PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Tri-Teva

Coated tablets

Composition:

Active ingredients:

Each coated tablet contains:

Efavirenz 600 mg

Emtricitabine 200 mg

Tenofovir disoproxil (fumarate) 245 mg

For information regarding inactive ingredients, see section 2 "Important information about some ingredients of the medicine" and section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

Tri-Teva is intended for use by adults, from 18 years old and older. The medicine has not been studied in children under 18 years of age or in adults above 65 years of age.

1. What is the medicine intended for?

Tri-Teva can be used by itself as a full treatment, or in combination with other antiretroviral medicines, for treatment of HIV-1 infection in adults.

The HIV virus destroys CD4+ T cells, which are important for the immune system. The immune system helps fighting infections. After a large number of T cells is destroyed, an Acquired Immune Deficiency Syndrome (AIDS) develops.

Tri-Teva helps to block the HIV-1 reverse transcriptase enzyme, which is a viral chemical that is found in the body and is required for the multiplication of HIV-1.

Tri-Teva reduces the amount of HIV-1 in the blood (viral load). Tri-Teva may also help increase the number of T cells (CD4+ cells), thereby improving the function of the immune system. Reducing the amount of HIV-1 in the blood reduces the risk for death or for infections that occur when the immune system is weak (opportunistic infections).

Tri-Teva does not cure a HIV-1 infection or AIDS, and you may continue to experience illnesses that are related to HIV-1 infection, including opportunistic infections. You need to remain under a doctor's supervision while using Tri-Teva. It has not been proven that Tri-Teva reduces the risk of passing the HIV-1 virus to other people through sexual intercourse, needle sharing or exposure to blood.

- Do not share your needles or other injection supplies with other people.
- Do not share with other people personal items that may have blood or body fluids on them, such as toothbrushes or razor blades.
- Do not engage in any sexual intercourse without protection. Sexual intercourse should always be done safely using latex or polyurethane condom, or by using

other barrier methods to reduce the risk for contact with sperm, vaginal discharges or blood.

Therapeutic class:

Tri-Teva contains three active ingredients that are used for treatment of the human immunodeficiency virus (HIV) infection:

- Efavirenz belongs to the non-nucleoside reverse transcriptase inhibitors (NNRTI) family.
- Emtricitabine is a nucleoside reverse transcriptase inhibitor (NRTI).
- Tenofovir is a nucleotide reverse transcriptase inhibitor (NtRTI).

2. Before using the medicine

☒ Do not use this medicine if:

- **You have hypersensitivity (allergy)** to the active ingredients: efavirenz, emtricitabine, tenofovir disoproxil, or to any other ingredient of Tri-Teva (the ingredients are listed in section 6).
- **You have a severe liver disease.**
- **You have a cardiac problem, such as prolongation in the electrical conduction of QT segment, which puts you in a high risk for severe heart rate problems (Torsades de Pointes).**
- A relative (parents, grandparents, brothers or sisters) has died unexpectedly due to cardiac problem or was born with a cardiac problem.
- Your doctor has told you that you have a high or low level of electrolytes such as potassium or magnesium in your blood.
- You are breastfeeding.
- **You are currently taking** one of the following medicines (see also “drug-drug interactions"):

- **Astemizole or terfenadine** (used for treatment of hay fever or other allergies).
- **Bepridil** (used for treatment of cardiac diseases).
- **Cisapride** (used for treatment of heartburn).
- **Elbasvir/grazoprevir** (used for treatment of hepatitis C).
- **Ergot alkaloids** (e.g. ergotamine, dihydroergotamine, ergonovine and methylergonovine) (used for treatment of migraine and cluster headaches).
- **Midazolam or triazolam** (used for sleep induction).
- **Pimozide, imipramine, amitriptyline or clomipramine** (used for treatment of certain mental disorders).
- **Hypericum perforatum (St. John's Wort -** a medicinal herb for treatment of depression and anxiety).
- **Voriconazole** (used for treatment of fungal infections).
- **Flecainide, metoprolol** (used for treatment of arrhythmias).
- **Certain antibiotics** (macrolides, fluoroquinolones, imidazole).
- **Anti-fungal triazole.**
- **Certain anti-malarial medicines.**
- **Methadone** (used for treatment of opiate dependence).

