Patient Information Leaflet

SCHEDULING STATUS: **S4**

ALUVIA ™ 200/50 film-coated tablets

(Lopinavir 200 mg / Ritonavir 50 mg)

"Sugar free"

Read all this leaflet carefully before you start taking ALUVIA

- 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.
- ALUVIA 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 ALUVIA is and what it is used for
2. What you need to know before you take ALUVIA
3. How to take ALUVIA
4. Possible side effects
5. How to store ALUVIA
6. Contents of the pack and other information

1. WHAT ALUVIA is and what it is used for

ALUVIA film-coated tablets contain 200 mg of lopinavir and 50 mg of ritonavir.

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ALUVIA is an inhibitor of the human immunodeficiency virus (HIV) protease enzyme. It helps control HIV infection by inhibiting or interfering with the protease enzyme that HIV needs to multiply.

ALUVIA is used by adults and children with a body surface area of 1,3 m^2 or greater who are infected with HIV, the virus which causes AIDS. Your doctor has prescribed ALUVIA to help control your HIV infection.

ALUVIA is prescribed for use in combination with other antiviral medicines. Your doctor will determine which medicines are best for you.

2. What you need to know before you take Aluvia

Do not take ALUVIA

- If you are allergic (hypersensitive) to lopinavir, ritonavir or to any of the other ingredients of Aluvia (listed in section 6).
- If you have severe liver problems.

If you are currently taking any of the following medicines:

- Alfuzosin (used in men to treat symptoms of enlarged prostate)
- Apalutamide (used for prostate cancer)
- Amiodarone, dronedarone (used to correct irregular heartbeat)
- Astemizole (used to treat allergy symptoms – this medicine may be available without prescription)
- Avanafil or vardenafil (used to treat erectile dysfunction)
- Blonanserin (used to treat psychosis)

- Cisapride (used to relieve certain stomach problems)
- Colchicine (medicine used to treat gout) - if you have kidney and/or liver problems
- Elbasvir/grazoprevir (used to treat chronic hepatitis C virus [HCV])
- Ergotamine, dihydroergotamine, ergonovine, methylergonovine (used to treat headaches)
- Lomitapide- (used to lower blood cholesterol)
- Lovastatin, Simvastatin (used to treat high blood cholesterol)
- Lurasidone (used to treat depression)
- Midazolam, triazolam (used to relieve anxiety and/or trouble sleeping)
- Neratinib (used to treat breast cancer)
- Ombitasvir/paritaprevir /ritonavir with or without dasabuvir (used to treat chronic hepatitis C virus)
- Pimozide (used to treat schizophrenia)
- Quetiapine (used to treat schizophrenia, bipolar disorder and major depressive disorder)
- Salmeterol (used to treat asthma)
- Ranolazine (used to treat chronic chest pain [angina])
- Sildenafil, tadalafil and vardenafil (for the treatment of pulmonary arterial hypertension)

- Patients taking ALUVIA must not take products containing St John's Wort *(Hypericum perforatum)* as this may stop ALUVIA from working properly.

If you are currently taking any of these medicines, ask your doctor about switching to another medicine while you are taking ALUVIA.

Warnings and precautions

Talk to your doctor or pharmacist before taking ALUVIA:

- ALUVIA is not a cure for HIV infection or AIDS. People taking ALUVIA may still develop infections or other illnesses associated with HIV disease and AIDS. It is therefore important that you remain under the supervision of your doctor while taking ALUVIA.
- ALUVIA does not reduce the risk of passing HIV to others through sexual contact or blood contamination. You should use appropriate precautions.

- In some patients with advanced HIV infection (AIDS) and a history of opportunistic infection, signs and symptoms of inflammation from previous infections may occur soon after anti-HIV treatment is started. It is believed 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. If you notice any symptoms or infection, please inform your doctor immediately.

