

Package leaflet: Information for the user

Darunavir Clonmel 400mg Film-coated Tablets Darunavir Clonmel 800mg Film-coated Tablets

Darunavir

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 doctor or pharmacist.
- 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 doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Darunavir Clonmel is and what it is used for

What is Darunavir Clonmel?

Darunavir Clonmel contains the active substance darunavir. Darunavir Clonmel 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 Clonmel 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.

What it is used for?

Darunavir Clonmel 400 mg/800mg is used to treat adults and children (3 years of age and above, at least 40 kg body weight) who are infected by HIV and

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

Darunavir Clonmel must be taken in combination with a low dose of cobicistat or ritonavir and other anti-HIV medicines. Your doctor will discuss with you which combination of medicines is best for you.

2. What you need to know before you take Darunavir Clonmel

Do not take Darunavir Clonmel

- if you are **allergic** to darunavir or any of the other ingredients of this medicine (listed in section 6) or to cobicistat or ritonavir.
- if you have **severe liver problems**. Ask your doctor if you are unsure about the severity of your liver disease. Some additional tests might be necessary.

Do not combine Darunavir Clonmel with any of the following medicines

If you are taking any of these, ask your doctor 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>methylergonovine</i>	to treat migraine and headaches
<i>Amiodarone</i> , <i>bepiridil</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 Clonmel
<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 Clonmel with products that contain St John's wort (*Hypericum perforatum*).

Warnings and precautions

Talk to your doctor or pharmacist before taking Darunavir Clonmel.

Darunavir Clonmel 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 physician the precautions needed to avoid infecting other people.

People taking Darunavir Clonmel may still develop infections or other illnesses associated with HIV infection. You must keep in regular contact with your doctor.

People taking Darunavir Clonmel may develop a skin rash. Infrequently a rash may become severe or potentially life-threatening. Please contact your doctor whenever you develop a rash.

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

Darunavir has only been used in limited numbers of patients 65 years or older. If you belong to this age group, please discuss with your doctor if you can use Darunavir Clonmel.

Tell your doctor about your situation BEFORE and DURING your treatment

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

- Tell your doctor if you have had **problems with your liver** before, including hepatitis B or C. Your doctor may evaluate how severe your liver disease is before deciding if you can take Darunavir Clonmel.
- Tell your doctor if you have **diabetes**. Darunavir Clonmel might increase sugar levels in the blood.
- Tell your doctor 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 doctor immediately to seek necessary treatment.
- Tell your doctor if you have **haemophilia**. Darunavir Clonmel might increase the risk of bleeding.
- Tell your doctor if you are **allergic to sulphonamides** (e.g. used to treat certain infections).
- Tell your doctor 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 doctor.

Children and adolescents

Darunavir Clonmel 400 mg/800mg is not for use in children younger than 3 years of age or weighing less than 15 kg.

Other medicines and Darunavir Clonmel

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

There are some medicines that **you must not combine** with Darunavir Clonmel. These are mentioned above under the heading 'Do not combine Darunavir Clonmel with any of the following medicines.'

In most cases, Darunavir Clonmel 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 with cobicistat or 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 doctor if you take other anti-HIV medicines and follow your doctor's instruction carefully on which medicines can be combined.

The effects of Darunavir Clonmel might be reduced if you take any of the following products. Tell your doctor 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 Clonmel. Tell your doctor 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 doctor may have to check your blood.
- Oestrogen-based hormonal contraceptives and hormonal replacement therapy. Darunavir Clonmel 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 doctor 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 doctor 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 doctor 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 Darunavir Clonmel's therapeutic effect or side effects may be influenced when combined.

Tell your doctor 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, zolpidem* (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 Clonmel with food and drink

See section 3 'How to take Darunavir Clonmel'.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnant or breast-feeding mothers must not take Darunavir Clonmel unless specifically directed by the doctor. It is recommended that HIV infected women must not breast-feed their infants because of both the possibility of your baby becoming infected with HIV through your breast milk and because of the unknown effects of the medicine on your baby.

Driving and using machines

Do not operate machines or drive if you feel dizzy after taking Darunavir Clonmel.

Darunavir Clonmel 400 mg tablets contain sunset yellow FCF (E110) which may cause allergic reactions.

