Patient Information Leaflet

SCHEDULING STATUS:

Schedule 4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

MIVIRDO (film-coated tablet)

Lamivudine 150 mg / Nevirapine 200 mg / Zidovudine 300 mg film-coated tablets

Read all of this leaflet carefully before you start taking MIVIRDO

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

1. WHAT MIVIRDO CONTAINS:

Each film-coated tablet contains the active substances:

Lamivudine 150 mg

Nevirapine 200 mg

Zidovudine 300 mg

Contains lactose monohydrate (sugar) 100 mg

The other ingredients are: Colloidal silicon dioxide, hydroxypropyl methyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate, titanium dioxide and triacetin {colourant: FD&C Blue # 2

2. WHAT MIVIRDO IS USED FOR:

MIVIRDO belongs to a group of medicines known as antiretrovirals. These are used to treat Human Immunodeficiency Virus (HIV) infection.

3. BEFORE YOU TAKE MIVIRDO:

Do not take MIVIRDO:

- if you are allergic to lamivudine or nevirapine or zidovudine or any of the other ingredients contained in **MIVIRDO** tablets
- if you have a very low red blood cell count (anaemia) or a very low white blood cell count (neutropenia)
- if you have taken **MIVIRDO** or a product containing any of the active ingredients before and had to stop taking it because you suffered from:
  - inflammation of the liver (hepatitis)
  - severe liver disease
  - severe skin rash
  - skin rash with other symptoms for example: fever or blistering
- if you have renal failure and your are not on haemodialysis
- if you are currently taking any of the following:

- other medicines containing lamivudine, nevirapine, zidovudine or emtricitabine because these medicines contain the same or similar active ingredients as the ingredients in **MIVIRDO**
- other antiretroviral medicines called ribavirin or stavudine. Taking **MIVIRDO** with these could cause serious and life-threatening side-effects
- St John's Wort (*Hypericum perforatum*) (a herbal remedy used for depression and anxiety). This herbal substance may stop **MIVIRDO** from working properly

• if you are pregnant or planning to become pregnant or breast-feeding a baby (see **Pregnancy and Breast-feeding**)

• **MIVIRDO** must not be given to children of younger than 12 years.

Take special care with MIVIRDO:

WARNING:

PATIENTS TAKING NEVIRAPINE, WHICH IS AN INGREDIENT IN MIVIRDO, MAY DEVELOP SEVERE LIVER DISEASE OR SKIN REACTIONS THAT CAN CAUSE DEATH. THE RISK OF THESE REACTIONS IS GREATEST DURING THE FIRST 18 WEEKS OF TREATMENT, BUT THESE REACTIONS CAN ALSO OCCUR LATER (see HOW TO TAKE MIVIRDO).

• if you develop severe rash of hypersensitivity (allergic) reactions that may appear in the form of a rash accompanied by other side-effects such as: fever, blistering, mouth sores, eye inflammation, facial swelling, general swelling, shortness of breath, muscle or joint aches, general feeling of illness and abdominal pain, YOU SHOULD DISCONTINUE TAKING **MIVIRDO** and contact your doctor IMMEDIATELY. These reactions are potentially life-threatening and could lead to death (see **POSSIBLE SIDE-EFFECTS**).

• If you have ever had liver disease, including hepatitis B or C and take **MIVIRDO**, you are at an increased risk of severe and potentially fatal liver effects and may require blood tests to monitor your liver function. Do not stop taking **MIVIRDO** without your doctor's advice, as your hepatitis may come back. If liver function abnormalities recur **MIVIRDO** should be stopped permanently.

• Blood disorders can be expected to occur in patients receiving zidovudine, and therefore **MIVIRDO.**

• If you develop nausea, vomiting or have stomach pain, these may be signs of inflammation of the pancreas. If you notice any of these symptoms, contact your doctor.

• Look out for signs of possible lactic acidosis (excess of lactic acid in your blood) once you start taking **MIVIRDO**. Possible signs of lactic acidosis are:

- deep, rapid breathing
- drowsiness
- numbness or weakness in the limbs
- nausea, vomiting and stomach pain

This can cause enlargement of the liver and has occasionally been fatal. It usually develops after a few months of treatment.
Lactic acidosis is more likely to develop in people who have liver disease, or in obese (very overweight) people, especially women.
During treatment with **MIVIRDO**, your doctor will monitor you for signs that you may be developing lactic acidosis.

• Patients with advanced HIV infection (AIDS) have weak immune systems and are more likely to develop serious infections (opportunistic infections). When these patients start taking **MIVIRDO**, they may find that old, hidden infections flare up, causing signs and symptoms of inflammation. These symptoms are probably caused by the body's immune system becoming stronger, so that the body starts to fight these infections.

• Patients taking combination therapy for HIV may find that their body shape changes, because of changes in fat redistribution:

- Fat may be lost from your legs, arms or face
- Extra fact may build up around your tummy (abdomen), or on the breasts of internal organs
- Fatty lumps (sometimes called buffalo hump) may appear on the back of your neck

If you notice changes in your body shape, tell your doctor.

• Patients taking **MIVIRDO** may develop a condition called osteonecrosis. With this condition, parts of the bone tissue die because of reduced blood supply to the bone. Signs of osteonecrosis include:

- stiffness in the joints
- aches and pains (especially in the hip, knee or shoulder)
- difficulty moving.

If you notice any of these symptoms, tell your doctor.

• Patients taking **MIVIRDO** may continue to develop opportunistic illnesses associated with advanced HIV-1 infection. Patients should therefore remain under close supervision by medical practitioners experienced in the treatment of patients with HIV-associated diseases.

• **MIVIRDO** will not cure or prevent HIV infection or AIDS; however, it helps to keep HIV from reproducing and appears to slow down the destruction of the immune system.

