

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PART III: PATIENT MEDICATION INFORMATION

PrHOLKIRA[®] PAK

ombitasvir/paritaprevir/ritonavir film-coated tablets and dasabuvir film-coated tablets

Read this carefully before you start taking HOLKIRA PAK and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your doctor about your medical condition and treatment and ask if there is any new information about HOLKIRA PAK.

Serious Warnings and Precautions

Hepatitis B activity (e.g., inflamed liver) may increase when taking antiviral drugs like HOLKIRA PAK, sometimes leading to liver failure and death. (See the “To help avoid side effects...” section, *Hepatitis B Reactivation*)

What is HOLKIRA PAK used for?

HOLKIRA PAK treats long-lasting hepatitis C virus (HCV) infection in adults 18 years and older. It treats one kind of HCV infection called HCV genotype 1.

HOLKIRA PAK is sometimes used with ribavirin, but not always. Read the ribavirin patient medication information if your doctor says you should also take ribavirin.

How does HOLKIRA PAK work?

HOLKIRA PAK with ribavirin can cure HCV infection in most patients. Cure means HCV is cleared from your blood 3 months after finishing the medicine.

HOLKIRA PAK has 3 types of HCV medicines. These 3 medicines stop HCV from multiplying in different ways.

Curing HCV infection can help lower the chance you will have problems or die from HCV.

Taking HOLKIRA PAK does not keep you from getting infected again. Talk with your doctor about ways to avoid getting infected again with HCV.

Can I still pass on HCV to others if I take HOLKIRA PAK?

Yes, you can still pass on HCV to others while you are taking HOLKIRA PAK. For example, some ways that HCV can be passed on is by sharing needles or through unprotected sex. Talk with your doctor about ways to avoid passing on HCV.

What are the ingredients in HOLKIRA PAK?

Ombitasvir/paritaprevir/ritonavir tablets

Each tablet contains the following medicinal ingredients: ombitasvir, paritaprevir and ritonavir.

Each tablet has the following ingredients that are not medicines: colloidal silicon dioxide/anhydrous colloidal silica, copovidone, propylene glycol monolaurate, sodium stearyl fumarate, sorbitan monolaurate, vitamin E polyethylene glycol succinate.

Each tablet is covered with the following ingredients that are not medicines: iron oxide red, polyethylene glycol/macrogol, polyvinyl alcohol, purified water, talc, and titanium dioxide.

The tablets do not contain gluten.

Dasabuvir film-coated tablets

Each tablet contains the following medicinal ingredients: dasabuvir.

Each tablet has the following ingredients that are not medicines: colloidal silicon dioxide/anhydrous colloidal silica, copovidone, croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose.

Each tablet is covered with the following ingredients that are not medicines: iron oxide black, iron oxide red, iron oxide yellow, polyethylene glycol/macrogol, polyvinyl alcohol, purified water, talc, and titanium dioxide.

The tablets do not contain gluten.

HOLKIRA PAK comes in the following dosage forms:

HOLKIRA PAK has two different tablets. One tablet has 12.5 mg of ombitasvir, 75 mg of paritaprevir and 50 mg of ritonavir. The other tablet has 250 mg of dasabuvir.

Do not use HOLKIRA PAK if:

- your doctor says you should also use ribavirin and you are pregnant or want to be pregnant (or your partner is pregnant or wants to become pregnant). Ribavirin may cause birth defects or death of your unborn baby.
- you are allergic to any of the medicines or other ingredients in HOLKIRA PAK (see the section **What are the ingredients in HOLKIRA PAK?** to see all the medicines and ingredients).
- your doctor has told you that you have moderate or severe loss of liver function.

