PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: **S4**

ALUVIA 100/25 ™ Film-coated Tablets

(Lopinavir 100 mg / Ritonavir 25 mg)

"Sugar free"

Read all this leaflet carefully before you start taking ALUVIA 100/25

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- ALUVIA 100/25 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 100/25 is and what it is used for
2. What you need to know before you or your child take Aluvia 100/25
3. How to take Aluvia 100/25
4. Possible side effects
5. How to store Aluvia 100/25
6. Contents of the pack and other information

1. WHAT ALUVIA 100/25 is and what it is used for

ALUVIA 100/25 film-coated tablets contain 100 mg of lopinavir and 25 mg of ritonavir

PATIENT INFORMATION LEAFLET

ALUVIA 100/25 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 100/25 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 100/25 to help control your HIV infection.

ALUVIA 100/25 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 100/25

Do not take Aluvia 100/25:

- If you are allergic (hypersensitive) to lopinavir, ritonavir or to any of the other ingredients of Aluvia 100/25 (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)
  - Astemizole (used to treat allergy symptoms – this medicine may be available without prescription).
  - 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

- Amiodarone, dronedarone (used to correct irregular heartbeat)
- Ergotamine, dihydroergotamine, ergonovine, methylergonovine (used to treat headaches)
- Elbasvir/grazoprevir (used to treat chronic hepatitis C virus [HCV])
- Fusidic acid (used to treat bacterial infection)
- HMG – CoA Reductase Inhibitors:- Lovastatin, simvastatin, rosuvastatin, atorvastatin (used to treat high blood cholesterol)
- Lomitapide- (used to lower 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])
- PDE5 inhibitors: sildenafil, tadalafil and vardenafil (for the treatment of pulmonary arterial hypertension)
- Avanafil or vardenafil (used to treat erectile dysfunction)

- Patients taking ALUVIA 100/25 must not take products containing St John's Wort *(Hypericum perforatum)* as this may stop ALUVIA 100/25 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 100/25.

Warnings and precautions

Talk to your doctor or pharmacist before taking **ALUVIA 100/25**:

- ALUVIA 100/25 is not a cure for HIV infection or AIDS. People taking ALUVIA 100/25 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 100/25.

- ALUVIA 100/25 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 100/25 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 100/25 may cause changes in your heart rhythm and the electrical activity of your heart. These changes may be seen on an ECG (electrocardiogram).
- Combination antiretroviral therapy, including ALUVIA 100/25, may also cause raised lactic acid and sugar in the blood, hyperlipidaemia (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 amount 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.

- 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 100/25

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 100/25 may interact with certain other medicines with possible clinical effects. The use of the following medicines together with ALUVIA 100/25 should only take place based on medical advice:
    - Certain antibiotics (e.g. rifampicin, rifabutin, clarithromycin).
    - Abemaciclib – used to treat breast cancer
    - Anticancer medicine (e.g abemaciclib, afatinib, ceritinib, ibrutinib, nilotinib, dasatinib, venetoclax, vincristine, vinblastine).
    - Anticoagulants - medicines used to prevent blood clots (e.g. warfarin, rivaroxaban) and may cause bleeding.
    - Antidepressants (e.g. bupropion, trazodone)
    - 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)
- Medicines used to lower blood cholesterol (e.g. lovastatin, simvastatin, rosuvastatin or atorvastatin)
- Some medicines affecting the immune system (e.g. ciclosporin, sirolimus, rapamycin, tacrolimus)
- Various steroids (e.g. budesonide, dexamethasone, fluticasone propionate, ethinyl oestradiol, triamcinolone)
- Other protease inhibitors (fosamprenavir, indinavir, ritonavir, saquinavir, tipranavir)
- certain heart medicines such as calcium channel antagonists (e.g. felodipine, nifedipine, nicardipine)
- Medicines used to correct heart rhythm (e.g. amiodarone, bepridil, systemic lidocaine (lignocaine), quinidine)
- Morphine-like medicines (e.g. methadone)
- pain tablets (e.g. fentanyl)
- other antiretrovirals (maraviroc)
- Antiviral medicines used to treat chronic hepatitis C virus infection in adults (boceprevir, simeprevir, telaprevir, glecaprevir/pibrentasvir and sofosbuvir/velpatasvir/voxilaprevir)

