

PATIENT INFORMATION LEAFLET

Information for the Patient about REYDIN (Film-coated tablets)

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

REYDIN containing lamivudine 300 mg, tenofovir disoproxil fumarate 300 mg and dolutegravir 50 mg (film-coated tablets).

Read all of this leaflet carefully before you start taking REYDIN:

- **Keep this leaflet, you may need to read it again.**
- **If you have further questions, please ask your doctor or pharmacist.**
- **REYDIN 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 REYDIN CONTAINS:

The active ingredients in **REYDIN** are dolutegravir (as dolutegravir sodium), lamivudine and tenofovir disoproxil (equivalent to tenofovir disoproxil fumarate).

The other ingredients are croscarmellose sodium, hydroxypropyl methyl

cellulose, magnesium stearate, mannitol, microcrystalline cellulose, opadry blue (containing polyvinyl alcohol, talc, titanium dioxide, indigo carmine, glycerol esters of fatty acids, sodium lauryl sulfate, brilliant blue aluminum lake), povidone, sodium starch glycolate.

Contains mannitol 145 mg (sugar).

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 “TAKE SPECIAL CARE WITH REYDIN”). REYDIN IS NOT INDICATED FOR TREATMENT OF CHRONIC HEPATITIS B VIRUS (HBV) INFECTION. THE SAFETY AND EFFICACY OF REYDIN HAS NOT BEEN ESTABLISHED IN PATIENTS INFECTED WITH BOTH HBV AND HIV. SEVERE ACUTE WORSENING OF HEPATITIS B HAVE 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 HEPTATITIS B MAY NEED TO BE PRESCRIBED (SEE “TAKE SPECIAL CARE WITH REYDIN”).

WHAT REYDIN IS USED FOR:

REYDIN tablets are used to treat Human Immunodeficiency Virus-1 (HIV-1) infected adults over 18 years of age.

BEFORE YOU TAKE REYDIN

Do not take REYDIN:

- If you are hypersensitive (allergic) to dolutegravir, lamivudine or tenofovir disoproxil fumarate, or any of the ingredients in **REYDIN** (see "**WHAT REYDIN CONTAINS**").
- If you have kidney failure.
- If you have liver disease.
- If you are pregnant or breast feeding your baby.
- If you plan on becoming pregnant.
- If you are a woman of child bearing age and not using effective contraceptives to prevent falling pregnant.
- If you are also taking heart medication for irregular heart beat 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 medicine containing didanosine.
- If you are younger than 18 years of age.

Take special care with REYDIN:

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 aches, sores, oral scrapes, eye infection, facial swelling, a serious liver infection or swelling of the skin.
- If you develop changes in body fat have been seen in some patients taking **REYDIN** 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 **REYDIN**. 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 and/or deep breathing, or muscle weakness.
- If you are female, very overweight (obese), or have been medicines used 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 **REYDIN** can cause liver toxicity.
- If your child experience 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) 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 movement, you may suffer from osteonecrosis.
- If you are elderly and suffer from kidney or liver damage or failure.

REYDIN should not be used in children under the age of 18 years. Safety have not been established (see "**BEFORE YOU TAKE REYDIN**").

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

REYDIN should not be taken with other medicine containing any of the active ingredients, namely: dolutegravir, lamivudine or tenofovir disoproxil fumarate (see "**Taking other medicines with REYDIN**").

REYDIN 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 other.

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.

Pregnancy and breastfeeding:

Do not take **REYDIN** if you are pregnant or breastfeeding. (see "**Do not take REYDIN if**"). **REYDIN** could seriously harm your unborn child if you fall pregnant while on treatment or if you start taking **REYDIN** in the first few weeks

of your pregnancy.

If you are pregnant or breastfeeding your baby, please consult your healthcare professional for advice before taking **REYDIN**. You should ensure that you always use effective contraception while you are taking **REYDIN**. Your healthcare professional can advise you on which contraceptives to take. Never stop taking **REYDIN** 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 **REYDIN** 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.

Mothers should not breastfeed their infants while taking **REYDIN**.

If you are pregnant, planning on becoming pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking REYDIN.

Driving and using machinery:

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

Important information about some of the ingredients of REYDIN:

REYDIN contains mannitol and may have a laxative effect.

Taking other medicines with REYDIN:

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

If you are taking any of the following medicines, please inform your doctor before taking **REYDIN**:

- Other products that contain dolutegravir, lamivudine or tenofovir, either alone or as combined formulations. **REYDIN** should not be used with these medicines because they contain the same or similar active ingredients as **REYDIN**.
- Rifampicin, used for treatment of tuberculosis, can decrease blood concentrations of **REYDIN**.
- **REYDIN** can increase blood concentrations of metformin (for the treatment of Type 2 Diabetes), when used simultaneously.
- Other medicine used for the treatment of HIV infections that decreases **REYDIN** levels includes efavirenz, nevirapine, ritonavir, tipranavir.
- **REYDIN** can increase levels of the following heart medicine for the treatment of irregular heartbeat – dofetilide and pilsicainide.
- **REYDIN** can increase blood concentration levels of isoniazid used for treatment of tuberculosis.

