

INSTRUCTIONS FOR USE

EVASIF® 245 mg film coated tablet

Administered orally.

- **Effective Substance:** Each tablet contains 300 mg tenofovir disoproxil fumarate, equivalent to 245 mg tenofovir disoproxil.
- **Excipients:** Pregelatinized starch, croscarmellose sodium, lactose monohydrate, microcrystalline cellulose, magnesium stearate, hypromellose, titanium dioxide, triacetate, FD&C Blue#2/indigo carmine aluminum salt.

Please read the USAGE INSTRUCTIONS carefully before starting the use of this pharmaceutical, since it contains important information for you.

- *Keep the usage instructions. You may need to read it again later.*
- *In case you have additional questions, please consult to your physician or your pharmacist.*
- *This pharmaceutical has been personally prescribed for you; do not give it to other persons.*
- *During the use of this pharmaceutical, tell your physician that you are using this pharmaceutical during your visit to the physician or hospital.*
- *Please comply with the instructions herein. Do not use a dose, **lower or higher** than the recommended dose.*

In these Usage Instructions:

1. **What is EVASIF® and what is it used for?**
2. **Issues prior to the use of EVASIF®**
3. **How is EVASIF® used?**
4. **What are the possible side effects?**
5. **Storage of EVASIF®**

are explained.

1. What is EVASIF® and what is it used for?

EVASIF® consists of blue, almond-shaped film coated tablets and is presented in white HDPE bottles, containing 30 tablets with silica gel desiccant within a box.

EVASIF® is used in the treatment of chronic hepatitis in adults, caused by a hepatitis B virus (HBV).

In addition, EVASIF® is a treatment for Human Immune Deficiency Virus (HIV) infection in adults over 18 years of age.

For treatment of hepatitis B virus (HBV) with EVASIF®, you do not have to have HIV infection.

EVASIF® contains tenofovir disoproxil as effective substance. This effective substance is an antiviral or antiretroviral agent, used in the treatment of hepatitis B virus or HIV or both. Tenofovir is a nucleoside reverse transcriptase inhibitor, known as NRTI, and acts by

preventing normal operation of the enzymes (DNA polymerase in hepatitis B and reverse transcriptase in HIV), required for reproduction of viruses. In HIV, EVASIF[®] must always be used in combination with other pharmaceuticals for treatment of HIV infection.

This pharmaceutical is not a cure for HIV infection. When taking EVASIF[®] other infections or other diseases, associated with HIV infection, may develop.

In addition, you may infect HIV or HBV to others; therefore it is important to take measures to prevent other from being infected.

2. Issues prior to the use of EVASIF[®]

DO NOT USE EVASIF[®] in following cases

- If you are **allergic** (hypersensitive) to tenofovir disoproxil fumarate or any one of other components of EVASIF[®] listed in the beginning of this instruction.

If this is the case for you, tell it to your physician immediately.

USE EVASIF[®] WITH CAUTION in case of following

- **If you have kidney disease or in case problems have been observed in tests in your kidneys, tell this to your physician.** EVASIF[®] may affect your kidneys. Before starting treatment, your physician may request blood tests to assess your kidney functions or may recommend you to take tablets less frequently. In addition, your physician may also request blood tests during the treatment to monitor your kidneys.

EVASIF[®] is generally not taken in combination with other drugs, which may damage your kidneys. Administration in combination with other drugs). In case this is inevitable, your physician will monitor your kidney functions on a daily basis.

- **Talk to your physician in case you are over 65.** Tenofovir disoproxil fumarate has not been studied in patients over 65 years of age. If you are over this age and if you have been prescribed EVASIF[®], your physician will carefully monitor you.
- **Do not give EVASIF[®] to children and adolescents below 18 years of age.**
- **Talk to your physician if you have a liver disease history, including hepatitis.** Patients with liver diseases, including chronic hepatitis B or C and treated with antiretrovirals, are under a higher risk with respect to severe and potentially fatal liver complications. If you have hepatitis B infection, your physician will carefully consider the best treatment regime for you. If you have a history of liver disease or chronic hepatitis B infection, blood tests may be conducted to monitor your liver functions.