→ **If you are taking any of the abovementioned medicines, inform your doctor immediately.** Taking these medicines together with Tri-Teva may cause severe or life-threatening side effects, or compromise the efficacy of the medicines.

! Special warnings regarding the use of the medicine

You may still pass HIV to others while taking the medicine, although effective medicinal treatment decreases the risk. Consult a doctor regarding the required precautions to avoid infecting other people.

This medicine does not cure HIV infection. During treatment with Tri-Teva you may still develop other infections or illnesses related to the HIV infection.

During treatment with Tri-Teva you should remain under a doctor's supervision.

Before starting treatment with Tri-Teva, tell the doctor if:

- **You are taking other medicines** that contain efavirenz, emtricitabine, tenofovir disoproxil, tenofovir alafenamide, lamivudine or adefovir dipivoxil. Do not take Tri-Teva together with these medicines.
- **You have kidney disease or had such disease in the past,** or if test results showed that you have kidney problems. It is not recommended to use Tri-Teva if you have moderate to severe kidney disease (see also section 3, "Tests and follow-up"). Tri-Teva may affect the kidneys. Your doctor may instruct you to have your blood tested in order to evaluate your kidney function before starting the treatment. Your doctor may instruct you to have your blood tested also during the treatment, in order to follow your kidney function.
  Usually no other medicines that may damage the kidneys should be taken while taking Tri-Teva (see the "Drug-drug interactions" section). Nevertheless, if a combination therapy is necessary, the doctor will follow your kidney function once a week.
- **You have a cardiac problem, such as abnormal electrical conduction called QT prolongation.**
- **You have a history of mental illness,** including depression, or of drug/medicine or alcohol dependence. Inform the doctor immediately if you feel depressed, or if you have suicidal or strange thoughts (see section 4, "Side effects").
- **You have a history of convulsions (attacks or spasms)** or you are receiving anti-convulsant treatment such as carbamazepine, phenobarbital or phenytoin. If you are taking any of these medicines, the doctor may need to check the level of the anti-convulsant medicine in your blood in order to make sure it is not changing while taking Tri-Teva. The doctor may give you a different anti-convulsant.
- **You have a history of liver disease, including chronic active hepatitis (liver inflammation). Patients with liver disease, including hepatitis B or C,** who are treated with a combination of anti-retroviral medicines, have an increased risk for severe liver problems which may be life-threatening. The doctor may refer you for blood tests in order to check your liver function, or he may change your medicine.
  If you have a severe liver disease, do not take Tri-Teva (See also section 3, "Tests and follow-up").
  If you have a hepatitis B infection, the doctor will carefully consider what would be the best treatment regimen for you.

Tenofovir disoproxil and emtricitabine - two of the active ingredients in Tri-Teva - have a certain activity against the hepatitis B virus, even though emtricitabine is not approved for treatment of hepatitis B infection. Hepatitis symptoms may worsen after stopping treatment with Tri-Teva. The doctor may order blood tests at regular intervals in order to check liver function (see also section 3, “Tests and follow-up”). Regardless of liver diseases you might have had in the past, the doctor will consider ordering blood tests in regular intervals in order to evaluate your liver function.

- **You are over 65 years old.** The number of studied patients above 65 years of age is not sufficient. If you are above 65 years of age and have been prescribed with Tri-Teva, the doctor will closely follow your condition.

After starting to take Tri-Teva, pay attention to the following:

- **Signs of dizziness, sleeplessness, sleepiness, difficulty focusing or abnormal dreams.** These side effects may appear on the first or second day of the treatment and they usually disappear after two to four weeks from the beginning of the treatment.
- **Any signs of skin rash.** Tri-Teva may cause rash. If you observe any signs of severe rash with blisters or fever, stop taking Tri-Teva and immediately inform the doctor. If you had a rash while taking another medicine of the NNRT family, you may have a higher risk for rash from Tri-Teva.
- **Any signs of inflammation or infection.** In some patients with advanced HIV (AIDS) infection and a history of an opportunistic infection, signs and symptoms of inflammation from previous infections may appear shortly after the beginning of an anti-HIV treatment. It is hypothesized that these symptoms may be occurring due to an improvement of the body’s immune reaction, which enables the body to fight infections that existed in the body without observable symptoms. If you observe any symptoms of infection, inform the doctor immediately.

