PATIENT INFORMATION LEAFLET FOR AEDATRI

SCHEDULING STATUS: S4

AEDATRI film-coated tablets

Lamivudine 300 mg, tenofovir disoproxil fumarate 300 mg and dolutegravir 50 mg.

Contains sugar: mannitol 145 mg.

Read all of this leaflet carefully before you start taking AEDATRI

- 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.
- AEDATRI 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

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1. What AEDATRI is and what it is used for

AEDATRI is an antiviral medicine.

AEDATRI tablets are used to treat human immunodeficiency virus-1 (HIV-1) infected adults over 18 years of age.

WARNING

TOO MUCH ACID IN THE BODY DUE TO LACTIC ACID AND SERIOUS ENLARGED, FATTY LIVER, INCLUDING CASES RESULTING IN DEATH, HAVE BEEN REPORTED WITH THE USE OF NUCLEOSIDE ANALOGUES (MEDICINES USED FOR THE TREATMENT OF HIV) ALONE OR IN COMBINATION WITH OTHER ANTIRETROVIRALS (SEE WARNINGS AND PRECAUTIONS). AEDATRI IS NOT INDICATED FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF AEDATRI HAS NOT BEEN ESTABLISHED IN PATIENTS INFECTED WITH BOTH HBV AND HIV. SEVERE ACUTE WORSENING OF HEPATITIS B HAS BEEN REPORTED IN PATIENTS WHO ARE INFECTED WITH BOTH HBV AND HIV AND HAVE STOPPED TAKING THE COMBINATION TABLET. LIVER FUNCTION SHOULD BE MONITORED CLOSELY BY A HEALTH CARE PRACTITIONER FOR AT LEAST SEVERAL MONTHS IN PATIENTS WHO ARE INFECTED WITH BOTH HIV AND HBV AND WHO STOPPED TAKING THE COMBINATION TABLET. IF APPROPRIATE, MEDICINE TO TREAT HEPATITIS B MAY NEED TO BE PRESCRIBED (SEE WARNINGS AND PRECAUTIONS).

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2. What you need to know before you take AEDATRI

Do not take AEDATRI:

- If you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir disoproxil fumarate, or any of the ingredients of AEDATRI (listed in **section 6**).
- If you have kidney failure.
- If you have liver disease.
- If you are pregnant or breastfeeding your baby.
- If you plan on becoming pregnant.
- If you are a woman of childbearing age and not using effective contraceptives to prevent falling pregnant.
- If you are also taking heart medication for irregular heartbeat containing dofetilide and pilsicainide.
- If you are taking metformin, for the treatment of type 2 diabetes.
- If you are taking chronic medication for hepatitis B infection, containing adefovir dipivoxil.
- If you are taking other anti-retroviral medicines containing didanosine.
- If you are younger than 18 years of age.

Warnings and precautions

Take special care with AEDATRI:

Tell your doctor:

- If you develop a rash, or show any general signs of allergy (rash, accompanied by fever, general feeling of being ill, tiredness, muscle or joint

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aches, sores, oral scrapes, eye infection, facial swelling, a serious liver infection or swelling of the skin).

- If you develop changes in body fat, as changes have been seen in some patients taking AEDATRI and other anti-HIV medicines. These changes may include increased amount of fat in the upper back and neck (“buffalo hump”), breast, and around the main part of your body (trunk). Loss of fat from the legs, arms and face may also happen. The cause and long-term health effect of these conditions are not known at this time.
- If you show any symptoms of infection while you are taking AEDATRI**.** People with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (opportunistic infections). When these people start with the treatment, they may find that old hidden infections (such as tuberculosis) flare up, causing signs and symptoms of inflammation (such as localised swelling, area appears red and hot, painful). These symptoms are probably caused by the body’s immune system becoming stronger, so that the body starts to fight these infections.
- If you have abnormal metabolic processes, such as increased cholesterol, glucose or lactate in the blood, or are resistant to insulin. Your healthcare professional may perform regular blood tests to confirm normal metabolic processes.
- If you have liver problems including hepatitis B virus (HBV) infection.
- If you show signs of liver injury.
- If you show symptoms such as nausea, vomiting, abdominal pain, non-specific general feeling of being ill, loss of appetite, weight loss, rapid

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and/or deep breathing, or muscle weakness.

