



PATIENT INFORMATION LEAFLET

Darunavir and Ritonavir Tablets 400 mg/50 mg

Please read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:

1. What Darunavir and Ritonavir tablets is and what it is used for
2. What you need to know before you take Darunavir and Ritonavir
3. How to take Darunavir and Ritonavir tablets
4. Possible side effects
5. How to store Darunavir and Ritonavir tablets
6. Contents of the pack and other information

1. What Darunavir and Ritonavir tablets 400mg/50mg is and what it is used for

Darunavir and Ritonavir contains the active ingredients Darunavir and Ritonavir. Darunavir and Ritonavir is an antiretroviral medicine used in the treatment of Human Immunodeficiency virus (HIV) infection. It belongs to a group of medicines called protease inhibitors. Darunavir and Ritonavir works by reducing the amount of HIV in your body. This will improve your immune system and reduces the risk of developing illness linked to HIV infection.

Darunavir and Ritonavir is used to treat adults and children of 3 years of age and above weighing at least 15 kilograms who are infected by HIV and who have already used other antiretroviral medicines.

It is very important that you also read the package leaflets for the other medicines that you will be taking with Darunavir and Ritonavir tablet 400mg/50mg. If you have any questions about your medicines, please ask your doctor or pharmacist.

**2. What you need to know before you take Darunavir and Ritonavir tablet 400mg/50mg****Do not take Darunavir and Ritonavir**

- If you are allergic to Darunavir and Ritonavir or any of the other ingredients of this medicine (listed in section 6 of this leaflet)
- If you have severe liver problems. Ask your health care provider if you are unsure about the severity of your liver disease. Some additional tests might be necessary.
- If you he/she is currently taking any of the following medicines, ask your healthcare provider about switching to a different medicine while you are taking Darunavir and Ritonavir tablet 400mg/50mg. Often, there are other medicines you can take instead.

Medicine	Purpose of the medicine
astemizole or terfenadine	commonly used to treat allergy symptoms – these medicines may be available without prescription)
amiodarone, bepridil, dronedarone encainide, flecainide, propafenone, quinidine, ranolazine and systemic lidocaine	used to correct irregular heartbeats);
Ergot alkaloids like ergotamine , dihydroergotamine, ergometrine , methylergonovone	used to treat migraine headache
ergonovine, methylergonovine	used to stop excessive bleeding that may occur following childbirth or an abortion
clorazepate, diazepam, estazolam, flurazepam, triazolam or oral (taken by mouth) midazolam	used to help you sleep and/or relieve anxiety
clozapine, pimozide, quetiapine or sertindole	used to treat abnormal thoughts or feelings
pethidine, piroxicam, propoxyphene	used to relieve pain
cisapride	used to relieve certain stomach problems



rifabutin	used to prevent/treat certain infections
voriconazole	(used to treat fungal infections)
simvastatin, lovastatin	used to lower blood cholesterol
alfuzosin	used to treat enlarged prostate gland
fusidic acid	used to treat bacterial infections
avanafil or vardenafil	used to treat erectile dysfunction in adult patients
Rifampicin	To treat some infection such as tuberculosis
Ticagrelor	To help stop the clumping of platelets in the treatment of patients with a history of a heart attack
Sildenafil	To treat high blood pressure in the pulmonary circulation.

Products containing St John's wort (*Hypericum perforatum*) as this may stop Ritonavir Darunavir and Ritonavir from working properly. St John's wort is often used in herbal medicines that you can buy yourself.

Warnings and precautions

Talk to your healthcare provider before taking Darunavir and Ritonavir tablet 400mg/50mg.

Important information

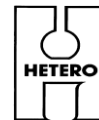
- If Darunavir and Ritonavir is taken in combination with other antiretroviral medicines, it is important that you also carefully read the leaflets that are provided with these other medicines. There may be additional information in those leaflets about situations when Darunavir and Ritonavir should be avoided. If you have any further questions about Darunavir and Ritonavir
- Darunavir and Ritonavir 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 need to avoid infecting other people.
- People taking Darunavir and Ritonavir may still develop infections or illness associated with HIV infection. You must keep in regular contact with your health care provider.

