1.3.2 PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

VULANTE 300 mg/ 300 mg/ 50 mg film-coated tablets

Tenofovir disoproxil fumarate, lamivudine and dolutegravir

Contains sugar: Lactose monohydrate 150,4 mg; mannitol 131,38 mg

Read all of this leaflet carefully before you start taking VULANTE

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- VULANTE 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 VULANTE is and what it is used for
2. What you need to know before you take VULANTE
3. How to take VULANTE
4. Possible side effects
5. How to store VULANTE
6. Contents of the pack and other information

1. What VULANTE is and what it is used for

VULANTE belongs to a group of medicines called antivirals, for treatment of HIV (human immunodeficiency virus) infection in adults aged 18 years and older.

2. What you need to know before you take VULANTE

Do not take VULANTE:

- if you are hypersensitive (allergic) to dolutegravir, lamivudine, tenofovir or any of the other ingredients of VULANTE (see section 6).
- if you are taking a medicine called metformin (to treat diabetes).
- if you are taking medicine called adefovir dipivoxil (used to treat Hepatitis B infection).
- if you are taking medicine called dofetilide or pilsicainide (to treat heart rhythm problems).
- if you are taking medicine called didanosine (to treat HIV).
- if you have liver or kidney disease.
- if you are a woman of child-bearing age not using effective contraception.
- if you are below the age of 18 years.
- if you are pregnant (in your first trimester) or breastfeeding your baby. VULANTE could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking VULANTE in the first few weeks of your pregnancy (see Take Special care with VULANTE and Pregnancy and breastfeeding).

Warnings and precautions

LACTIC ACIDOSIS (EXCESS LACTIC ACID IN THE BLOOD) IS A RARE BUT

SERIOUS POSSIBLE SIDE EFFECT THAT CAN BE FATAL. THE FOLLOWING SIDE EFFECTS MAY BE SIGNS OF LACTIC ACIDOSIS:

- **DEEP, RAPID BREATHING**
- **WEIGHT LOSS, LOSS OF APPETITE**
- **GENERAL FEELING OF DISCOMFORT**
- **FEELING SICK (NAUSEA), BEING SICK (VOMITING) AND STOMACH PAIN**

IF YOU THINK THAT YOU MAY HAVE LACTIC ACIDOSIS, CONTACT YOUR DOCTOR IMMEDIATELY.

AN ENLARGED LIVER WITH FATTY LIVER DISEASE HAVE BEEN REPORTED WITH THE USE OF VULANTE. IF YOU HAVE A LIVER DISEASE, TELL YOUR HEALTHCARE PROVIDER AS VULANTE CAN WORSEN OR CAUSE LIVER DISEASE.

VULANTE IS NOT INDICATED TO TREAT HEPATITIS B (AN INFECTION OF YOUR LIVER THAT CAUSES INFLAMMATION AND SCARRING OF YOUR LIVER). IF YOU HAVE BEEN DIAGNOSED WITH HEPATITIS B, TELL YOUR HEALTHCARE PROVIDER AS VULANTE CAN WORSEN SYMPTOMS OF HEPATITIS B. YOUR DOCTOR WILL SEND YOU FOR REGULAR BLOOD TESTS TO MONITOR YOUR LIVER FUNCTION IF YOU HAVE HAD TO STOP VULANTE DUE TO HEPATITIS B INFECTION.

Take special care with VULANTE:

- if you are pregnant or suspect that you might be pregnant, you should immediately tell your healthcare provider. Taking VULANTE when conception takes place may cause serious birth defects in your baby. If you want to become pregnant, while on VULANTE treatment, consult your healthcare provider before trying to conceive a baby. You might need to be switched to another type of medicine (see Pregnancy and breastfeeding).
- if you get any symptoms of infection while you are taking VULANTE. Patients 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 or hidden” 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, headache, stomach ache or 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 (such as Graves’ disease, Guillain-Barre Syndrome, polymyositis) 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.

