

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.**

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

* https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[HA697 trade name][†]

Lopinavir/ritonavir

*The warnings and instructions in this leaflet are intended for the person taking the medicine.
If you are a parent or carer responsible for giving the medicine to someone else such as a child,
you will need to apply the instructions accordingly.*

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine is for you only. Do not pass it on to others. It may harm them, even if their illness seems to be the same as yours.
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [HA697 trade name] is and what it is used for
2. What you need to know before you take [HA697 trade name]
3. How to take [HA697 trade name]
4. Possible side effects
5. How to store [HA697 trade name]
6. Contents of the pack and other information

1. What [HA697 trade name] is and what it is used for

[HA697 trade name] is used in combination with other antiviral medicines for the treatment of human immunodeficiency virus (HIV) infection in adults and children aged over 2 weeks.

The medicines reduce the amount of viruses in your body and keep it at a very low level. They are not a cure for HIV infection but if taken correctly, the combination will improve your immune system and reduce the risk of developing illnesses linked to HIV infection.

[HA697 trade name] contains the active substances lopinavir and ritonavir. It is an antiretroviral medicine. It belongs to a group of medicines called protease inhibitors.

2. What you need to know before you take [HA697 trade name]

Do not take [HA697 trade name]:

- if you are allergic (hypersensitive) to lopinavir, ritonavir, or any of the other ingredients of [HA697 trade name] listed in section 6.
- if you have severe liver problems
- if you are taking any of the following medicines:
 - amiodarone, dronedarone, bepridil, quinidine, (drugs used to treat abnormal heartbeat)
 - pimozide (used to treat schizophrenia)
 - lurasidone (used to treat depression)
 - quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder);

[†] Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- astemizole, terfenadine (commonly used to treat allergy symptoms);
- triazolam, diazepam, flurazepam (used to relieve anxiety or trouble sleeping)
- midazolam taken by mouth and clorazepate (sedative, used to treat epilepsy)
- alfuzosin (used in men to treat symptoms of an enlarged prostate [benign prostatic hyperplasia])
- ranolazine (used to treat chronic chest pain [angina])
- cisapride (used to relieve certain stomach problems)
- ergotamine, dihydroergotamine, ergonovine, methylergonovine (used to treat migraine headaches)
- lomitapide, simvastatin, lovastatin (used to lower blood cholesterol)
- colchicine (anti-gout medicine) – patients with renal or hepatic impairment. (See the section on Taking Other Medicines).
- fusidic acid (used to treat skin infections such as impetigo and infected dermatitis). (See the section on Taking Other Medicines).
- elbasvir/grazoprevir, ombitasvir/paritaprevir/ritonavir with or without dasabuvir (used to treat chronic hepatitis C virus [HCV]);
- neratinib (used to treat breast cancer)
- sildenafil used to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery). Sildenafil used to treat erectile dysfunction may be taken under doctor’s supervision (see “Warnings and precautions” section)
- avanafil or vardenafil (used to treat erectile dysfunction)
- products that contain St John’s Wort (*Hypericum perforatum*))

Read the list of medicines under ‘Taking other medicines’ for information on certain other medicines which require special care.

If you are taking any of these medicines, ask your healthcare provider about making changes either in the treatment for your other condition(s) or in your HIV treatment.

Warnings and precautions

Talk to your health care provider before you take [HA697 trade name] if you:

- have had liver disease—if you have chronic hepatitis B or C, you may be at greater risk of severe and dangerous liver problems, HIV medicines such as [HA697 trade name] and your health care provider may need to give you regular blood tests to check your liver function.
- have haemophilia type A and B (a disorder of blood coagulation)—[HA697 trade name] may increase the risk of bleeding.
- have diabetes—treatment with HIV protease inhibitors like [HA697 trade name] may occasionally cause or aggravate diabetes.

This medicine helps to control HIV infection, but it is not a cure for it. You may still develop other infections and other illnesses associated with HIV disease (e.g. opportunistic infections). These require specific and sometimes preventive treatment. You should keep in regular contact with your health care provider. Do not stop the medicine without first talking to your health care provider. It is important that your health care provider knows about all your symptoms even when you think they are not related to HIV infection. Tell your health care provider if your blood cholesterol is high. Treatment with [HA697 trade name] may increase blood cholesterol and other blood lipids. Therefore, you may require blood tests during treatment.

