

Package leaflet: Information for the patient

Efavirenz Rowex 600 mg film-coated tablets

efavirenz

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 Efavirenz Rowex is and what it is used for
2. What you need to know before you take Efavirenz Rowex
3. How to take Efavirenz Rowex
4. Possible side effects
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1 What Efavirenz Rowex is and what it is used for

Efavirenz Rowex, which contains the active substance efavirenz, belongs to a class of antiretroviral medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs). It is an **antiretroviral medicine that fights human immunodeficiency virus (HIV) infection** by reducing the amount of the virus in blood. It is used by adults, adolescents and children weighing ≥ 40 kg.

Your doctor has prescribed Efavirenz Rowex for you because you have HIV infection. Efavirenz Rowex taken in combination with other antiretroviral medicines reduces the amount of the virus in the blood. This will strengthen your immune system and reduce the risk of developing illnesses linked to HIV infection.

2 What you need to know before you take Efavirenz Rowex

Do not take Efavirenz Rowex

- **if you are allergic** to efavirenz or any of the other ingredients of this medicine (listed in section 6). Contact your doctor or pharmacist for advice.
- **if you have severe liver disease.**
- **if you have a heart condition, such as changes in the rhythm or rate of the heartbeat, a slow heartbeat, or severe heart disease.**
- if any member of your family (parents, grandparents, brothers or sisters) has died suddenly due to a heart problem or was born with heart problems.
- if your doctor has told you that you have high or low levels of electrolytes such as potassium or magnesium in your blood.
- **if you are currently taking** any of the following medicines (see also ‘other medicines and Efavirenz Rowex’):
 - **astemizole or terfenadine** (used to treat allergy symptoms)
 - **bepridil** (used to treat heart disease)
 - **cisapride** (used to treat heartburn)

- **ergot alkaloids** (for example, ergotamine, dihydroergotamine, ergonovine, and methylergonovine) (used to treat migraine and cluster headaches)
- **midazolam or triazolam** (used to help you sleep)
- **pimozide, imipramine, amitriptyline or clomipramine** (used to treat certain mental conditions)
- **St. John's wort** (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety)
- **flecainide, metoprolol** (used to treat irregular heartbeat)
- **certain antibiotics** (macrolides, fluoroquinolones, imidazole)
- **triazole antifungal agents**
- certain **antimalarial treatments**
- **methadone** (used to treat opiate addiction)
- elbasvir/grazoprevir.

If you are taking any of these medicines, tell your doctor immediately. Taking these medicines with Efavirenz Rowex could create the potential for serious and/or life-threatening side-effects or stop Efavirenz Rowex from working properly.

Warnings and precautions

Talk to your doctor or pharmacist before taking Efavirenz Rowex

- **Efavirenz Rowex must be taken with other medicines that act against the HIV virus.** If Efavirenz Rowex is started because your current treatment has not prevented the virus from multiplying, another medicine you have not taken before must be started at the same time.
- **You can still pass on HIV** when taking this medicine, although the risk is lowered by effective antiretroviral therapy. It is important to take precautions to avoid infecting other people through sexual contact or blood transfer. Discuss with your doctor the precautions needed to avoid infecting other people. This medicine is not a cure for HIV infection and you may continue to develop infections or other illnesses associated with HIV disease.
- You must remain under the care of your doctor while taking Efavirenz Rowex.
- **Tell your doctor:**
 - **if you have a history of mental illness**, including depression, or of substance or alcohol abuse. Tell your doctor immediately if you feel depressed, have suicidal thoughts or have strange thoughts (see section 4. Possible side effects).
 - **if you have a history of convulsions (fits or seizures)** or if you are being treated with anticonvulsant therapy such as carbamazepine, phenobarbital and phenytoin. If you are taking any of these medicines, your doctor may need to check the level of anticonvulsant medicine in your blood to ensure that it is not affected while taking Efavirenz Rowex. Your doctor may give you a different anticonvulsant.
 - **if you have a history of liver disease, including active chronic hepatitis.** Patients with chronic hepatitis B or C and treated with combination antiretroviral agents have a higher risk for severe and potentially life-threatening liver problems. Your doctor may conduct blood tests in order to check how well your liver is working or may switch you to another medicine. **If you have severe liver disease, do not take Efavirenz Rowex** (see section 2. Do not take Efavirenz Rowex).
 - **if you have a heart disorder, such as abnormal electrical signal called prolongation of the QT interval.**
- **Once you start taking Efavirenz Rowex, look out for:**
 - **signs of dizziness, difficulty sleeping, drowsiness, difficulty concentrating or abnormal dreaming.** These side effects may start in the first 1 or 2 days of treatment and usually go away after the first 2 to 4 weeks.
 - signs of confusion, slow thoughts and physical movement, and delusions (false beliefs) or hallucinations (seeing or hearing things that others do not see or hear). These side effects may occur months to years after beginning Efavirenz Rowex therapy. If you notice any symptoms, please inform your doctor.