3. How to take Darunavir Clonmel

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Even if you feel better, do not stop taking Darunavir Clonmel and cobicistat or ritonavir without talking to your doctor.

After therapy has been initiated, the dose must not be changed or therapy must not be stopped without instruction of the doctor.

Darunavir Clonmel is not suitable for all dosages described below. For these dosages, other medicinal products containing darunavir should be used.

Darunavir Clonmel 400 mg tablets are only to be used to construct the once daily 800 mg regimen.

Darunavir Clonmel 800 mg tablets are intended for once daily use only.

Dose for adults who have not taken antiretroviral medicines before (your doctor will determine this)

The usual dose of Darunavir Clonmel is 800 mg (2 tablets containing 400 mg of Darunavir Clonmel or 1 tablet containing 800 mg of Darunavir Clonmel) once daily.

You must take Darunavir Clonmel every day and always in combination with 150 mg of cobicistat or 100 mg of ritonavir and with food. Darunavir Clonmel cannot work properly without cobicistat or ritonavir and food. You must eat a meal or a snack within 30 minutes prior to taking your Darunavir Clonmel and cobicistat or ritonavir. The type of food is not important. Even if you feel better, do not stop taking Darunavir Clonmel and cobicistat or ritonavir without talking to your doctor.

Instructions for adults

- Take two 400 mg tablets/one 800 mg tablet at the same time, once a day, every day.
- Take Darunavir Clonmel always together with 150 mg of cobicistat or 100 mg of ritonavir.
- Take Darunavir Clonmel with food.
- Swallow the tablets/tablet with a drink such as water or milk.
- Take your other HIV medicines used in combination with Darunavir Clonmel and cobicistat or ritonavir as recommended by your doctor.

Dose for adults who have taken antiretroviral medicines before (your doctor will determine this)

The dose is either:

- 800 mg Darunavir Clonmel (2 tablets containing 400 mg of Darunavir Clonmel or 1 tablet containing 800 mg of Darunavir Clonmel) together with 150 mg cobicistat or 100 mg ritonavir once daily.
- OR
- 600 mg darunavir (2 tablets containing 300 mg of Darunavir Clonmel or 1 tablet containing 600 mg of Darunavir Clonmel) together with 100 mg ritonavir twice daily.

Please discuss with your doctor which dose is right for you.

Dose for children 3 years of age and above, weighing more than 40 kg who have not taken antiretroviral medicines before (your child's doctor will determine this)

- The usual dose of Darunavir Clonmel is 800 mg (2 tablets containing 400 mg of Darunavir Clonmel or 1 tablet containing 800 mg of Darunavir Clonmel) together with 100 mg ritonavir once daily.

Dose for children 3 years of age and above, weighing more than 40 kg who have taken antiretroviral medicines before (your child's doctor will determine this)

The dose is either:

- 800 mg Darunavir Clonmel (2 tablets containing 400 mg of Darunavir Clonmel or 1 tablet containing 800 mg of Darunavir Clonmel) together with 100 mg ritonavir once daily.
- OR
- 600 mg darunavir (2 tablets containing 300 mg of Darunavir Clonmel or 1 tablet containing 600 mg of Darunavir Clonmel) together with 100 mg ritonavir twice daily.

Please discuss with your doctor which dose is right for you.

Instructions for children 3 years of age and above, weighing more than 40 kg

- Take 800 mg Darunavir Clonmel (2 tablets containing 400 mg of Darunavir Clonmel or 1 tablet containing 800 mg of Darunavir Clonmel) at the same time, once a day, every day.
- Take Darunavir Clonmel always together with 100 mg of ritonavir.
- Take Darunavir Clonmel with food.
- Swallow the tablets with a drink such as water or milk.
- Take your other HIV medicines used in combination with Darunavir Clonmel and ritonavir as recommended by your doctor.

Removing the child resistant cap



The plastic bottle comes with a child resistant cap and must be opened as follows:

- Push the plastic screw cap down while turning it counter clockwise.
- Remove the unscrewed cap.

If you take more Darunavir Clonmel than you should

Contact your doctor or pharmacist immediately.