  In addition to opportunistic infections, autoimmune disorders (a condition that occurs when the immune system attacks a healthy body tissue) may occur after you start taking medicines for treatment of HIV infection. Autoimmune disorders may occur many months after starting treatment. If you observe any symptoms of infection or other symptoms, such as muscle weakness, weakness that starts in the hands and feet and rises towards the center of the body, palpitations, tremor or hyperactivity, inform the doctor immediately in order to receive the necessary treatment.
- **Bone problems.** In some patients that receive combined anti-retroviral treatment, a bone disease called osteonecrosis (death of bone tissue as a result of loss of blood supply to the bone) may develop. The many risk factors for the development of this disease may include, among other things: the duration of treatment with a combination of antiretroviral medicines, use of corticosteroids, alcohol consumption, severe immunosuppression and high body mass index. Signs for osteonecrosis are joint rigidity, pain and aches (particularly in the hip, knee and shoulder) and movement difficulties. If you observe any of these symptoms, inform the doctor.

Bone problems (which sometimes cause fractures) may also occur due to the damage caused to the renal tubule cells (see section 4, “Side effects”).

! Children and adolescents

Tri-Teva should not be given to children and adolescents under 18 years of age. Use of the medicine in children and adolescents has not yet been studied.

! Drug-drug interactions

Tri-Teva should not be taken together with certain medicines. These medicines are listed in the beginning of section 2 under “Do not use this medicine if”. Some of those are common medicines and some are herbal medicines (including hypericum perforatum, St. John’s wort) which can cause severe drug-drug interactions.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including non-prescription medicines, vitamins, herbal medicines and nutritional supplements.

Additionally, Tri-Teva should not be taken together with other medicines that contain efavirenz (unless recommended by a doctor), emtricitabine, tenofovir disoproxil, tenofovir alafenamide, lamivudine or adefovir dipivoxil.

Inform the doctor if you are taking other medicines that may cause kidney damage. For example:

- Aminoglycosides, vancomycin (for treatment of bacterial infections).
- Foscarnet, ganciclovir, cidofovir (for treatment of viral infections).
- Amphotericin B, pentamidine (for treatment of fungal infections).
- Interleukin-2 (for treatment of cancer).
- Non-steroidal anti-inflammatory drugs (NSAIDs, for relief of bone and muscle pain).

Tri-Teva may react with other medicines, including herbal medicines such as ginkgo biloba extract. As a result, the amount of the medicine or other medicines in the blood may be affected. This may compromise the effect of the medicine or may worsen side effects. In certain cases, the doctor may adjust the dosage of the medicine or check blood values.

! It is important to inform the doctor or pharmacist if you are taking:

- **Medicines containing didanosine (for HIV infection):** taking Tri-Teva together with anti-viral medicines that contain didanosine may cause elevation in didanosine blood levels and reduce the CD4 cells count. Pancreatitis and lactic acidosis (excess of lactic acid in the blood), which can sometimes be fatal, have been rarely reported when medicines containing tenofovir disoproxil and didanosine have been taken together. The doctor will carefully consider whether to treat you with medicines containing tenofovir and didanosine.
- **Other medicines used for treatment of HIV infection:** the following protease inhibitors: darunavir, indinavir, lopinavir/ritonavir, ritonavir or ritonavir as booster with atazanavir or saquinavir. The doctor may consider giving an alternative medicine or changing the dosage of the protease inhibitors. In addition, inform the doctor if you are taking maraviroc.
- **Medicines used for treatment of viral hepatitis C infection:** boceprevir, elbasvir/ grazoprevir, simeprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir.

