

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

<b>Darunavir Teva 600 mg</b>	<b>Darunavir Teva 800 mg</b>
Film coated tablets	Film coated tablets

<b>Composition:</b>	<b>Composition:</b>
Each tablet contains:	Each tablet contains:
Darunavir 600 mg	Darunavir 800 mg

For information about inactive ingredients, see section 6 – ‘Additional information’.

**Read the entire leaflet carefully before you start using this medicine.** This leaflet contains concise information about this medicine. If you have any further questions, consult with your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Darunavir Teva, co-administered with ritonavir, and with other anti-HIV agents, is indicated for the treatment of Human Immunodeficiency Virus (HIV) infection in patients over 18 years of age.

**Therapeutic group:** anti-HIV medicines of the protease inhibitors family.

Darunavir Teva contains the active substance darunavir. Darunavir Teva is an antiretroviral medicine used in the treatment of HIV infection. It belongs to a group of medicines called protease inhibitors. Darunavir Teva works by reducing the amount of HIV in your body. This will improve your immune system and reduce the risk of developing a disease linked to HIV infection.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient or to any of the other ingredients of this medicine (see section 6 – ‘Additional information’) or to ritonavir.
- you are a child or adolescent under 18 years of age.
- you have **severe liver problems**. Ask your doctor if you are uncertain about the severity of your liver disease. Some additional tests may be necessary.
- **Do not take Darunavir Teva with any of the following medicines:** if you are taking any of these, ask your doctor about the possibility of switching to another medicine.
  - Avanafil (for treatment of erectile dysfunction),
  - Astemizole or terfenadine (for treatment of allergy symptoms),
  - Triazolam and midazolam (taken orally) (for sleep induction and/or sedation),
  - Cisapride (for stomach problems),
  - Colchicine (if you have kidney and/or liver problems) (for treatment of gout or familial Mediterranean fever),
  - Lurasidone, pimozide, quetiapine or sertindole (for treatment of psychiatric conditions),
  - Ergot alkaloids, such as ergotamine, dihydroergotamine, ergometrine and methylexgonovine (for treatment of migraine headaches),
  - Amiodarone, bepridil, dronedarone, ivabradine, quinidine, ranolazine (for treatment of certain heart disorders, like for example, abnormal heart beat),
  - Lovastatin, simvastatin and lomitapide (for lowering blood cholesterol levels),
  - Rifampicin (for treatment of some infections such as tuberculosis),
  - The combination product lopinavir/ritonavir (this anti-HIV medicine belongs to the same class as Darunavir Teva),
  - Elbasvir/grazoprevir (for treatment of hepatitis C viral infection),
  - Alfuzosin (for treatment of enlarged prostate),
  - Sildenafil (for treatment of pulmonary hypertension),
  - Dabigatran, ticagrelor (to help stop the clumping of platelets in the treatment of patients with a history of heart attack),
  - Naloxegol (for treatment of opioid-induced constipation),
  - Dapoxetine (for treatment of premature ejaculation),
  - Domperidone (for treatment of nausea and vomiting),
- Do not combine Darunavir Teva with products containing St. John's Wort (hypericum perforatum).

**Special warnings about using this medicine:**  
**Consult with a doctor,** pharmacist or nurse **before** taking Darunavir Teva if:

- Treatment with Darunavir Teva does not cure HIV infection. You can still transmit HIV to others while taking this medicine, although the risk is lowered by taking effective antiretroviral therapy. Consult with your doctor about the precautions that you need to avoid infecting others.
- People taking Darunavir Teva may develop a skin rash. Infrequently, a rash may become severe and even life-threatening. Contact your doctor whenever you develop a rash.
- In patients taking Darunavir Teva and raltegravir (for treatment of HIV) rash (generally mild or moderate) may occur more frequently than in patients taking either medicine separately.

**Tell your doctor about your condition before and during the treatment with Darunavir Teva.**

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 a hepatitis B or C infection. Your doctor may evaluate how severe your liver disease is, in order to decide whether you are able to be treated with Darunavir Teva.
- Tell your doctor if you have diabetes, because Darunavir Teva may increase the blood sugar level.
- 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 HIV infection. Autoimmune disorders may also 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 **hemophilia** (defect in blood clotting ability), because Darunavir Teva may increase the risk of bleeding.
- Tell your doctor if you are **sensitive (allergic) to medicines from the sulfonamide family** (such as medicines 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, pain (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms please inform your doctor.