- If you have a history of liver disease, please speak with your doctor. Patients with chronic hepatitis B or C and treated with antiretroviral medicines are at increased risk for severe and potentially fatal liver adverse events and may require blood tests for control of liver functions.

- Autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking ALUVIA 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.
- Symptoms of dizziness, lightheadedness, fainting or sensation of abnormal heartbeats. ALUVIA may cause changes in your heart rhythm and the electrical activity of your heart. These changes may be seen on an ECG (electrocardiogram).
- Joint stiffness, aches and pains (especially of the hip, knee and shoulder) and difficulty in movement as some of the patients taking these medicines 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 (reduction in the activity of the immune system), higher body mass index, among others, may be some of many risk factors for the developing this disease.

Other medicines and ALUVIA

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

If you are taking certain other medicines. ALUVIA may interact with certain other medications with possible clinical effects.

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The use of the following medicines together with ALUVIA should only take place on the basis of medical advice:

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines

- Antibiotics: Clarithromycin, rifabutin, rifampicin
- Abemaciclib – used to treat breast cancer
- Anticancer medicines: abemaciclib, afatinib, Ceritinib, ibrutinib Dasatinib, nilotinib, venetoclax, vincristine and vinblastine
- Antidepressants: Trazodone, bupropion
- Anti-tuberculosis: Bedaquiline, delamanid
- Heart medicines including:
    - Digoxin
    - calcium channel antagonists (e.g. felodipine, nifedipine, nicardipine);
    - Medicine used to correct the heart rhythm: Bepridil, systemic lidocaine (lignocaine), quinidine, amiodarone, dronedarone
- Ombitasvir/paritaprevir/ritonavir with or without dasabuvir, Boceprevir, Simeprevir and Telaprevir: antiviral medicines used to treat chronic hepatitis C virus in adults
- Fentanyl: Pain relieving medicine
- Quetiapine: used to treat schizophrenia, bipolar and major depression
- HIV CCR5-antagonist (e.g. maraviroc)
- Anti-epilepsy medicines (e.g. carbamazepine, phenytoin, phenobarbital, lamotrigine and valproate)
- Antifungals (e.g. ketoconazole, itraconazole, voriconazole)

- Elagolix (used for moderate to severe pain associated with endometriosis)
- Encorafenib (used for skin cancer)
- Fostamatinib (used for low blood platelet count)
- Ivosidenib (used for a type of leukemia)
- Anti-gout medicines (e.g. colchicine). You must not take ALUVIA with colchicine if you have kidney and/or liver problems (see also '**Do not take** ALUVIA' above)
- Various steroids (dexamethasone, fluticasone propionate, ethinyl oestradiol, budesonide, triamcinolone)
- protease inhibitors (e.g. fosamprenavir, indinavir, ritonavir, saquinavir, tipranavir)
- Antiparasitic (Atovaquone)
- Medicines used to lower blood cholesterol (e.g. atorvastatin, lovastatin, rosuvastatin or simvastatin)
- Medicines affecting the immune system (e.g. ciclosporin, sirolimus (rapamycin), tacrolimus)
- morphine-like medicines (e.g. methadone)
- Medicines used for smoking cessation (e.g. bupropion)
- Non -nucleoside reverse transcriptase inhibitors (NNRTI's) (e.g. efavirenz, nevirapine)
- Levothyroxine (used to treat thyroid problems).
- HIV-1 integrase inhibitor (e.g. Raltegravir)

- ALUVIA may interact with dabigatran etexilate, edoxaban, warfarin and rivaroxaban (medicines used to prevent blood clots) and may cause bleeding.
- ALUVIA may interact antiviral medicines used to treat chronic hepatitis C virus infection in adults (boceprevir, simeprevir, telaprevir, glecaprevir/pibrentasvir,

sofosbuvir/velpatasvir/voxilaprevir, ombitasvir/paritaprevir/ritonavir with or without dasabuvir).

