a combination of two different tablets.

The first tablet is a co-formulation of ombitasvir and paritaprevir boosted with ritonavir. The second tablet contains dasabuvir.

The following table shows when to take the tablets and how many to take:

Tablet name	Time of day it is taken	How many
ombitasvir/ paritaprevir/ ritonavir	morning	2 tablets
dasabuvir	morning	1 tablet
	evening	1 tablet

Holkira Pak should be taken with food, but it does not matter what kind of food.

Holkira Pak may also be taken with ribavirin. The following groups of people take Holkira Pak with ribavirin:

- people with genotype 1a virus
- people with genotype 1b virus and cirrhosis

Your doctor will tell you if you need ribavirin, how many ribavirin tablets to take and when to take them.

Holkira Pak is approved in Canada for people over the age of 18 with genotype 1 hepatitis C virus.

How long is treatment?

The majority of people take Holkira Pak (with or without ribavirin) for 12 weeks.

People with genotype 1a virus who have cirrhosis and who have been previously treated with peg-interferon and ribavirin but did not have any response to treatment (these people are referred to as prior null responders) are recommended to take treatment for 24 weeks.

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 as well and the chance of being cured is lower.

With some Hep C medications, there is also a chance that the virus can become resistant to the medication if it is not taken as prescribed and directed. In this case, the medication will not be effective against the virus and can no longer be used to treat the infection. (See the Resistance section to learn about the potential for resistance to the medications in Holkira Pak.)

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

If you miss taking a dose of ombitasvir + paritaprevir/ritonavir and it is within 12 hours of when you were supposed to take it, take it as soon as possible. If it is after 12 hours from when you were supposed to take it, wait and take the next dose at your regular time. Do not take a double dose.

If you miss taking a dose of dasabuvir and it is within six hours of when you were supposed to take it, take it as soon as possible. If it is after six hours from when you were supposed to take it, wait and take the next dose 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 Holkira Pak?

Hep C treatment can cure a person from Hep C.

In late-stage clinical trials of Holkira Pak with or without ribavirin, participants had approximately the following cure rates:

People with virus genotype	Treatment	Cure rate
genotype 1a	Holkira Pak + ribavirin	93% to 97%
genotype 1b	Holkira Pak	99% to 100%

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

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

Warnings

1. Combination therapy

In some cases, Holkira Pak must be taken in combination with ribavirin, so all of the warnings that apply to ribavirin also apply to people considering Holkira Pak.

2. Pregnancy

Some of the drugs used to treat Hep C can harm a fetus, so talk to a doctor if you are pregnant or thinking about having a baby.

People on Hep C treatment who could get pregnant or who are sex partners with someone who could get pregnant should use two forms of reliable contraception.

3. Breastfeeding/nursing

People with infants and who are taking Holkira Pak should not breastfeed or nurse their children.

4. 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.

5. Special populations

People who should not be treated with Holkira Pak

- people with Hep C genotypes other than genotype 1
- people under the age of 18
- people who have severe liver damage (Child-Pugh Class B or C¹)

Groups of people for whom there is limited or no information about the effectiveness of Holkira Pak

- people who have previously taken other DAAs and were not cured

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

- people who are co-infected with hepatitis B virus
- people on kidney dialysis
- people who have had a liver transplant. In a late-stage trial of Holkira Pak and ribavirin in people who had a liver transplant the cure rate was 97%. Participants received 24 weeks of treatment.
- people who are co-infected with HIV. In a late-stage trial of Holkira Pak and ribavirin in people co-infected with hepatitis C and HIV, cure rates ranged from 91% to 94%. Participants received either 12 or 24 weeks of treatment.

If you are in one of the groups for which there is limited or no information, the risks and benefits of taking Holkira Pak need to be carefully weighed, so speak to your doctor about the most appropriate treatment options. Your doctor or specialist may have experience treating these specific populations.

Holkira Pak is a new medication and some things are unknown about its effect in people. Make sure your doctor knows about all of your medical conditions when you are discussing Holkira Pak as a treatment option.