- if your body shape changes, because of changes in fat distribution. People taking combination therapy, such as VULANTE, for HIV may find that their body shape changes, and that they have higher blood sugar and blood lipid (fat in the blood) levels.
- if you experience joint pain, joint stiffness or difficulty in movement, you should see your doctor immediately.
- if you have any bone problems. It is not known whether long-term use of VULANTE will cause damage to your bones. If you have had bone problems in the past, your healthcare provider may need to do tests to check your bone mineral density or may prescribe medicines to treat or prevent further bone mineral density loss. Some adult patients with HIV taking combination antiretroviral therapy may develop a bone disease called osteonecrosis (death of bone tissue caused by loss of blood supply to the bone). The length of combination antiretroviral therapy, corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index, among others, may be some of the many risk factors for developing this disease. Signs of osteonecrosis are joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement. If you notice any of these symptoms tell your doctor as you may need to take calcium and vitamin D supplements to prevent further damage to your bones that may be caused by VULANTE. Bone problems (sometimes resulting in fractures) may also occur due to damage to kidneys (see section 4).
- if you do not see your doctor regularly. Keep in touch with your doctor, and do not stop taking VULANTE without your doctor’s advice. You might still develop infections. For as long as you are taking VULANTE, your doctor will arrange

regular blood tests to check for side effects.

- if you have regular sexual contact with someone or if there is transfer of your blood to another person by sharing needles. 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). VULANTE will not stop you passing HIV infection on to other people. To protect other people from becoming infected with HIV, use a condom when you have oral or penetrative sex and do not risk blood transfer (for example, don't share needles). HIV can still be transmitted despite taking VULANTE. VULANTE does not cure HIV infection, it reduces the amount of virus in your body.
- if you are female, overweight (obese), or have been taking a type of HIV medicine called a nucleoside reverse transcriptase inhibitors (e.g. abacavir, zidovudine, stavudine, lamivudine, tenofovir etc.) for a long time as you may be more likely to get lactic acidosis (build-up of lactic acid in the body) (see section 4).
- if you experience pain in the stomach, nausea, vomiting or any changes in laboratory (blood) test values, as this can be a symptom of pancreatitis (inflammation in the pancreas) (see section 4).
- if you have kidney problems. Before starting treatment, your doctor may order blood tests to assess your kidney function. VULANTE may affect your kidneys during treatment. Your doctor may order blood tests during treatment to monitor how your kidneys work. VULANTE is not usually taken with other medicines that can damage your kidneys (see Other medicines and VULANTE). If this is unavoidable, your healthcare provider will monitor your kidney function once a week.

- if you have liver problems or if you have an infection in your liver called hepatitis B or C. Your doctor will monitor your liver enzymes as VULANTE can cause or worsen liver disease. It is very important not to stop treatment with VULANTE without talking to your doctor first. Some patients have had blood tests or symptoms indicating that their hepatitis has got worse after stopping VULANTE. You may require blood tests for several 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.
- if you are taking or have taken any other medicine you need to tell your doctor about it. This includes natural medicine and medicine that you are taking that does not need a prescription (see Other medicines and VULANTE).
- if you have been told by your doctor that you have a mutation called the K65R mutation.
- if you experience nausea, vomiting, abdominal pain, generalised weakness, anorexia, and sudden unexplained weight loss, and difficulty breathing you should tell your doctor immediately as you may be experiencing lactic acidosis. This usually occurs after a few months of treatment with VULANTE.
- if you experience any symptoms of anaemia such as extreme tiredness or paler skin than usual, or if you start experiencing fits, a change in your muscle tone or unusual behaviour from yourself you may be experiencing mitochondrial dysfunction and should therefore inform your doctor immediately.

Elderly

If you are elderly, there is insufficient experience with VULANTE in patients aged 65 and over to determine whether you will respond differently from younger patients.

Children and adolescents

There is no experience with VULANTE in children younger than 18 years.

Other medicines and VULANTE

Always tell your healthcare provider if you are taking any other medicines (this includes complementary or traditional medicines).

