

PATIENT INFORMATION LEAFLET: INFORMATION FOR THE USER

Darunavir (as ethanolate) 400mg Tablets ¹

Darunavir (as ethanolate)

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 any further questions, 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 are the same as yours.
- If you get 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 Darunavir (as ethanolate) 400mg Tablets is and what it is used for
2. What you need to know before you take Darunavir (as ethanolate) 400mg Tablets
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1. What Darunavir (as ethanolate) 400mg Tablets is and what it is used for

Darunavir (as ethanolate) 400mg Tablets contains the active substance darunavir. Darunavir (as ethanolate) 400mg Tablets 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 (as ethanolate) 400mg Tablets works by reducing the amount of HIV in your body. This will improve your immune system and reduces the risk of developing illnesses linked to HIV infection.

Darunavir (as ethanolate) 400mg Tablets is used to treat adults and adolescents weighing at least 40 kilograms who are infected by HIV and

- who have not used antiretroviral medicines before.
- in certain patients who have used antiretroviral medicines before (your health care provider will determine this).

Darunavir (as ethanolate) 400mg Tablets must be taken in combination with a low dose of ritonavir and other anti-HIV medicines. Your health care provider will discuss with you which combination of medicines is best for you.

¹ Trade names are not prequalified by WHO. This is the national medicines regulatory authority's (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

2. What you need to know before you take Darunavir (as ethanolate) 400mg Tablets

Do not take Darunavir (as ethanolate) 400mg Tablets

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

- 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.

Do not combine Darunavir (as ethanolate) 400mg Tablets with any of the following medicines

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

Medicine	Purpose of the medicine
<i>Avanafil</i>	to treat erectile dysfunction
<i>Astemizole</i> or <i>terfenadine</i>	to treat allergy symptoms
<i>Triazolam</i> and <i>oral</i> (taken by mouth) <i>midazolam</i>	to help you sleep and/or relieve anxiety
<i>Cisapride</i>	to treat some stomach conditions
<i>Colchicine</i> (if you have kidney and/or liver problems)	to treat gout
<i>Pimozide</i> , <i>quetiapine</i> or <i>sertindole</i>	to treat psychiatric conditions
<i>Ergot alkaloids</i> like <i>ergotamine</i> , <i>dihydroergotamine</i> , <i>ergometrine</i> and <i>methylethergonovine</i>	to treat migraine and headaches
<i>Amiodarone</i> , <i>bepidil</i> , <i>dronedarone</i> , <i>quinidine</i> , <i>ranolazine</i> and <i>systemic lidocaine</i>	to treat certain heart disorders e.g. abnormal heart beat
<i>Lovastatin</i> and <i>simvastatin</i>	to lower cholesterol levels
<i>Rifampicin</i>	to treat some infections such as tuberculosis
The combination product <i>lopinavir/ritonavir</i>	this anti-HIV medicine belongs to the same class as darunavir
<i>Alfuzosin</i>	to treat enlarged prostate
<i>Sildenafil</i>	to treat high blood pressure in the pulmonary circulation
<i>Ticagrelor</i>	to help stop the clumping of platelets in the treatment of patients with a history of a heart attack.

Do not combine Darunavir (as ethanolate) 400mg Tablets with products that contain St John's wort (*Hypericum perforatum*).

Warnings and precautions

Talk to your health care provider before taking Darunavir (as ethanolate) 400mg Tablets.

Darunavir (as ethanolate) 400mg Tablets 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 needed to avoid infecting other people.

People taking Darunavir (as ethanolate) 400mg Tablets may still develop infections or other illnesses associated with HIV infection. You must keep in regular contact with your health care provider.

People taking Darunavir (as ethanolate) 400mg Tablets may develop a skin rash. Infrequently a rash may become severe or potentially life-threatening. Please contact your health care provider whenever you develop a rash.

In patients taking Darunavir (as ethanolate) 400mg Tablets and raltegravir (for HIV infection), rashes (generally mild or moderate) may occur more frequently than in patients taking either medicine separately.

Darunavir (as ethanolate) 400mg Tablets has only been used in limited numbers of patients 65 years or older. If you belong to this age group, please discuss with your health care provider if you can use Darunavir (as ethanolate) 400mg Tablets.

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

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 (as ethanolate) 400mg Tablets.
- Tell your health care provider if you have **diabetes**. Darunavir (as ethanolate) 400mg Tablets 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, 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 infections that may have been present with no obvious symptoms.
- In addition to the opportunistic infections, autoimmune 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 (as ethanolate) 400mg Tablets, might increase the risk of bleeding.
- Tell your health care provider if you are **allergic to sulphonamides** (e.g. used to treat certain infections).

- Tell your health care provider if you notice any **musculoskeletal problems**. Some patients taking 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 these symptoms please inform your health care provider.

Children and adolescents

Darunavir (as ethanolate) 400mg Tablets is not for use in children younger than 3 years of age or weighing less than 15 kilograms.

