Package leaflet: Information for the user

Eviplera 200 mg/25 mg/245 mg film-coated tablets
emtricitabine/rilpivirine/tenofovir disoproxil

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 Eviplera is and what it is used for

Eviplera contains three active substances that are used to treat Human Immunodeficiency Virus (HIV) infection:

- Emtricitabine, a nucleoside reverse transcriptase inhibitor (NRTI).
- Rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI).
- Tenofovir disoproxil, a nucleotide reverse transcriptase inhibitor (NtRTI).

Each of these active substances, also known as antiretroviral medicines, works by interfering with an enzyme (a protein called 'reverse transcriptase') that is essential for the virus to multiply.

Eviplera reduces the amount of HIV in your body. This, will improve your immune system and reduces the risk of developing illnesses linked to HIV infection.

Eviplera is a treatment for Human Immunodeficiency Virus (HIV) infection in adults aged 18 years and over.

2. What you need to know before you take Eviplera

Do not take Eviplera

- **If you are allergic** to emtricitabine, rilpivirine, tenofovir disoproxil, or any of the other ingredients of this medicine (listed in section 6 of this leaflet).

→ If this applies to you, tell your doctor immediately.

- **If you are currently taking any of the following medicines**
  - **carbamazepine, oxcarbazepine, phenobarbital and phenytoin** (medicines to treat epilepsy and prevent seizures)
  - **rifampicin and rifapentine** (used to treat some bacterial infections such as tuberculosis)
  - **omeprazole, lansoprazole, rabeprazole, pantoprazole and esomeprazole** (proton pump inhibitors that are medicines used to prevent and treat stomach ulcers, heartburn, acid reflux disease)
  - **dexamethasone** (a corticosteroid used to treat inflammation and suppress the immune system) when taken by mouth or injected (except as a single dose treatment)
  - **products that contain St. John's wort** (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety)

Warnings and precautions

You must remain under the care of your doctor while taking Eviplera.

- This medicine is not a cure for HIV infection. While taking Eviplera you may still develop infections or other illnesses associated with HIV infection.

- **Tell your doctor if you had kidney disease,** or if tests have shown kidney problems. Eviplera may affect your kidneys. Before and during treatment, your doctor may order blood tests to measure kidney function. Eviplera is not recommended if you have moderate to severe kidney disease.

  Eviplera is not usually taken with other medicines that can damage your kidneys (see *Other medicines and Eviplera*). If this is unavoidable, your doctor will monitor your kidney function once a week.

- **Talk to your doctor if you have a history of liver disease, including hepatitis.** HIV patients with liver disease (including chronic hepatitis B or C), who are treated with antiretrovirals, have a higher risk of severe and potentially fatal liver complications. If you have hepatitis B, your doctor will carefully consider the best treatment regimen for you. Two of the active substances in Eviplera (tenofovir disoproxil and emtricitabine) show some activity against hepatitis B virus. If you have a history of liver disease, or chronic hepatitis B infection, your doctor may conduct blood tests in order to monitor liver function.

  If you have hepatitis B infection, liver problems may become worse after you stop taking Eviplera. It is important not to stop taking Eviplera without talking to your doctor: see section 3, *Do not stop taking Eviplera*.

- **Tell your doctor immediately and stop taking Eviplera if you develop a skin rash with the following symptoms: fever, blisters, redness in your eyes and swelling of your face, mouth or body.** This may become severe or potentially life-threatening.

- **Talk to your doctor if you are over 65 years of age.** Not enough patients over the age of 65 have been studied. If you are over 65 years of age and are prescribed Eviplera, your doctor will monitor you carefully.

While you take Eviplera
Once you start taking Eviplera, look out for:

- any signs of inflammation or infection
- bone problems (manifesting as persistent or worsening bone pain and sometimes resulting in fractures) may also occur due to damage to kidney tubule cells (see section 4, *Possible side effects*). Tell your doctor if you have bone pain or fractures.

Tenofovir disoproxil (a component of Eviplera) may also cause loss of bone mass. Overall, the effects of tenofovir disoproxil on long-term bone health and future fracture risk in adult patients are uncertain. Tell your doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk for fractures.

→ If you notice any of these symptoms, tell your doctor immediately.

Children and adolescents

Do not give this medicine to children and adolescents under 18 years of age.

Other medicines and Eviplera

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines and herbal medicines obtained without a prescription.

