

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/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[HA627 trade name][†]
Darunavir (ethanolate)

*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 has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem 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 [HA627 trade name] is and what it is used for
2. What you need to know before you take [HA627 trade name]
3. How to take [HA627 trade name]
4. Possible side effects
5. How to store [HA627 trade name]
6. Contents of the pack and other information

1. What [HA627 trade name] is and what it is used for

[HA627 trade name] contains the active substance darunavir. [HA627 trade name] is an antiretroviral medicine used in the treatment of human immunodeficiency virus (HIV) infection. It belongs to a group of medicines called protease inhibitors.

[HA627 trade name] is used with other HIV medicines to treat patients weighing at least 25 kilograms who are infected by HIV and

- who have not used protease inhibitors before, or
- in certain patients who have used antiretroviral medicines before (your health care provider will check this if you are given this medicine).

[HA627 trade name] is used in combination with other HIV medicines to reduce the amount of virus in your blood and keep it at a low level. It is 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. Your health care provider will discuss with you which combination of medicines is best for you.

[HA627 trade name] may also be recommended by your health care provider as part of the treatment if you have been exposed to HIV, to reduce the risk of getting the infection.

2. What you need to know before you take [HA627 trade name]

Do not take [HA627 trade name]

- if you are **allergic** to darunavir or any of the other ingredients of this medicine (listed in section 6).

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

- if you have **severe liver problems**. Ask your health care provider if you are not sure if you have severe liver disease. You may need some additional tests.

Do not combine [HA627 trade name] with any of the following medicines

If you are taking any of these, ask your health care provider about switching to another medicine.

Medicine	Usual purpose of the medicine
Alfuzosin	to treat enlarged prostate
Amiodarone, bepridil, dronedarone, ivabradine, quinidine, ranolazine	to treat certain heart disorders e.g. abnormal heartbeat
Apixaban, rivaroxaban, clopidogrel, ticagrelor	to prevent platelets clumping together and blocking blood vessels (e.g. in patients who have had a heart attack).
Astemizole or terfenadine	to treat allergy symptoms
Avanafil	to treat erectile dysfunction
Budesonide, fluticasone	to stop inflammatory symptoms
Cisapride	to treat some stomach conditions
Colchicine (if you have kidney or liver problems)	to treat gout or familial Mediterranean fever
Dapoxetine	to treat premature ejaculation
Domperidone	to treat nausea and vomiting
Elbasvir/grazoprevir, glecaprevir/pibrentasvir	to treat hepatitis C infection
Ergot alkaloids like ergotamine, dihydroergotamine, ergometrine and methylergonovine	to treat migraine and headaches
Halofantrine	to treat malaria
Lopinavir/ritonavir	HIV medicine in the same class as darunavir
Lovastatin and simvastatin, and lomitapide	to lower cholesterol levels
Lurasidone, pimozide, quetiapine or sertindole	to treat psychiatric conditions
Naloxegol	to treat constipation caused by certain painkillers
Phenobarbital, phenytoin	to prevent seizures
Rifampicin, rifapentine	to treat some infections such as tuberculosis
Sildenafil	to treat high blood pressure in the pulmonary circulation
Triazolam and midazolam	to help you sleep and relieve anxiety

Do not combine [HA627 trade name] with products that contain St John's wort (*Hypericum perforatum*).

Warnings and precautions

Talk to your health care provider before taking [HA627 trade name].

[HA627 trade name] is not a cure for HIV infection. You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your health care provider the precautions you should take to avoid infecting other people.

People taking [HA627 trade name] may still develop infections or other illnesses associated with HIV infection. You must keep in regular contact with your health care provider.

People taking [HA627 trade name] may develop a skin rash. Infrequently a rash may become severe or life-threatening. Please contact your health care provider if you develop a rash.

In patients taking [HA627 trade name] and raltegravir (for HIV infection), rashes (generally mild or moderate) may occur more frequently than in patients taking either medicine without the other.

[HA627 trade name] has been used in very few patients aged 65 years or older. If you are in this group, please discuss with your health care provider if you can use [HA627 trade name].

Tell your health care provider about your situation BEFORE and DURING your treatment

Check the following points and tell your health care provider if any of them apply to you.