- you are taking any of the following medicines or natural substances:
 - alfuzosin hydrochloride (Xatral[®])
 - astemizole*
 - atorvastatin (Lipitor[®])
 - bosentan (Tracleer[®])
 - carbamazepine (Tegretol[®])
 - cisapride*
 - colchicine for patients who have certain kidney or liver problems
 - disopyramide (Rythmodan[®])
 - dronedarone (Multaq[®])
 - efavirenz-containing medicines (Sustiva[®], Atripla[®])
 - ergot-containing medicines including:
 - ergonovine*
 - ergotamine tartrate*
 - ergotamine (Bellergal Spacetabs[®])
 - dihydroergotamine mesylate (Migranal[®])
 - methylergonovine*
 - ethinyl estradiol-containing medicines such as those contained in most contraceptive pills and vaginal rings used for contraception
 - etravirine (Intelence[®])
 - fusidic acid (systemic)*
 - gemfibrozil
 - lovastatin
 - lurasidone (Latuda[®])
 - midazolam (when taken by mouth)
 - modafinil (Alertec[®])
 - nevirapine (Viramune[®])
 - phenytoin (Dilantin[®])
 - phenobarbital
 - pimozide (Orap[®])
 - rifampin (Rifadin[®], Rifater[®], Rofact[®])
 - salmeterol (Advair Diskus[®], Serevent Diskus[®])
 - sildenafil citrate (Revatio[®]) for the lung problem, pulmonary artery hypertension (PAH)
 - simvastatin
 - St. John's wort (*Hypericum perforatum*) or products containing St. John's wort
 - terfenadine*
 - triazolam

*** Drugs not sold in Canada.**

To help avoid side effects and make sure you are using your medicines correctly, talk to your doctor before you take HOLKIRA PAK. Talk about any health problems you may have, including if you:

- are taking birth control medicines of any kind or using a medicine that has ethinyl estradiol. Ethinyl estradiol is usually found in birth control pills. However, not all birth control pills have ethinyl estradiol. You must not use medicines that have ethinyl estradiol while taking HOLKIRA PAK. Your doctor will ask you to stop or change to a different type of birth control while you are taking HOLKIRA PAK.
- have any other medical condition.
- have had a kidney and/or liver transplant.
 - You should not take HOLKIRA PAK if you are taking everolimus. The dose of everolimus cannot be adjusted to maintain the correct drug levels when given with HOLKIRA PAK.
 - If you are taking tacrolimus or sirolimus you should talk to your doctor about the risks and benefits of taking HOLKIRA PAK at the same time and consider:
 - Serious and life-threatening side effects have occurred when taking HOLKIRA PAK with tacrolimus or sirolimus
 - Your doctor may order blood tests to check tacrolimus or sirolimus levels in your blood at the beginning and during treatment with HOLKIRA PAK
 - Talk with your doctor if you are taking cyclosporine for your transplant. The levels of this medicine can change when taken with HOLKIRA PAK. Your doctor will choose how much cyclosporine you need to take:
 - with HOLKIRA PAK.
 - when you have completed HOLKIRA PAK.
 - if you have to stop taking HOLKIRA PAK for any reason.
- have liver problems other than HCV infection.
- also have HIV infection.
- are breastfeeding or plan to breastfeed. It is not known if HOLKIRA PAK passes into your breast milk. You and your doctor should decide if you will take HOLKIRA PAK or breastfeed. You should not do both.

Hepatitis B Reactivation

Taking antiviral drugs such as HOLKIRA PAK may increase hepatitis B activity. This can lead to liver problems such as liver failure and death. Contact your doctor if:

- you have never been tested for hepatitis B
- you know you have a current hepatitis B infection
- you have had a previous hepatitis B infection

Your healthcare professional may do blood tests:

- before hepatitis C treatment
- to see the hepatitis B levels in your blood
- and may order hepatitis B treatment

Pregnancy and Birth Control

- Females must have negative pregnancy test before starting HOLKIRA PAK and ribavirin, every month while on the medicine, and for 6 months after stopping them.
- You or your partner should not become pregnant while taking HOLKIRA PAK with ribavirin and for 6 months after you have stopped taking them.
- You and your partner must use 2 kinds of birth control while taking HOLKIRA PAK and ribavirin and for 6 months after you have stopped taking them.
- Talk with your doctor about the kind of birth control that you can use.
- If you or your partner becomes pregnant while taking HOLKIRA PAK and ribavirin or within 6 months after you stop taking them, tell your doctor right away.