Do not stop taking EVASIF[®] without recommendation by your physician. After stopping EVASIF[®] report all new, extraordinary or deteriorating symptoms, noticed after the discontinuance of treatment, to your physician. In case you have hepatitis B (mono-infection) or hepatitis B and HIV at the same time (co-infection) in some patients, there are symptoms or blood tests, showing a deterioration in hepatitis after discontinuance of tenofovir disoproxil treatment. It is best for the physician to monitor your health after discontinuing treatment with EVASIF[®]. You may need to have blood tests for several months after discontinuance of treatment.

- **After starting EVASIF[®] treatment, pay attention to possible lactic acidosis symptoms.**

EVASIF[®] may cause lactic acidosis (excessive lactic acid in your blood) together with enlargement of liver. Data in animals and in humans show that the risk of acidosis development during EVASIF[®] treatment is low. Non-specific symptoms, such as deep and rapid breathing, numbness and nausea, vomiting and stomach pain may point to the development of lactic acidosis. This rare, yet severe side effect may sometimes be lethal. Lactic acidosis, caused by nucleoside analogues, is more frequently seen in women, in particular in the obese. If you have liver disease, you may be under a greater risk for the development of this condition. During treatment with EVASIF[®] your physician will monitor you closely for development of lactic acidosis.

- **Pay attention not to infect others.** EVASIF[®] does not mitigate the risk of transmission of Hepatitis B virus (HBV) or HIV to other persons via sexual intercourse or blood. To avoid this, you must continue taking measures.

Other Measures

In HIV treatment, antiretroviral combination therapies (including EVASIF) may increase blood glucose, blood lipids (hyperlipidemia), and may cause changes in body fat distribution and blood glucose levels, secondary to insulin resistance (see, Section 4. Possible Side Effects).

If you have diabetes, are obese or have high cholesterol levels, talk to your physician.

Be careful for infections. If you have advanced HIV infection (AIDS) or an infection after starting EVASIF[®] treatment, inflammatory symptoms may occur or a deterioration may be seen in existing inflammatory symptoms. These symptoms may point that improved immune system of your body is fighting against infection. Immediately after starting to take EVASIF[®] be careful about inflammatory symptoms. If you notice inflammatory symptoms, **report to your physician immediately.**

Bone disorders. In some HIV patients, receiving combination antiretroviral therapy, osteonecrosis (death of bone tissue as a result of loss of supply of blood to bone tissue). Inter alia, the duration of antiretroviral combination therapy, corticosteroid use, alcohol consumption, severe immunosuppression or high body mass index may be among many risk factors for development of osteonecrosis. Osteonecrosis symptoms are stiffness, pain and ache in joints (in particular in hip, knee and shoulder) and difficulty of movement. If you notice any one of these symptoms, report to your physician.

Do not discontinue the treatment without consulting your physician.

In case these warnings apply to you, even if for any period in the past, please consult to your physician.

Use of EVASIF[®] with food and beverage

- **EVASIF[®]** may be taken with or without food.

Pregnancy

Please consult your physician or pharmacist before using the pharmaceutical.

- Unless you talk to your physician specifically, **you must not take EVASIF[®] during**

pregnancy. There is no clinical data concerning use of EVASIF[®] in pregnant women and generally it is not used unless it is absolutely necessary.

- In case you have the potential to get pregnant during EVASIF treatment, you must use an effective contraception method to avoid getting pregnant.
- If you get pregnant or you are planning to get pregnant, ask your physician concerning possible benefits and risks of antiretroviral therapy on you and your child.

If you take EVASIF[®] during pregnancy, your physician may request blood tests and other diagnostic tests to monitor the development of your child. In the children of mothers, receiving NRTI during pregnancy, benefit from protection against the virus has prevailed over the risk of side effects.

Consult your physician or your pharmacist immediately in case you realize that you are pregnant during treatment.

Lactation:

Please consult your physician or pharmacist before using the pharmaceutical.

- Do not breastfeed **during treatment with EVASIF[®]**. It is not known whether the effective substances in this pharmaceutical are excreted in breastmilk.
- If you are a woman with hepatitis B virus (HBV) or HIV, it is recommended not to breastfeed in order to avoid transmission of virus to the baby.

Driving and Operating Machinery

EVASIF[®] may cause dizziness. When taking EVASIF[®] if you feel dizzy, do not drive or use any tools or machinery.