In rare cases, patients receiving lopinavir and ritonavir (contained in [HA697 trade name]) have developed pancreatitis (inflammation of the pancreas). You should contact the health care provider if you get symptoms such as abdominal pain, nausea and vomiting, which may be due to pancreatitis.

In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed that these symptoms are due to an improvement in the body’s immune response, enabling the body

to fight infection that may have been present with no obvious symptoms. If you notice any symptoms of infection, tell your health care provider immediately.

In addition to opportunistic infections, autoimmune disorders (resulting from the immune system attacking healthy body tissue) may also occur after you start taking medicines for treating HIV infection. Autoimmune disorders may occur many months after starting treatment. If you notice any symptoms of infection or other symptoms such as muscle weakness, weakness beginning in the hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, tell your health care provider immediately.

Some patients taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue). The risk of developing this disease may be higher, e.g. when the immune system is severely compromised or when drinking alcohol regularly. If you notice joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement, tell the health care provider.

Muscle pain, tenderness or weakness, particularly in combination with these medicines. On rare occasions these muscle disorders have been serious.

[HA697 trade name] may affect the electrical activity or rhythm of your heart. If you have or have had any heart problems, you should tell your healthcare provider before taking [HA697 trade name]. Tell your doctor if you faint or become dizzy or light-headed, or your heart rhythm feels strange.

[HA697 trade name] may interact with other medications, which may alter their effects (see also the section above, 'do not take [HA697 trade name]', and below 'taking other medicines'). Prior to taking [HA697 trade name], you should inform your health care provider about all other medications that you are taking. While taking [HA697 trade name], you should not start any new medications without informing your health care provider.

If you are taking an oral contraceptive or using a patch contraceptive to prevent pregnancy, you should use an additional or different type of contraception (e.g. barrier contraceptives such as condoms) since [HA697 trade name] may reduce the effectiveness of oral and patch contraceptives.

[HA697 trade name] may interact with medicines used for erectile dysfunction (e.g. sildenafil, tadalafil, vardenafil). You should never take vardenafil with [HA697 trade name]. If you are taking sildenafil or tadalafil with [HA697 trade name], you should talk to your health care provider about possible interactions with other medicines and side effects.

Tell your health care provider if you are taking corticosteroids such as dexamethasone, prednisolone or fluticasone. This includes use of nasal or oral inhalators against rhinitis and asthma. [HA697 trade name] may raise the blood levels of these drugs and cause serious side effect (Cushing's syndrome with hypertension, diabetes, a rounded face, loss of fat on arms and legs as well as a reduction in the body's production of the hormone cortisol). Your health care provider may wish to reduce the steroid dose or monitor the side effects more closely.

Other medicines and [HA697 trade name]

Tell your health care provider if you are taking any other medicine or if you have recently taken other medicines, including medicines obtained without a prescription. These may affect the action of [HA697 trade name] or [HA697 trade name] may affect their action (see also above, sections 'do not take [HA697 trade name]' and "Warnings and precautions"). Side effects of either medicine may become worse or the medicines may become less effective. Sometimes your health care provider may adjust the dose of [HA697 trade name] or of the other drug. Examples of drugs that are or may be unsuitable to take with [HA697 trade name] or where dose adjustments may be necessary include:

- amprenavir, efavirenz, fosamprenavir, indinavir, maraviroc, nelfinavir, nevirapine, saquinavir, tipranavir (against HIV)
- rifampicin, rifabutin, bedaquiline, delamanid (anti-tuberculosis medicine)
- clarithromycin (antibiotic)
- voriconazole, itraconazole, ketoconazole (against fungal infections)
- methadone, fentanyl, propoxyphene, pethidine (opioid analgesics, to treat severe pain)
- medicines to treat asthma and other lung-related problems such as chronic obstructive pulmonary disease (COPD) (e.g. salmeterol)