Other medicines and Darunavir (as ethanolate) 400mg Tablets

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 Darunavir (as ethanolate) 400mg Tablets. These are mentioned above under the heading ‘Do not combine Darunavir (as ethanolate) 400mg Tablets with any of the following medicines:’

In most cases, Darunavir (as ethanolate) 400mg Tablets can be combined with anti-HIV medicines belonging to another class [e.g. NRTIs (nucleoside reverse transcriptase inhibitors), NNRTIs (non-nucleoside reverse transcriptase inhibitors), CCR5 antagonists and FIs (fusion inhibitors)]. Darunavir (as ethanolate) 400mg Tablets with ritonavir has not been tested with all PIs (protease inhibitors) and must not be used with other HIV PIs. In some cases dosage of other medicines might need to be changed. Therefore always tell your health care provider if you take other anti-HIV medicines and follow your health care provider’s instruction carefully on which medicines can be combined.

The effects of Darunavir (as ethanolate) 400mg Tablets 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, boceprevir* (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 (as ethanolate) 400mg Tablets. Tell your health care provider if you take:

- *Amlodipine, diltiazem, disopyramide, carvedilol, felodipine, flecainide, metoprolol, mexiletine, nifedipine, nicardipine, propafenone, timolol, verapamil* (for heart disease) as the therapeutic effect or side effects of these medicines may be increased.

- *Apixaban, dabigatran 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.

- Oestrogen-based hormonal contraceptives and hormonal replacement therapy. Darunavir (as ethanolate) 400mg Tablets might reduce its effectiveness. When used for birth control, alternative methods of non-hormonal contraception are recommended.

- *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.

- *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* (medicines to treat opiate dependence)

- *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 (as ethanolate) 400mg Tablets 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 procedures)

- *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 psychiatric conditions)
- *Metformin* (to treat type 2 diabetes).

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

Darunavir (as ethanolate) 400mg Tablets with food and drink

You must eat a meal or a snack within 30 minutes prior to taking your Darunavir (as ethanolate) 400mg Tablets and ritonavir. 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 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

Do not operate machines or drive if you feel dizzy after taking Darunavir (as ethanolate) 400mg Tablets.

Excipients

This medicine contains FD&C yellow #6/Sunset yellow FCF Aluminium Lake, a colouring agent which may cause allergic reactions.

3. How to take Darunavir (as ethanolate) 400mg Tablets

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 (as ethanolate) 400mg Tablets and ritonavir without talking to your health care provider.

After therapy has been initiated, the dose or dosage form must not be changed or therapy must not be stopped without instruction of the health care provider.

You must take Darunavir (as ethanolate) 400mg Tablets every day and always in combination with 100 milligram of ritonavir and with food. Darunavir (as ethanolate) 400mg Tablets cannot work properly without ritonavir and food. You must eat a meal or a snack within 30 minutes prior to taking your Darunavir (as ethanolate) 400mg Tablets and ritonavir. Swallow the tablets with a drink such as water or milk. The type of

food is not important. Even if you feel better, do not stop taking Darunavir (as ethanolate) 400mg Tablets and ritonavir without talking to your health care provider.

Dose for adults and for children of 3 years of age and above, weighing at least 40 kilograms

The recommended dose is 800 milligram (2 tablets of Darunavir (as ethanolate) 400mg Tablets together with 100 milligram ritonavir once daily taken with food.

If you take more Darunavir (as ethanolate) 400mg Tablets than you should

Contact your health care provider immediately.

If you forget to take Darunavir (as ethanolate) 400mg Tablets

If you notice **within 12 hours**, you must take the tablets immediately. Always take with ritonavir and 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 (as ethanolate) 400mg Tablets 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 (as ethanolate) 400mg Tablets. 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, this medicine can cause side effects, although not everybody gets them.

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 (as ethanolate) 400mg Tablets. 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 (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 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 (as ethanolate) 400mg Tablets 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 (as ethanolate) 400mg Tablets . 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 (as ethanolate) 400mg Tablets

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 Darunavir (as ethanolate) 400mg Tablets contains

The active ingredient is 433.648 mg darunavir ethanolate equivalent to 400 mg darunavir.

The other ingredients are:

Core tablet:

Silicified microcrystalline cellulose

Crospovidone

Colloidal silicon dioxide

Magnesium stearate

Film coat:

Polyvinyl alcohol part hydrolysed

Titanium dioxide

Macrogol/PEG

Talc

FD&C yellow #6/Sunset yellow FCF Aluminium Lake

What Darunavir (as ethanolate) 400mg Tablets looks like and contents of the pack

Light orange coloured, oval shaped, biconvex, film coated tablet, debossed with 'DNV' on one side & '400' on the other side.

No score line.

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	Manufacturer
Cipla Ltd. Cipla House Peninsula Business Park Ganpatrao Kadam Marg Lower Parel Mumbai: 400013 India	Cipla Limited Unit -II, A-42, MIDC Patalganga: 410220 District: Raigad, Maharashtra India

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

This leaflet was last approved in June 2017

Detailed information on this medicine is available on the World Health Organization (WHO) web site:
<https://extranet.who.int/prequal>.

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