Important information concerning some of the excipients, contained in EVASIF[®]:

Tell your physician if you have intolerance to lactose or other sugars. EVASIF[®] contains lactose monohydrate. If you know that you are lactose intolerant or in case you are told that you are intolerant to any other sugars, talk to your physicians before taking this drug.

This medicinal product contains less than 1 mmol (23 mg) sodium in each film coated tablet; at these doses, no side effects are expected.

Use with other pharmaceuticals:

You should not take EVASIF[®] **if you are using other pharmaceuticals, comprising tenofovir disoproxil fumarate.** You should not take EVASIF[®] and adefovir dipivoxil concurrently.

- **If you are taking other drugs, which may damage your kidneys, it is important to tell these to your physician.**

These include the following:

- aminoglycosides (for bacterial infection)
- amphotericin B (for fungal infection)
- foscarnet (for viral infection)
- ganciclovir (for viral infection)
- pentamidine (for infections)

- vancomycin (for bacterial infection)
- interleukin-2 (used in cancer treatment)
- cidofovir (for viral infection)
- adefovir dipivoxil (for HBV)
- tacrolimus and cyclosporin (for immune system suppression)
- **Other drugs, containing didanosine (for HIV infection):** Administration of EVASIF in combination with other antiviral drugs, comprising didanosine, may increase didanosine levels in your blood and may decrease CD4 cell counts. When tenofovir disoproxil fumarate and drugs, containing didanosine are administered in combination, pancreatic inflammation and lactic acidosis (excessive lactic acid in blood), which may sometimes be fatal, have been reported rarely. Your physician will carefully consider whether to treat you with tenofovir and didanosine combinations.

In case you are using or have recently used any prescription or over-the-counter pharmaceuticals please report these to your physician or your pharmacist.

3. How is EVASIF[®] used?

Instructions for appropriate usage and dosage/application frequency:

- **Adults:** One tablet daily.

Administration route and method:

May be taken with or without food.

If you have problems in swallowing, you may use the tip of a spoon to crush the tablet.

Then mix the powder with approximately 100 ml (half glass) of water, orange juice or grape juice and drink immediately.

- **Always use EVASIF[®] as prescribed by your physician.** If you are not sure, check with your physician or your pharmacist.
- **Always take the dose, recommended by your physician.** This allows to ensure complete efficacy of your pharmaceutical and to decrease the risk of development of resistance against treatment. Do not change the dose unless told by your physician.
- **If you have HIV, your physician will prescribe EVASIF[®] to you in combination with other antiretroviral drugs.** If you have both hepatitis B virus (HBV) and HIV (co-infection), it is important to take EVASIF[®] together with other antiretroviral drugs, to be prescribed by your physician. If you have hepatitis B, your physician may recommend you to have a HIV test to see whether you have both hepatitis B and HIV viruses.

For instructions on how to take these drugs, please see the patient leaflets of other antiretrovirals.

Different age groups:

- **Use in children: Not for children and adolescents.**

Special usage conditions:

- **If you have problems with your kidneys, your physician** may recommend you to take EVASIF[®] less frequently.

If you used more EVASIF[®] than you should have used

In case you used EVASIF[®] at an amount that is more than you were supposed to, talk to a physician or a pharmacist.

In order to explain what you took easily, keep the tablet bottle with you.

If you forget to use EVASIF[®]:

It is important not to skip EVASIF[®] doses. Do not forget to take your medication on time.

If you have skipped EVASIF[®] take the dose as soon as possible and take the next dose at due time.

If the time for your next dose has almost come, ignore the skipped dose. Wait and take the next dose in due time.

Do not take double doses to compensate for forgotten doses.

If you vomit within one hour after taking **EVASIF[®]**, take another tablet. If you get sick more than one hour after taking EVASIF[®], there is no need to take an additional tablet.

If you discontinue using EVASIF[®]:

- Do not stop taking EVASIF[®] without recommendation by your physician. Discontinuing EVASIF[®] treatment may reduce the efficacy of the treatment, recommended by your physician. Before discontinuing EVASIF[®] for any reason, and in particular if you are experiencing side effects or in case you have any other conditions, talk to your physician. Talk to your physician before you resume taking EVASIF[®] tablets.