- **any signs of skin rash.** If you see any signs of a severe rash with blistering or fever, stop taking Efavirenz Rowex and tell your doctor at once. If you had a rash while taking another NNRTI, you may be at a higher risk of getting a rash with Efavirenz Rowex.
- **any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) 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. If you notice any symptoms of infection, please tell your doctor immediately.
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.
- **bone 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

Efavirenz Rowex is not recommended for children weighing less than 40 kg because it has not been adequately studied in these patients.

Other medicines and Efavirenz Rowex

You must not take Efavirenz Rowex with certain medicines. These are listed under 'Do not take Efavirenz Rowex', at the start of Section 2. They include some common medicines and a herbal remedy (St. John's wort) which can cause serious interactions.

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. Efavirenz Rowex may interact with other medicines, including herbal preparations such as *Ginkgo biloba* extracts. As a result, the amounts of Efavirenz Rowex or other medicines in your blood may be affected. This may stop the medicines from working properly, or may make any side effects worse. In some cases, your doctor may need to adjust your dose or check your blood levels. **It is important to tell your doctor or pharmacist if you are taking any of the following:**

- **Other medicines used for HIV infection:**
 - protease inhibitors: darunavir, indinavir, lopinavir/ritonavir, ritonavir, ritonavir boosted atazanavir, saquinavir or fosamprenavir/saquinavir. Your doctor may consider giving you an alternative medicine or changing the dose of the protease inhibitors.
 - maraviroc
 - the combination tablet containing efavirenz, emtricitabine and tenofovir, should not be taken with Efavirenz Rowex unless recommended by your doctor since it contains efavirenz, the active ingredient of Efavirenz Rowex.
- **Medicines used to treat infection with the hepatitis C virus:** boceprevir, telaprevir, simeprevir, sofosbuvir/velpatasvir, glecaprevir/pibrentasvir and sofosbuvir/velpatasvir/voxilaprevir.

- **Medicines used to treat bacterial infections**, including tuberculosis and AIDS-related mycobacterium avium complex: clarithromycin, rifabutin, rifampicin. Your doctor may consider changing your dose or giving you an alternative antibiotic. In addition, your doctor may prescribe a higher dose of Efavirenz Rowex.
- **Medicines used to treat fungal infections (antifungals):**
 - voriconazole. Efavirenz Rowex may reduce the amount of voriconazole in your blood and voriconazole may increase the amount of efavirenz in your blood. If you take these two medicines together, the dose of voriconazole must be increased and the dose of efavirenz must be reduced. You must check with your doctor first.
 - itraconazole. Efavirenz Rowex may reduce the amount of itraconazole in your blood.
 - posaconazole. Efavirenz Rowex may reduce the amount of posaconazole in your blood.
- **Medicines used to treat malaria:**
 - artemether/lumefantrine: Efavirenz Rowex may reduce the amount of artemether/lumefantrine in your blood.
 - atovaquone/proguanil: Efavirenz Rowex may reduce the amount of atovaquone/proguanil in your blood.
- **Medicines used to treat convulsions/seizures (anticonvulsants):** carbamazepine, phenytoin, phenobarbital. Efavirenz Rowex can reduce or increase the amount of anticonvulsant in your blood. Carbamazepine may make Efavirenz Rowex less likely to work. Your doctor may need to consider giving you a different anticonvulsant.
- **Medicines used to lower blood fats (also called statins):** atorvastatin, pravastatin, simvastatin. Efavirenz Rowex can reduce the amount of statins in your blood. Your doctor will check your cholesterol levels and will consider changing the dose of your statin, if needed.
- **Methadone** (a medicine used to treat opiate addiction): your doctor may recommend an alternative treatment.
- **Sertraline** (a medicine used to treat depression): your doctor may need to change your dose of sertraline.
- **Praziquantel** (a medicine used to treat schistosomiasis): Efavirenz Rowex may reduce the amount of praziquantel in your blood. If you take these two medicines together, you must check with your doctor first.
- **Bupropion** (a medicine used to treat depression or to help you stop smoking): your doctor may need to change your dose of bupropion.
- **Diltiazem or similar medicines (called calcium channel blockers which are medicines typically used for high blood pressure or heart problems):** when you start taking Efavirenz Rowex, your doctor may need to adjust your dose of the calcium channel blocker.
- **Immunosuppressants such as cyclosporine, sirolimus, or tacrolimus** (medicines used to prevent organ transplant rejection): when you start or stop taking Efavirenz Rowex, your doctor will closely monitor your plasma levels of the immunosuppressant and may need to adjust its dose.
- **Hormonal contraceptive, such as birth control pills, an injected contraceptive (for example, Depo-Provera), or a contraceptive implant (for example, Implanon):** you must also use a reliable

barrier method of contraception (see Pregnancy, breast-feeding and fertility). Efavirenz Rowex may make hormonal contraceptives less likely to work. Pregnancies have occurred in women taking Efavirenz Rowex while using a contraceptive implant, although it has not been established that the Efavirenz Rowex therapy caused the contraceptive to fail.