Tell your doctor if you are taking any of the following:

- **Any other medicines containing:**
  - emtricitabine
  - rilpivirine
  - tenofovir disoproxil
  - tenofovir alafenamide
  - any other antiviral medicines that contain lamivudine or adefovir dipivoxil

Eviplera may interact with other medicines. As a result, the amounts of Eviplera or other medicines in your blood may be affected. This may stop your 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.

- **Medicines that may damage your kidneys,** examples include:
  - aminoglycosides (such as streptomycin, neomycin and gentamicin), vancomycin (for bacterial infections)
  - foscarnet, ganciclovir, cidofovir (for viral infections)
  - amphotericin B, pentamidine (for fungal infections)
  - interleukin-2, also called aldesleukin (to treat cancer)
  - non-steroidal anti-inflammatory drugs (NSAIDs, to relieve bone or muscle pains)

- **Medicines containing didanosine (for HIV infection):** Taking Eviplera with other antiviral medicines that contain didanosine can raise the levels of didanosine in your blood and may reduce CD4+ cell counts. Inflammation of the pancreas and lactic acidosis (excess lactic acid in the blood), which sometimes caused death, have been reported rarely when medicines containing tenofovir disoproxil and didanosine were taken together. Your doctor will carefully consider whether to treat you with other medicines used for treating HIV infection (see *Other medicines used for HIV infection*).

- **Other medicines used for HIV infection:** Non-nucleoside reverse transcriptase inhibitors (NNRTIs). Eviplera contains an NNRTI (rilpivirine) and so Eviplera is not to be combined with other medicines of this type. Your doctor will discuss a different medicine if required.

- **Rifabutin,** a medicine to treat some bacterial infections. This medicine can decrease the amount of rilpivirine (a component of Eviplera) in your blood. Your doctor may need to give you an additional dose of rilpivirine to treat your HIV infection (see section 3, *How to take Eviplera*).

- **Antibiotics used to treat bacterial infections** including tuberculosis containing:
  - clarithromycin
  - erythromycin

  These medicines can increase the amount of rilpivirine (a component of Eviplera) in your blood. Your doctor may need to change the dose of the antibiotic or give you a different antibiotic.

- **Medicines for stomach ulcers, heartburn or acid reflux** such as:
  - antacids (aluminium/magnesium hydroxide or calcium carbonate)
  - H_2-antagonists (famotidine, cimetidine, nizatidine or ranitidine)

  These medicines can decrease the amount of rilpivirine (a component of Eviplera) in your blood. If you are taking one of these medicines your doctor will either give you a different medicine for stomach ulcers, heartburn or acid reflux, or recommend how and when you take that medicine.

- **If you are taking an antacid** (such as medicines containing magnesium or potassium), take it at least 2 hours before or at least 4 hours after Eviplera (see section 3, *How to take Eviplera*).

- **If you are taking an H_2-antagonist** (also used to treat stomach acid or acid reflux disease), take it at least 12 hours before or at least 4 hours after Eviplera. H_2-antagonists can only be taken once a day if you take Eviplera. H_2-antagonists should not be taken in a twice a day regimen. Talk to your doctor about an alternative regimen (see section 3, *How to take Eviplera*).

- **Methadone,** a medicine used to treat opiate addiction, as your doctor may need to change your methadone dose.

- **Dabigatran etexilate,** a medicine used to treat heart conditions, as your doctor may need to monitor the levels of this medicine in your blood.

→ **Tell your doctor if you are taking any of these medicines.** Do not stop your treatment without contacting your doctor.

Pregnancy and breast-feeding

If you are pregnant or breast‑feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- **Use effective contraception** while taking Eviplera.
- **Tell your doctor immediately if you become pregnant or if you plan to become pregnant.** Pregnant women should discuss the use of Eviplera with their doctor. Your doctor will discuss the potential benefits and risks of taking Eviplera to you and your child.
- **If you have taken Eviplera** during your pregnancy, your doctor may request regular blood tests and other diagnostic tests to monitor the development of your child. In children whose mothers took NRTIs during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Do not breast-feed during treatment with Eviplera. This is because the active substances in this medicine pass into human breast milk.

Breast-feeding is not recommended in women living with HIV because HIV infection can be passed on to the baby in breast milk.

If you are breast-feeding, or thinking about breast-feeding, you should **discuss it with your doctor as soon as possible**.

Driving and using machines

Do not drive or operate machines if you feel tired, sleepy or dizzy after taking your medicine.