- Certain antacids can also decrease **REYDIN** levels, that contains for example magnesium, aluminium or calcium.
- **REYDIN** must be taken 2 hours before or 6 hours after taking products containing magnesium, calcium, iron or aluminium.
- **REYDIN** may hinder the breakdown of zalcitabine, also used in the treatment of HIV infections.
- Taking **REYDIN** 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.
- The use of **REYDIN** with etravirine for HIV infections is not recommended.
- Medicine that can cause toxicity in the kidneys, for example antibiotics e.g. vancomycin, aminoglycosides (gentamycin, amikacin, tobramycin, neomycin), antifungals, e.g. amphotericin B, antiviral, e.g. foscarnet, ganciclovir, antimicrobials, e.g. pentamidine.
- **REYDIN** 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 decreases levels of **REYDIN**.
- **REYDIN** increases levels of abacavir used in the treatment of HIV and may need to be adjusted.
- **REYDIN** is not affected and does not influence the levels of emtricitabine, lopinavir and ritonavir used in the treatment of HIV.
- **REYDIN** 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 decreases levels of **REYDIN**.
- Medicines used in the treatment of hepatitis B containing adefovir dipivoxil may increase levels of **REYDIN** in the blood especially if you have kidney failure. Whereas medicines containing ribavirin used in the treatment for hepatitis B, is not affected and does not alter the levels of **REYDIN**.
- Medicines that contain didanosine: **REYDIN** may increase the amount of didanosine used for the treatment of HIV in your blood. You may need to be monitored more carefully if you are taking **REYDIN** and didanosine together. The dose of didanosine may also need to be reduced.

HOW TO TAKE REYDIN:

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

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

Always take REYDIN exactly as your healthcare professional has instructed you. You should check with your doctor or pharmacist if you are unsure.

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

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

Your healthcare professional will tell you how long your treatment with **REYDIN** 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 **REYDIN** is too strong or too weak tell your healthcare professional or pharmacist.

If you take medicine for tuberculosis containing rifampicin, please consult your healthcare professional. (see “**Taking other medicines with REYDIN:**”)

If you take more REYDIN than you should:

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

If you forget to take REYDIN:

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

POSSIBLE SIDE EFFECTS:

REYDIN can have side effects.

Not all side effects reported for **REYDIN** 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 you experience any of the following side effects, stop taking **REYDIN** and contact your healthcare professional 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;
- Rash or itching;
- Fainting;
- Yellowing of the skin and eyes, also called jaundice;

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

- Hypersensitivity reactions:
 - Bronchospasm (sudden constriction of the muscles in the walls of the lungs)
 - Fast or irregular breathing
 - Puffiness or swelling around the face
 - Shortness of breath
 - Sudden decrease in blood pressure
- Swelling (inflammation) of the liver (hepatitis), that may include the following symptoms:
 - Fatigue
 - Nausea and vomiting
 - Stomach pain or discomfort, especially in the area of your liver on your right side beneath your lower ribs
 - Clay-coloured bowel movements
 - Loss of appetite

- Low-grade fever
- Dark urine
- Joint pain
- Yellowing of the skin and eyes (jaundice)

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

Tell your healthcare professional if you notice any of the following:

- Neutropenia (an abnormal low concentration of white blood cells).

Symptoms include a

- fever,
 - painful swallowing,
 - gingival pain,
 - skin abscesses
 - painful ears.
- Anaemia (when you have a low red blood cell count). Symptoms include:
 - tiredness,
 - unusually rapid heartbeat,
 - shortness of breath,
 - difficulty concentrating,
 - dizziness,
 - pale skin,
 - leg cramps,
 - sleeplessness.
 - If you have a blood clotting problem, symptoms include:
 - serious bleeding,

- purple, red or brown bruises.
- Patients who take **REYDIN** can develop a serious condition called lactic acidosis/hyperlactataemia (build-up of acid in the blood). Symptoms include:
 - You feel very weak or tired
 - You have unusual (not normal) muscle pain
 - You have trouble breathing
 - You have stomach pain with nausea and vomiting
 - You feel cold, especially in your arms and legs
 - You feel dizzy or light-headed
 - You have a fast or irregular heartbeat.
- You may be more likely to get lactic acidosis or liver problems if you are female, very overweight (obese), or have been taking **REYDIN**, for a long time.
- Red blood cell aplasia (decreased number of red blood cells). Symptoms include:
 - Fatigue.
 - Lethargy.
 - Decreased exercise tolerance.
 - Paleness.
- Lipodystrophy – abnormal distribution or loss of body fat in certain areas such as:
 - Increased waist or breast size.
 - Fat accumulation around neck, jaw or upper back (referred to as “moon face” or “buffalo hump”).