- **Warfarin** or acenocoumarol (medicines used to reduce clotting of the blood): your doctor may need to adjust your dose of warfarin or acenocoumarol.
- *Ginkgo biloba* extracts (a herbal preparation).
- Metamizole, a medicine used to treat pain and fever.
- Medicines that impact heart rhythm:
 - **Medicines used to treat heart rhythm problems** such as flecainide or metoprolol
 - **Medicines used to treat depression** such as imipramine, amitriptyline or clomipramine
 - **Antibiotics**, including the following types: macrolides, fluoroquinolones or imidazole.

Efavirenz Rowex with food and drink

Taking Efavirenz Rowex on an empty stomach, may reduce the undesirable effects. Grapefruit juice should be avoided when taking Efavirenz Rowex.

Pregnancy and breast-feeding

Women should not get pregnant during treatment with Efavirenz Rowex and for **12 weeks thereafter**.

Your doctor may require you to take a pregnancy test to ensure you are not pregnant before starting treatment with Efavirenz Rowex.

If you could get pregnant while receiving Efavirenz Rowex, you need to use a reliable form of barrier contraception (for example, a condom) with other methods of contraception including oral (pill) or other hormonal contraceptives (for example, implants, injection). Efavirenz may remain in your blood for a time after therapy is stopped. Therefore, you should continue to use contraceptive measures, as above, for 12 weeks after you stop taking Efavirenz Rowex.

Tell your doctor immediately if you are pregnant or intend to become pregnant. If you are pregnant, you should take Efavirenz Rowex only if you and your doctor decide it is clearly needed. Ask your doctor or pharmacist for advice before taking any medicine.

Serious birth defects have been seen in unborn animals and in the babies of women treated with efavirenz or a combination medicine containing efavirenz, emtricitabine and tenofovir during pregnancy. If you have taken Efavirenz Rowex or the combination tablet containing efavirenz, emtricitabine, and tenofovir during your pregnancy, your doctor may request regular blood tests and other diagnostic tests to monitor the development of your child.

You should not breast-feed your baby if you are taking Efavirenz Rowex.

Driving and using machines

Efavirenz Rowex contains efavirenz and may cause dizziness, impaired concentration, and drowsiness. If you are affected, do not drive and do not use any tools or machines.

Efavirenz Rowex contains sodium and lactose

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. Other efavirenz formulations are available in the market for these patients.

3 How to take Efavirenz Rowex

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will give you instructions for proper dosing.

- The dose for adults is 600 mg once daily.
- The dose for Efavirenz Rowex may need to be increased or decreased if you are also taking certain medicines (see ‘Other medicines and Efavirenz Rowex’).
- Efavirenz Rowex is for oral use. Efavirenz Rowex is recommended to be taken on an empty stomach preferably at bedtime. This may make some side effects (for example, dizziness, drowsiness) less troublesome. An empty stomach is commonly defined as 1 hour before or 2 hours after a meal.
- It is recommended that the tablet be swallowed whole with water.
- Efavirenz Rowex must be taken every day.
- Efavirenz Rowex should never be used alone to treat HIV. Efavirenz Rowex must always be taken in combination with other anti-HIV medicines.

Use in children and adolescents

- Efavirenz Rowex 600 mg film-coated tablets are not suitable for children weighing less than 40 kg.
- The dose for children weighing 40 kg or more is 600 mg once daily.

If you take more Efavirenz Rowex than you should

If you take too much Efavirenz Rowex, contact your doctor or nearest emergency department for advice. Keep the medicine container with you so that you can easily describe what you have taken.

If you forget to take Efavirenz Rowex

Try not to miss a dose. If you do miss a dose, take the next dose as soon as possible, but do not take a double dose to make up for a forgotten dose. If you need help in planning the best times to take your medicine, ask your doctor or pharmacist.

If you stop taking Efavirenz Rowex

When your Efavirenz Rowex supply starts to run low, get more from your doctor or pharmacist. This is very important because the amount of virus may start to increase if the medicine is stopped for even a short time. The virus may then become harder to treat.

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

4 Possible Side Effects

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

When treating HIV infection, it is not always possible to tell whether some of the unwanted effects are caused by Efavirenz Rowex or by other medicines that you are taking at the same time, or by the HIV disease itself.

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.