Eviplera contains lactose, sunset yellow aluminium lake (E110) and sodium

- If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
- **Tell your doctor if you have an allergy to sunset yellow aluminium lake (E110).** Eviplera contains sunset yellow aluminium lake also called "E110" which may cause allergic reactions.
- This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Eviplera

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose is one tablet taken each day by mouth. The tablet must be taken with food. This is important to get the right levels of active substance in your body. A nutritional drink alone does not replace food.

Swallow the tablet whole with water.

Do not chew, crush or split the tablet – if you do it may affect the way the medicine is released into your body.

If your doctor decides to stop one of the components of Eviplera or change the dose of Eviplera, you may be given emtricitabine, rilpivirine and/or tenofovir disoproxil separately or with other medicines for the treatment of HIV infection.

If you are taking an antacid such as medicines containing magnesium or potassium. Take it at least 2 hours before or at least 4 hours after Eviplera.

If you are taking an H_2-antagonist such as famotidine, cimetidine, nizatidine or ranitidine. Take it at least 12 hours before or at least 4 hours after Eviplera. H_2-antagonists can only be taken once a day if you take Eviplera. H_2-antagonists should not be taken twice a day. Talk to your doctor about an alternative regimen.

If you are taking rifabutin. Your doctor may need to give you an additional dose of rilpivirine. Take the rilpivirine tablet at the same time you take Eviplera. Check with your doctor or pharmacist if you are not sure.

If you take more Eviplera than you should

If you accidentally take more than the recommended dose of Eviplera you may be at increased risk of experiencing possible side effects with this medicine (see section 4, *Possible side effects*).

Contact your doctor or nearest emergency department immediately for advice. Keep the tablet bottle with you so that you can easily describe what you have taken.

If you forget to take Eviplera

It is important not to miss a dose of Eviplera.

If you do miss a dose:

- **If you notice within 12 hours** of the time you usually take Eviplera, you must take the tablet as soon as possible. Always take the tablet with food. Then take the next dose as usual.
- **If you notice after 12 hours or more** of the time you usually take Eviplera, then do not take the missed dose. Wait and take the next dose, with food, at your usual time.

If you vomit less than 4 hours after taking Eviplera, take another tablet with food. **If you vomit more than 4 hours after taking Eviplera** you do not need to take another tablet until your next regularly scheduled tablet.

Do not stop taking Eviplera

Do not stop taking Eviplera without talking to your doctor. Stopping Eviplera can seriously affect your response to future treatment. If Eviplera for any reason is stopped, speak to your doctor before you restart taking Eviplera tablets. Your doctor may consider giving you the components of Eviplera separately if you are having problems or need your dose adjusted.

When your supply of Eviplera 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 HIV infection and hepatitis B, it is especially important not to stop your Eviplera treatment without talking to your doctor first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping emtricitabine or tenofovir disoproxil (two of the three active substances of Eviplera). If Eviplera is stopped your doctor may recommend that you resume hepatitis B treatment. You may need blood tests to check how your liver is working for 4 months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment is not recommended as this may lead to worsening of your hepatitis, which may be life-threatening.

→ **Tell your doctor immediately** about new or unusual symptoms after you stop treatment, particularly symptoms you associate with hepatitis B infection.

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

4. Possible side effects

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

Possible side effects: tell a doctor immediately

- **Lactic acidosis** (excess lactic acid in the blood) is a rare but potentially life-threatening side effect of some HIV medicines. Lactic acidosis occurs more often in women – particularly if they are overweight, and in people with liver disease. The following may be signs of lactic acidosis:
  - Deep, rapid breathing
  - Tiredness or drowsiness
  - Feeling sick (*nausea*), being sick (*vomiting*)
  - Stomach pain

→ **If you think you may have lactic acidosis, tell your doctor immediately.**

Any signs of inflammation or infection. In some patients with advanced HIV infection (AIDS) and a history of opportunistic infections (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is thought 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 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.
→ If you notice any symptoms of inflammation or infection, tell your doctor immediately.

Very common side effects
(*may affect more than 1 in 10 people*)
- Diarrhoea, being sick (*vomiting*), feeling sick (*nausea*)
- Difficulty sleeping (*insomnia*)
- Dizziness, headache
- Rash
- Feeling weak

Tests may also show:
- Decreases in phosphate levels in the blood
- Increased levels of creatine kinase in the blood that may result in muscle pain and weakness
- Increased levels of cholesterol and/or pancreatic amylase in the blood
- Increased levels of liver enzymes in the blood

→ If any of the side effects get serious tell your doctor.