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

- metformin, to treat diabetes (see Do not take VULANTE),
- medicines called antacids, that contain magnesium and aluminium, to treat indigestion and heartburn. Do not take an antacid during the 2 hours before you take VULANTE, or for at least 6 hours after you take it,
- multivitamins, calcium and iron supplements. Do not take a multivitamin, calcium or iron supplement during the 2 hours before you take VULANTE, or for at least 6 hours after you take it,
- etravirine, efavirenz, fosamprenavir/ritonavir, nevirapine or tipranavir/ritonavir, to treat HIV infection,
- rifampicin or isoniazid, to treat tuberculosis,
- phenytoin and phenobarbitone, to treat epilepsy,
- oxcarbazepine and carbamazepine, to treat epilepsy and bipolar disorder,

- St. John's wort (*Hypericum perforatum*), a herbal remedy used for depression,
- other medicines that contain tenofovir, dolutegravir, emtricitabine, or lamivudine, either alone or as co-formulations. VULANTE should not be used with these medicines because they contain the same or similar active ingredients as VULANTE (see How to take VULANTE),
- adefovir dipivoxil, used to treat hepatitis B,
- medicines that contain didanosine. Tenofovir (a component of VULANTE) may increase the amount of didanosine in your blood. You may need to be monitored more carefully if you are taking VULANTE and didanosine together. The dose of didanosine may also need to be reduced,
- ribavirin, medicine used to treat hepatitis C,
- medicines that are excreted by the kidneys as they may reduce the kidney function and may increase the concentration of lamivudine, tenofovir and/or the medicines given with VULANTE. Some examples of medicines excreted by the kidneys include, but are not limited to adefovir dipivoxil (for hepatitis B infection), cidofovir, acyclovir, valacyclovir, foscarnet and ganciclovir (all used to treat viral infections), amphotericin B (for a fungal infection), aminoglycosides, pentamidine, vancomycin (all used to treat bacterial infections), interleukin 2 (used to boost the immune system in cancer therapy), non-steroidal anti-inflammatory drugs (NSAIDs) (used to relieve pain and inflammation) and tacrolimus (used to suppress the immune system after an organ transplant),
- atazanavir sulphate or lopinavir and ritonavir co-formulation. These medicines may increase the amount of tenofovir (a component of VULANTE) in your blood, which could result in more side effects. You may need to be monitored more

carefully if you are taking VULANTE and atazanavir sulphate or lopinavir and ritonavir co-formulation together. VULANTE may decrease the amount of atazanavir sulphate in your blood,

- other medicines used for HIV infection: the following protease inhibitors: amprenavir, nelfinavir, indinavir, ritonavir boosted atazanavir or saquinavir. Your doctor may consider giving you an alternative medicine or changing the dose of the protease inhibitors,
- cladribine, a medicine used to treat cancer in the blood (leukaemia),
- trimethoprim/sulfamethoxazole, used to treat or prevent bacterial infections.

Your healthcare provider can advise you on which contraceptives to take.

Tell your healthcare provider if you are taking any of these medicines.
Your doctor may decide to adjust your dose or that you need extra check-ups.
These are not all the medicines that may cause problems if you take VULANTE. Be sure to tell your healthcare provider about all medicines that you take.
Keep a complete list of all the medicines that you take. Make a new list when medicines are added or stopped, or if the dose changes. Give copies of this list to all of your healthcare providers and pharmacist every time you visit your healthcare provider or fill a prescription. This will give your healthcare provider a complete picture of the medicines you use. Then he or she can decide the best approach for your situation.

VULANTE with food and drink

VULANTE may be taken at any time of the day, with or without food. Take VULANTE at the same time every day.

Pregnancy and breastfeeding

Pregnancy

You should not take VULANTE if you are planning to become pregnant (see Do not take VULANTE).

You should not take VULANTE if you are pregnant (in your first trimester) or breastfeeding your baby (see Do not take VULANTE).

If you are a woman of child-bearing age you could get pregnant while taking VULANTE, you need to use a reliable method of barrier contraception (for example, a condom) with other methods of contraception including oral (pill) or other hormonal contraceptives (for example, implants, injection), to prevent pregnancy.

VULANTE can harm your baby if you become pregnant or are in the early stages of pregnancy. You should not take VULANTE if you have become pregnant, as there is potential risk of neural tube defects that will affect your unborn baby. Tell your doctor immediately if you think you may have become pregnant.

If you are thinking about having a baby, do not stop using VULANTE and contraception before you have talked to your healthcare professional. If you think you are pregnant, go to your healthcare professional to get a pregnancy test and to be advised on your future HIV treatment and on a pregnancy management plan.