- abemaciclib, afatinib, apalutamide, ceritinib, encorafenib, ibrutinib, venetoclax, most tyrosine kinases inhibitors such as dasatinib, ifosfamide, vincristine, vinblastine, etoposide, dasatinib and nilotinib (medicines used to treat cancer)
- warfarin, rivaroxaban, vorapaxar (to prevent blood clots)
- carbamazepine, phenytoin, lamotrigine, phenobarbital , valproate (anti-epilepsy medicines)
- trazodone, bupropion (against depression)
- colchicine (Anti-gout medicine)
- glecaprevir/pibrentasvir, simeprevir and sofosbuvir/velpatasvir/voxilaprevir (medicine used to treat chronic hepatitis C in adults)
- sildenafil and tadalafil (erectile dysfunction medicines));
- digoxin, verapamil (to treat heart conditions)
- diltiazem, amlodipine, felodipine, nifedipine, nicardipine (calcium channel blockers, to treat high blood pressure)
- bepridil, systemic lidocain, quinidine (used to correct heart rhythm)
- maracivoc (HIV CCR5-antagonist)
- raltegravir (HIV-1 integrase inhibitor)
- fostamatinib (medicines used to treat low blood platelet count)
- simvastatin, atorvastatin, rosuvastatin, lovastatin (to lower blood cholesterol)
- cyclosporin, sirolimus (rapamycin), tacrolimus (to reduce the body's immune response, e.g. after organ transplantation)
- medicines to treat pulmonary arterial hypertension (high blood pressure in the pulmonary artery) (e.g. bosentan, sildenafil, tadalafil)
- sedative, used to treat anxiety and to help you sleep (e.g. midazolam by injection)
- fusidic acid used to treat long-term infections of the bones and joints (e.g. osteomyelitis)
- medicines used for smoking cessation (e.g. bupropion);
- oral contraceptive or using a patch contraceptive to prevent pregnancy ;
- steroids (e.g. budesonide, dexamethasone, fluticasone propionate, ethinylestradiol, triamcinolone.

Pregnancy and breast-feeding

Pregnant or breast-feeding women should not take [HA697 trade name] unless specifically directed by the health care provider. The health-care provider should be told immediately if you are pregnant or think you are pregnant.

If a mother wants to breast-feed her baby, her healthcare provider should be asked for advice on the risks and benefits. Treatment of mother and/or child with medicines may be needed.

Generally, it is recommended that HIV-infected women should not breast-feed their infants because of the possibility that the baby may be infected with HIV through the breast milk.

Driving and using machines

[HA697 trade name] may cause side effects such as drowsiness or headache, that can reduce the ability to drive and to use machines.

Other ingredients of [HA697 trade name]

[HA697 trade name] contains mannitol, which may have a mild laxative effect.

3. How to take [HA697 trade name]

[HA697 trade name] should always be given exactly as described by the health care provider. You should check with the health care provider if you are not sure.

The recommended doses of [HA697 trade name] in infants and children weighing over 3 kg are as follows:

Child's weight	Dose (twice daily)
2 to less than 3 kg (and at least 2 weeks old)*	1 sachet in the morning 1 sachet in the evening

3kg to less than 6 kg	2 sachets in the morning 2 sachets in the evening
6 kg to less than 10 kg	3 sachets in the morning 3 sachets in the evening
10 kg to less than 14 kg	4 sachets in the morning 4 sachets in the evening
14 kg to less than 20 kg	5 sachets in the morning 5 sachets in the evening
20 kg to less than 25 kg	6 sachets in the morning 6 sachets in the evening
*For children weighing 2 to less than 3 kg who are at least 2 weeks old, another medicine may be used instead, but if your health care provider decides to use [HA697 trade name], this is the suggested dose	

Your health care provider may adjust the dose if you are receiving certain other medicines.

Take the morning and evening doses of [HA697 trade name] about 12 hours apart.

Patients weighing more than 25 kg should be given another form of the medicine supplying more of the active substances in each dose.

[HA697 trade name] should be taken with food. After opening the sachets, the granules should be mixed with soft food such as applesauce or porridge, or a liquid such as clean drinking water or expressed breast milk before consumption.