Other warnings you should know about:

HOLKIRA PAK may cause severe liver problems, especially in people with advanced cirrhosis (liver scarring). These severe liver problems can lead to the need for a liver transplant, or can lead to death.

Rises in liver tests have occurred when the medicines that are in HOLKIRA PAK were taken in studies. Contact your doctor right away if you have symptoms like those listed below since these may mean you have a serious problem with your liver:

- loss of appetite (do not feel like eating)
- stomachache

- swelling of your stomach area
- nausea (feeling sick in the stomach)
- vomiting
- feeling tired or weak
- yellowing of the skin and eyes
- confusion
- dark urine and pale stool.

It is not known if taking HOLKIRA PAK is safe or will work in children under 18 years of age.

Your doctor may do blood tests before you start taking, and while you are on your medicines. This is to help check if the medicines are working for you.

Tell your doctor all the medicines, drugs, vitamins and minerals, natural supplements or alternative medicines you are already taking. Also tell your doctor if you stop any of these or start any new ones.

Do not take HOLKIRA PAK with the following medicines:

- other ritonavir-containing medicines (Norvir[®], Kaletra[®]). When given with HOLKIRA PAK, atazanavir and darunavir should be taken without ritonavir.
- amiodarone (Cordarone[®])
- alfentanil
- everolimus (Affinitor[®], Affinitor[®] Disperz)
- fentanyl (Abstral[®], Duragesic[®])
- flecainamide
- lidocaine (systemic)
- propafenone (Rythmol[®])
- quetiapine (Seroquel[®])
- quinidine
- rilpivirine (Edurant[®], Complera[®])
- sirolimus (Rapamune[®])

The following medicines may interact with HOLKIRA PAK:

- alprazolam (Xanax[®])
- amlodipine (Norvasc[®])
- atazanavir (Reyataz[®])
- atorvastatin (Lipitor[®])
- carisoprodol*
- candesartan (Atacand[®]/Atacand[®] Plus)

- cyclobenzaprine
- cyclosporine (Neoral[®], Sandimmune[®])
- darunavir (Prezista[®])
- diazepam (Valium[®])
- digoxin (Lanoxin[®])
- diltiazem (Cardizem[®] CD)
- fluticasone (Advair[®], Flonase[®], Flovent Diskus[®], Flovent HFA[®])
- fluvastatin (Lescol[®])
- furosemide (Lasix[®])
- hydrocodone (Hycodan[®], Novahistex[®], Novahistine[®], Tussionex[®])
- itraconazole (Sporanox[®])
- ketoconazole (Nizoral[®])
- losartan (Cozaar[®]/Hyzaar[®])
- nifedipine (Adalat[®] XL)
- omeprazole (Losec[®])
- pitavastatin*
- posaconazole (Posanol[®])
- pravastatin (Pravachol[®])
- rosuvastatin (Crestor[®])
- tacrolimus (Prograf[®])
- valsartan (Diovan[®]/Diovan[®] HCT)
- verapamil (Isoptin[®] SR)
- voriconazole (Vfend[®])
- warfarin (Coumadin[®]), or other similar medicines called vitamin K antagonists

*** Drugs not sold in Canada.**

Ask your doctor or pharmacist if you are not sure if your medicine is one that is listed above.

Keep a list of all the medicines you take. Show it to your doctor or pharmacist when you get a new medicine or stop a medicine.

If you change or stop one of your other medicines while you are taking HOLKIRA PAK, ask your doctor about changing back when you are finished taking HOLKIRA PAK.

How to take HOLKIRA PAK:

- Take HOLKIRA PAK exactly as your doctor tells you. Do not change your dose or stop unless your doctor tells you to.
- Take HOLKIRA PAK at about the same time every day with food. The type of food is not important.
- Swallow HOLKIRA PAK tablets whole with water or another liquid if needed.
- Do not chew, break, or crush HOLKIRA PAK tablets.

