Package leaflet: Information for the patient

SPEGRA 50 mg/200 mg/25 mg film-coated tablets

Dolutegravir/Emtricitabine/Tenofovir Alafenamide

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of these 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.
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What is in this leaflet

1. What SPEGRA is and what it is used for

SPEGRA contains three active substances:

Emtricitabine, an antiretroviral medicine of a type known as a nucleoside reverse transcriptase inhibitor (NRTI).

Tenofovir alafenamide, an antiretroviral medicine of a type known as a nucleotide reverse transcriptase inhibitor (NtRTI).

Dolutegravir (INIs) an anti-retroviral medicines type known as integrase inhibitors.

SPEGRA blocks the action of the reverse transcriptase enzyme, which is essential for the virus to multiply. SPEGRA therefore reduces the amount of HIV in your body.
SPEGRA does not cure HIV infection; it reduces the amount of virus in your body, and keeps it at a low level. As a result of that, it also increases the CD4 cell count in your blood. CD4 cells are a type of white blood cells that are important in helping your body to fight infection.

SPEGRA in combination with other medicines is used for the **treatment of human immunodeficiency virus 1 (HIV-1) infection** in adults and adolescents 12 years of age and above, weighing at least 40 kg.

2. What you need to know before you take SPEGRA Tablets

Do not take SPEGRA:

- **If you are allergic to emtricitabine, tenofovir alafenamide, dolutegravir** or any of the other ingredients of this medicine (listed in section 6 of this leaflet).
- If you are taking another medicine called dofetilide (to treat heart conditions).

→ If you think any of these apply to you, tell your doctor.

Warnings and precautions

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

You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people. This medicine is not a cure for HIV infection. While taking SPEGRA you may still develop infections or other illnesses associated with HIV infection.

Look out for important symptoms

Some people taking medicines for HIV infection develop other conditions, which can be serious. These include:

- symptoms of infections and inflammation
- joint pain, stiffness and bone problems

→ **If you notice any of these symptoms, tell your doctor immediately.** For more information, see section 4, *Possible side effects*.

Although kidney problems have not been observed with Dolutegravir, Emtricitabine and Tenofovir alafenamide, there is a possibility that you may experience kidney problems when taking SPEGRA over a long period of time.

Protect other people

HIV infection is spread by sexual contact with someone who has the infection, or by transfer of infected blood (for example, by sharing injection needles). You can still pass on HIV when taking this medicine, although the risk is lowered by effective antiretroviral therapy. Discuss with your doctor the precautions needed to avoid infecting other people.

Talk to your doctor before taking SPEGRA:

- **If you have liver problems or have suffered liver disease, includinghepatitis.** Patients with liver disease including chronic hepatitis B or C, who are treated with anti retrovirals, have a higher risk of severe and potentially fatal liver complications. If you have hepatitis B infection, your doctor will carefully consider the best treatment regimen for you.

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

- Your doctor may not prescribe SPEGRA to you if the virus has a K65R mutation.

Other medicines and SPEGRA

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. SPEGRA may interact with other medicines. As a result, the amounts of SPEGRA or other medicines in your blood may change. 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.

Tell your doctor if you are taking any of the medicines *in the following list*:

- Metformin, to treat **diabetes**
- Medicines called **antacids**, to treat **indigestion** and **heartburn. Do not take an antacid** during the 6 hours before you take Dolutegravir, or for at least 2 hours after you take it. (*See also Section 3).*
- Calcium supplements, iron supplements and multivitamins. **Do not take a calcium supplement, iron supplement or multivitamin** during the 6 hours before you take Dolutegravir, or for at least 2 hours after you take it *(see also Section 3).*
- **Antiviral medicines used to treat HIV**
    - Etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir,
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- **Antibiotics used to treat bacterial infections including tuberculosis, containing:**
    - Rifabutin, rifampicin and rifapentine
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- **Antiviral medicines used to treat hepatitis C**
    - Telaprevir and boceprevir
- **Anticonvulsants used to treat epilepsy such as:**
    - Phenytoin, phenobarbital, Oxcarbazepine and carbamazepine
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- **Herbal remedies used to treat depression and anxiety containing:**
    - **St. John's wort** (*Hypericum perforatum*),
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- **Medicines used in treating hepatitis B infection:**
    - **Tenofovir disoproxil fumarate**
    - **Lamivudine**
    - **Adefovir dipivoxil**

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

Children and adolescents

Do not give this medicine to children aged 12 years or under, or weighing less than 40 kg.

