Approved Patient Information Leaflet

RELIVZATE

SCHEDULING STATUS: S4

RELIVZATE 300 mg/ 300 mg film-coated tablets

Lamivudine and tenofovir disoproxil fumarate 300 mg/ 300 mg

Contains sugar (lactose monohydrate: 49,4 mg/ tablet)

WARNING

RELIVZATE may cause serious liver damage or too much acid in your blood. This may result in death if left untreated. Report to your doctor immediately if you develop nausea, vomiting, stomach pain, loss of appetite, generally feel unwell or develop rapid or shallow breathing. This condition may develop after a few or several months of treatment.

The safety and efficacy of RELIVZATE in patients who are infected with both human immunodeficiency virus (HIV) and hepatitis B virus (HBV) have not been established. RELIVZATE should not be used for the treatment of chronic HBV infection. You should be closely monitored by your doctor for several months if you are infected with HBV and stop taking RELIVZATE.

Read all of this leaflet carefully before you start taking RELIVZATE

- Keep this leaflet. You may need to read it again.

- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- RELIVZATE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What RELIVZATE is and what it is used for

RELIVZATE contains lamivudine 300 mg and tenofovir disoproxil fumarate 300 mg, one of a group of medicines called reverse transcriptase inhibitors.

RELIVZATE is used

- to treat Human Immunodeficiency Virus (HIV) infection in adults over 18 years of age.

2. What you need to know before you RELIVZATE

Do not take RELIVZATE

- if you are allergic (hypersensitive) to lamivudine or tenofovir, or any of the other ingredients in RELIVZATE (listed in section 6)
- if you have moderate to severe impairment of kidney function

- if you are pregnant or breastfeeding
- if you are younger than 18 years of age
- if you are taking zalcitabine (see "Other medicines and RELIVZATE").

Warnings and precautions

Take special care with RELIVZATE

- you have symptoms such as deep, rapid breathing, drowsiness, and non-specific symptoms, such as nausea, vomiting and stomach pain. This is a serious, life-threatening side effect known as lactic acidosis (excess of lactic acid in your blood). Lactic acidosis occurs more often in women, particularly if they are very overweight. If you have liver disease you may also be more at risk of getting this condition. While you are being treated with RELIVZATE, please report any of these symptoms to your doctor as a matter of urgency
- you have hepatitis B virus (HBV) infection (see boxed "WARNING")
- you have a kidney disorder (see "Possible side effects"). Please report to your doctor immediately if you develop swelling of the lower limbs, hands, body or face, are short of breath and if you pass very little or no urine. You may have to go for regular blood tests to monitor your kidney function
- you develop excess fat on your abdomen (stomach), behind your neck, or your breasts may enlarge, while your legs and arms become thinner. Contact your doctor as soon as possible if you notice changes in body fat distribution. You may require blood tests to monitor your cholesterol and blood sugar (glucose) levels
- you develop severe stomach pain or cramps accompanied by fever, chills, and severe nausea and vomiting
- you are taking RELIVZATE you may still develop infections or other illnesses associated with HIV infection as RELIVZATE is not a cure for HIV infection

- RELIVZATE does not reduce the risk of passing HIV to others through sexual contact or contamination with blood. Therefore, it is important to continue to take appropriate precautions to prevent passing HIV to others
- you develop signs and symptoms of inflammation from previous infections soon after treatment with RELIVZATE is started. It is believed that these symptoms are due to an improvement in the body's immune response, causing inflammation in response to infections that may have been present with no obvious symptoms. If you notice any symptoms of infection, please inform your doctor immediately
- Bone problems:
    - 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 may also cause loss of bone mass. The most pronounced bone loss was seen in clinical studies when patients were treated with tenofovir disoproxil in combination with a boosted protease inhibitor.
    - Overall, the effects of tenofovir disoproxil on long-term bone health and future fracture risk in adult and paediatric patients are uncertain.

Tell you doctor if you know you suffer from osteoporosis. Patients with osteoporosis are at a higher risk for fractures.