If you have hepatitis B or HIV and hepatitis B concomitantly (co-infection), it is especially important not to discontinue EVASIF[®] treatment without talking to your physician. In some patients, blood tests or symptoms, showing deterioration of hepatitis after discontinuing EVASIF[®] have been found. You may need to have blood tests for several months after discontinuance of treatment (see, Section 2).

After discontinuing the treatment, please report new or extraordinary symptoms, in particular the ones, associated with hepatitis B infection, to your physician.

If you have any further questions concerning the use of this product, ask your physician or pharmacist.

4. What are the possible side effects?

As in all pharmaceuticals, EVASIF[®] may cause side effects, although not seen in every patient.

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

Very common side effects

(These may affect at least 10 patients out of every 100 treated patients)

- Diarrhea, vomiting, nausea, dizziness

Test may also show the following:

- Decrease in blood phosphate levels

Common side effects

(These may affect 1 to 10 patients out of every 100 treated patients)

- Gas

Rare side effects

(These may affect at least 1 patient out of 10,000 treated patients, but less than 1 patient out of 1,000 treated patients)

- Lactic acidosis (excessive lactic acid in blood, a severe side effect, which may be lethal). The following may be symptoms of lactic acidosis:
 - Deep and rapid breathing
 - Numbness
 - Nausea, vomiting and stomach pain.

If you think that you may have lactic acidosis, consult your physician immediately.

Other rare side effects

- Pain in the abdomen, caused by pancreas inflammation
- Increase in urine quantity, dehydration and back pain, caused by kidney problems, including kidney failure
- Rashes

Test may also show the following.

- Increase in blood creatinine
- Liver and pancreas disorders

Very rare side effects

(These may affect less than 1 patient out of every 10,000 treated patients)

- Shortness of breath
- Pain in the abdomen, caused by pancreas inflammation
- Feeling weak

Test may also show the following.

- Damage in kidney tubular cells

Other possible effects

In addition, in connection with muscle pain or weakness or bone mineral loss, weakening of bones (related to kidney problems), inflammation in kidneys, frequent urination or feeling of thirst.

In HIV treatment, antiretroviral combination therapy (including EVASIF[®]), may alter body fat distribution and may cause changes in your body form. You may lose fat from your legs, arms and face, fat may build in your abdomen or your internal organs, your breasts may enlarge or fat nodules may form behind your neck ("buffalo hump"). The reasons and long-term effects of these changes are not known.

In HIV treatment, antiretroviral combination therapy may cause hyperlipidemia (increase in blood lipids) and in blood glucose levels, secondary to insulin resistance. Your physician will apply tests for these changes.

In case any of the side effects increases in severity or in case you notice any side effects, not listed in the package leaflet, report to your physician.

Reporting of side effects

In case of a side effect, which is given in the Usage Instructions or not, consult your physician, pharmacist or nurse. In addition, report your side effects to Turkey Pharmacovigilance Center (TÜFAM) by clicking on "Pharmaceutical Side Effect Report" button on www.titck.gov.tr website or via side effect report line 0 800 314 00 08. By reporting side effects, you will provide a contribution to obtain greater information concerning safety of the pharmaceutical you use.

5. Storage of EVASIF®

Keep EVASIF® away from reach and sight of children and in package.

Keep at room temperature below 25°C.

Do not use EVASIF® after the expiry date, given on the box and the bottle.

This medical product does not require any special storage conditions

In case you notice irregularities on the product and/or package, do not use EVASIF®.

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These usage instructions have been approved on .../.../....



