

Package leaflet: Information for the patient

Darunavir Aurobindo 400 mg filmomhulde tabletten

Darunavir Aurobindo 800 mg filmomhulde tabletten

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

What is in this leaflet

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

1. What <Invented name> is and what it is used for

What is <Invented name>?

<Invented name> contains the active substance darunavir. <Invented 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. <Invented name> 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?

The <Invented name> 400 and 800 milligram tablets are used to treat adults and children (3 years of age and above, at least 40 kilograms 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).

<Invented name> 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 <Invented name>

Do not take <Invented name>

- 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 <Invented name> 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
Avanafil	to treat erectile dysfunction
Astemizole or terfenadine	to treat allergy symptoms
Triazolam and oral (taken by mouth) midazolam	to help you sleep and/or relieve anxiety
Cisapride	to treat some stomach conditions
Colchicine (if you have kidney and/or liver problems)	to treat gout or familial Mediterranean fever
Lurasidone, pimozide, quetiapine or sertindole	to treat psychiatric conditions
Ergot alkaloids like ergotamine, dihydroergotamine, ergometrine and methylergonovine	to treat migraine and headaches
Amiodarone, bepridil, dronedarone, ivabradine, quinidine, ranolazine	to treat certain heart disorders e.g. abnormal heart beat
Lovastatin, simvastatin and lomitapide	to lower cholesterol levels
Rifampicin	to treat some infections such as tuberculosis
The combination product lopinavir/ritonavir	this anti-HIV medicine belongs to the same class as darunavir
Elbasvir/grazoprevir	to treat hepatitis C infection
Alfuzosin	to treat enlarged prostate
Sildenafil	to treat high blood pressure in the pulmonary circulation
Dabigatran, ticagrelor	to help stop the clumping of platelets in the treatment of patients with a history of a heart attack
Naloxegol	to treat opioid induced constipation
Dapoxetine	to treat premature ejaculation
Domperidone	to treat nausea and vomiting

Do not combine <Invented name> with products that contain St John's wort (*Hypericum perforatum*).

Warnings and Precautions

Talk to your doctor, pharmacist or nurse before taking <Invented name>.

<Invented 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 physician the precautions needed to avoid infecting other people.

People taking <Invented name> may still develop infections or other illnesses associated with HIV infection. You must keep in regular contact with your doctor.

People taking <Invented name> 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 <Invented name> and raltegravir (for HIV infection), rashes (generally mild or moderate) may occur more frequently than in patients taking either medicine separately.

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 infection. Your doctor may evaluate how severe your liver disease is before deciding if you can take <Invented name>.
- Tell your doctor if you have diabetes. <Invented name> 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. <Invented name> 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.

Elderly

<Invented name> 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 <Invented name>.

Children and adolescents

<Invented name> is not for use in children younger than 3 years of age or weighing less than 40 kilograms.

Other medicines and <Invented name>

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

There are some medicines that **you must not combine** with <Invented name>. These are mentioned above under the heading 'Do not combine <Invented name> with any of the following medicines:'

In most cases, <Invented name> 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)]. <Invented name> 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 <Invented name> 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)
- Boceprevir (hepatitis C 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 <Invented name>. Tell your doctor if you take:

- Amlodipine, diltiazem, disopyramide, carvedilol, felodipine, flecainide, lidocaine, metoprolol, mexiletine, nifedipine, nicardipine, propafenone, timolol, verapamil (for heart disease) as the therapeutic effect or side effects of these medicines may be increased.
- Apixaban, edoxaban, 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. <Invented name> might reduce its effectiveness. When used for birth control, alternative methods of non-hormonal contraception are recommended.
- Ethinylestradiol/drospirenone. <Invented name> might increase the risk for elevated potassium levels by drospirenone.
- Atorvastatin, pravastatin, rosuvastatin (to lower cholesterol levels). The risk of muscle damage might be increased. Your doctor will evaluate which cholesterol lowering regimen is best for your specific situation.
- Clarithromycin (antibiotic)
- Ciclosporin, everolimus, tacrolimus, sirolimus (for dampening down 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.
- Corticosteroids including betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone. These medicines are used to treat allergies, asthma, inflammatory bowel diseases, inflammatory conditions of the eyes, joints and muscles and other inflammatory conditions. If alternatives cannot be used, 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 opioid dependence)
- Salmeterol (medicine to treat asthma)
- Artemether/lumefantrine (a combination medicine to treat malaria)
- Dasatinib, everolimus, irinotecan, nilotinib, vinblastine, vincristine (to treat cancer)
- Sildenafil, tadalafil, vardenafil (for erectile dysfunction or to treat a heart and lung disorder called pulmonary arterial hypertension)
- Glecaprevir/pibrentasvir, simeprevir (to treat hepatitis C infection).
- Fentanyl, oxycodone, tramadol (to treat pain)
- Fesoterodine, solifenacin (to treat urologic disorders)