- **Medicines used for lowering lipid blood levels (also called statins):** atorvastatin, pravastatin, simvastatin. Tri-Teva may decrease statins blood levels. The doctor will check your cholesterol blood level and will consider adjusting your statins dosage if necessary.
- **Medicines used for treatment of convulsions/attacks (anti-convulsants):** carbamazepine, phenytoin, phenobarbital. Tri-Teva may decrease the anti-convulsant blood levels. Carbamazepine can decrease the amount of efavirenz, one of Tri-Teva's components, in the blood. The doctor will consider whether to give another anti-convulsant medicine.
- **Medicines used for treatment of bacterial infections,** including tuberculosis and accompanying infection in AIDS-related mycobacterium avium complex: clarithromycin, rifabutin, rifampicin. The doctor will consider changing the dosage or giving an alternative antibiotic medicine. In addition, the doctor will consider giving another dose of efavirenz for treatment of the HIV infection.
- **Medicines used for treatment of fungal infections (anti-fungals):** itraconazole or posaconazole. Tri-Teva may decrease itraconazole or posaconazole blood levels. The doctor may consider giving an alternative anti-fungal.
- **Medicines used for treatment of malaria:** atovaquone/proguanil or artemether/lumefantrine. Tri-Teva may reduce the amounts of atovaquone/proguanil or artemether lumefantrine in the blood.
- **Hormonal contraceptives, such as contraceptive pills, injection (such as depo-provera), or contraceptive implant (intrauterine device, Implanon):** reliable barrier contraceptives should also be used (see "Pregnancy and breastfeeding"). Tri-Teva may render hormonal contraceptives less effective. Pregnancies in women taking efavirenz, which is a component of Tri-Teva, while using a contraceptive implant have been documented, although it has not been proven that treatment with efavirenz is responsible to impairment of the contraceptive activity.
- **Sertraline,** a medicine used for treatment of depression, the doctor may adjust the dosage of sertraline.
- **Bupropion,** a medicine used for treatment of depression or for assisting in smoking cessation, the doctor may adjust the dosage of bupropion.
- **Diltiazem or similar medicines (called calcium channel blockers):** While starting treatment with Tri-Teva, the doctor may adjust the calcium channel blockers dosage.
- **Medicines used for prevention of transplanted organs rejection (also called immunosuppressant medicines),** such as ciclosporin, sirolimus or tacrolimus. When starting or stopping Tri-Teva, the doctor will check the level of immune system antibodies in the plasma and may adjust the dose.
- **Warfarin or acenocoumarol** (medicines used for reducing blood coagulation): the doctor may adjust the dosage of warfarin or acenocoumarol.
- **Ginkgo biloba extract** (herbal preparation).

For more information, speak to the doctor or pharmacist.

! Use of the medicine and food

Tri-Teva should be taken on an empty stomach.

! Use of the medicine and alcohol consumption
Taking Tri-Teva together with alcohol or other medicines which cause side effects that are similar to the effects of Tri-Teva, such as sleepiness, may increase these side effects.
! Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you might be pregnant or planning to become pregnant, consult a doctor or a pharmacist before taking medicines.
Women must not become pregnant during treatment with Tri-Teva and also for 12 weeks after discontinuation of the medicine. The doctor may order a pregnancy test to make sure you are not pregnant before starting treatment with Tri-Teva.
If there is a chance of becoming pregnant during treatment with Tri-Teva, you should use reliable barrier contraceptives (e.g. condom) together with other contraceptives, including oral contraceptives (pills) or other hormonal contraceptives (e.g. implant or injection). Efavirenz, one of the active ingredients of Tri-Teva, may remain in the blood for a certain period of time after discontinuing the treatment. Therefore, you should continue using contraceptives as described above for 12 weeks after discontinuing Tri-Teva.
Inform the doctor immediately if you are pregnant or planning to become pregnant. If you are pregnant, you should take Tri-Teva only if you and your doctor have decided that this is absolutely necessary.
Severe birth defects have been observed in animal embryos and in babies of women who were treated with efavirenz during pregnancy.
Consult with a doctor or a pharmacist before taking any medicine.
If you have taken Tri-Teva during pregnancy, the doctor may ask to perform blood tests and other diagnostic tests regularly in order to follow the fetus's development. In children whose mothers have taken NRTIs during pregnancy, the benefit of protection against HIV outweighed the risk for side effects.
Do not breastfeed if you are taking Tri-Teva. Both the HIV virus and the Tri-Teva ingredients may pass into breastmilk and cause severe harm to the baby.
! Driving and operating machinery
Tri-Teva may cause dizziness, impaired concentration and drowsiness. If you observe these effects, do not drive and do not operate tools or machinery.
! Important information about some of the ingredients of the medicine
The medicine Tri-Teva contains a sugar called lactose. If you have been told by your doctor that you have an intolerance to certain sugars, speak to your doctor before taking this medicine.
This medicine contains less than 23 mg of sodium in a tablet, and is therefore considered sodium-free.

