PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S4**

Darunavir Ritonavir 450 mg Mylan

Film coated tablets

Darunavir 400 mg and Ritonavir 50 mg

WARNING:

If you are taking **Darunavir Ritonavir 450 mg Mylan** with some medicines

- used to treat **allergies**,
- used to relieve anxiety and/or trouble sleeping,
- used to correct irregular heart beat,
- used to treat migraine headache,

they may cause serious adverse events

Read all of this leaflet carefully before you start taking Darunavir Ritonavir 450 mg Mylan

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- **Darunavir Ritonavir 450 mg Mylan** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What **Darunavir Ritonavir 450 mg Mylan** is and what it is used for
2. What you need to know before you take **Darunavir Ritonavir 450 mg Mylan**
3. How to take **Darunavir Ritonavir 450 mg Mylan**
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5. How to store **Darunavir Ritonavir 450 mg Mylan**
6. Contents of the pack and other information.

1. What Darunavir Ritonavir 450 mg Mylan is and what it is used for

Darunavir Ritonavir 450 mg Mylan contains two active substances.

Darunavir, a HIV-1 protease inhibitor (PI)

Ritonavir, a HIV-1 and HIV-2 protease inhibitor (PI)

Each of these active substances, is also known as an antiretroviral medicine, works by inhibiting the proteases enzymes.

Darunavir Ritonavir 450 mg Mylan is used for the treatment of Human Immunodeficiency Virus (HIV) infection. It belongs to a group of HIV medicines called protease inhibitors (PIs). **Darunavir Ritonavir 450 mg Mylan** 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.

It is important that you see your healthcare professional regularly while you are taking Darunavir Ritonavir 450 mg Mylan.

2. What you need to know before you take Darunavir Ritonavir 450 mg Mylan

Do not take Darunavir Ritonavir 450 mg Mylan:

- If you previously suffered an allergic reaction to any of the active ingredients, darunavir or ritonavir, or any other ingredient of **Darunavir Ritonavir 450 mg Mylan** (listed in section 6).
- If you have liver problems
- If you are taking medicines to treat tuberculosis (TB).
- If you are pregnant or breastfeeding your baby.

Do not take Darunavir Ritonavir 450 mg Mylan with any of the following medicines:

- medicines to treat convulsions (epilepsy) (*phenobarbitone or phenytoin*)
- medicines to treat allergy symptoms (*astemizole*)
- medicines to treat tuberculosis (*rifampicin, rifabutin*)
- medicines to treat high blood pressure as a result of problems with your lungs (*sildenafil, bosentan*)
- medicines to treat gout if you have liver or kidney problems (colchicine)
- medicines to treat prostate problems (alfuzosin)
- medicines to treat migraine and headaches (dihydroergotamine, ergonovine, ergotamine, methylergonovine)
- medicines to treat some stomach conditions (cisapride)
- medicines to treat hepatitis C virus (*boceprevir, telaprevir*)
- herbal products containing St John's wort (usually used for depression)
- medicines to treat high cholesterol (*lovastatin and simvastatin*)
- medicines to treat psychiatric conditions such as schizophrenia (*pimozide, blonanserin*)
- medicines to treat trouble with sleeping and/or anxiety (*midazolam or triazolam*)
- medicines to treat fungal infections (*ketoconazole, itraconazole,*

voriconazole)

- medicines to treat narcotic dependence (*buprenorphine/naloxone*)
- medicines to treat heart conditions (*amiodarone, bepridil, flecainide, propafenone, quinidine, encainide, digoxin*)
- medicines to treat asthma or difficulty in breathing (*salmeterol*)

If you are taking any of these medicines above, tell your doctor immediately.
Taking these medicines with **Darunavir Ritonavir 450 mg Mylan** could cause serious or life-threatening side effects or stop these medicines from working properly.

Warnings and precautions

Take special care with Darunavir Ritonavir 450 mg Mylan:

Darunavir Ritonavir 450 mg Mylan is not a cure for HIV infection. You can still pass on HIV to others through sexual contact or blood contaminations. Therefore, you must continue to use appropriate precautions, such as condoms. People taking **Darunavir Ritonavir 450 mg Mylan** may still develop infections or other illnesses associated with HIV infection. You must keep in regular contact with your doctor.