Usual Adult Dose:

- Every day in the morning, take the two pink ombitasvir/paritaprevir/ritonavir tablets and one beige dasabuvir tablet with food.
- Every day in the evening, take the remaining beige dasabuvir tablet with food.
- HOLKIRA PAK is taken for either 12 or 24 weeks. Your doctor will tell you exactly how long you need to take HOLKIRA PAK.
- If your doctor has also prescribed ribavirin, your doctor will provide you dosage directions for the ribavirin.

Overdose:

If you think you have taken too much HOLKIRA PAK, contact your doctor or pharmacist, hospital emergency department or regional Poison Control Centre immediately, even if you do not have symptoms.

Missed Dose:

- If you miss a dose of the pink ombitasvir/paritaprevir/ritonavir tablets and it is:
 - less than 12 hours from the time you usually take ombitasvir/paritaprevir/ritonavir, you should take the missed dose with food as soon as possible. Then take your next dose at your usual time.
 - more than 12 hours from the time you usually take ombitasvir/paritaprevir/ritonavir, you should not take the missed dose. Take your next dose as usual with food.
- If you miss a dose of the beige dasabuvir tablets and it is:
 - less than 6 hours from the time you usually take dasabuvir, you should take the missed dose with food as soon as possible. Then take your next dose at your usual time.
 - more than 6 hours from the time you usually take dasabuvir, you should not take the missed dose. Take your next dose as usual with food.

What are possible side effects from using HOLKIRA PAK?

If your side effect is not listed here, contact your doctor or pharmacist. Also see **Other warnings you should know about**.

Common side effects of HOLKIRA PAK:

- feeling tired or weak
- headache

Common side effects of HOLKIRA PAK when used with ribavirin:

- feeling tired or weak
- headache
- itching
- nausea (feeling sick in the stomach)
- trouble sleeping

If you have a side effect that is not listed here or becomes bad enough to get in the way of your daily tasks, talk to your doctor.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Erythema multiforme: serious or life-threatening skin rashes and blisters			✓
Serious allergic reactions: difficulty breathing or swallowing; dizziness or light-headedness which may be due to low blood pressure; swelling of the face, lips, tongue or throat; severe itching of the skin, with a red rash or raised bumps			✓

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](http://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting) (www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting);
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 1908C
Ottawa, ON
K1A 0K9Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](http://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting) (www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting).

NOTE: Contact your doctor if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 2 and 30°C. Keep away from moisture.

Keep HOLKIRA PAK out of the reach and sight of children.

If you want more information about HOLKIRA PAK:

- Talk to your doctor.
- Find the most recent version of the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the [Health Canada website](http://www.canada.ca/en/health-canada) (www.canada.ca/en/health-canada); the manufacturer's website (abbvie.ca), or by calling 1-888-704-8271.

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Abstral, Adalat XL, Advair, Advair Diskus, Affinitor, Affinitor Disperz, AlerteC, Atacand, Atacand Plus, Atripla, Bellergal Spacetabs, Cardizem CD, Complera, Cordarone, Coumadin, Cozaar, Crestor, Dilantin, Diovan, Diovan HCT, Duragesic, Edurant, Flonase, Flovent Diskus,

Flovent HFA, Hycodan, Hyzaar, Intelence, Isoptin SR, Lanoxin, Lasix, Latuda, Lescol, Lipitor, Losec, Migranal, Multaq, Neoral, Nizoral, Norvasc, Novahistex, Novahistine, Orap, Posanol, Pravachol, Prezista, Prograf, Rapamune, Revatio, Reyataz, Rifadin, Rifater, Rofact, Rythmodan, Rythmol, Sandimmune, Serevent Diskus, Seroquel, Sporanox, Sustiva, Tegretol, Tracleer, Tussionex, Valium, Vfend, Viramune, Xanax, Xatral are trademarks of their respective owners and are not trademarks of AbbVie Corporation. The makers of these brands are not affiliated with and do not endorse AbbVie or its products.