Common side effects
(*may affect up to 1 in 10 people*)
- Decreased appetite
- Depression and depressed mood
- Tiredness, feeling sleepy (*somnolence*)
- Drowsiness
- Pain, stomach pain or discomfort, feeling bloated, dry mouth
- Abnormal dreams, sleep disorders
- Problems with digestion resulting in discomfort after meals, wind (*flatulence*)
- Rashes (including red spots or blotches sometimes with blistering and swelling of the skin), which may be allergic reactions, itching, changes in skin colour including darkening of the skin in patches
- Other allergic reactions, such as wheezing, swelling or feeling light-headed

Tests may also show:
- Low white blood cell count (a reduced white blood cell count can make you more prone to infection)
- Low platelet count (a type of blood cell involved in clotting blood)
- Decrease in haemoglobin in your blood (low red blood cell count)
- Increased fatty acids (*triglycerides*), bilirubin or sugar in the blood
- Pancreas problems

→ If any of the side effects get serious tell your doctor.

Uncommon side effects
(*may affect up to 1 in 100 people*)
- Anaemia (low red blood cell count)
- Pain in the abdomen (tummy) caused by inflammation of the pancreas
- Breakdown of muscle, muscle pain or weakness
- Swelling of the face, lips, tongue or throat

- Signs or symptoms of inflammation or infection
- Severe skin reactions including rash accompanied by fever, swelling and liver problems
- Damage to kidney tubule cells

Tests may also show:
- Decreases in potassium in the blood
- Increases in creatinine in your blood
- Changes to your urine

→ **If any of the side effects get serious tell your doctor.**

Rare side effects
(*may affect up to 1 in 1,000 people*)
- Lactic acidosis (see *Possible side effects: tell a doctor immediately*)
- Back pain caused by kidney problems, including kidney failure. Your doctor may do blood tests to see if your kidneys are working properly
- Fatty liver
- Yellow skin or eyes, itching or pain in the abdomen (tummy) caused by inflammation of the liver
- Inflammation of the kidney, passing a lot of urine and feeling thirsty
- Softening of the bones (with bone pain and sometimes resulting in fractures)

The breakdown of muscle, softening of the bones (with bone pain and sometimes resulting in fractures), muscle pain, muscle weakness and decreases in potassium or phosphate in the blood may occur due to damage to kidney tubule cells.

→ **If any of the side effects get serious tell your doctor.**

Other effects that may be seen during HIV treatment

The frequency of the following side effects is not known (frequency cannot be estimated from the available data).

- **Bone problems.** Some patients taking combination antiretroviral medicines such as Eviplera may develop a bone disease called *osteonecrosis* (death of bone tissue caused by loss of blood supply to the bone). Taking this type of medicine for a long time, taking corticosteroids, drinking alcohol, having a very weak immune system, and being overweight, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are:
  - Joint stiffness
  - Joint aches and pains (especially of the hip, knee and shoulder)
  - Difficulty with movement

→ **If you notice any of these symptoms tell your doctor.**

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.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the *Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.*

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Eviplera

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 and carton after {EXP}. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture. Keep the bottle tightly closed.

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 Eviplera contains

- **The active substances are** *emtricitabine, rilpivirine* and *tenofovir disoproxil.* Each Eviplera film-coated tablet contains 200 mg of emtricitabine, 25 mg of rilpivirine (as hydrochloride) and 245 mg of tenofovir disoproxil (as fumarate).

- **The other ingredients are:**
  Tablet core:
  Microcrystalline cellulose, lactose monohydrate, povidone, pregelatinised maize starch, polysorbate 20, croscarmellose sodium, and magnesium stearate.

  Film-coating:
  Hypromellose, indigo carmine aluminium lake, lactose monohydrate, polyethylene glycol, red iron oxide, sunset yellow aluminium lake (E110), titanium dioxide, and triacetin.

What Eviplera looks like and contents of the pack

Eviplera is a purplish-pink, capsule-shaped, film-coated tablet debossed on one side with "GSI" and plain on the other side. Eviplera comes in bottles of 30 tablets and in packs made up of 3 bottles, each containing 30 tablets. Each bottle contains a silica gel desiccant that must be kept in the bottle to help protect your tablets. The silica gel desiccant is contained in a separate sachet or canister and should not be swallowed.

Not all pack sizes may be marketed.

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