If you forget to take Darunavir Clonmel

If you notice **within 12 hours**, you must take the tablets immediately. Always take with cobicistat or 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 Clonmel without talking to your doctor first

HIV therapy may increase your sense of well-being. Even when you feel better, do not stop taking Darunavir Clonmel. Talk to your doctor first.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

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 doctor will test for these changes.

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

Tell your doctor if you develop any of the following side effects.

Liver problems that may occasionally be severe have been reported. Your doctor should do blood tests prior to initiating Darunavir Clonmel. If you have chronic hepatitis B or C infection, your doctor should check your blood tests more often because you have an increased chance of developing liver problems. Talk to your doctor 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 doctor if you develop a rash. Your doctor will advise you how to deal with your symptoms or whether Darunavir Clonmel 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 doctor 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 Clonmel. These are:

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

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Darunavir Clonmel

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

Do not use this medicine after the expiry date which is stated on the carton, bottle and blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

For bottles: Use within 6 months after first opening; do not store above 25°C.

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

6. Contents of the pack and other information

What Darunavir Clonmel contains

- The active substance is darunavir.
Darunavir Clonmel 400 mg: Each tablet contains 400 mg of darunavir.
Darunavir Clonmel 800 mg: Each tablet contains 800 mg of darunavir.
- The other ingredients are:
Darunavir Clonmel 400 mg: cellulose, microcrystalline (E460), crospovidone (type A) (E1202), silica, colloidal anhydrous (E551), magnesium stearate (E470b). The film-coating contains poly (vinyl alcohol) (E1203), titanium dioxide (E171), macrogol (3350) (E1521), talc (E553b), sunset yellow FCF (E110).
Darunavir Clonmel 800 mg: cellulose, microcrystalline (E460), crospovidone (type A) (E1202), silica, colloidal anhydrous (E551), magnesium stearate (E470b). The film-coating contains poly (vinyl alcohol) (E1203), titanium dioxide (E171), macrogol (3350) (E1521), talc (E553b), iron oxide red (E172).

What Darunavir Clonmel looks like and contents of the pack

Darunavir Clonmel 400 mg: Light orange oval shaped film-coated tablets, debossed with '400' on one side and plain on the other side, with dimensions of approximately 17.1 mm x 8.6 mm.
Darunavir Clonmel 800 mg: Dark red oval shaped film-coated tablets, debossed with '800' on one side and plain on the other side, with dimensions of approximately 20.2 mm x 10.1 mm.

Darunavir Clonmel 400 mg tablets are available in a plastic bottle of 60 tablets and perforated blister packs of 30, 35, 70, 90 tablets.

Darunavir Clonmel 800 mg tablets are available in a plastic bottle of 30 tablets and a multipack containing 90 (3 packs of 30) tablets.

Product name> 800 mg tablets are also available in perforated blister packs of 35, 60, 70 tablets.

Not all pack sizes may be marketed.

Darunavir Clonmel is also available as 600 mg film-coated tablets.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

Manufacturer

Remedica Ltd, Aharnon Street, Limassol Industrial Estate, 3056 Limassol, Cyprus

STADA Arzneimittel AG, Stadastrasse 2-18, D-61118 Bad Vilbel, Germany

STADA Arzneimittel GmbH, Muthgasse 36/2, 1190 Wien, Austria

Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

Centrafarm Services B.V., Nieuwe Donk 9, 4879 AC Etten-Leur, The Netherlands

This medicinal product is authorised in the Member States of the EEA under the following names:

- AT: Darunavir STADA 800 mg Filmtabletten
- BE: Darunavir EG 400/600/800 mg filmomhulde tabletten
- DE: Darunavir AL 400/600/800 mg Filmtabletten
- DK: Darunavir STADA
- FI: Darunavir STADA 400/600/800 mg kalvopäällysteinen tabletti
- FR: DARUNAVIR EG 400/600/800 mg, comprimé pelliculé
- IE: Darunavir Clonmel 400/600/800 mg film-coated tablets
- IT: Darunavir EG

LU: Darunavir EG 400/600/800 mg comprimés pelliculés
NL: Darunavir CF 400/600/800 mg, filmomhulde tabletten
PL: Darunavir Stada
SE: Darunavir STADA 400/600/800 mg filmdragerad tablett

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