**Elderly**  
Darunavir has been evaluated in limited numbers of patients at the age of 65 and older. If you belong to this age group, discuss with your doctor if you can take Darunavir Teva.

**Children and adolescents**  
Not for use in children and adolescents under 18 years of age.

**Drug interactions**  
**If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.** Particularly if you are taking:

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

- In most cases, Darunavir Teva may be combined with anti-HIV medicines belonging to another class [such as nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), antagonists to CCR5 and fusion inhibitors (FIs)]. Darunavir Teva co-administered with ritonavir has not been tested with all protease inhibitors and must not be used concomitantly with other anti-HIV medicines of the protease inhibitor group.

In some cases, the dosage of other medicines might need to be changed. Therefore, always tell your doctor if you take other anti-HIV medicine, and follow your doctor's instruction carefully about which medicines can be combined.

The effect of Darunavir Teva may be reduced if you take any of the following medicines. Tell your doctor if you take:

- Dexamethasone (corticosteroid).
- Phenobarbital, phenytoin (to prevent epileptic seizures).
- Efavirenz (for treatment of HIV infection).
- Boceprevir (for treatment of hepatitis C infection).
- Rifapentine, rifabutin (for treatment of certain infections, such as tuberculosis).
- Saquinavir (for treatment of HIV infection).

The effects of the following medicines may be altered if you take Darunavir Teva. Tell your doctor if you take:

- Amlodipine, diltiazem, disopyramide, carvedilol, felodipine, flecainide, lidocaine, metoprolol, mexiletine, nifedipine, nicardipine, propafenone, timolol, verapamil (for treatment of heart problems), because the effect or the side effects of these medicines may be increased.
- Apixaban, edoxaban, rivaroxaban, warfarin (for treatment of coagulation problems); their side effects or their effect may be altered. The doctor may need to conduct a blood test.
- Estrogen-based hormonal medicinal products used for contraception and as hormone replacement therapy. Darunavir Teva may reduce their efficacy.
- When the products are used for contraception, alternative nonhormonal methods of contraception are recommended.
- Ethinylestradiol/drospirenone. Darunavir Teva may increase the risk that drospirenone will elevate potassium levels.
- Atorvastatin, pravastatin, rosuvastatin (to lower cholesterol levels). The risk of muscle tissue damage may increase. Your doctor will decide which cholesterol-lowering regimen is the best for you.
- Clarithromycin (antibiotic).
- Ciclosporin, everolimus, tacrolimus, sirolimus (for immune system suppression). Because the effect or the side effects of these medicines may be increased. Your doctor may want to do some additional tests.
- Corticosteroids, including betamethasone, budesonide, fluticasone, mometasone, prednisone, triamcinolone. These medicines are used for treatment of allergies, asthma, inflammatory bowel diseases, inflammatory conditions of the eyes, joints and muscles and other inflammatory conditions. If alternatives cannot be used, their use should only take place after medical evaluation and under close monitoring by your doctor for corticosteroid side effects.
- Buprenorphine/naloxone (medicines for treatment of opioid dependence).
- Salmeterol (for treatment of asthma).
- Artemether/lumefantrine (a combination medicine for treatment of malaria).
- Dasatinib, everolimus, irinotecan, nilotinib, vinblastine, vincristine (for treatment of cancer).
- Sildenafil, tadalafil, vardenafil (for treatment of erectile

- dysfunction or for treatment of a heart and lung disorder called pulmonary hypertension).
- Glecaprevir/pibrentasvir, simeprevir (for treatment of hepatitis C infection).
- Fentanyl, oxycodone, tramadol (for treatment of pain).
- Fesoterodine, solifenacin (for treatment of urologic disorders).

The dosage of other medicines may need to be changed either because their own or Darunavir Teva's therapeutic effect or side effects may be altered when taken together:

- Alfentanil (a strong, short-term analgesic administered by injection during surgical procedures).
- Digoxin (for treatment of certain heart disorders).
- Clarithromycin (antibiotic).
- Itraconazole, isoconazole, fluconazole, posaconazole, clotrimazole (for treatment of fungal infections); voriconazole may only be taken after medical evaluation.
- Rifabutin (for treatment of bacterial infections).
- Sildenafil, vardenafil, tadalafil (for treatment of erectile dysfunction or for treatment of pulmonary hypertension).
- Amitriptyline, desipramine, imipramine, nortriptyline, paroxetine, sertraline, trazodone (for treatment of depression and anxiety).
- Maraviroc (for treatment of HIV infection).
- Methadone (for treatment of opiate dependence).
- Carbamazepine, clonazepam (for prevention of epileptic seizures or for treatment of certain types of nerve pain).
- Colchicine (for treatment of gout or familial Mediterranean fever).
- Bosentan (for treatment of pulmonary hypertension).
- Buspirone, clorazepate, diazepam, estazolam, flurazepam, midazolam via injection, zolpidem (sedative agents).
- Perphenazine, risperidone, thioridazine (for treatment of psychiatric conditions).
- Metformin (for treatment of type 2 diabetes).