- ALUVIA may interact with erectile dysfunction medicines and used to treat pulmonary hypertension (e.g. sildenafil, tadalafil, vardenafil). Your doctor should prescribe lower doses of these medicines if you are also taking ALUVIA. If you are taking sildenafil, tadalafil or vardenafil with ALUVIA talk to your doctor about possible interactions with other medicines and side-effects. If you take sildenafil, tadalafil or vardenafil and ALUVIA together, you may be at risk of side effects such as low blood pressure, passing out, visual changes and penile erection lasting more than 4 hours. If an erection lasts longer than 4 hours, you should get medical help immediately to avoid permanent damage to your penis. Your doctor can explain these symptoms to you.

- ALUVIA may interact with medicines to treat pulmonary arterial hypertension (bosentan).

- ALUVIA may interact with bedaquiline (tuberculosis medicine) and delamanid (used for treatment of multi-drug-resistant tuberculosis).

- ALUVIA may interact with digoxin (heart medicine). Your doctor should monitor you if you are taking digoxin and ALUVIA.

- If you are taking certain medicines with ALUVIA it may result in increased levels in the body of these other medicines and could increase or prolong their effect and/or adverse reactions. You must tell your doctor about all the medicines, including those

medicines you can buy without a prescription, you are taking or are planning to take before you take ALUVIA. This is because taking ALUVIA with some medicines can result in serious or life-threatening problems.

- If you are taking an oral contraceptive or using a patch contraceptive to prevent pregnancy, you should use an additional or different type of contraception since ALUVIA may reduce the effectiveness of oral and patch contraceptives.

- Talk to your doctor if you are taking or are planning to take fluticasone propionate. Taking fluticasone propionate or triamcinolone with ALUVIA, can increase the levels of fluticasone or triamcinolone in your blood and could cause serious side effects.
- ALUVIA can be taken with acid reducing medicines (such as omeprazole and ranitidine) with no dose adjustment.

You should not take any medicines, which you obtain without a prescription i.e. over-the-counter (OTC), or medicine-like products without consulting your doctor. Inform any doctor who prescribes medicine for you that you are taking ALUVIA.

Taking ALUVIA with food and drink and alcohol

Refer to section 3" **How to take ALUVIA"**

Pregnancy and breastfeeding and fertility

Pregnant or breastfeeding mothers should not take ALUVIA. Be sure to tell your doctor immediately if you are or may be pregnant or if you are breastfeeding your baby. It is

recommended that HIV-infected women should not breastfeed their infants because of the possibility that your baby can be infected with HIV through your breast milk.

If you are pregnant or breastfeeding your baby while taking ALUVIA, please consult your doctor, pharmacist, or other healthcare professional for advice.

If you are taking an oral contraceptive or using patch contraceptive to prevent pregnancy, you should use an additional or different type of contraception since ALUVIA may reduce the effectiveness of oral and patch contraceptives.

Driving and using machines

ALUVIA has not specifically been tested for its possible effects on the ability to drive a car or operate machines. Do not drive a car or operate machinery if you experience any side effects (e.g. nausea) that impact your ability to do so safely. Instead, contact your doctor.

3. HOW TO TAKE ALUVIA

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

For medicines available on prescription only:

Always take ALUVIA exactly the way your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

It is important that you take ALUVIA every day exactly as your doctor prescribed it. Even if you feel better, do not stop taking ALUVIA without talking to your doctor. Using ALUVIA as recommended should give you the best chance to delay the development of resistance to the product.

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Use in adults

- The usual adult dose is 400 mg/100 mg twice a day i.e. every 12 hours, in combination with other anti-HIV medicines.

- Adult patients who have not previously taken other antiviral medicines can also take ALUVIA tablets once daily as an 800 mg/200 mg dose.

- Your doctor will advise on the number of tablets to be taken. Adult patients who have previously taken other antiviral medicines can take ALUVIA tablets once daily as an 800 mg/200 mg dose if their doctor decides it is appropriate.