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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 for advice before taking this medicine.
- **Use effective contraception** while taking SPEGRA.

Ask your doctor or pharmacist for advice before taking any medicine when pregnant.

If you have taken SPEGRA 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 medicines for HIV during pregnancy, the benefit from the protection against HIV outweighed the risk of side effects.

Do not breast-feed during treatment with SPEGRA. Women who are HIV positive must not be breastfed because HIV infection can be passed on to the baby in breast milk. It is recommended that you do not breast-feed to avoid passing the virus to the baby through breast milk.

Driving and using machines

SPEGRA can cause dizziness. If you feel dizzy when taking SPEGRA, do not drive and do not use any tools or machines.

3. How to take SPEGRA Tablets

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

The recommended dose of SPEGRA is one tablet once a day in adults and adolescents aged 12 years and older who weigh at least 40 kg.

Swallow the tablet with some liquid and can be taken with or without food.
Do not chew, crush or split the tablet.

Always take the dose recommended by your doctor. This is to make sure that your medicine is fully effective, and to reduce the risk of developing resistance to the treatment. Do not change the dose unless your doctor tells you to.

Antacid medicines

- Antacids, to treat indigestion and heartburn, can stop this medicine from being absorbed into your body and make it less effective.
- Do not take an antacid during the 6 hours before you take SPEGRA, or for at least 2 hours after you take it.
- Other acid-lowering medicines like ranitidine and omeprazole can be taken at the same time as SPEGRA.

→ Talk to your doctor for further advice on taking acid-lowering medicines with SPEGRA.

Calcium supplements, iron supplements or multivitamins

- Calcium supplements, iron supplements or multivitamins can stop this medicine from being absorbed into your body and make it less effective.
- Do not take a calcium supplement, iron supplement or multivitamin during the 6 hours before you take SPEGRA, or for at least 2 hours after you take it.

→ Talk to your doctor for further advice on taking calcium supplements, iron supplements or multivitamins with this medicine.

If you take more SPEGRA than you should

If you take more than the recommended dose of SPEGRA you may be at higher risk of side effects of this medicine (see section 4, *Possible side effects*).
Contact your doctor or nearest emergency department immediately for advice.

If you forget to take SPEGRA

It is important not to miss a dose of SPEGRA.

If you do miss a dose:

- **If you notice within 18 hours** of the time you usually take SPEGRA, you must take the tablet as soon as possible. Then take the next dose as usual.
- **If you notice 18 hours or more** after the time you usually take SPEGRA, then do not take the missed dose. Wait and take the next dose at your usual time.

If you vomit less than 1 hour after taking SPEGRA, take another tablet.

Do not stop taking SPEGRA

Do not stop taking SPEGRA without talking to your doctor. Stopping SPEGRA can seriously affect how well future treatment works. Take this medicine for as long as your doctor recommends. Don’t stop unless your doctor advises you to.

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

When your supply of SPEGRA 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 disease may then become harder to treat.

If you have both HIV infection and hepatitis B, it is very important not to stop taking SPEGRA without talking to your doctor first. You may require blood tests for several months after stopping treatment. In some patients with advanced liver disease or cirrhosis, stopping treatment may lead to worsening of 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.

When you're being treated for HIV, it can be hard to tell whether a symptom is a side effect of SPEGRA or other medicines you are taking, or an effect of the HIV disease itself. So it is very important to talk to your doctor about any changes in your health.

Allergic reactions
These are uncommon in people taking SPEGRA. Signs include:
- skin rash
- a high temperature (fever)
- lack of energy (fatigue)
- swelling, sometimes of the face or mouth (angioedema), causing difficulty in breathing
- muscle or joint aches.

→ **See a doctor straight away.** Your doctor may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking SPEGRA.

Possible serious side effects: tell a doctor immediately

- **Any signs of inflammation or infection.** In some patients with advanced HIV infection (AIDS) and who have had opportunistic infections in the past (infections that occur in people with a weak immune system), signs and symptoms of inflammation from previous infections may occur soon after antiretroviral 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.