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

**Using this medicine and food**  
See section 3 – ‘How to use this medicine’.

**Pregnancy and breastfeeding**  
Tell your doctor immediately if you are pregnant, planning to become pregnant, or if you are breastfeeding. Pregnant or breastfeeding mothers should not take Darunavir Teva with ritonavir unless specifically directed by the doctor. Pregnant women or breastfeeding mothers should not take Darunavir Teva with cobicistat. It is recommended that HIV infected women must not breastfeed 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 drive a vehicle or operate dangerous machines if you feel dizzy after taking Darunavir Teva.

3. How to use this medicine?

Always use a medicinal product according to your doctor's instructions.  
Check with your doctor or pharmacist if you are not sure about your dosage or about the treatment regimen with the medicinal product.  
Only your doctor will determine your dosage and treatment regimen.

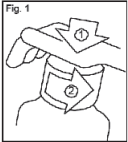
**Do not exceed the recommended dose.**

- The medicine should be taken every day at the same time, and always with 100 mg of ritonavir and food. The medicine will not work properly without ritonavir and food. The type of food does not matter. Take Darunavir Teva and ritonavir within 30 minutes of eating any food (the type of food is unimportant).
- No information is available regarding chewing or crushing the tablet.
- It can be halved at the score line. There is a score line on the tablet.
- The medicine should be swallowed whole with a drink, such as water, milk.
- Take the other medicines for treatment of HIV that you are taking according to the instructions given to you by your doctor.

Instructions for opening the bottle:

The bottle has a safety cap that prevents accidental opening by children.

Open the bottle by pushing downward on the cap (1) while turning it counterclockwise (2).



This medicine should be used at set intervals as determined by the treating physician.

- **If you accidentally took a higher dose**, immediately contact your doctor or pharmacist.  
If you took an overdose, or if a child has accidentally swallowed some of the medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.
- **If you forgot to take the medicine**
  - If you are taking Darunavir Teva once a day and you forgot to take this medicine at the scheduled time, and you remember within up to 12 hours of the time you were supposed to take the medicine, take a dose as soon as you remember (together with 100 mg ritonavir and food). If more than 12 hours have passed since the time you were supposed to take the medicine, skip the forgotten dose. Take the next dose as scheduled. Never take a double dose!
  - If you are taking Darunavir Teva twice a day and you forgot to take this medicine at the scheduled time, and you remember within up to 6 hours of the time you were supposed to take the medicine, take a dose as soon as you remember (together with 100 mg ritonavir and food). If more than 6 hours have passed since the time you were supposed to take the medicine, skip the forgotten dose. Take the next dose as scheduled. Never take a double dose!

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking Darunavir Teva in combination with ritonavir without explicit instruction from your doctor.

**Do not stop taking the medicine without consulting with your doctor.**

**Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.**

**If you have any further questions about using this medicine, consult with your doctor or pharmacist.**

4. 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 with all medicines, using Darunavir Teva may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

**Tell your doctor if you develop any side effect.**  
**Effects requiring special attention:**

- Liver problems that may occasionally be severe have been reported. Your doctor should do blood tests before you start using Darunavir Teva. 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. Contact your doctor if you notice signs and symptoms that may indicate liver problems, such as yellowing of your skin or whites of your eyes, dark urine (tea colored), pale-colored stools (bowel movements), nausea, vomiting, loss of appetite, or pain or aching 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 may also be a symptom of a rare severe situation. Therefore, it is important that you speak with your doctor if a rash appears. Your doctor will advise you how to deal with your symptoms or whether you should stop using Darunavir Teva.
- Other severe side effects were diabetes (common), and inflammation of the pancreas (uncommon).

**Additional side effects**  
Very common side effects (occur in more than one in ten users):

- Diarrhea.