People taking **Darunavir Ritonavir 450 mg Mylan** may develop a skin rash. Contact your doctor immediately if you develop a rash.
Tell your doctor if you have a sulphonamide (antimicrobial used to treat certain infections) allergy. It is possible that patients allergic to sulphonamides may react to **Darunavir Ritonavir 450 mg Mylan**.
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.

Your doctor may evaluate how severe your liver disease is before deciding if you can take **Darunavir Ritonavir 450 mg Mylan**.

- Tell your doctor if you have diabetes (blood sugar). Anti-HIV medicines such as **Darunavir Ritonavir 450 mg Mylan** may increase sugar levels in the blood.
- Tell your doctor immediately if you notice any symptoms of infection.

In some patients with advanced HIV and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started.

- Tell your doctor if you notice changes in body fat. Redistribution, accumulation or loss of body fat may occur in patients receiving a combination of anti-HIV medicines.
- Tell your doctor if you have haemophilia (bleeding disease). Anti-HIV medicines, such as **Darunavir Ritonavir 450 mg Mylan**, may increase the risk of bleeding.
- Tell your doctor if you experience joint aches and pain, joint stiffness or difficulty in movement, because some people taking anti-HIV medicines may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone).
- Tell your doctor if you are taking contraceptive medicines as alternative methods of contraception may be necessary.
- -Tell your doctor if you experience nausea, vomiting or abdominal pain
- Combination antiretroviral medicines, including **Darunavir Ritonavir 450 mg Mylan**, may raise blood sugar levels, increase blood fats (*hyperlipidaemia*), cause changes to body fat, and resistance to insulin (insulin becomes less effective at controlling the sugar levels in your body, which can lead to

diabetes). *See Possible side-effects*.

- Tell your doctor if you are older than 65 years of age.

Other medicines and Darunavir Ritonavir 450 mg Mylan

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

There are some medicines that you must not combine with **Darunavir Ritonavir 450 mg Mylan**. These are mentioned above under the heading "**Do not take Darunavir Ritonavir 450 mg Mylan with any of the following medicines**".

Tell your doctor if you take any other anti-HIV medicines. **Darunavir Ritonavir 450 mg Mylan** can be combined with some other anti-HIV medicines while other combinations are not recommended.

Tell your doctor if you take:

- medicines to prevent seizures (*carbamazepine*)
- steroids (*dexamethasone*)
- medicines for heart disease or high blood pressure (*amiodarone, bepridil, felodipine, lignocaine, nifedipine, nicardipine, quinidine, digoxin*)
- medicines used to reduce clotting of the blood (*warfarin*)
- oestrogen based hormonal contraceptives. **Darunavir Ritonavir 450 mg Mylan** might reduce the effectiveness of hormonal contraceptives. Therefore, alternative methods of non-hormonal contraception are recommended.
- medicines to lower cholesterol levels (*e.g. atorvastatin, pravastatin and rosuvastatin*). The risk of muscle tissue disorder might be increased. Atorvastatin, pravastatin or rosuvastatin, at a reduced starting dose, could be used.
- medicines for your immune system (*ciclosporin, tacrolimus, sirolimus*).

Your doctor might want to do some additional tests.

- medicines to control asthma (*fluticasone and salmeterol and theophylline*)
- medicines for erectile dysfunction (*sildenafil, vardenafil, tadalafil*)
- antibiotics (*clarithromycin, fusidic acid*)
- medicines to treat depression and anxiety (*paroxetine, sertraline, amitriptyline, alprazolam, fluoxetine, nefazodone, venlafaxine)*
- medicines to treat narcotic dependence (*methadone)*
- medicines to treat gout or familial Mediterranean fever (*colchicine*)
- a combination medicine to treat malaria *(artemether/lumefantrine*).
- medicines to treat blood pressure abnormalities (*felodipine, nifedipine, nicardipine, beperidil*)
- medicines used to treat headaches
- medicines used as sedatives (*midazolam, triazolam*)
- medicines used as stimulants (dexfenfluramine, metamphetamine, methylphenidate)
- bupropion (used to treat depression)
- buspirone (sedative agent)
- desimipramine (used to treat depression)
- metronidazole (used to fight bacteria)
- if you smoke
- trazodone (used to treat depression)
- vincristine, vinblastine (used for cancer)
- medicines to treat ulcers or indigestion (*omeprazole, ranitidine*)

Darunavir Ritonavir 450 mg Mylan with food and drink:

It is important that you take **Darunavir Ritonavir 450 mg Mylan** with a meal. A meal is important to get the right drug levels in your body. A protein drink alone does not replace a meal.