The dosage of other medicines might need to be changed since either their own or <Invented name>'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)
- Itraconazole, isavuconazole, 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, clonazepam (to prevent seizures or to treat certain types of nerve pain)
- Colchicine (to treat gout or familial Mediterranean fever)
- Bosentan (to treat high blood pressure in the pulmonary circulation)
- Buspirone, clorazepate, diazepam, estazolam, flurazepam, midazolam when used as injection, 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.

<Invented name> with food and drink

See section 3 ‘How to take <Invented name>.’

Pregnancy and breast-feeding

Tell your doctor immediately if you are pregnant, planning to become pregnant or if you are breast-feeding. Pregnant or breast-feeding mothers should not take <Invented name> with ritonavir unless specifically directed by the doctor. Pregnant or breast-feeding mothers should not take <Invented name> with cobicistat.

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 <Invented name>.

<Invented name> 400 mg tablets contains propylene glycol

This medicine contains 55.56 mg propylene glycol in each film-coated tablet. If your baby is less than 4 weeks old, talk to your doctor or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol.

<Invented name> 400 mg tablets contain sunset yellow FCF (E110) which may cause allergic reactions.

<Invented name> 800 mg tablets contains propylene glycol

This medicine contains 111.12 mg propylene glycol in each film-coated tablet. If your baby is less than 4 weeks old, talk to your doctor or pharmacist before giving them this medicine, in particular if the baby is given other medicines that contain propylene glycol or alcohol.

3. How to take <Invented name>

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are unsure. Your doctor will tell you how much <Invented name> you must take.

Even if you feel better, do not stop taking <Invented name> and cobicistat or ritonavir without talking to your doctor.

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

<Invented name> 400 milligram tablets are only to be used to construct the once daily 800 milligram regimen or <Invented name> 800 milligram tablets are intended for once daily use only.

This product is only available as film coated tablets and is thus not suitable for patients who are unable to swallow intact tablets, for example young children. For use in these patients, more suitable formulations containing darunavir should be checked for their availability.

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

The usual dose of <Invented name> is 800 milligram (2 tablets containing 400 milligram of <Invented name> or 1 tablet containing 800 milligram of <Invented name>) once daily.

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

Instructions for adults

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

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

Maybe you will require a different dose of <Invented name> which cannot be administered with these 400 or 800 milligram tablets. Other strengths of <Invented name> are available.

The dose is either:

- 800 milligram <Invented name> (2 tablets containing 400 milligram of <Invented name> or 1 tablet containing 800 milligram of <Invented name>) together with 150 milligram cobicistat or 100 milligram ritonavir once daily.
OR
- 600 milligram <Invented name> (1 tablet containing 600 milligram of <Invented name>) together with 100 milligram 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 kilograms who have not taken antiretroviral medicines before (your child's doctor will determine this)

- The usual dose of <Invented name> is 800 milligram (2 tablets containing 400 milligram of <Invented name> or 1 tablet containing 800 milligram of <Invented name>) together with 100 milligram ritonavir once daily.

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

The dose is either:

- 800 milligram <Invented name> (2 tablets containing 400 milligram of <Invented name> or 1 tablet containing 800 milligram of <Invented name>) together with 100 milligram ritonavir once daily.
OR
- 600 milligram <Invented name> (1 tablet containing 600 milligram of <Invented name>) together with 100 milligram 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 kilograms

- Take 800 milligram <Invented name> (2 tablets containing 400 milligram of <Invented name> or 1 tablet containing 800 milligram of <Invented name>) at the same time, once a day, every day.
- Take <Invented name> always together with 100 milligram of ritonavir.
- Take <Invented name> with food.
- Swallow the tablets with a drink such as water or milk.
- Take your other HIV medicines used in combination with <Invented name> 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 <Invented name> than you should

Contact your doctor, pharmacist or nurse immediately.