Pantone 225 C



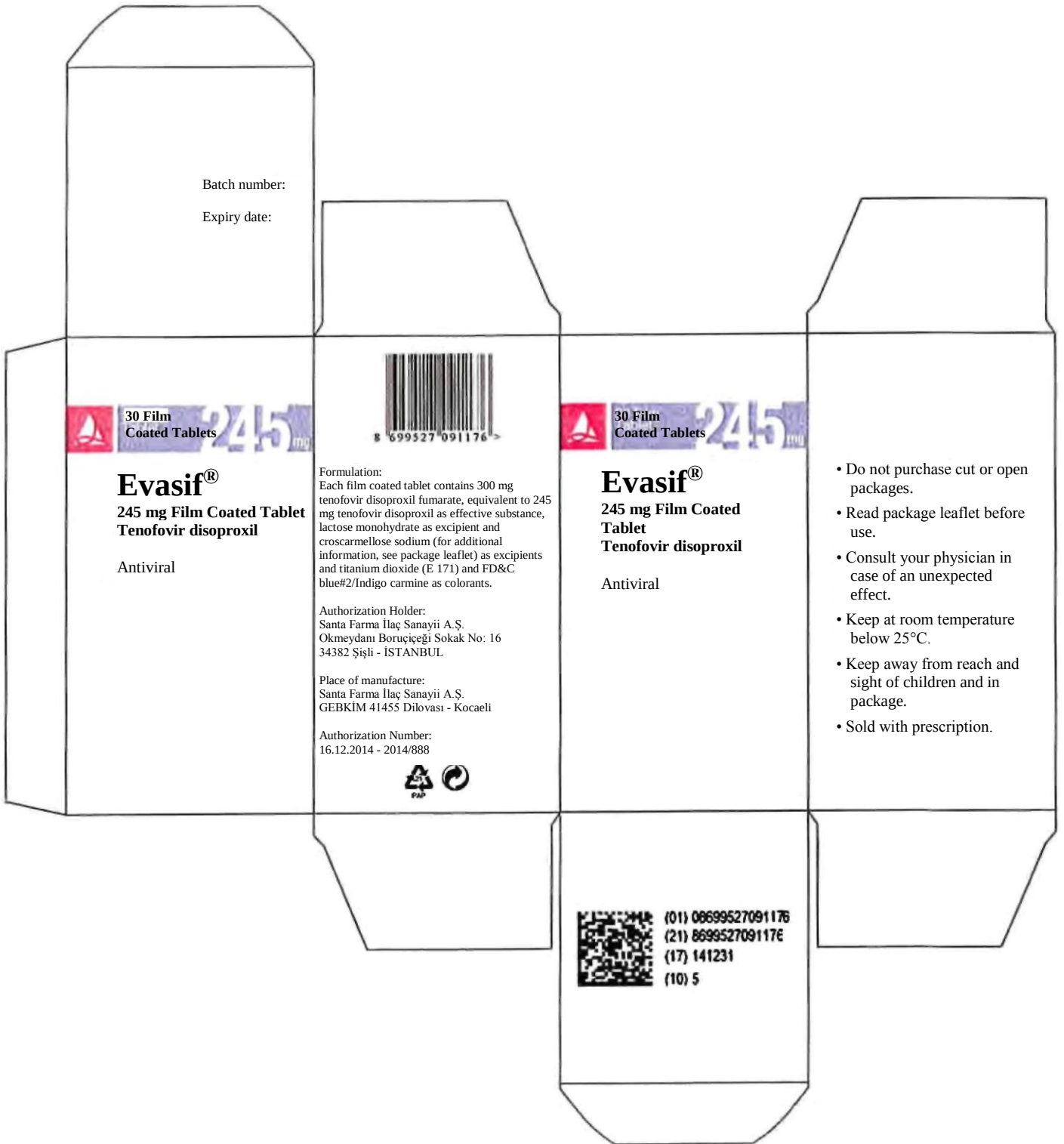
Pantone 536 C



Pantone Cool Gray 11 C



Black





Pantone 225 C



Pantone 536 C



Pantone Cool Gray 11 C



Black

	30 Film Coated Tablets	245 mg
Evasif®		
245 mg Film Coated Tablet		
Tenofovir disoproxil		
Antiviral		
Formulation: Each film coated tablet contains 300 mg tenofovir disoproxil fumarate, equivalent to 245 mg tenofovir disoproxil as effective substance, lactose monohydrate as excipient and croscarmellose sodium (for additional information, see package leaflet) as excipients and titanium dioxide (E 171) and FD&C blue#2/Indigo carmine as colorants.		
Authorization Holder: Santa Farma İlaç Sanayii A.Ş. 34382 Şişli-İstanbul Place of Manufacture: Santa Farma İlaç Sanayii A.Ş. GEBKİM 41455 Dilovası-Kocaeli Authorization Number: 16.12.2014-2014/888		
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