Children and adolescents

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 child's doctor if your child has bone pain or fractures.

Tenofovir disoproxil may also cause loss of bone mass. The most pronounced bone loss was seen in clinical studies when patients were treated with tenofovir disoproxil in combination with a boosted protease inhibitor.

Overall, the effects of tenofovir disoproxil on long-term bone health and future fracture risk in adult and paediatric patients are uncertain.

Tell your child's doctor if your child suffers from osteoporosis. Patients with osteoporosis are at a higher risk for fractures.

Other medicines and RELIVZATE

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

- do not take RELIVZATE with any other medicines containing lamivudine, tenofovir disoproxil fumarate, abacavir, emtricitabine adefovir dipivoxil
- it is not recommended to take didanosine, or zalcitabine (see "Do not take RELIVZATE") in combination with RELIVZATE
- atazanavir, atazanavir/ritonavir combination, lopinavir/ritonavir combination darunavir/ritonavir combination (medicines used to treat HIV infection) taken in combination with RELIVZATE can increase the effect of RELIVZATE and can lead to kidney problems
- taking sofosbuvir and RELIVZATE together can increase the effect of RELIVZATE and lower the effect of sofosbuvir
- taking RELIVZATE in combination with ledipasvir/sofosbuvir combination may

increase the effect of RELIVZATE and side effect may occur

- taking co-trimoxazole (antibiotic used to treat infection) may increase the effect of RELIVZATE and should be avoided if high doses of co-trimoxazole is prescribed for treatment of lung infection and infection from a parasite called *Toxoplasma gondii*
- do not take RELIVZATE if you recently used or are using medicine which can influence the kidneys i.e., aminoglycosides (antibiotics), amphotericin B (used to treat fungal infections), foscarnet (used to treat virus infections), ganciclovir (used to treat the viral infection - cytomegalovirus), pentamidine (used to treat lung infection), vancomycin (antibiotic), cidofovir (used to treat viral infections) or interleukin-2 (used to treat cancer)
- tacrolimus (used to suppress the immune system) can influence the kidneys and should be used with care when taken in combination with RELIVZATE.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking RELIVZATE.

Adult patients

If you are a mother with HBV, and your baby has been given treatment to prevent hepatitis B transmission at birth, you may be able to breast-feed your infant, but first talk to your doctor to get more information.

If you are mother with HIV do not breastfeed, to avoid passing the virus to the baby in breast milk.

Paediatric patients

If your child has HBV, and their baby has been given treatment to prevent hepatitis B transmission at birth, your child may be able to breast-feed their infant, but first talk to your child's doctor to get more information.

If your child has HIV they must not breast-feed, to avoid passing the virus to the baby in breast milk.

Driving and using machines

It is not always possible to predict to what extent RELIVZATE may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which RELIVZATE affects them.

- RELIVZATE may cause dizziness. If you feel dizzy while taking RELIVZATE, do not drive and do not use any tools or machines.

RELIVZATE contains lactose monohydrate

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking RELIVZATE.

3. How to take RELIVZATE

Do not share medicines prescribed for you with any other person.

Always take RELIVZATE exactly as your doctor or pharmacist has told you.

Check with your doctor or pharmacist if you are not sure.

Adults

The usual dose is on RELIVZATE tablet once daily with food.

Duration of administration

Your doctor will tell you how long your treatment with RELIVZATE will last. Do not stop taking RELIVZATE without discussing it with your doctor. If you have the impression that the effect of RELIVZATE is too strong or too weak, please discuss this with your doctor.

Method of administration

Take RELIVZATE once a day, every day, at about the same time each day with food.

If you take more RELIVZATE than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.
Always take RELIVZATE exactly as your doctor has instructed you.

If you forget to take RELIVZATE

If you forget to take RELIVZATE, take a dose as soon as you remember, then continue to take RELIVZATE at the usual times. Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

RELIVZATE can have side effects.

Not all side effects reported for RELIVZATE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking RELIVZATE, please consult your health care provider for advice.