- Loss of fat under the skin, most visibly on the face (especially cheeks), arms and legs.
- Prominent leg veins due to loss of fat under the skin.
- Thrombocytopenia (low levels of platelets (clotting agents in your blood)).
Symptoms include:
 - Bleeding in the skin that look like tiny red or purple spots on the skin, called petechiae, or bruising.
 - Bleeding outside or inside your body including nosebleeds or bleeding gums.
 - Blood in your urine or bowel movement.
 - Heavy menstrual periods.
- Pancreatitis (swelling of the pancreas). Symptoms include:
 - Stomach pain
 - Nausea
 - Vomiting
 - Abnormal urine tests
- Rhabdomyolysis (breakdown of muscle fibres that leads to the release of muscle fibre contents into the bloodstream). Symptoms include:
 - Abnormal urine colour (dark, red, or cola coloured).
 - Decreased urine production
 - General weakness
 - Muscle stiffness or pain (myalgia)
 - Muscle tenderness
 - Weakness of the affected muscles.
- Increased levels of amylase, an enzyme that is produced by the pancreas

that help break down food in the intestines. Symptoms include:

- severe abdominal pain,
 - loss of appetite,
 - fever and nausea.
- Temporary increase in liver enzymes. Symptoms include:
 - Fatigue
 - Nausea
 - Anorexia
 - Discomfort over the liver area (upper right quadrant of the body).
 - Softening of bones and occasionally contributing to breaks.
 - Kidney damage or failure that includes the following symptoms:
 - Weakness & shortness of breath
 - Confusion
 - Abnormal heart rhythm,
 - Loss of appetite
 - High blood pressure

Side effects with **REYDIN** that may occur at the beginning of the treatment. Tell your healthcare professional immediately.

- IRS (Immune reconstitution syndrome): This has been reported in patients treated with combination antiretroviral therapy such as **REYDIN**. During the initial phase of combination antiretroviral treatment, patients' immune system response may develop an allergic reaction to other infections such as *Mycobacterium avium* infection (an infection that can produce severe illness in people with advanced AIDS), cytomegalovirus (a virus),

Pneumocystis jirovecii pneumonia (or PCP – a severe infection found in people with HIV) or tuberculosis, which may necessitate, further evaluation and treatment. Contact your doctor immediately if you experience any of the following, but not limited to the following effects; fever, cough, troubled breathing, blurred vision, painful swallowing, weakness and numbness in the legs, night sweats, weight loss, mouth ulcers or blisters.

The following side effects have frequently been reported. Contact your healthcare professional as soon as possible if you notice any of the following.

- Sleeplessness, headaches, dizziness, abnormal dreams.
- Diarrhoea, nausea, vomiting, upper abdominal pain, abdominal pain, abdominal discomfort, abdominal swelling, cramps, flatulence or wind, loss of appetite, indigestion.
- Rash, itching, hair loss.
- Tiredness, feeling of discomfort, fever, lack of energy.
- Increase in liver enzymes in the blood (ALT & AST), symptoms include tiredness.
- Muscle disorders, painful joints and muscles.
- Damage to or disease affecting nerves, which may harm sensation, movement, gland or organ function, or other aspects of health, depending on the type of nerve affected (peripheral neuropathy).

If you notice any side effects not mentioned in this leaflet, please inform your healthcare professional.

STORAGE AND DISPOSING OF REYDIN:

Store at or below 30 °C.

Keep the container tightly closed.

Store in the original container until required for use.

Do not store in a bathroom.

STORE ALL MEDICINES OUT OF REACH AND SIGHT OF CHILDREN.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

PRESENTATION OF REYDIN:

Containers of 28's: **REYDIN** is packed in a 85 cc white HDPE bottle with 38 mm white Non Child Resistant Cap containing 28 tablets and two silica gel bags of 2 g each, packed in a cardboard carton.

Containers of 30's: **REYDIN** is packed in a 85 cc HDPE bottle with 38 mm white Non Child Resistant Cap containing 30 tablets and two silica gel bags of 2 g each, packed in a cardboard carton.

IDENTIFICATION OF REYDIN:

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

REGISTRATION NUMBERS:

52/20.2.8/0451.450

NAME AND ADDRESS OF REGISTRATION HOLDER:

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