For infants and young children who are able to take soft foods:

1. Work out the number of sachets needed for the correct dose.
2. Gently tap the sachet(s) to ensure all the granules are at the bottom of the sachets, so they are not lost when opening.
3. Completely tear or cut off the top of the sachet(s) so that the sachet(s) are fully open.
4. Mix with the chosen material:
 - **soft food** such as applesauce or porridge:
 - Place the food (approximately 1 teaspoon of soft food for each sachet) into a small clean cup or bowl.
 - sprinkle the full contents of the sachet onto the food. Make sure no granules/powder are left inside the sachet(s).
 - using a spoon, mix the contents of the sachet into the food.
 - Give or take all of the mixture. If any granules are left in the small cup/bowl or spoon, add more soft food to the granules and mix. Then give or take the mixture along with adequate drinking water, to ensure that no granules are left behind in the mouth.
 - Mixing with **liquid** such as drinking water:
 - Add the appropriate amount of clean drinking water into a cup or bowl (1 teaspoon of water for 2 sachets; 2 teaspoons of water for 3 to 8 sachets; 3 teaspoons or 1 tablespoon for 10 sachets).
 - Sprinkle the entire contents of the sachet(s) into the water and stir gently with a spoon to mix. Make sure no granules/powder are left inside the sachet(s).

- Give or take all of the mixture. If any granules are left in the spoon, add a little more liquid (water) and mix. Then give or take the additional mixture.
5. The mixture must be made up freshly each time and used straight away. It must not be stored. Throw away any unused mixture.

For infants not yet taking solid food, i.e. less than 6 months of age:

1. Work out the number of sachets needed for the correct dose.
2. Gently tap the sachets to ensure all the granules are at the bottom of the sachets, so they are not lost when opening.
3. Completely tear or cut off the top of the sachet(s) so that the sachet(s) are fully open.
4. Add the granules to a small volume of expressed breast milk or formula in a spoon and give to the infant, or put the granules directly on the infant's tongue before breastfeeding. It is important to limit the amount of breast milk (or formula) used to an amount the infant is able to easily consume (2 or 3 teaspoons).
5. Give some additional breast milk (or formula) to make sure the infant has taken the entire dose of granules
6. The mixture must be made up freshly each time and used straight away. It must not be stored. Throw away any unused mixture

If you take more [HA697 trade name] than you should

If you accidentally take too much medicine, tell your health care provider or contact your nearest hospital emergency department for advice.

You may need medical attention. Remember to take the medicine container with you to show to the health care provider.

If you forget to take [HA697 trade name]

If you forget to take a dose and

- if you notice you miss a dose within 6 hours of your normal dosing time, take your missed dose as soon as possible, and then continue with your normal dose at the regular time as prescribed by your health care provider.
- if you notice you miss a dose by more than 6 hours after your normal dosing time, do not take the missed dose. Take the next dose as usual.

Do not take a double dose to make up for a missed dose.

If you stop taking [HA697 trade name]

You should continue taking the medicine to keep the infection in control. Talk with your health care provider if you are thinking of stopping treatment and don't stop it unless the health care provider says you can.

If you have any questions about the use of this medicine, ask your health care provider.

4. Possible side effects

Like all medicines, [HA697 trade name] can cause side effects, but not everybody gets them. When treating HIV infection, it is not always possible to tell which unwanted effects are caused by [HA697 trade name] and which are caused by any other medicines you may be taking at the same time, and by the HIV disease.

Tell your health care provider of any change in your health.

Very common side effects (these may affect more than 1 in 10 patients treated):

- diarrhoea
- nausea

- upper respiratory tract infection

Common side effects (these may affect up to 1 in 10 patients treated):

- headache including migraine
- difficulty in sleeping
- dizziness, anxiety
- feeling, tired, lack of strength and energy
- vomiting, enlarged abdomen, abdominal pain, passing wind, indigestion, decreased appetite, reflux from your stomach to your oesophagus which may cause pain.
- swelling or inflammation of the stomach, intestines and colon
- increased cholesterol, increased triglycerides
- high blood pressure
- inflammation of the pancreas.
- decreased ability of the body to handle sugar including diabetes mellitus, weight loss.
- low number of red blood cells, low number of white blood cells which are usually used to fight infection.
- inflammation of the liver including increased liver enzymes
- muscle disorders such as weakness and spasms, pain in the joints, muscles and back
- night sweats
- rash, eczema, accumulation of scales or greasy skin
- itching, rash including raised bumps on the skin, infection of the skin, inflammation of skin or hair pores, accumulation of fluid in cells or tissues
- allergic reactions including hives and inflammation in the mouth
- tingling, prickling or numbness of the skin.
- haemorrhoids
- lower respiratory tract infection
- enlargement of the lymph nodes
- impotence, abnormally heavy or extended menstrual flow or a lack of menstruation

Further information about nausea, vomiting or abdominal pain

Tell your health care provider if you have nausea, vomiting or abdominal pain as these may be suggestive of pancreatitis (inflammation of the pancreas).