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



Make sure that you check the following points and tell your health care provider if any of these apply to you.

- Tell your health care provider if you have had **problems with your liver** before, including hepatitis B or C. Your health care provider may evaluate how severe your liver disease is before deciding if you can take Darunavir and Ritonavir tablet 400mg/50mg.
- Tell your health care provider if you have **diabetes**. Darunavir and Ritonavir tablet 400mg/50mg.
- 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, signs and symptoms of inflammation from previous infection 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 infections that may have been present with no obvious symptoms.
- In addition to the opportunistic infections, auto immune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of 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, please inform your health care provider immediately to seek necessary treatment.
- Tell your health care provider if you have **haemophilia**. Darunavir and Ritonavir might increase the risk of bleeding. The reason for this is not known. Your child may need additional medicine to help your blood clot (factor VIII), in order to control any bleeding.
- Tell your healthcare provider if you are **allergic to sulphonamides** (e.g. used to treat certain infections).
- Tell your health care provider if you have notice any **musculoskeletal problems**. Darunavir and Ritonavir as it is a combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination antiretroviral therapy, corticosteroid use, alcohol



consumption, severe immunosuppression, higher body mass index, among others, may be some of the many risk factors 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 those symptoms please inform your health care provider.

- **Erectile dysfunction** (in adult patients), as the medicines used to treat erectile dysfunction can cause hypotension and prolonged erection.
- **Kidney (renal) disease**, since your health care provider may need to check the dose of the other medicines (such as protease inhibitors) your child is taking.
- **Dizziness, lightheadness, fainting** spells or **abnormal heartbeat**. Some patients taking Darunavir and Ritonavir may experience changes in the electrocardiogram (ECG). Tell your healthcare provider if your child has a heart defect or conduction defect.

Other medicines and Darunavir and Ritonavir tablet 400mg/50mg

Please tell your healthcare provider if you he/she is taking or has recently taken any other medicines, including medicines obtained without a prescription. There are some medicines cannot take at all with Darunavir and Ritonavir tablet 400mg/50mg. These are listed earlier in section 2, under 'Do not use Darunavir and Ritonavir tablet 400mg/50mg' under certain circumstances, as described below.

The effects of Darunavir and Ritonavir might be reduced if you take any of the following products. Tell your health care provider if you take:

- *Phenobarbital, phenytoin* (to prevent seizures)
- *Dexamethasone* (Corticosteroid)
- *Efavirenz* (HIV infection)
- *Telaprevir, bocoprevir* (hepatitis C virus infection)
- *Rifapentine, rifabutin* (medicines to treat some infections such as tuberculosis)
- *Saquinavir* (HIV infection)

The effects of other medicines might be influenced if you take Darunavir and Ritonavir tablet 400mg/50mg. Tell your health care provider if you take:



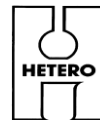
- *Amloipine, diltiazem, disopyramide, carvedilol, felodipine, flecainide, metoprolol, mexiletine, nifedipine, nocardipine, propafenone, timolol, verapamil* (for heart disease) as the therapeutic effect or side effects of these medicines may be increased.
- *Apixam, dabigatram etexilate, rivaroxaban, warfarin* (to reduce clotting of the blood) as their therapeutic effect or side effects may be altered; your health care provider may have to check your blood.
- *Atorvastatin, pravastatin, rosuvastatin* (to lower cholesterol levels). The risk of muscle tissue disorder might be increased. Your health care provider will evaluate which cholesterol lowering regimen is best for your specific situation.
- Oestrogen-based hormonal contraceptives and hormonal replacement therapy. Darunavir and Ritonavir might reduce its effectiveness. When used for birth control, alternative methods of non-hormonal contraception are recommended.
- *Clarithromycin* (antibiotic)
- *Ciclosporin, everolimus, tacrolimus, sirolimus* (to treat your immune system) as the therapeutic effect or side effects of these medicines might be increased. Your health care provider might want to do some additional tests.
- *Fluticasone, budesonide* (to control asthma). Its use should only take place after medical evaluation and under close monitoring by your health care provider for corticosteroid side effects.
- *Buprenorphine/naloxone* (dependence) medicines to treat opiate
- *Salmeterol* (medicine to treat asthma)
- *Artemether/lumefantrine* (a combination medicine to treat malaria).
- *Dasatinib, everolimus, nilotinib, vinblastine, vincristine* (to treat cancer)
- *Prednisone* (corticosteroid)
- *Sildenafil, tadalafil, vardenafil* (for erectile dysfunction or to treat a heart and lung disorder called pulmonary arterial hypertension).