3. How should you use the medicine?

Always use the medicine according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.
Dosage:
Dosage is according to the doctor's instructions only.

Never change the prescribed dosage by yourself. Do not discontinue the medicine without an explicit order from the doctor.
The dosage and treatment regimen will be determined only by the doctor.
The generally accepted dosage is one tablet of Tri-Teva a day.
Tri-Teva should be taken on an empty stomach (the accepted definition is one hour before or two hours after a meal), preferably at bedtime. Taking Tri-Teva at bedtime may make some side effects (e.g. dizziness, sleepiness) more tolerable.
The tablet should be swallowed whole with water.
Do not chew, crush or halve the tablet, as no information is available about such practices.
Tri-Teva should be taken every day.
If the doctor has decided to stop treatment with one of Tri-Teva's ingredients, you may receive efavirenz, emtricitabine and/or tenofovir disoproxil separately or with other medicines for treatment of the HIV infection.
This medicine should be used at set intervals as determined by the treating doctor.
Do not skip doses of Tri-Teva.
Do not exceed the recommended dosage.
Tests and follow-up:

- Tri-Teva may affect the kidneys. Before starting to use the medicine, the doctor will refer you for blood tests in order to evaluate your kidney function. During the treatment period you may also be referred for blood tests in order to follow your kidneys' condition. Usually Tri-Teva is not taken together with other medicines that may damage the kidneys (see section 2, "Before using the medicine"). If this is unavoidable, the doctor will refer you for a kidney function test once a week.
- Patients with liver disease, including chronic hepatitis B or C, who are treated with a combination of anti-retroviral medicines, have an increased risk for severe liver problems which may be life-threatening. The doctor may refer you for blood tests in order to check your liver function, or he may give you another medicine. If you have a severe liver disease, do not take Tri-Teva (see also section 2, "Before using the medicine").
- If you have a hepatitis B infection, the doctor will carefully consider what would be the best treatment regimen for you. Tenofovir disoproxil and emtricitabine - two of the active ingredients in Tri-Teva - are active to some degree against the hepatitis B virus, although emtricitabine is not approved for treatment of hepatitis B infection. Hepatitis symptoms may worsen after stopping treatment with Tri-Teva. In this case, the doctor may refer you to regular blood tests in order to check your liver function (see also section 3, "If you stop taking the medicine").
- Regardless of liver disease history, the doctor will consider referring you to regular blood tests in order to check liver function.

If you accidentally take a higher dosage
If you have accidentally taken too many Tri-Teva tablets you may have an increased risk for possible side effects of this medicine (see section 4, "Side effects"). Contact a doctor or a hospital's emergency room immediately for consultation. Bring the package of the medicine with you so that the medical staff will know for certain what you have taken.

If a child swallowed this medicine by mistake, immediately go to the doctor or the emergency room of the hospital and bring the package of the medicine with you.
Do not induce vomiting without an explicit instruction from the doctor!

If you have forgotten to take the medicine

If you have forgotten to take a dose of Tri-Teva within 12 hours from the usual time, take the dose when you remember, and take the next dose at the usual time.
If it is almost time (less than 12 hours) for the next dose, do not take the forgotten dose.
Wait and take the next dose at the scheduled time.
Do not take a double dose in place of the forgotten dose.
Follow the treatment as recommended by the doctor.