- If you are female, very overweight (obese), or have been using medicines for the treatment of HIV for a long time as you may be more likely to get lactic acidosis (build-up of lactic acid in the body) (see **Possible side effects**).
- If you suffer from kidney disease.
- If you experience pain in the stomach, as this can be a symptom of pancreatitis (swelling of the pancreas) (see **Possible side effects**).
- If you suffer from liver disease including hepatitis B or C, as the use of antiviral medicine can cause fatal unfavourable liver symptoms. Your doctor will monitor your liver enzymes as AEDATRI can cause liver toxicity.
- If your child experiences symptoms of poor growth, loss of muscle coordination, muscle weakness, visual problems, hearing problems, learning disabilities, heart disease, liver disease, kidney disease, gastrointestinal disorders, respiratory disorders, nervous system problems (brain, spine and nerves), loss of voluntary body functions (such as breathing, bladder function, heartbeat and digestive processes) and dementia (loss of memory) it can be a sign of mitochondrial (part of the cell that creates energy) disorder. These findings should be considered for any child exposed to treatment, before being born.
- 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 help your bone mineral density.
- If you experience joint aches and pain, joint stiffness or difficulty in

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movement, you may suffer from osteonecrosis.

- If you are elderly and suffer from kidney or liver damage or failure.
- If you have a history of depression or mental illness as AEDATRI may cause depression and suicidal thoughts.

AEDATRI should be used with caution in the elderly (65 years and over), due to decreased liver and kidney function.

AEDATRI should not be taken with other medicines containing any of the active ingredients, namely: dolutegravir, lamivudine or tenofovir disoproxil fumarate (see **Other medicines and AEDATRI**).

AEDATRI does not reduce the risk of passing HIV to others through sexual contact or blood contamination. Therefore, it is important to continue to take appropriate precautions to prevent passing HIV to others.

Even if you are receiving treatment for HIV, you are still at risk of contracting other infections and other complications of the HIV infection. Therefore, you should remain under close observation by your doctor.

Other medicines and AEDATRI

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

If you are taking any of the following medicines, please inform your doctor

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before taking AEDATRI:

- Other products that contain dolutegravir, lamivudine or tenofovir, either alone or as combined formulations. AEDATRI should not be used with these medicines because they contain the same or similar active ingredients as AEDATRI.
- Rifampicin, used for treatment of tuberculosis, can decrease blood concentrations of AEDATRI.
- AEDATRI can increase blood concentrations of metformin (for the treatment of type 2 diabetes), when used simultaneously.
- Other medicines used for the treatment of HIV infections that decrease AEDATRI levels include efavirenz, nevirapine, ritonavir, tipranavir.
- AEDATRI can increase levels of the following heart medicine for the treatment of irregular heartbeat – dofetilide and pilsicainide.
- AEDATRI can increase blood concentration levels of isoniazid used for treatment of tuberculosis.
- Certain antacids can also decrease AEDATRI levels, that contain for example magnesium, aluminium or calcium.
- AEDATRI must be taken 2 hours before or 6 hours after taking products containing magnesium, calcium, iron or aluminium.
- AEDATRI may hinder the breakdown of zalcitabine, also used in the treatment of HIV infections.
- Taking AEDATRI in combination with high doses of co-trimoxazole or trimethoprim (used for the treatment of bacterial infections) must be avoided if you have a kidney condition or disease.