- Tell your health care provider if you have ever had **problems with your liver**, including hepatitis B or C. Your health care provider may check how severe your liver disease is before deciding if you can take [HA627 trade name].
- Tell your health care provider if you have **diabetes**. [HA627 trade name] might increase sugar levels in the blood.
- Tell your health care provider immediately if you notice any **symptoms of infection** (for example enlarged lymph nodes and fever). In some patients with advanced HIV infection and a history of opportunistic infection, inflammation from previous infections may occur soon after starting HIV treatment. These symptoms may occur because of an improvement in the body's immune system, enabling the body to fight infections that may have been present with no obvious symptoms.
- Tell your health care provider immediately 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. These are symptoms of autoimmune disorders (conditions that occur when the immune system attacks healthy body tissue) which may also occur after you start taking HIV medicines. Autoimmune disorders may occur many months after the start of treatment.
- Tell your health care provider if you have **haemophilia**. [HA627 trade name] might increase the risk of bleeding.
- Tell your health care provider if you are **allergic to sulfonamides** (medicines used to treat certain infections).
- Tell your health care provider if you notice any **muscle or bone problems**. Some patients taking antiretroviral medicines may develop a bone disease called osteonecrosis (permanent damage to bone tissue caused by loss of blood supply to the bone). The duration of antiretroviral therapy, corticosteroid use, alcohol consumption, severe immunosuppression, being overweight, among others, may increase the risk for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms, please inform your health care provider.

Children and adolescents

[HA627 trade name] is not for use in children weighing less than 25 kilograms.

Other medicines and [HA627 trade name]

Tell your health care provider if you are taking or have recently taken any other medicines.

There are some medicines that **you must not combine** with [HA627 trade name]. These are mentioned above under the heading 'Do not combine [HA627 trade name] with any of the following medicines:'

In most cases, [HA627 trade name] can be combined with HIV medicines belonging to another class. [HA627 trade name] has not been tested with all PIs (protease inhibitors) and must not be used with certain PIs. In some cases, dosage of other medicines might need to be changed. Therefore, always tell your health care provider if you take other HIV medicines and follow your health care provider's instruction carefully on which medicines can be combined.

Tell your health care provider of **all** the medicines you take. The following is a list of some of the medicines that can either have an effect on how [HA627 trade name] works or [HA627 trade name] may have an effect

on how the medicines work. Taking these medicines together may increase side effects or the medicines may not work well enough, so your health care provider may need to adjust your treatment.

Type of medicine	Examples of medicines
Anaesthetics	ketamine
Antibiotics (including medicines for tuberculosis)	bedaquilline, clarithromycin, delamanid, moxifloxacin, rifabutin
Anticoagulants and antiplatelet medicines (medicines to prevent blood clots and blocked blood vessels)	dabigatran, edoxaban, warfarin
Antidepressants	amitriptyline, desipramine, imipramine, nortriptyline, paroxetine, sertraline, trazodone
Antifungal medicines	clotrimazole, fluconazole, isavuconazole, itraconazole, ketoconazole, posaconazole, voriconazole
Asthma medicine	salmeterol
Cancer medicines	cisplatin, cyclophosphamide, dacarbazine, dasatinib, docetaxel, everolimus, ifosfamide, imatinib, irinotecan, nilotinib, paclitaxel, tamoxifen, vinblastine, vincristine, vinorelbine,
Contraceptive medicines containing an oestrogen and progestogen	ethinylestradiol/drospirenone, ethinylestradiol/norethindrone, medroxyprogesterone etonogestrel (vaginal ring)
Hormone replacement therapy	dydrogesterone, norethisterone
Corticosteroids, usually used for inflammatory condition	betamethasone, dexamethasone, mometasone, prednisone, triamcinolone
HIV medicines	efavirenz, elvitegravir, indinavir, maraviroc, saquinavir, tenofovir disoproxil
Medicines for worm infections	albendazole
Medicines for malaria	artemisinin, mefloquine, proguanil, quinine
Medicines for epilepsy or fits and nerve pain	carbamazepine, clonazepam, lamotrigine, oxcarbazepine, valproate
Medicines for Parkinson's disease	carbidopa, levodopa
Medicines for diabetes	glibenclamide, gliclazide
Medicines for heart problems and high blood pressure	amlodipine, digoxin, diltiazem, disopyramide, carvedilol, felodipine, flecainide, lidocaine, metoprolol, mexiletine, nifedipine, nicardipine, propafenone, timolol, verapamil
Medicines for psychiatric disorders such as schizophrenia	perphenazine, risperidone, thioridazine
Medicines for urinary disorders	fesoterodine, solifenacin
Medicines to control the immune system (e.g. to prevent rejection after transplantation)	ciclosporin, everolimus, sirolimus, tacrolimus
Medicines to increase blood flow (to treat high blood pressure in the lungs and also erectile disorders)	bosentan, sildenafil, vardenafil, tadalafil
Medicines to lower cholesterol in the blood	atorvastatin, pravastatin, rosuvastatin
Medicines to reduce anxiety and to help	bupirone, clorazepate, diazepam, estazolam, flurazepam,

Type of medicine	Examples of medicines
sleep	midazolam injection, zolpidem
Opioid medicines (for treating pain or opioid addiction)	alfentanil, buprenorphine/naloxone, fentanyl, methadone, morphine, oxycodone, tramadol

This is **not** a complete list of medicines. Tell your healthcare provider about **all** medicines that you are taking.