Pregnancy, breastfeeding and fertility

You must not take **Darunavir Ritonavir 450 mg Mylan** during pregnancy and breastfeeding. The safe use of **Darunavir Ritonavir 450 mg Mylan** in pregnancy and during breastfeeding has not been established.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before you start taking **Darunavir Ritonavir 450 mg Mylan**.

Studies in animals do not indicate direct harmful effects of darunavir with respect to pregnancy, development in the womb, birth or development after birth.

There is a large amount of information on the use of ritonavir during pregnancy. In general, pregnant mothers received ritonavir after the first three months of pregnancy at a lower dose (booster) along with other protease inhibitors. Ritonavir did not appear to increase the chance of developing birth defects compared to the general population.

Driving and using machines

Do not drive or operate machines if you feel tired, sleepy or dizzy after taking your **Darunavir Ritonavir 450 mg Mylan**.

3. How to take Darunavir Ritonavir 450 mg Mylan

Do not share medicines prescribed for you with any other person.

Always take **Darunavir Ritonavir 450 mg Mylan** exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose of **Darunavir Ritonavir 450 mg Mylan** is two tablets taken each day by mouth. The tablets must be taken with food. This is important to get the right levels of active substance in your body. A nutritional drink alone does not replace food.

Do not change your dose of **Darunavir Ritonavir 450 mg Mylan** without first talking to your doctor. See your doctor regularly while taking **Darunavir Ritonavir 450 mg Mylan**.

- When your supply of **Darunavir Ritonavir 450 mg Mylan** starts to run low, get more from your doctor or pharmacy. It is important not to run out of **Darunavir Ritonavir 450 mg Mylan**. The amount of HIV in your blood may increase if the medicine is stopped for a short time.

Your doctor will tell you how long your treatment with **Darunavir Ritonavir 450 mg Mylan** will last. Do not stop treatment early.

If you have the impression that the effect of **Darunavir Ritonavir 450 mg Mylan** is too strong or too weak, talk to the doctor or pharmacist.

If you take more Darunavir Ritonavir 450 mg Mylan than you should:

In the event of overdosage, speak to a doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre for help.

If you forget to take Darunavir Ritonavir 450 mg Mylan:

If you notice within 12 hours of the time you usually take **Darunavir Ritonavir 450 mg Mylan**, you must take the tablets as soon as possible. Always take the tablets with a meal. Then take the next dose as usual.

If you notice after 12 hours, then skip the dose and take the next dose as usual.

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

Effects when treatment with Darunavir Ritonavir 450 mg Mylan is stopped:

Do not stop using **Darunavir Ritonavir 450 mg Mylan** without talking to your doctor first. HIV therapy may increase your sense of well-being. Even if you feel better, do not stop taking **Darunavir Ritonavir 450 mg Mylan** or your other HIV medicines. Doing so could increase the risk of the virus developing resistance. Talk to your doctor first.

4. Possible side effects

Darunavir Ritonavir 450 mg Mylan can have side effects.

Not all side effects reported for **Darunavir Ritonavir 450 mg Mylan** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **Darunavir Ritonavir 450 mg Mylan**, please consult your health-care provider for advice.

If any of the following happens, stop taking **Darunavir Ritonavir 450 mg Mylan** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing.
- rash or itching,
- fainting,
- yellowing of the skin or eyes.