Common side effects (occur in 1-10 in 100 users):

- Vomiting, nausea, abdominal pain or bloating, dyspepsia, flatulence
- Headaches, tiredness, dizziness, drowsiness, numbness, tingling or pain in the hands or legs, weakness, difficulty falling asleep.

Uncommon side effects (occur in 1-10 in 1,000 users):

- Chest pain, changes in ECG, rapid heart beating
- Decrease or change in skin sensitivity, tingling, attention disturbance, memory loss, problems with your balance
- Difficulty breathing, cough, nosebleed, throat irritation
- Inflammation of the stomach or mouth, heartburn, retching, dry mouth, abdominal discomfort, constipation, belching
- Kidney failure, kidney stones, urination problems, more frequent urination or increased urine output, sometimes at night
- Skin rash (urticaria), severe swelling of the skin and other tissues (especially the lips or the eyes), eczema, excessive sweating, night sweats, hair loss, acne, scaly skin, discoloration of the nails
- Muscle pain, muscle cramps or weakness, extremity pain, osteoporosis
- Slowdown 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 accumulation, malaise, irritability, pain
- Symptoms of infection, herpes simplex
- Erectile dysfunction, enlargement of breasts
- Sleeping problems, sleepiness, depression, anxiety, abnormal dreams, decreased in sexual drive.

Rare side effects (occur in 1-10 in 10,000 users):

- A reaction called DRESS: severe skin rash that may be accompanied by fever, fatigue, swelling of the face or lymph glands, increase of eosinophils (type of white blood cells), effect on the liver, kidneys or lungs
- Heart attack, slow heart beating, palpitations
- Vision disturbances
- Chills, feeling unwell
- A feeling of confusion or disorientation, altered mood, restlessness
- Fainting, epileptic fits, change in or loss of the sense of taste
- Mouth sores, vomiting blood, inflammation of the lips, dry lips, coated tongue
- Runny nose
- Skin lesions, dry skin
- Muscle or joint stiffness, joint pain with or without inflammation
- Changes in some indicators of blood cells or chemistry. This can be seen in particular indicators in the results of blood and/or urine tests. The doctor will explain these to you. For example, increase in the level of particular white blood cells.

The following effects are typical for anti-HIV medicines of the same group to which Darunavir Teva belongs:

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

**If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult with your doctor.**

Reporting of side effects  
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page ([www.health.gov.il](http://www.health.gov.il)) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

## **5. How to store the medicine?**

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date), which is stated on the package. The expiry date refers to the last day of that month.
- **Store in a dry place, below 25°C.**
- Keep the medicine in its original package.
- If you are using the plastic bottle package of Darunavir Teva, the medicine should be used within 60 days of the initial opening of the bottle, but not after the expiry date.

**Note:** The bottle of Darunavir Teva 800 mg contains a desiccant. Do not swallow it! Leave the desiccant inside the bottle and close the bottle tightly after each use!

## **6. Additional information**

**In addition to the active ingredient, this medicine also contains:**

Microcrystalline cellulose, Anhydrous calcium hydrogen phosphate, Crospovidone, Copovidone, Colloidal anhydrous silica, Polyvinyl alcohol, Magnesium stearate

- Present in 800 mg tablet: Iron Oxide red, Macrogol, Talc
- Present in 600 mg tablet: Macrogol, Titanium dioxide, Talc, Iron Oxide yellow, Iron Oxide red

### **What the medicine looks like and contents of the pack:**

Darunavir Teva 800 mg: red, film coated, oval shaped tablet, scored on one side, and debossed with "800" on the other side. Darunavir Teva 800 mg is marketed in a blister containing 28, 30, 56 or 60 tablets, or in a plastic bottle containing 30 tablets.

Darunavir Teva 600 mg: orange, film coated, oval shaped tablet, scored and debossed with "600" on the left side of the score on one side and plain on the other side.

Darunavir Teva 600 mg is marketed in a blister containing 28 or 56 tablets, or in a plastic bottle containing 60 tablets.

Not all package types or sizes may be marketed.

### **Name and address of the manufacturer and registration-holder:**

Teva Pharmaceutical Industries Ltd., POB 3190, Petah Tikva.

The leaflet was revised in December 2020.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Darunavir Teva 800 mg: 161.07.35135

Darunavir Teva 600 mg: 165.06.35798

DOR-Dar-PIL-1220-06

The Teva logo, consisting of the word "teva" in a bold, lowercase, sans-serif font. The letters are black, and the 'v' is stylized with a slight gap between the two vertical strokes.