- ALUVIA must not be taken once daily with efavirenz, nevirapine, carbamazepine, phenobarbital and phenytoin.

- ALUVIA tablets can be taken with or without food.

Use in children

The adult dose of ALUVIA film-coated tablets (two 200/50 mg tablets twice daily) may be used in children with a Body Surface Area (BSA)* greater than 1,3 m^2.

For children, your doctor will decide the right dose (number of tablets) based on the child's height and weight.
ALUVIA should not be given once daily in children.
ALUVIA tablets can be taken with or without food.

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ALUVIA tablets can be taken with or without food. It is important that ALUVIA tablets are swallowed whole and not chewed, broken or crushed.

Do not alter or discontinue the daily dose of ALUVIA without first consulting with your doctor.

ALUVIA should be taken every day exactly as prescribed by your doctor to help control your HIV, no matter how much better you feel. If a side effect is preventing you from taking ALUVIA as directed, tell your doctor right away. Always keep enough ALUVIA on hand so you don't run out. When you travel or need to stay in the hospital make sure you will have enough ALUVIA to last until you can get a new supply.
Continue to take ALUVIA until your doctor tells you otherwise.

If you take more ALUVIA than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take ALUVIA

It is important to take the total daily dose prescribed to ensure you get maximum benefit. If you miss a dose, take the missed dose as soon as possible and then continue as before. However, if a dose is skipped, do not double the next dose. Continue with your normal dose on the regular schedule as prescribed by your doctor.

4. Possible side effects

ALUVIA can have side effects.

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

If any of the following happens, stop taking ALUVIA and tell your doctor immediately or go to 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
- rash or itching

These are all very serious side-effects. If you have them, you may have a serious allergic reaction to ALUVIA. You may need urgent medical attention or hospitalisation.

More frequent:

- diarrhoea;
- nausea;
- upper respiratory tract infection

Frequent:

- vomiting, enlarged abdomen, pain in the lower and upper stomach area, passing wind, indigestion, decreased appetite, reflux from your stomach to your oesophagus which may cause pain- **Tell your doctor** if you experience nausea, vomiting or abdominal pain as these may be suggestive of pancreatitis (inflammation of the pancreas).

- swelling or inflammation of the stomach, intestines and colon
- increased cholesterol levels in your blood, increased triglycerides (a form of fat) levels in your blood, high blood pressure
- decreased ability of the body to handle sugar including diabetes mellitus, weight loss
- low number of red blood cells, low number of white blood cells which are usually used to fight infection
- rash, eczema, accumulation of scales of greasy skin
- dizziness, anxiety, difficulty in sleeping
- feeling tired, lack of strength and energy, headache including migraine
- haemorrhoids
- inflammation of the liver including increased liver enzymes
- allergic reactions including hives and inflammation in the mouth
- lower respiratory tract infection
- enlargement of the lymph nodes
- impotence, abnormally heavy or extended menstrual flow or a lack of menstruation
- muscle disorders such as weakness and spasms, pain in the joints, muscles and back
- damage to nerves of the peripheral nervous system
- night sweats, itching, rash including raised bumps on the skin, infection of the skin
- inflammation of skin or hair pores, accumulation of fluid in the cells or tissues

Less frequent:

- abnormal dreams
- loss or changed sense of taste

- hair loss
- an abnormality in your electrocardiogram (ECG) called atrioventricular block
- plaque building up inside your arteries which could lead to heart attack and stroke
- abnormal closure of one of the valves (tricuspid valve in your heart)
- inflammation of blood vessels and capillaries
- inflammation of the bile duct
- constipation
- deep vein inflammation related to a blood clot
- dry mouth
- inability to control your bowels
- inflammation of the first section of the small intestine just after the stomach, wound or ulcer in the digestive tract, bleeding from the intestinal tract or rectum
- red blood cells in the urine
- fatty deposits in the liver, enlarged liver
- inflammation of the bile duct
- abnormally high level of bilirubin (a pigment produced from the breakdown of red blood cells) in the blood
- a flare-up of symptoms related to an inactive infection in your body (immune reconstitution)
- increased appetite; Weight gain.
- decreased sexual desire
- inflammation of the kidney; kidney failure;
- bone death caused by poor blood supply to the area
- mouth sores or ulcerations, inflammation of the stomach and intestine