If any of the following happens, stop taking RELIVZATE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are very serious side effects. If you have them, you may have had a serious reaction to RELIVZATE. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- shortness of breath (dyspnoea)
- lung infection (symptoms include severe coughing with the production of yellow, green, or brown phlegm, with shortness of breath and/or chest pain)
- lactic acidosis (symptoms include deep, rapid breathing, drowsiness, and non-specific symptoms, such as nausea, vomiting and stomach pain)
- inflammation of your pancreas (symptoms include severe stomach pain or cramps, fever, nausea, vomiting)
- problems with your liver (symptoms include yellow discolouration of the skin or whites of the eyes with pain over the liver area discoloured urine and stools, diarrhoea, abdominal swelling, distention or bloating, loss of appetite)
- peripheral neuropathy (symptoms include pins and needles in the hands or feet, or burning, intractable pain in the limbs
- kidney problems, kidney failure (symptoms include swelling of your legs, ankles, and feet from retention of fluids, confusion, pain in the pelvis, pain of

a burning sensation while urinating, reduced amount of urine, nausea, drowsiness or fatigue)

- breakdown of muscle fibres (symptoms include muscle weakness, fatigue, dark coloured urine)
- muscle weakness, softening of the bones (bone pain and fractures easy)
- abnormal distribution of fat.

These are serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- dizziness, headache and difficulty sleeping
- blood test indicating low levels of phosphate in the blood
- cough, runny or blocked nose
- diarrhoea, nausea, vomiting, pain in the stomach, indigestion, flatulence (wind)
- rash and hair loss
- blood test indicating raised liver enzyme levels
- hives, itching, sweating
- muscle pain, joint pain
- lack of energy, tiredness, fever, back or chest pain, pain
- weight loss
- depression, anxiety
- blood tests indicating abnormal levels for the following: cholesterol or triglycerides, amylase (indication of pancreas infections), creatine kinase (indication of muscle damage), white blood cell count, glucose
- blood in urine, glucose in urine as detected with urine analyses.

Less frequent side effects:

- low white blood cell counts (symptoms include repeated fevers and infections) and red blood cell counts (symptoms include fatigue, dizziness, weakness and light-headedness, pale skin), low platelet count (symptoms include easy and excessive bruising, prolonged bleeding from cuts), abnormal organ or tissue development and function
- proteins in the urine as detected with urine tests.

Side effects with frequency unknown:

- a condition called immune reconstitution syndrome (where the immune system starts to recover but then responds to a previous infection). Symptoms include fever and worsening of breathing issues
- a low level of the electrolyte potassium in the blood as detected with blood tests. Symptoms can include weakness and fatigue, heart palpitations, muscle cramps.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of RELIVZATE.

Suspected side effects can also be reported directly to the Holder of the Certificate of Registration via medsafety@austell.co.za

5. How to store RELIVZATE

- Store all medicines out of reach of children
- Store at or below 30 °C in original container.
- Keep the container tightly closed
- Do not use after the expiry date stated on the label/carton/bottle.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What RELIVZATE contains

- The active substances are lamivudine and tenofovir disoproxil fumarate.
- The other ingredients are microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide, hypromellose, talc. The film-coating of the tablet contains Opadry II 32K58000 (White), which contains hydroxypropyl methyl cellulose, lactose monohydrate, titanium dioxide and triacetin.

What RELIVZATE looks like and contents of the pack

RELIVZATE tablets are white coloured, capsule shaped, biconvex, film-coated tablets plain on both sides.

RELIVZATE tablets are packed in a 120CC white HDPE bottle along with either a 5 g silica gel desiccant sachet or a 5 g molecular sieve desiccant sachet. The bottle is closed with a 38 mm non-child resistant closure. Pack size of 28 or 30 tablets.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

JOHANNESBURG, 2193

South Africa

Tel: +2711 611 1400 or +27 860 287 835

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Access to the corresponding Professional Information

Professional Information for this medicine is available on the following URL:

https://austell.co.za/product-info/

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Tel: +27 11 611 1400 or +27 860 287 835