[HA627 trade name] with food and drink

You must take [HA627 trade name] within 30 minutes of eating a meal or a taking a snack. The type of food you take is not important

Pregnancy and breast-feeding

If you become pregnant, or are planning to become pregnant, you must contact your healthcare provider to discuss the potential benefits and risks of your antiretroviral therapy to you and your child.

Pregnant or breast-feeding mothers should not take [HA627 trade name] with cobicistat.

It is not known whether darunavir and ritonavir pass into milk. If you want to breast-feed your baby, you should ask your healthcare provider for advice on the risks and benefits.

Driving and using machines

Do not operate machines or drive if you feel dizzy after taking [HA627 trade name].

3. How to take [HA627 trade name]

Always take this medicine exactly as your health care provider has told you. Check with your health care provider if you are not sure.

Even if you feel better, do not stop taking [HA627 trade name] without talking to your health care provider.

You must not change the dose, change your HIV medicines or stop treatment without checking with your health care provider.

You must take [HA627 trade name] every day around the same time and always in combination with ritonavir and with food. [HA627 trade name] cannot work properly without ritonavir and food. You should take [HA627 trade name] within 30 minutes of eating a meal or taking a snack. The type of food is not important. Swallow the tablets with a drink such as water or milk.

Dose

The recommended dose of [HA627 trade name] is 1 or 2 tablets of [HA627 trade name] in combination with 100 mg ritonavir, taken once daily with food at around the same time each day.

If you take more [HA627 trade name] than you should:

If you accidentally take too many [HA627 trade name], contact your health care provider immediately.

If you forget to take [HA627 trade name]

It is important not to miss a dose.

If you miss a dose **within 12 hours of when you usually take it**, take it as soon as you can, and then take your next dose at its regular time.

If you miss a dose and **it is less than 12 hours before you usually take a dose**, do not take the missed dose. Wait and take the next dose at the usual time. Do not take a double dose to make up for a forgotten tablet.

If you vomit (throw up) within 4 hours of taking [HA627 trade name], take another tablet straightaway with some food. Do not wait until your next dose is due. You do not need to take another tablet if you vomited more than 4 hours after taking [HA627 trade name].

Stopping [HA627 trade name]

Do not stop taking [HA627 trade name] without talking to your health care provider first. HIV treatment may increase your sense of well-being. Even when you feel better, do not stop taking {DotWPProductName}. Talk to your health care provider first if you are thinking of stopping your medicine. If you have any questions about this medicine, ask your health care provider.

4. Possible side effects

During HIV therapy you may put on weight and levels of blood lipids (fats in the blood) and glucose (blood sugar) may rise. This is partly linked to restored health and lifestyle, and in the case of blood lipids sometimes to the HIV medicines. Your health care provider will test for these changes.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your health care provider if you have:

- yellowing of your skin or whites of your eyes, dark (tea-coloured) urine, pale stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching, or discomfort on your right side below your ribs. These are symptoms of liver problems that may occasionally be severe. Your health care provider should do blood tests before starting [HA627 trade name]. If you have chronic hepatitis B or C infection, your health care provider should check your blood tests more often because your chances of liver problems may be increased.
- skin rash (more often when used in combination with raltegravir), itching. The rash is usually mild to moderate. A skin rash might also be a symptom of a rare severe condition. It is therefore important to contact your health care provider if you develop a rash. Your health care provider will say how to deal with your symptoms or whether [HA627 trade name] must be stopped.

Other important severe side effects are diabetes (common) and inflammation of the pancreas (uncommon).

Very common side effects (that may affect more than 1 in 10 people):

- diarrhoea.

Common side effects (may affect up to 1 in 10 people)

- vomiting, nausea, abdominal (belly) pain or distension (swelling), indigestion, flatulence (gas)
- headache, tiredness, dizziness, numbness, tingling or pain in hands or feet, loss of strength, difficulty falling asleep
- rash
- blood tests showing changes in certain enzymes (indicating stress on the liver and pancreas), raised cholesterol, blood lipids and glucose (blood sugar).