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- The use of AEDATRI with etravirine for HIV infections is not recommended.
- Medicines that can cause toxicity in the kidneys, for example antibiotics e.g., vancomycin, aminoglycosides (gentamycin, amikacin, tobramycin, neomycin), antifungals, e.g., amphotericin B, antivirals, e.g., foscarnet, ganciclovir, antimicrobials, e.g., pentamidine.
- AEDATRI increases the levels of atazanavir (also used for the treatment of HIV infection) and may need to be adjusted.
- Phenobarbitone, phenytoin, oxcarbazepine, carbamazepine and St. John's Wort decrease levels of AEDATRI.
- AEDATRI increases levels of abacavir used in the treatment of HIV and may need to be adjusted.
- AEDATRI is not affected and does not influence the levels of emtricitabine, lopinavir and ritonavir used in the treatment of HIV.
- AEDATRI is not affected and does not change levels of methadone, used in the treatment of opioid abuse.
- Combination medicines for treatment of HIV containing fosamprenavir and ritonavir, or darunavir and ritonavir decrease levels of AEDATRI.
- Medicines containing ribavirin used in the treatment of hepatitis B, is not affected and does not alter the levels of AEDATRI.

Pregnancy, breastfeeding and fertility

AEDATRI is contraindicated in pregnancy and breastfeeding.

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If you are a woman who is able to have children, you should be counselled about the potential risk of neural tube defects with dolutegravir.

A pregnancy test should be performed before you start taking AEDATRI, if you are able to bear children, to exclude the unintentional use of AEDATRI during the first trimester of pregnancy.

If you plan on becoming pregnant, your doctor will need to discuss the risks and benefits of starting or continuing treatment with AEDATRI versus another medicine regimen.

It should be noted that the use of dolutegravir, as contained in AEDATRI, was associated with a small increase in the likelihood of neural tube defects (birth defects) compared to non-dolutegravir regimens. Most neural tube defects occur within the first 4 weeks of pregnancy which is approximately 6 weeks after your last menstrual cycle (period).

If you are pregnant or breastfeeding your baby, please consult your healthcare professional for advice before taking AEDATRI. You should ensure that you always use effective contraception while you are taking AEDATRI. Your healthcare professional can advise you on which contraceptives to take. Never stop taking AEDATRI without first consulting your healthcare professional as your HIV condition may become worse.

If you are thinking about having a baby, do not stop using AEDATRI and

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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.

Mothers should not breastfeed their infants while taking AEDATRI, to avoid transmission of HIV.

There are no data on the effects of dolutegravir, as contained in AEDATRI, on human male or female fertility. Animal studies indicate no effects of dolutegravir on male or female fertility.

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 AEDATRI.

Driving and using machines

AEDATRI may cause dizziness, impaired concentration, and/or drowsiness. You should not drive or operate machinery until you are sure AEDATRI does not affect your ability to drive or use machines.

It is not always possible to predict to what extent AEDATRI 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 AEDATRI affects them.

AEDATRI contains

AEDATRI contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium free’.

3. How to take AEDATRI

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

AEDATRI therapy should be initiated by a healthcare professional experienced in the management of HIV infections.

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

The usual dose for AEDATRI is one tablet taken orally, once daily, with or without food.

AEDATRI can only be used by adults over the age of 18 years.

Your doctor will tell you how long your treatment with AEDATRI will last. Do not stop treatment early because this may worsen your condition and make your body resistant to the medicine. If you have an impression that the effect of AEDATRI is too strong or too weak tell your doctor or pharmacist.

If you take medicine for tuberculosis containing rifampicin, please consult your healthcare professional (see **Other medicines and AEDATRI**).

If you take more AEDATRI than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is

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available, contact the nearest hospital or poison control centre.

If you forget to take AEDATRI

Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

AEDATRI can have side effects.

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

If any of the following happens, stop taking AEDATRI 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 all very serious side effects. If you have them, you may have had a serious reaction to AEDATRI. 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:

- Pancreatitis (inflammation of the pancreas, which causes severe pain in the abdomen and back).

- Thrombocytopenia (bleeding into the skin, bruising and slow blood clotting after an injury).
- Hepatitis (swelling and inflammation of the liver, characterised by symptoms such as abdominal pain, dark urine and pale or clay-coloured stools, fatigue, fever, general itching, yellowing of the skin or eyes, loss of appetite, nausea and vomiting).
- Thoughts of killing or harming yourself, or attempting to commit suicide.
- Rhabdomyolysis (a condition affecting the muscles with symptoms such as dark urine and difficulty moving arms or legs).
- Kidney failure.
- Lactic acidosis (excess lactic acid in the blood with symptoms including deep, rapid breathing, drowsiness, nausea, vomiting and stomach pain).