- **Autoimmune disorders** (the immune system attacks healthy body tissue), may also occur after you start taking medicines for HIV infection. Autoimmune disorders may occur many months after the start of treatment. Look out for 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

→ If you notice the side effects described above, tell your doctor immediately.

Very common side effects

(*may affect more than 1 in 10 people*)

- feeling sick (*nausea*)
- headache
- diarrhoea

Common side effects

(*may affect up to 1 in 10 people*)

- abnormal dreams
- headache
- dizziness
- diarrhoea
- stomach pain (abdominal pain)
- stomach (abdominal discomfort)
- rash
- tiredness (*fatigue*)
- itching (*pruritus*)
- being sick (*vomiting*)

- insomnia
- depression (feelings of deep sadness and unworthiness)
- lack of energy (fatigue)
- wind (*flatulence*)
- increase in the level of liver enzymes
- increase in the level of enzymes produced in the muscles (*creatine phosphokinase*).

Uncommon side effects

(*may affect up to 1 in 100 people*)

- low red blood cell count (*anaemia*).
- problems with digestion resulting in discomfort after meals (*dyspepsia*).
- swelling of the face, lips, tongue or throat (*angioedema*).
- .
- joint pain *(arthralgia).*
- inflammation of the liver (*hepatitis*).
- suicidal thoughts and behaviours (particularly in patients who have had depression or mental health problems before).
- muscle pain.

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 SPEGRA may develop a bone disease called *osteonecrosis* (death of bone tissue caused by loss of blood supply to the bone).

The people mentioned below may be more likely to get this condition:

- if they have been taking combination therapy for a long time
- if they are also taking anti-inflammatory medicines called corticosteroids
- if they drink alcohol
- if their immune systems are very weak
- if they are overweight.

- 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**.

If you get any side effects
→ **Talk to your doctor**. This includes any possible side effects not listed in this leaflet.
If any of the side effects get serious tell your doctor.

Other possible side effects

People taking combination therapy for HIV may get other side effects.

Symptoms of infection and inflammation

People with advanced HIV infection (AIDS) have weak immune systems, and are more likely to develop serious infections (*opportunistic infections*). Such infections may have been "silent" and not detected by the weak immune system before treatment was started. After starting treatment, the immune system becomes stronger, and may attack the infections, which can cause symptoms of infection or inflammation. Symptoms usually include **fever**, plus some of the following:

- headache
- stomach ache
- difficulty breathing

In rare cases, as the immune system becomes stronger, it can also attack healthy body tissue (*autoimmune disorders*). The symptoms of autoimmune disorders may develop many months after you start taking medicine to treat your HIV infection. Symptoms may include:

- palpitations (rapid or irregular heartbeat) or tremor
- hyperactivity (excessive restlessness and movement)
- weakness beginning in the hands and feet and moving up towards the trunk of the body.

If you get any symptoms of infection and inflammation or if you notice any of the symptoms above:
→ Tell your doctor immediately. Don't take other medicines for the infection without your doctor's advice.

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.

4. How to store SPEGRA

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

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30° C (59° to 86° F) [See USP Controlled Room Temperature].
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.

5. Contents of the pack and other information

What SPEGRA contains

The active substances are Dolutegravir, Emtricitabine and Tenofovir Alafenamide. Each SPEGRA film-coated tablet contains Dolutegravir 50 mg, 200 mg of Emtricitabine and Tenofovir Alafenamide Fumarate equivalent to 25 mg of Tenofovir Alafenamide.

The other ingrediens are

Mannitol, Microcrystalline cellulose, Sodium starch glycolate, Povidone K30, Sodium stearyl Fumarate, Croscarmellose sodium, Magnesium stearate, Opadry II white 85F18422 (Containing Polyvinyl alcohol-part hydrolyzed, Macrogol/PEG, Talc, Titanium dioxide)

What SPEGRA looks like and contents of the pack

White to off white, capsule shaped, film coated tablets, debossed with HP602 on one side and plain on the another side.

30 tablets are packed in HDPE bottle container

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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Manufacturer

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