These are all very serious side effects. If you have them, you may have had a serious reaction to **Darunavir Ritonavir 450 mg Mylan**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- symptoms of infection (such as fever, aches and pains, feeling tired, coughing or sneezing, nausea, vomiting or diarrhoea) or inflammation after the start of treatment (immune reconstitution inflammatory syndrome)
- inflammation of the liver or pancreas (symptoms may include belly pain, nausea and vomiting)
- diabetes (high blood sugar)

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

<u>Frequent side effects:</u>

- headache
- vomiting, nausea (feeling sick)
- diarrhoea, stomach pain, flatulence (gas)
- rash
- high cholesterol and other fats in the blood
- high blood sugar
- tingling in the fingers and toes
- bad taste in the mouth
- sore throat and cough
- weight loss and lack of appetite

- nutrition disorders
- anxiety and trouble falling and/or staying asleep
- confusion, feelings of sadness (depression)
- abnormal vision and visual disturbances (problems with eyes and eyesight)
- muscle and joint pain
- kidney problems and difficulty with urination (passing water)
- fever and pain
- dilation of the blood vessels (veins get bigger)

Less frequent side effects:

- changes in body fats (fat redistribution)
- abdominal (belly) swelling, indigestion, flatulence (gas)
- itching
- muscle pain
- loss of strength and energy, tiredness
- increase in pancreatic enzymes (digest fats, starches and proteins)
- seizure (convulsions)
- dehydration (thirsty due to loss of body water) because of vomiting and diarrhoea sometimes resulting in fainting
- fainting
- chest pains and cardiac (heart) problems, difficulty breathing
- menstrual bleeding (periods) with heavy flow (menorrhagia)
- blood disorders (changes the results in some values of your blood tests)
- dizziness
- ear pain and hearing problems
- impotence (decrease in sexual drive)

Darunavir Ritonavir 450 mg Mylan may change some values of your blood chemistry. These can be seen in the results of blood tests. Your doctor will explain these to you.

In some patients, **Darunavir Ritonavir 450 mg Mylan** has been reported to cause a severe or life-threatening rash. In patients taking **Darunavir Ritonavir 450 mg Mylan** and raltegravir, rashes (generally mild or moderate) may occur more frequently than in patients taking either medicine separately. Contact your doctor if you develop a rash. Your doctor will advise you whether your symptoms can be managed on therapy or whether **Darunavir Ritonavir 450 mg Mylan** should be stopped. **Darunavir Ritonavir 450 mg Mylan** should not be taken if you suffer from liver problems. Some side effects are typical for anti-HIV medicines in the same family as **Darunavir Ritonavir 450 mg Mylan**.

These include:

- raised blood sugar and worsening of diabetes.
- muscle pain, tenderness or weakness. On rare occasions, these muscle disorders have been serious.
- changes in body shape due to fat redistribution. These may include loss of fat from legs, arms and face, increased fat in the abdomen (belly) and other internal organs, breast enlargement and fatty lumps on the back of the neck (buffalo hump).
- joint aches and pains, joint stiffness or difficulty in movement. The cause and long-term health effects of these conditions are not known at this time.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse.

You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

By reporting side effects, you can help provide more information on the safety of **Darunavir Ritonavir 450 mg Mylan**.

5. How to store Darunavir Ritonavir 450 mg Mylan

Store all medicines out of reach of children.

Store at or below 30 °C. Protect from light. Store in the original container.

Do not remove from the carton until required for use.

Keep the bottle tightly closed.

Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What Darunavir Ritonavir 450 mg Mylan contains

The active substances are darunavir and ritonavir in one tablet.

Each **Darunavir Ritonavir 450 mg Mylan** film coated tablet contains:

Darunavir ethanolate equivalent to darunavir 400 mg and ritonavir 50 mg.

Darunavir Ritonavir 450 mg Mylan also contains the following other ingredients:

Colloidal silicon dioxide; copovidone; crospovidone; microcrystalline cellulose; ferric oxide yellow, sodium chloride; sodium stearyl fumarate; sorbitan monolaurate; coating: Opadry Yellow 20C520058

What Darunavir Ritonavir 450 mg Mylan looks like and contents of the pack

A light yellow film-coated ovaloid, biconvex, bevelled edge tablet debossed with "M" on one side of the tablet and "DRL" on the other side.

Darunavir Ritonavir 450 mg Mylan are presented in the following:

HDPE bottle pack comprises of opaque HDPE bottle with opaque polypropylene closure and desiccant. HDPE container may be packed in a carton. Pack size 60's.

Holder of Certificate of Registration

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