  HIV-1 integrase inhibitor (e.g. Raltegravir)
- Levothyroxine (used to treat thyroid problems)

- Medicines used for smoking cessation (e.g. Bupropion)
- Non -nucleoside reverse transcriptase inhibitors (NNRTI's) (e.g. efavirenz, nevirapine)
- Sedatives (midazolam administered by injection)
- Antiviral medicines used to treat chronic hepatitis C virus infection (ombitasvir/paritaprevir/ritonavir with or without dasabuvir)
- ALUVIA 100/25 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 100/25.
- ALUVIA 100/25 may interact with medicines to treat pulmonary arterial hypertension (bosentan)
- ALUVIA 100/25 may interact with bedaquiline (tuberculosis medicine) and delamanid (used for treatment of multi-drug-resistant tuberculosis)
- ALUVIA 100/25 may interact with digoxin (heart medicine). Your doctor should monitor you if you are taking digoxin and ALUVIA 100/25.

- 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 100/25 may reduce the effectiveness of oral contraceptives.

- If you are taking certain medicines with ALUVIA 100/25 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 100/25. This is because taking

ALUVIA 100/25 with some medicines can result in serious or life-threatening problems.

ALUVIA 100/25 may interact with other medicines, including those you take without prescription. It is possible that your doctor may increase or decrease the dose of other medicines when you are also taking ALUVIA 100/25. You should tell your doctor about any medicines, including those medicines you can buy without a prescription; you are taking, or planning to take, before you take ALUVIA 100/25. See Section 3, before you take ALUVIA 100/25, for further information.

- ALUVIA 100/25 can be taken with acid reducing medicines (such as omeprazole and ranitidine) with no dose adjustment.
- If you are taking sildenafil, tadalafil or vardenafil with ALUVIA 100/25 talk to your doctor about possible interactions with other medicines and side-effects. If you take sildenafil, tadalafil or vardenafil and ALUVIA 100/25 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. Do not take ALUVIA 100/25 if you are currently taking avanafil or vardenafil.
- 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 100/25 may reduce the effectiveness of oral and patch contraceptives.

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 100/25.

ALUVIA 100/25 with food and drink and alcohol

Refer to section 3 (below)

Pregnancy and breastfeeding and fertility

Pregnant or breastfeeding mothers should not take ALUVIA 100/25. 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 100/25, please consult your doctor, pharmacist or other healthcare professional for advice.

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 100/25 may reduce the effectiveness of oral and patch contraceptives.

Driving and using machinery

ALUVIA 100/25 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 100/25

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

Always take ALUVIA 100/25 exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

It is important that you take ALUVIA 100/25 every day exactly as your doctor prescribed it. Even if you feel better, do not stop taking ALUVIA 100/25 without talking to your doctor. Using ALUVIA 100/25 as recommended should give you the best chance to delay the development of resistance to the product.

Your doctor or pharmacist will advise on the number of tablets to be taken.

The recommended oral dose of ALUVIA 100/25 film-coated tablets are as follows:

Use in adults

- ALUVIA 100/25 film-coated tablets adult usual dose is 400/100 mg twice daily (i.e. every 12 hours), in combination with other antiretroviral medicines.
- Alternatively, ALUVIA 100/25 film-coated tablets may be dosed as 800/200 mg) once daily.

ALUVIA 100/25 must not be taken once daily with efavirenz, nevirapine, carbamazepine, phenobarbital and phenytoin.

Use in children

Aluvia 100/25 should not be given once daily in children.