The dosage of other medicines might need to be changed since either their own or the therapeutic effect or side effects of Darunavir and Ritonavir may be influenced when combined.

Tell your health care provider if you take

- *Alfentanil* (injectable strong and short-acting painkiller that is used for surgical procedure)
- *Digoxin* (to treat certain heart disorders)
- *Clarithromycin* (antibiotic)
- *Ketoconazole, itraconazole, fluconazole, posaconazole, clotrimazole* (to treat fungal infections). Voriconazole should only be taken after medical evaluation.
- *Rifabutin* (against bacterial infections)
- *Sildenafil, vardenafil, tadalafil* (for erectile dysfunction or high blood pressure in the pulmonary circulation)
- *Amitriptyline, desipramine, imipramine, nortriptyline, paroxetine, sertraline, trazodone* (to treat depression and anxiety)
- *Maraviroc* (to treat HIV infection)
- *Methadone* (to treat opiate dependence)
- *Carbamazepine* (to prevent seizures or to treat certain types of nerve pain)
- *Colchicine* (to treat gout)
- *Bosentan* (to treat high blood pressure in the pulmonary circulation)
- *Buspirone, clorazepate, diazepam, estazolam, flurazepam, midazolam that is not taken orally, zoldipem* (sedative agents)
- *Perphenazine, risperidone, thioridazine* (to treat conditions) psychiatric
- *Metformin* (to treat type 2 diabetes).



Darunavir and Ritonavir with food and drink

You must eat a meal or a snack within 30 minutes prior to taking your Darunavir and Ritonavir tablet 400mg/50mg. The type of food 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.

It is not known whether Darunavir and Ritonavir is excreted in human 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

Darunavir and Ritonavir can cause sleepiness and dizziness. If the ability to drive or use machines seems to be affected then one should not drive or use machinery.

Important information about some of the ingredients of Darunavir and Ritonavir tablet 400mg/50mg

This medicine contains Opadry yellow 16C82767, a colouring agent which may cause allergic reactions.

3. How to take Darunavir and Ritonavir tablet 400mg/50mg

Always use this medicine exactly as described in this leaflet or 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 Darunavir and Ritonavir without talking to your health care provider.

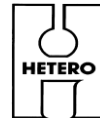
Swallow the tablets with a drink such as water or milk. The type of food is not important. **Recommended dose**

Your health care provider will advise you on the dosage to be taken.

Dose for adults who have taken certain antiretroviral medicines before

The recommended dose is 400 milligram of Darunavir and 50 milligrams of Ritonavir (1 tablet of Darunavir and Ritonavir 400mg/50mg) per day.

If you take more Darunavir and Ritonavir than you should



Contact your health care provider immediately.

If you forget to take Darunavir and Ritonavir tablet 400mg/50mg

If you notice within 12 hours, you must take the tablets immediately. Always take with food. If you notice after 12 hours, then skip the intake and take the next doses as usual.

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

Do not stop taking Darunavir and Ritonavir without talking to your health care provider first

HIV therapy may increase your sense of well-being. Even when you feel better, do not stop taking Darunavir and Ritonavir tablet 400mg/50mg. Talk to your health care provider first.

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

4. POSSIBLE SIDE EFFECTS

During HIV therapy there may be an increase in weight and in levels of blood lipids and glucose. This is partly linked to restored health and life style, and in the case of blood lipids sometimes to the HIV medicines themselves. Your health care provider will test for these changes.

Like all medicines, Darunavir and Ritonavir can cause side effects, although not everybody gets them. Also, the side effects of Darunavir and Ritonavir when used with other antiretroviral medicines are dependent on the other medicines. It is important that you carefully read the side effects section of the leaflets that are provided with these other medicines. Tell your health care provider if you develop any of the following side effects.