- breakdown of muscle fibers resulting in the release of muscle fiber contents (myoglobin) into the bloodstream;
- a sound in one ear or both ears, such as buzzing, ringing or whistling;
- vertigo (spinning feeling);
- eye disorder, abnormal vision
- tremor
- uncontrolled shaking of the body

Side effects where frequency is not known:

- yellowing of the skin and/or white of the eyes, also called jaundice
- Severe or life-threatening skin rashes and blisters (Stevens-Johnson syndrome and erythema multiforme).
- Kidney stones

Combination antiretroviral therapy, including ALUVIA, may cause changes in body shape due to changes in fat distribution. These may include loss of fat from legs, arms and face, increased fat in the abdomen (belly) and other internal organs, breast enlargement and fatty lumps on the back of the neck ('buffalo hump'). The cause and long-term health effects of these conditions are not known at this time.

Combination antiretroviral therapy, including ALUVIA, may also cause raised lactic acid and sugar in the blood, hyperlipaemia (increased fats in the blood) and resistance to insulin. The long-term risks for complications such as heart attacks or stroke due to

increases in triglycerides and cholesterol are not known at this time. Your doctor will monitor you and may prescribe other medicines if needed.

In addition, large increases in the number of triglycerides (fats in the blood) have also been considered a risk factor for pancreatitis. Pancreatitis should be considered if you experience clinical symptoms (nausea, vomiting, abdominal pain), which may be suggestive of this condition. If you experience these symptoms, tell your doctor.

In patients with haemophilia type A and B, there have been reports of increased bleeding while taking this treatment or another protease inhibitor. Should this happen to you, seek immediate advice from your doctor.

Cases of diabetes mellitus or increased blood sugars have been reported in patients receiving ALUVIA.

Abnormal liver function tests, hepatitis and jaundice, have been reported in patients taking ALUVIA. Some people had other illnesses or were taking other medicines. People with pre-existing liver disease or hepatitis may have worsening of liver disease.

There have been reports of muscle pain, tenderness or weakness, particularly in combination with antiretroviral therapy including protease inhibitors and nucleoside analogues. On occasions these muscle disorders have been serious (rhabdomyolysis).

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

Healthcare professionals, patients and caregivers are also asked to report any suspected adverse reaction to AbbVie (Pty) Ltd via this e-mail address: MEAPV@abbvie.com

5. How to store ALUVIA

ALUVIA film-coated tablets do not require any special storage conditions. Store at room temperature (below 30 ºC) in its original package. Do not transfer it to any other container.

Keep ALUVIA out of the reach and sight of children.

Do not keep medicine that is out of date or that you no longer need. Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets). Be sure that if you throw any medicine away, it is out of reach of children.

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6. Contents of the pack and other information

What ALUVIA contains

ALUVIA film-coated tablets contain 200 mg of lopinavir and 50 mg of ritonavir.

Other ingredients include copovidone, sorbitan laurate, colloidal anhydrous silica, sodium stearyl fumarate, hypromellose, titanium dioxide, macrogols type 400, hydroxypropyl cellulose, talc, macrogols type 3350, red ferric oxide E172 and polysorbate 80.

What ALUVIA looks like and contents of the pack

ALUVIA tablets are red film-coated tablets embossed with the code '**AL**' on one side.

ALUVIA film-coated tablets come in a white plastic bottle containing 112 tablets.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

For the professional information please email medicalinfo.za@abbvie.com

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