The doctor will decide the correct dose (i.e. number of tablets) based on the child's height and weight.

Paediatric Dosing Guidelines Based on Body Surface Area (without concomitant efavirenz, nevirapine, nelfinavir or amprenavir)	
Body Surface Area (m^2)	**Recommended number of ALUVIA 100/25 Tablets**
≥ 0,6 to < 0,9	2 tablets (200/50 mg) twice daily with or without food
≥ 0,9 to < 1,4	3 tablets (300/75 mg) twice daily with or without food
≥ 1,4	4 tablets (400/100 mg) twice daily with or without food

The following table contains dosing guidelines for **ALUVIA 100/25** tablets based on body weight.

Paediatric Dosing Guidelines Based on Body Weight (without concomitant efavirenz, nevirapine Nelfinavir or Amprenavir)		
Weight (kg)	**Dose (mg/kg) ***	**Number of ALUVIA 100/25 tablets**
7 kg to < 15 kg	12 mg/kg twice daily	Tablets are not recommended. This formulation is not suitable for children weighing less than 15 kg use oral solution.
15 kg to 40 kg	10 mg/kg twice daily	

Paediatric Dosing Guidelines Based on Body Weight (without concomitant efavirenz, nevirapine Nelfinavir or Amprenavir)		
Weight (kg)	**Dose (mg/kg) ***	**Number of ALUVIA 100/25 tablets**
15 kg to 25 kg		2 tablets (200/50 mg) twice daily with or without food
> 25 kg to 35 kg		3 tablets (300/75 mg) twice daily with or without food
> 35 kg to 40 kg		4 tablets (400/100 mg) twice daily with or without food
> 40 kg	400 mg twice daily	4 tablets (400/100 mg) twice daily with or without food

* dosing based on the lopinavir component of lopinavir/ritonavir solution (80 mg lopinavir / 20 mg ritonavir per mL)

ALUVIA 100/25 tablets can be taken with or without food.

It is important that ALUVIA 100/25 tablets are swallowed whole and not chewed, broken or crushed.

If you take more ALUVIA 100/25 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 100/25

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.

If you stop taking ALUVIA 100/25

ALUVIA 100/25 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 100/25 as directed, tell your doctor right away. Always keep enough ALUVIA 100/25 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 100/25 to last until you can get a new supply.
Continue to take ALUVIA 100/25 until your doctor tells you otherwise.

4. Possible side effects

ALUVIA 100/25 can have side effects.
Not all side effects reported for ALUVIA 100/25 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop taking ALUVIA 100/25 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 100/25. 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 100/25, 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.

Cases of diabetes mellitus or increased blood sugars have been reported in patients receiving ALUVIA 100/25.

Abnormal liver function tests, hepatitis and jaundice have been reported in patients taking ALUVIA 100/25. 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 "**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 **ALUVIA 100/25**.

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 100/25

Keep ALUVIA 100/25 out of the reach and sight of children.

ALUVIA 100/25 film-coated tablets do not require any special storage conditions.

Store at or below room temperature (below 30 ºC) in its original package. Do not transfer it to any other container.

Do not use after the expiry date 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). Be sure that if you throw any medicine away, it is out of reach of children.

6. Contents of the pack and other information

What Aluvia 100/25 contains

The active substances are lopinavir and ritonavir.

Each tablet of Aluvia contains 100 mg of lopinavir and 25 mg of ritonavir

The other ingredients include copovidone, sorbitan laurate, colloidal anhydrous silica, sodium stearyl fumarate, polyvinyl alcohol, titanium dioxide, talc, macrogols type 3350 (polyethylene glycol 3350) and red ferric oxide E172.

What Aluvia 100/25 looks like and contents of the pack

ALUVIA 100/25 tablets are pale pink film-coated tablets embossed with the debossed with '**AC**' on one side·

ALUVIA 100/25 film-coated tablets come in a white plastic bottle containing 60 or 56 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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