The most notable unwanted effects reported with efavirenz in combination with other anti-HIV medicines are skin rash and nervous system symptoms.

You should consult your doctor if you have a rash, since some rashes may be serious; however, most cases of rash disappear without any change to your treatment with Efavirenz Rowex. Rash was more common in children than in adults treated with efavirenz.

The nervous system symptoms tend to occur when treatment is first started, but generally decrease in the first few weeks. In one study, nervous system symptoms often occurred during the first 1-3 hours after taking a dose. If you are affected your doctor may suggest that you take Efavirenz Rowex at bedtime and on an empty stomach. Some patients have more serious symptoms that may affect mood or the ability to think clearly. Some patients have actually committed suicide. These problems tend to occur more often in those who have a history of mental illness. In addition, some nervous system symptoms (e.g. confusion, slow thoughts and physical movement, and delusions [false beliefs] or hallucinations [seeing or hearing things that others do not see or hear]) may occur months to years after beginning Efavirenz Rowex therapy. Always notify your doctor immediately if you have these symptoms or any side effects while taking Efavirenz Rowex.

Tell your doctor if you notice any of the following side effects:

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

- skin rash.

Common (may affect up to 1 in 10 people)

- abnormal dreams, difficulty concentrating, dizziness, headache, difficulty sleeping, drowsiness, problems with coordination or balance
- stomach pain, diarrhoea, feeling sick (nausea), vomiting
- itching
- tiredness
- feeling anxious, feeling depressed.

Tests may show:

- increased liver enzymes in the blood
- increased triglycerides (fatty acids) in the blood.

Uncommon (may affect up to 1 in 100 people)

- nervousness, forgetfulness, confusion, fitting (seizures), abnormal thoughts
- blurred vision
- a feeling of spinning or tilting (vertigo)
- pain in the abdomen (stomach) caused by inflammation of the pancreas
- allergic reaction (hypersensitivity) that may cause severe skin reactions (erythema multiforme, Stevens-Johnson syndrome)
- yellow skin or eyes, itching, or pain in the abdomen (stomach) caused by inflammation of the liver
- breast enlargement in males
- angry behaviour, mood being affected, seeing or hearing things that are not really there (hallucinations), mania (mental condition characterised by episodes of overactivity, elation or irritability), paranoia, suicidal thoughts, catatonia (condition in which the patient is rendered motionless and speechless for a period)
- whistling, ringing or other persistent noise in the ears
- tremor (shaking)
- flushing.

Tests may show:

- increased cholesterol in the blood.

Rare (may affect up to 1 in 1,000 people)

- itchy rash caused by a reaction to sunlight
- liver failure, in some cases leading to death or liver transplant, has occurred with efavirenz. Most cases occurred in patients who already had liver disease, but there have been a few reports in patients without any existing liver disease.
- unexplained feelings of distress not associated with hallucinations, but it may be difficult to think clearly or sensibly
- suicide.

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: HPRA Pharmacovigilance; website: www.hpra.ie. By reporting side effects, you can help provide more information on the safety of this medicine.

5 How to store Efavirenz Rowex

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

This medicine does not require any special storage conditions.
After first opening of the bottle: use within 2 months.

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

6 Contents of the pack and other information

What Efavirenz Rowex contains

- The active substance is efavirenz. Each film-coated tablet contains 600 mg of efavirenz.
- The other ingredients are: croscarmellose sodium, microcrystalline cellulose, sodium laurylsulfate, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate in the tablet core; hypromellose (E464), quinoline yellow aluminium lake (E104), titanium dioxide (E171), macrogol, iron oxide red (E172) in the film-coating.

What Efavirenz Rowex looks like and contents of the pack

Efavirenz Rowex is a yellow film-coated tablet of capsule shape (9.6 x 19.2 mm) with a break line on both sides.

Efavirenz Rowex are supplied in:

- HDPE bottles with a child-resistant polypropylene closure sealed with liner and containing a silica gel packet: 30 or 90 (3x30) film-coated tablets.
- PVC/Aclar/Al blisters: 10, 28, 30, 84 or 90 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturers

Marketing Authorisation Holder

Rowex Ltd., Bantry, Co. Cork, Ireland.

Manufacturers

Lek Pharmaceuticals d.d., Verovškova 57, 1526 Ljubljana, Slovenia.
Salutas Pharma GmbH, Otto-von-Guericke-Allee 1, 39179 Barleben, Germany.
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S.C. Sandoz, S.R.L., Str. Livezeni nr. 7A, RO-540472 Targu-Mures, Romania.

This medicine is authorised in the Member States of the European Economic Area under the following names:

Germany	Efavirenz HEXAL 600 mg Filmtabletten
Ireland	Efavirenz Rowex 600 mg film-coated tablets

This leaflet was last revised in 03/2022.