Breastfeeding

You should not breastfeed your baby while you are taking VULANTE.

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

Driving and using machines

It is not always possible to predict to what extent VULANTE may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which VULANTE affects you (see section 4).

VULANTE contains lactose monohydrate and mannitol

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

VULANTE may have a mild laxative effect.

3. How to take VULANTE

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

Always take VULANTE exactly as your doctor or pharmacist has instructed you.

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

The usual dose of VULANTE is one tablet once a day.

Your doctor will decide on the correct dose of VULANTE for you.

Swallow the tablet with some liquid.

VULANTE can be taken with or without food.

Your doctor will tell you how long your treatment with VULANTE will last. Do not stop treatment unless your doctor advises you to.

If you have the impression that the effect of VULANTE is too strong or too weak, tell your doctor or pharmacist.

If you take more VULANTE than you should

In the event of overdosage, consult your doctor or pharmacist. If your healthcare provider is not available, contact the nearest hospital or poison control centre.

If you forget to take VULANTE

Do not take a double dose to make up for forgotten individual doses. If you have missed a dose of VULANTE, take the dose that you have missed as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. If you have forgotten to take several doses, contact your doctor without delay.

If you stop taking VULANTE

Take VULANTE for as long as your doctor recommends. Do not stop taking VULANTE unless your doctor advises you to because stopping your treatment may cause resistance. Even if you decide to take VULANTE again at a later stage, VULANTE might not work.

For these reasons, it is vital to take VULANTE exactly as your doctor or pharmacist has instructed you.

4. Possible side effects

VULANTE can have side effects.

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

It is very important to talk to your doctor about any changes in your health.
Some side effects may only be seen in your blood tests and may not appear immediately after you start taking VULANTE. If you get any of these effects and if they are severe, your doctor may advise you to stop taking VULANTE.

As well as the effects listed below for VULANTE, other conditions can develop during combination therapy for HIV (see section 2).
If any of the following happens, stop taking VULANTE and tell your doctor immediately or go to the casualty department at your nearest hospital:

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

These are all very serious side effects. If you have them, you may have had a serious

allergic reaction to VULANTE. 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:

- inflammation in your liver or pancreas (hepatitis or pancreatitis) or liver problems that causes yellowing of the skin and eyes, (jaundice) dark coloured urine, light coloured stools, abdominal pain, nausea and vomiting,
- any unusual or unexplained bruising or bleeding due to a low blood platelet count (thrombocytopenia),
- fever, chills, swelling, sore throat, fatigue, which may be signs of an infection due to low white blood cell count (neutropenia),
- kidney problems, including kidney failure. Due to the build-up of waste products and excess fluid in the body, symptoms may include, but are not limited to, weakness, shortness of breath, tiredness, swelling in your legs, ankles, and feet, confusion, abnormal heart rhythm, reduction in how much and how often you urinate and pain or pressure in your chest,
- lactic acidosis**.** Patients who take VULANTE can develop a serious condition called lactic acidosis (build-up of an acid in the blood). Call your doctor right away if you get the following signs or symptoms of lactic acidosis:
    - You feel very weak or tired,
    - You suddenly lose weight and do not have an appetite,
    - You have unusual (not normal) muscle pain,
    - You have trouble breathing,
- rhabdomyolysis. The breakdown of muscle fibers that leads to the release of

muscle fiber contents (myoglobin) into the bloodstream. Myoglobin is harmful to the kidney and often causes kidney damage. Call your doctor right away if you get the following signs or symptoms:

- Abnormal urine colour (dark, red, or cola coloured),
- Decreased urine production,
- General weakness,
- Muscle stiffness or aching (myalgia),
- Muscle tenderness,
- Weakness of the affected muscles,