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

Tell your doctor if you notice any of the following:

Frequent side effects:

- Hypophosphataemia (electrolyte disorder in which there is a low level of phosphate in the blood, with symptoms that may include weakness, trouble breathing and loss of appetite).
- Insomnia (difficulty sleeping), abnormal dreams, depression, anxiety.
- Headache, dizziness.
- Cough, nasal discharge and congestion.
- Nausea, diarrhoea, vomiting, flatulence, stomach pain or discomfort.
- Skin rash, hair loss, severe itching of the skin.

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- Fatigue, general feeling of being unwell, fever.
- Increased liver enzyme levels.

Less frequent side effects:

- Anaemia (not having enough healthy red blood cells), neutropenia (changes in the white blood cell counts), thrombocytopenia (low platelet count in your blood which is required for blood to clot) and pure red cell aplasia (type of anaemia which affects red blood cells).
- Peripheral neuropathy (damage to nerves outside the spinal cord, affecting the normal functioning of the body's organs and movement and/or feeling of sensation in the extremities, including your arms and legs).
- Dyspnoea (difficulty breathing).
- Increased digestive enzyme (amylase) levels.
- Joint pain, muscle pain.
- Kidney problems including kidney failure.
- Abnormal physical weakness or lack of energy.
- Redistribution of fat around your body.
- Decreased bone density, bone fractures.

Side effects with unknown frequency:

- Hypokalaemia (low blood potassium levels).
- Fatty liver disease (symptoms include weight loss, fatigue and abdominal pain).

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- Bone pain, muscle weakness, experiencing a decrease in height, stooped posture, and easily fractured bone (loss of bone mass).
- Inflammation of the kidney, diabetes insipidus (frequent urination and often feeling thirsty).
- Immune reconstitution syndrome (condition in which the immune system begins to recover but then responds to a previously acquired opportunistic infection with an overwhelming inflammatory response making the symptoms of infection worse).

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 [Ref 3.] or to Cipla Medpro (Pty) Ltd. by e-mail: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free). By reporting side effects, you can help provide more information on the safety of AEDATRI.

5. How to store AEDATRI

Store at or below 30 °C.

Keep the container tightly closed.

Store in the original container until required for use.

Store all medicines out of reach of children.

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Do not store in a bathroom.

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 AEDATRI contains

The active substances are lamivudine 300 mg, tenofovir disoproxil fumarate 300 mg and dolutegravir 50 mg.

The other ingredients are croscarmellose sodium, magnesium stearate, mannitol, microcrystalline cellulose, Insta Moistshield Aqua II A22G21202 (containing polyvinyl alcohol, triacetin, talc, sodium lauryl sulfate, titanium dioxide, FD&C Blue no. 2 aluminium lake, FD&C Blue no. 1 aluminium lake), povidone, sodium starch glycolate.

What AEDATRI looks like and contents of the pack

Blue coloured, capsule shaped, biconvex film-coated tablet, debossed with ‘C’ on one side and plain on other side.

Containers of 28’s:	AEDATRI is packed in a 85 cc white HDPE bottle with 38 mm white non-child resistant cap containing 28 tablets and two 2 g silica gel bags.
Containers of 30’s:	AEDATRI is packed in a 85 cc white HDPE bottle with 38 mm white non-child resistant cap containing

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30 tablets and two 2 g silica gel bags.

Containers of 84's: AEDATRI is packed in a 200 cc white HDPE bottle with 45 mm screw cap containing 84 tablets and five 2 g silica gel bags.

Containers of 90's: AEDATRI is packed in a 200 cc white HDPE bottle with 45 mm screw cap containing 90 tablets and five 2 g silica gel bags.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

CIPLA MEDPRO MANUFACTURING (PTY) LTD.

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Access to the corresponding Professional Information

To access corresponding Professional Information, scan the QR Code below.

PLACE HOLDER:

The QR Code to be generated and included after approval.

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