Side effects

The most common side effects with Holkira Pak are:

- lack of energy
- headache
- nausea

In most cases, these side effects are mild or moderate and temporary.

Drug interactions

Always consult your doctor and pharmacist about taking other prescription and non-prescription drugs, 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 the

drugs in Holkira Pak, 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.

The following medications should not be taken with Holkira Pak. This is not a complete list of medications that should not be taken with Holkira Pak:

- contraceptive pills or vaginal rings that contain ethinyl estradiol, which is a very common form of contraception
- medicine to treat the symptoms of an enlarged prostate gland, such as alfuzosin (Xatral)
- medicine to prevent seizures, such as carbamazepine (Tegretol)
- HIV medicines, such as etravirine (Intelence), rilpivirine (Edurant, Complera), those that contain efavirenz (Sustiva, Atripla) and those that contain ritonavir (Norvir), such as lopinavir/ritonavir (Kaletra)
- medicine to treat migraines that contain ergot, such as dihydroergotamine (Migranal)
- medicine to lower cholesterol, such as lovastatin
- medicine to treat sleep problems, such as modafinil (Alertec) and triazolam
- medicine to prevent seizures, such as phenytoin (Dilantin) and phenobarbital
- medicine to control verbal or motor tics, such as pimozide (Orap)
- tuberculosis medicine, such as rifampin (Rofact)
- medicine used to treat asthma, such as salmeterol (Serevent Diskus)
- medicine for the lung problem pulmonary hypertension, such as sildenafil (Revatio) and bosentan (Tracleer)
- medicine to reduce cholesterol levels or the likelihood of stroke or heart attack, such as simvastatin

- any medicinal herbs, especially an herb used to treat depression – St. John’s wort (*Hypericum perforatum*), or hyperforin and hypericin, active ingredients in St. John’s wort

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

- asthma medication, such as fluticasone (Advair, Flonase, Flovent Diskus, Flovent HFA)
- HIV medication, such as atazanavir (Reyataz) and darunavir (Prezista, Prezcofix)
- medicine to treat indigestion, heartburn or ulcers, such as omeprazole (Losec)
- medicine to treat fungal infection, such as ketoconazole
- pain medicine, such as alfentanil and fentanyl (Abstral, Duragesic)
- medicine to treat anxiety, such as alprazolam (Xanax)
- medicine to treat irregular heartbeat, such as amiodarone, digoxin (Toloxin), propafenone and quinidine
- medicine to treat heart disease, such as fluvastatin (Lescol)
- medicine to reduce swelling and fluid retention, such as furosemide
- calcium channel blockers, such as amlodipine (Norvasc)
- medicine to lower cholesterol, such as rosuvastatin (Crestor), atorvastatin (Lipitor) and pravastatin (Pravachol)
- medicine to lower immune response or prevent organ transplant failure, such as cyclosporine (Neoral, Sandimmune), tacrolimus (Prograf) and sirolimus (Rapamune)
- medicine to prevent blood clots, such as warfarin (Coumadin)

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.

Resistance

Drug resistance develops when a virus mutates, or changes, during the replication process. Some mutations of the virus may be able to resist Hep C medications. When this happens, the medication becomes less effective or stops working. Resistance can develop when a person does not take their medication as prescribed and directed.

In clinical trials, it was rare for the Hep C virus to develop resistance to the drugs in Holkira Pak. However, it is still important for people taking Holkira Pak to take it exactly as prescribed. If you skip or miss doses, the level of drugs inside Holkira Pak falls to low levels in your body. This can allow the Hep C virus to mutate and become able to resist the effect of treatment.

Availability

Holkira Pak, manufactured by AbbVie, 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 Holkira Pak 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.

Acknowledgement

We thank Lisa Barrett, MD, PhD, for expert review.

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Author: Anderson S

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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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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.

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CONTACT US

by telephone

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416-203-7122

by fax

416-203-8284

by e-mail

info@catie.ca

by mail

555 Richmond Street West
Suite 505, Box 1104
Toronto ON M5V 3B1