- if you are also infected with the Hepatitis B Virus (HBV), you need close medical follow up for several months after stopping treatment with VULANTE. Follow-up includes medical exams and blood tests to check for HBV that could be getting worse. Patients with hepatitis B Virus who take VULANTE and then stop it, may get “flare-ups” of their hepatitis. A “flare-up” is when the disease suddenly returns in a worse way than before. VULANTE is not approved for the treatment of Hepatitis B Virus infection,
- suicidal thoughts or an attempt to take one’s own life,
- convulsions (fits),
- neural tube defects (a group of birth defects involving the brain, spine and spinal cord) in babies born to women taking VULANTE (see section 2),
- abnormal results when your blood is tested, decrease in red blood cells, white blood cells and platelets,
- an inflammatory condition which may develop as the immune system becomes stronger (immune reconstitution syndrome or ‘IRIS’). Symptoms can include

fever, headache, stomach ache, difficulty breathing, rapid or irregular heartbeat or tremor, excessive restlessness and movement and weakness,

- blood in the urine (haematuria), protein in the urine (proteinuria), increased urine production (polyuria), frequently feeling thirsty,
- chest pain, inflammation of the lungs caused by a bacterial infection (pneumonia), difficulty breathing (dyspnoea),
- loss of blood flow to bone tissue, which causes the bone to die (osteonecrosis),
- painful joints and bones, bones that break more easily (osteomalacia),
- decreased levels of potassium in the blood (hypokalaemia).

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- difficulty in sleeping (insomnia), abnormal dreams, depression,
- headache, dizziness,
- feeling sick (nausea) and being sick (vomiting), wind (flatulence), outward expansion of stomach (stomach distension), diarrhoea, stomach pain or cramps (upper abdominal pain, abdominal pain), stomach discomfort (abdominal discomfort), heartburn (dyspepsia), lack of appetite (anorexia),
- lack of energy (fatigue),
- increase in the level of liver enzymes when your blood is tested,
- cough, nasal symptoms,
- hair loss (alopecia),
- pain in the joints (arthralgia), muscle disorders,

- a general feeling of discomfort or illness (malaise), fever, abnormal physical weakness or lack of energy (asthenia),
- decreased phosphate levels (hypophosphataemia),
- feeling of unease, such as worry or fear (anxiety).

Less frequent side effects:

- pain in the muscles (myalgia), disease of the muscles (myopathy),
- “pins and needles” in the hands and feet (peripheral neuropathy),
- increased enzyme levels (serum amylase, AST, ALT),
- increased cholesterol levels in the blood (hypercholesterolaemia) or an increase in a certain type of fat in the blood (hypertriglyceridaemia),
- increased blood sugar levels (hyperglycaemia) or an inability of the body to lower blood sugar levels normally (insulin resistance),
- increased lactate levels in the blood (hyperlactatemia),
- fat redistribution,
- bone pain.

Side effects with unknown frequency:

- sensation of spinning (vertigo).

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

By reporting side effects, you can help provide more information on the safety of VULANTE.

5. How to store VULANTE

Store all medicines out of reach of children

Store at or below 30 °C.

Keep the bottle tightly closed. Protect from moisture.

Keep the desiccant in the container. Do not remove the desiccant.

Keep in original packaging until required for use.

Do not store in a bathroom.

Do not use after the expiry date stated on the label.

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 VULANTE contains

The active substances are 300 mg of tenofovir disoproxil fumarate, 300 mg of lamivudine and dolutegravir sodium equivalent to 50 mg of dolutegravir.

The other ingredients are croscarmellose sodium, lactose monohydrate, macrogol, mannitol, microcrystalline cellulose, polyvinyl alcohol part hydrolysed, povidone, pregelatinised starch, sodium starch glycolate, sodium stearyl fumarate, talc, titanium dioxide.

Contains sugar: Lactose monohydrate 150,4 mg; mannitol 131,38 mg

What VULANTE looks like and contents of the pack

VULANTE is an oval, white film-coated, biconvex tablet marked II0 on one side and plain on the other side, free from cracking, peeling or chipping.

Pack size of 28, 30 or 84 tablets packed in a white, round, high density polyethylene bottle with a silica gel desiccant and closed with a white polypropylene cap with heat seal liner. The bottle may be packed in an outer cardboard carton.

Holder of Certificate of Registration

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912

This leaflet was last revised in:

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Registration number

53/20.2.8/0082

Access to the corresponding Professional Information

SAHPRA Repository of Professional Information and Patient Information

Leaflets:

https://www.sahpra.org.za/pi-pil-repository/

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

Tel: 0800 118 088

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