If you forget to take <Invented name>

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 <Invented name> without talking to your doctor first

Anti-HIV medicines may make you feel better. Even when you feel better, do not stop taking <Invented name>. Talk to your doctor first.

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

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 before you start <Invented name>. 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 pain and discomfort 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 talk to your doctor if you develop a rash. Your doctor will advise you how to deal with your symptoms or whether <Invented name> must be stopped.

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

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

- diarrhoea.

Common: (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: (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: (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 <Invented name>. 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 the national reporting system listed in Appendix V. By reporting side effects you can help to provide more information on the safety of this medicine.

5. How to store <Invented name>

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 blister, label, carton and on bottle after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not use this medicine if you notice any change in the appearance of the tablets.

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 to protect the environment.

6. Contents of the pack and other information

What <Invented name> contains

- The active substance is darunavir (as propylene glycolate).

<Invented name> 400 mg film-coated tablets

Each film-coated tablet contains 400 mg darunavir (as propylene glycolate).

<Invented name> 800 mg film-coated tablets

Each film-coated tablet contains 800 mg darunavir (as propylene glycolate).

- The other ingredients are:

Tablet core:

Cellulose microcrystalline (Grade 101), hydroxypropylcellulose, crospovidone (Type-B), silica colloidal anhydrous and magnesium stearate.

Tablet coating:

For 400 mg

Ready to use coating material (Orange colour):

Polyvinyl alcohol, macrogol 3350, titanium dioxide (E171), talc and sunset yellow FCF (E110).

For 800 mg

Ready to use coating material (Brown colour):

Polyvinyl alcohol, macrogol 3350, Iron oxide red (E172), titanium dioxide (E171) and talc.

What <Invented name> looks like and contents of the pack

<Invented name> 400 mg Film Coated Tablets

Light orange colored, oval shaped, biconvex, film coated tablets debossed with 'D' on one side and '400' on another side.

<Invented name> 800 mg Film Coated Tablets

Dark red colored, oval shaped, biconvex, film coated tablets debossed with 'D' on one side and '800' on another side.

<Invented name> film-coated tablets are available in blister packs and HDPE bottle packs with polypropylene child resistant closure.

Pack sizes

Blister packs: 30, 50, 60, 90, 100 and 120 film-coated tablets

HDPE bottle pack:

For 400 mg: 60 film-coated tablets

For 800 mg: 30 and 90 (3x30) film-coated tablets

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers

Marketing Authorisation Holder

Aurobindo Pharma B.V.

Baarnsche Dijk 1

3741 LN Baarn

Manufacturers

APL Swift Services (Malta) Ltd

HF26, Hal Far Industrial Estate

BBG 3000 Birzebbugia

Malta

Generis Farmacêutica S.A.

Rua Joao De Deus 19

2700-487 Lissabon

Portugal

Arrow Generiques

26 Avenue Tony Garnier

69007 Lyon

Frankrijk

In het register ingeschreven onder:

Darunavir Aurobindo 400 mg filmomhulde tabletten

RVG 122884

Darunavir Aurobindo 800 mg filmomhulde tabletten

RVG 122886

Dit geneesmiddel is geregistreerd in lidstaten van de EEA onder de volgende namen:

Frankrijk:	Darunavir Arrow 400 mg/ 800 mg comprimé pelliculé
Duitsland:	Darunavir PUREN 400 mg/ 800 mg Filmtabletten
Nederland:	Darunavir Aurobindo 400 mg/ 800 mg filmomhulde tabletten
Polen:	Darunavir Aurovitas
Portugal:	Darunavir Generis
Roemenië:	Darunavir Aurobindo 400mg comprimate filmate
Spanje:	Darunavir Aurovitas 800 mg comprimidos recubiertos con película EFG

Deze bijsluiter is voor het laatst goedgekeurd in juli 2019