Liver problems that may occasionally be severe have been reported. Your health care provider should do blood tests prior to initiating Darunavir and Ritonavir tablet 400mg/50mg. If you have chronic hepatitis B or C infection, your health care provider should check your blood tests more often because you have an increased chance of developing liver problems. Talk to your health care provider about the signs and symptoms of liver problems. These may include yellowing of your skin or whites of



your eyes, dark (tea coloured) urine, pale coloured stools (bowel movements), nausea, vomiting, loss of appetite, or pain, aching, or sensitivity on your right side below your ribs.

Skin rash. The rash is usually mild to moderate. A skin rash might also be a symptom of a rare severe situation. It is therefore important to contact your health care provider if you develop a rash. Your health care provider will advise you how to deal with your symptoms or whether Darunavir and Ritonavir must be stopped.

Other clinically relevant severe side effects were diabetes (common) and inflammation of the pancreas (uncommon).

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

- diarrhoea.

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

- vomiting, nausea, abdominal pain or distension, dyspepsia, flatulence
- headache, tiredness, dizziness, drowsiness, numbness, tingling or pain in hands or feet, loss of strength, difficulty falling asleep.

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

- chest pain, changes in electrocardiogram, rapid heart beating
- decreased or abnormal skin sensibility, pins and needles, attention disturbance, loss of memory, problems with your balance
- difficulty breathing, cough, nosebleed, throat irritation
- inflammation of the stomach or mouth, heartburn, retching, dry mouth, discomfort of the abdomen, constipation, belching
- kidney failure, kidney stones, difficult discharge of urine, frequent or excessive passage of urine, sometimes at night
- urticaria, severe swelling of the skin and other tissues (most often the lips or the eyes), eczema, excessive sweating, night sweats, hair loss, acne, scaly skin, colouration of nails
- muscle pain, muscle cramps or weakness, pain in extremity, osteoporosis
- slowing down of the thyroid gland function. This can be seen in a blood test.
- high blood pressure, flushing
- red or dry eyes



- fever, swelling of lower limbs due to fluids, malaise, irritability, pain
- symptoms of infection, herpes simplex
- erectile dysfunction, enlargement of breasts
- Sleeping problems, sleepiness, depression, anxiety, abnormal dreams, decrease in sexual drive.

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

- a reaction called DRESS [severe rash, which may be accompanied by fever, fatigue, swelling of the face or lymph glands, increase of eosinophils (type of white blood cells), effects on liver, kidney or lung]
- heart attack, slow heart beating, palpitations
- visual disturbance
- chills, feeling abnormal
- a feeling of confusion or disorientation, altered mood, restlessness
- fainting, epileptic fits, changes or loss of taste
- mouth sores, vomiting blood, inflammation of the lips, dry lips, coated tongue
- running nose
- skin lesions, dry skin
- stiffness of muscles or joints, joint pain with or without inflammation
- Changes in some values of your blood cells or chemistry. These can be seen in the results of blood and/or urine tests. Your health care provider will explain these to you. Examples are: increase in some white blood cells.

Some side effects are typical for anti-HIV medicines in the same family as Darunavir and Ritonavir tablet 400mg/50mg. 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.

5. How to store Darunavir and Ritonavir tablet 400mg/50mg

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 throw away any medicines via wastewater or household waste. Ask your pharmacist 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 tablet Darunavir and Ritonavir contains

Each film coated tablet contains Darunavir ethanolate equivalent to 400mg of Darunavir and Ritonavir USP 50mg

Core tablet:

- Silicified microcrystalline cellulose
- Crospovidone
- Colloidal silicon dioxide
- Magnesium stearate
- Dibasic Calcium phosphate anhydrous
- Sodium stearyl Fumarate

Film coat:

- Opadry yellow 16C82767
- Purified water

What Darunavir and Ritonavir looks like and contents of the pack

Yellow, capsule shaped, bevel edged, biconvex film coated tablets debossed with 'H' on one side and with 'D8' on the other side.

Marketing Authorization Holder

M/s. Hetero Labs Limited,

7-2-A2, Hetero Corporate,

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