If you stop taking the medicine

Do not stop taking Tri-Teva without consulting a doctor, even if you feel that your general condition is improving. Discontinuing treatment with Tri-Teva may severely affect your reaction to treatment in the future. If you stopped taking Tri-Teva, consult a doctor before starting to take Tri-Teva tablets again. If you have problems or if the dosage needs to be adjusted, the doctor may consider giving you Tri-Teva's ingredients separately.

How can you contribute to the success of the treatment?

When your stock of Tri-Teva is about to run out, you should renew the stock through the doctor or pharmacist. This is very important, since the amount of viruses may start rising if the medicine is stopped, even if stopped for a short time. In this case, it may be more difficult to treat the virus.

If the patient is vomiting

If you have vomited the tablet (within one hour of taking Tri-Teva), you should take another tablet. Do not wait for the time for the next dose. There is no need to take another tablet if the vomiting occurred more than one hour after taking Tri-Teva.

If you have both HIV infection and hepatitis B, it is highly important not to stop treatment with Tri-Teva without first consulting the doctor. In some patients there were blood tests and symptoms that indicated that the hepatitis worsened after emtricitabine or tenofovir disoproxil (two of the three ingredients of Tri-Teva) have been stopped. If Tri-Teva has been stopped, the doctor may recommend to continue with the hepatitis B treatment. You can ask for blood tests in order to check liver function for 4 months after treatment has been discontinued. In some patients with advanced liver disease or liver cirrhosis, discontinuing the treatment is not recommended since this may cause the hepatitis to worsen, which may be life-threatening.
Inform the doctor immediately about new or abnormal symptoms following discontinuation of treatment. In particular about symptoms that you attribute to hepatitis B infection.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

During treatment of HIV, there may be an increase in body weight and in lipid and glucose blood levels. This is partially related to health improvement and the return to normal lifestyle, while lipid blood level elevation is sometimes related to anti-HIV medicines themselves. The doctor will perform tests to identify these changes.
As with any medicine, using Tri-Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Tri-Teva may cause the following severe side effects:

Contact the doctor immediately if you develop:

Lactic acidosis (an excess of lactic acid in the blood) is **a rare side effect** (may occur in up to 1 of every 1,000 patients) but a severe one, which may sometimes be fatal.

The following side effects may be signs of lactic acidosis:

- Deep and fast breathing
- Drowsiness
- Nausea, vomiting and abdominal pain

Contact the doctor immediately if you think you might have lactic acidosis.

Other possible severe side effects

The following side effects are **not common** (may occur in up to 1 of every 100 patients):

- An allergic reaction (hypersensitivity) which may cause severe skin reactions (Stevens-Johnson syndrome, erythema multiforme, see section 2)
- Swelling of the face, lips, tongue and throat
- Angry behavior, suicidal thoughts, strange thoughts, paranoia, inability to think clearly, influence on your mood, seeing or hearing things that do not exist (hallucinations), suicide attempts, change of personality (psychosis), catatonia (a disorder that causes the patient to be unable to move and to speak for a period of time)
- Abdominal pain as a result of pancreatitis
- Forgetfulness, confusion, convulsions, confused speech, tremor
- Yellowing of the skin or eyes, itching or abdominal pain which originates from hepatitis
- Damage to renal tubules

Psychiatric side effects in addition to those mentioned above, including delusions, neurosis. Some patients have committed suicide. These problems tend to occur more frequently among patients with a history of mental disease. Always inform the doctor immediately if you observe these side effects.

Hepatic side effects: if you also have hepatitis B, it may worsen following treatment discontinuation (see section 3)

The following side effects are **rare** (may occur in up to 1 of every 1,000 patients):

- In some cases, liver failure may lead to death or to need of liver transplant. Most cases have occurred in patients that already had liver disease, but there were also several reports of patients without any existing liver disease
- Kidney inflammation, increased urination and feeling of thirst

- Back pain caused by kidney problems, including kidney failure. The doctor may order blood tests to check your kidney function
- Rickets (accompanied by bone pain and sometimes fractures as a result), which may result from damage to the renal tubule cells
- Fatty liver

→ If you think you may have any of these serious side effects, contact the doctor.