Uncommon side effects (may affect up to 1 in 100 people)

- pain because of blockage in blood supply to a part of the heart, changes in electrocardiogram (test of the heart's electrical activity), rapid heartbeat
- decreased or abnormal sensation to touch, pain and temperature, pins and needles, attention disturbance, loss of memory, lack of energy, sleepiness, taste disturbance
- difficulty breathing, cough, nosebleed, throat irritation
- inflammation of the stomach or mouth, abnormal sensation in the mouth, heartburn, retching, dry mouth, discomfort of the abdomen, constipation, belching
- inflammation of the liver, fat build-up in the liver, blood tests indicating liver damage
- kidney failure, kidney stones, pain and discomfort on passing urine, passing urine frequently sometimes at night; tests showing protein and bilirubin in the urine
- itchy rash, widespread rash, swelling of the skin and other tissues (most often the lips or the eyes), skin reddening, eczema, excessive sweating, night sweats, hair loss, acne, dry skin, discoloration of nails

- muscle pain, muscle cramps or weakness, pain in arms and legs, osteoporosis (bones become fragile), osteonecrosis (permanent bone damage); blood test showing markers for bone damage
- gout, weight loss, decreased appetite and weight loss, increased appetite and weight gain, excessive thirst
- reduced thyroid gland function. This can be seen in a blood test.
- high blood pressure, flushing
- red eyes, dry eyes
- fever, swelling of ankles due to build-up of fluids, feeling generally unwell, feeling hot, irritability, pain, spinning sensation
- immune reconstitution inflammatory syndrome, allergy
- herpes simplex (cold sores or genital herpes)
- erectile dysfunction, enlargement of breasts
- blood tests showing reduced white cells and platelets (components that help the blood to clot), anaemia
- sleeping problems, depression, disorientation, anxiety, abnormal dreams, decrease in sexual drive

Rare side effects (may affect up to 1 in 1,000 people)

- a reaction called DRESS (a severe reaction affecting the skin, blood and internal organs), Stevens-Johnson syndrome (serious reaction with flu-like symptoms and painful rash affecting the skin, mouth, eyes and genitals)
- heart attack, slow heartbeat, palpitations
- visual disturbance
- chills, feeling abnormal
- confusion, altered mood, restlessness
- fainting, convulsions (fits), loss of taste
- mouth sores, vomiting blood, inflammation of the lips, dry lips, coated tongue
- runny nose
- skin lesions (damage or abnormalities), seborrheic dermatitis (red skin and scaly patches on the scalp and dandruff)
- stiffness of muscles or joints, joint pain and inflammation
- blood tests showing increase in eosinophils (a type of white blood cells).

Side effects for which there is not enough information to work out how many people are affected:

- toxic epidermal necrolysis (life-threatening reaction with flu-like effects and blistering in the skin, mouth eyes and genitals), acute generalised exanthematous pustulosis (pus-filled pimples with red surrounding skin)

Some side effects are typical for HIV medicines in the same family as darunavir. These are:

- muscle pain, tenderness or weakness. On rare occasions, these muscle disorders have been serious.

If you get any side effects talk to your health care provider. This includes any possible side effects not listed in this leaflet.

Reporting of side effects

If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects you can help improve understanding about the safety of this medicine.

5. How to store [HA627 trade name]

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

Do not store above 30°C.

Do not use this medicine after the expiry date which is stated on the label 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 [HA627 trade name] contains

- The active ingredient is 433.648 mg darunavir ethanolate equivalent to 400 mg darunavir.
- The other ingredients of [HA627 trade name] are excipients:

Core tablet: Silicified microcrystalline cellulose, Crospovidone, Colloidal silicon dioxide and Magnesium stearate.

Film coat: Polyvinyl alcohol part hydrolysed, Titanium dioxide, Macrogol/PEG, Talc and FD&C yellow #6/Sunset yellow FCF Aluminium Lake

What [HA627 trade name] looks like and contents of the pack

[HA627 trade name] is a light orange coloured, oval shaped, biconvex, film coated tablet, debossed with 'DNV' on one side & '400' on the other side.

No score line.

[HA627 trade name] is available in an opaque, white, 85cc high density polyethylene (HDPE) plastic bottle containing 60 tablets, fitted with a HDPE non child resistant closure, and foil induction seal.

Supplier and Manufacturer

Supplier

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India

“For any information about this medicinal product, please contact the supplier”

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Detailed information on this medicine is available on the World Health Organization (WHO) website: <https://extranet.who.int/pqweb/medicines>