Further information about increased cholesterol and triglycerides

The long-term risks for complications such as heart attacks or stroke due to increased triglycerides and cholesterol are not known at this time.

Your health care provider will monitor you, and may prescribe other medicines if needed.

Large increases in the amount of triglycerides (fats in the blood) have been considered a risk factor for pancreatitis.

Tell your health care provider if you notice any changes in your body shape due to changes in fat distribution.

Uncommon side effects (these can affect up to 1 in every 100 patients treated):

- loss or changed sense of taste
- hearing a sound such as buzzing, ringing or whistling
- abnormal vision, eye disorder
- atrioventricular block—an abnormality in your electrocardiogram

- plaque building up inside your arteries which could lead to heart attack and stroke
- inflammation of blood vessels and capillaries
- inflammation of the bile duct
- uncontrolled shaking of the body
- constipation
- dry mouth
- inability to control your bowels
- inflammation of the first section of the small intestine just after the stomach, wound or ulcer in the digestive tract, bleeding from the intestinal tract or rectum
- red blood cells in the urine
- fatty deposits in the liver, enlarged liver
- lack of functioning of the testes
- a flare-up of symptoms related to an inactive infection in your body (immune reconstitution).
- increased appetite
- abnormally high level of bilirubin (a pigment produced from the breakdown of red blood cells) in the blood
- decreased sexual desire
- inflammation of the kidney
- bone death caused by poor blood supply to the area
- mouth sores or ulcerations, inflammation of the stomach and intestine
- kidney failure
- breakdown of muscle fibres resulting in the release of muscle fibre contents (myoglobin) into the bloodstream
- tremor
- abnormal closure of one of the heart valves (tricuspid valve)
- vertigo (spinning feeling)
- weight gain
- abnormal dreams,
- hair loss
- deep vein inflammation related to a blood clot
- yellowing of the skin or whites of eye (jaundice)
- damage to nerves of the peripheral nervous system

Rare side effects (these can affect up to 1 in 1000 patients treated):

- severe or life-threatening skin rashes and blisters (Stevens-Johnson syndrome and erythema multiforme).

Side effects whose **frequency cannot be estimated** from the available data:

- kidney stones.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your health care provider.

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

For reporting of adverse events and PV related queries please write to Email: ProductSafety@viatris.com

5. How to store [HA697 trade name]

Keep this medicine out of the sight and reach of children.

Do not store above 30°C. Store in the original container.

Do not use this medicine after the expiry date stated on the label and carton after 'EXP'. The expiry date refers to the last day of that month.

Do not use this medicine if you notice description of the visible signs of deterioration that it is different from the description below.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [HA697 trade name] contains

- The active ingredients are lopinavir 40 mg and ritonavir 10 mg
- The other ingredient(s) of [HA697 trade name] are; copovidone, sorbitan monolaurate, colloidal silicon dioxide, ethyl cellulose, mannitol, acesulfame potassium, sodium stearyl fumarate and vanilla flavour.

There is too little sodium in this medicine to have any effect, even if you are on a low-sodium diet.

What [HA697 trade name] looks like and contents of the pack

A white to creamish granular powder filled in a sachet.

Pack size: 120 sachets per carton

Supplier and Manufacturer

Supplier

Mylan Laboratories Limited
Plot No. 564/A/22, Road No. 92, Jubilee Hills
Hyderabad-500096
Telangana
India
Email: ProductSafety@viatris.com

Manufacturer

Mylan Laboratories Limited
F4 & F12, MIDC, Malegaon
Sinnar, Nashik – 422 113
Maharashtra
India

For any information about this medicine, contact the local representative of the supplier

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Detailed information on this medicine is available on the World Health Organization (WHO) website:
<https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products>