The most frequent side effects:

The following side effects are **very frequent** (may occur in more than 1 of every 10 patients):

- Dizziness, headaches, diarrhea, nausea, vomiting
- Rash (including red spots or patches, sometimes with blisters and swelling of the skin), which may be an allergic reaction
- Weakness

Tests may show:

- A decrease of phosphorus blood levels
- An increase in creatine kinase blood levels, which may cause muscle pain and weakness

Other possible side effects

The following side effects are **common** (may occur in up to 1 of every 10 patients):

- Allergic reactions
- Coordination and balance disturbances
- Feeling of anxiety or depression
- Difficulty falling asleep, strange dreams, difficulty focusing, sleepiness
- Pain, abdominal pain
- Indigestion which causes discomfort after meals, swelling sensation, flatulence
- Loss of appetite
- Tiredness
- Itching
- Skin discoloration, including darkening of the skin in patches, often starting in the hands and feet

Tests may show:

- Low counts of white blood cells (a decline in white blood cells counts may increase susceptibility to infections)
- Liver and pancreas problems
- Elevation in blood levels of fatty acids (triglycerides), bilirubin or sugar

The following side effects are **not common** (may occur in up to 1 of every 100 patients):

- Muscle tissue breakdown, muscle pain or muscle weakness
- Anemia (low red blood cells counts)
- Sensation of spinning or leaning sideways (vertigo), beeping, ringing or other types of continuous noise in the ears
- Blurry vision
- Chills
- Enlarged breasts in men
- Decreased libido

- Flushing
- dry mouth
- Increased appetite

Tests may show:

- A decrease in blood potassium level
- Elevation in creatinine blood levels
- Protein in the urine
- High level of blood cholesterol

Muscle tissue breakdown, rickets (bone pain and sometimes fractures), muscle pain, muscle weakness and decline in potassium or phosphorus blood levels may result from damage to renal tubule cells.

The following side effects are **rare** (may occur in up to 1 of every 1,000 patients):

- Itchy skin rash due to reaction to sunlight

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link “report side effects due to medicinal treatment” found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:
https://sideeffects.health.gov.il

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Storage:

- Store below 25°C.
- Keep in original package to protect from humidity.
- After first opening the bottle, the preparation can be used until the medicine’s expiry date.
- Even if medicines are kept in the original package under the recommended storage conditions, they are preserved only for a limited time.
- Pay attention to the medicine’s expiry date! In case of doubt, consult the pharmacist that dispensed the medicine to you.
- Different medicines should not be stored in the same package.
- Do not discard medicines in the wastewater or domestic trash. Consult the pharmacist on how to discard medicines that are no longer needed. These precautions will help to protect the environment.

6. Additional information

In addition to the active ingredients, the medicine also contains:

Inactive ingredients:

Tablet core:

Microcrystalline cellulose, lactose monohydrate, crospovidone, sodium starch glycolate, mannitol (E421), magnesium stearate, colloidal silicon dioxide, lutrol F 127, hydroxypropyl cellulose, povidone K-25.

Tablet coating:

Polyvinyl alcohol, titanium dioxide (E171), macrogol/PEG 3350, talc, carmine, iron oxide red, iron oxide yellow.

What does the medicine look like and what are the contents of the package

A plastic bottle containing 30 light-pink to pink, capsule-shaped, coated tablets. On one side they are imprinted with “TV” and on the other side with “5234”.

Inside the bottle there is a small bag containing silica gel, which is not to be swallowed.

It should be left inside the bottle in order to protect the tablets from humidity.

License holder and the address:

Abic Marketing Ltd. P.O.B 8077 Netanya (Teva Group).

Name and address of the manufacturer:

Teva Pharmaceutical Industries Ltd., P.O. box 3190, Petah Tikva.

This leaflet, dated January 2020, is formatted according to Ministry of Health guidelines and its content matches the original medicinal product leaflet reviewed and approved by the Ministry of Health in December 2016 and last revised in November 2018.**Registration number of the medicine in the National Drug Registry of the Ministry of Health: 163-36-35175**

DOR-Tri-T-PIL-t-0220-04