• Other effects may show up in blood tests

Combination therapy for HIV, as in **MIVIRDO**, can also cause:

- increased levels of lactic acid in the blood, which on rare occasions can lead to lactic acidosis
- increased levels of sugar and fats (triglycerides and cholesterol) in the blood
- resistance to insulin (so if you are diabetic, you have to change your insulin dose to control your blood sugar).

• 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). **MIVIRDO** will not stop you passing HIV infection on to other people. To protect other people from become infected with HIV:

Use a condom when you have oral or penetrative sex

Do not risk blood transfer – for example, do not share needles

Taking MIVIRDO with food and drink:

MIVIRDO can be taken with or without food.

Pregnancy and breast-feeding:

Speak to your medical practitioner if you become pregnant regarding the potential risks and benefits of taking **MIVIRDO** to you and your baby.

You should discontinue breast-feeding if you are taking **MIVIRDO**. It is recommended that HIV infected women must not breast-feed their infants under any circumstances in order to avoid the transmission of HIV.

If you are taking oral contraceptives (e.g. the “pill”) or other hormonal method of birth control during treatment with **MIVIRDO**, you should use a barrier method of contraception (e.g. condoms) in addition, to prevent pregnancy and further HIV transmission.

Driving and using machinery:

MIVIRDO may cause dizziness. Make sure you know how you react to **MIVIRDO** before you drive, use machines, or do anything else that could be dangerous

Important information about some of the ingredients of MIVIRDO:

MIVIRDO tablets contain lactose. If you have been told by your doctor that you have intolerance to some sugars contact your doctor before taking **MIVIRDO**.

Taking other medicines with MIVIRDO:

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **MIVIRDO** with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional for advice**.**

Especially tell your doctor, pharmacist or health care professional if you take:

- Amiodarone (medicine to treat certain heart conditions)
- Amphotericin (for fungal infection)
- Aspirin (pain and fever medicine)
- Carbamazepine (medicine to treat epilepsy, seizures, fits)
- Cimetidine (antacid medicine)
- Cisapride (used to treat gastro-intestinal disorders)
- Clarithromycin (an antibiotic which decreases the way your medicine works)
- Clonazepam (used for treatment of fits (seizures))
- Codeine (medicine for pain relief)
- Trimethoprim + sulfamethoxazole (co-trimoxazole) (these are two antibiotics which can be given together to treat some types of infections)
- Cyclophosphamade
- Ciclosporin (immunosuppressant medicine)
- Dapsone (used to prevent pneumonia and treat skin infections)
- Diltiazem (used for heart rhythm disturbances)
- Disopyramide (used for uneven heartbeats)
- Doxorubicin (used to treat cancer)
- Efavirenz (this is an anti-viral medicine)
- Ergotamine (used to treat migraines)
- Ethosuximide (anti-epileptic medicine)

- Fentanyl (medicine to relieve pain)
- Fluconazole (medicine to treat fungal infections)
- Flucytosine (used to treat fungal infections)
- Foscarnet (this belongs to a group of medicines called anti-viral medicines. It works by stopping viruses from multiplying in number and is used to treat different infections caused by viruses)
- Ganciclovir (this is an antiviral medicine used to treat infections caused by a virus called cytomegalovirus)
- Indinavir (antiretroviral medicine)
- Indomethacin (anti-inflammatory medicine to reduce swelling and inflammation)
- Interferon alfa (antiviral medicine)
- Itraconazole (medicine to treat fungal infections)
- Ketoconazole (medicine to treat fungal infections)
- Ketoprofen (anti-inflammatory medicine to reduce swelling and inflammation)
- Lidocaine (medicine to relieve pain)
- Lorazepam (medicine to relieve anxiety)
- Methadone (this medicine is used to prevent withdrawal symptoms in people who are addicted to opioid substances such as heroin)
- Morphine (medicine to relieve pain)
- Naproxen (anti-inflammatory medicine to reduce swelling and inflammation)
- Nelfinavir (anti-retroviral medicines)

- Nevirapine (anti-retroviral medicines)
- Oral contraceptives and other hormonal methods of birth control (it decreases the efficacy of your medicine)
- Oxazepam (used as a tranquilliser)
- Paracetamol (pain medicine)
- Pentamidine (for bacterial infection)
- Phenytoin (medicine to treat epilepsy, seizures, fits)
- Prednisone (a corticosteroid to treat various illnesses involving inflammation in the body)
- Probenecid (used to treat gout and similar conditions, and given with some antibiotics to make them more effective)
- Pyrimethamine (used to treat malaria and other parasitic infections)
- Ribavirin (anti-retroviral medicine)
- Rifabutin (medicine to treat tuberculosis)
- Rifampicin (used to treat tuberculosis and other infections)
- Saquinavir (antiviral medicine)
- Sirolimus (for suppression of the immune system)
- Staduvine (anti-retroviral medicine)
- St John's Wort (medicine to treat depression)
- Tacrolimus (for suppression of the immune system)
- Verapamil (used to treat certain heart conditions)
- Vinblastine (anticancer medicine)
- Vincristine (anticancer medicine)

- Warfarin (medicine to reduce blood clotting)

Keep a complete list of all the medicines that you are taking. Make a new list when medicines are added or stopped. Give copies of this list to your doctor, pharmacist or health care professional **EVERY TIME** you visit them or fill a prescription.

4. HOW TO TAKE MIVIRDO:

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

Always take **MIVIRDO** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose for adults and children older than 12 years is one tablet each day without regard to food. As this tablet contains a fixed dose combination the dose cannot be adjusted for the different ages.

You will therefore only start taking **MIVIRDO** after you are stabilised on the individual components at the same doses.or if you have completed a two (2) week lead-in period on the three individual components at the following doses:

- Lamivudine 300 mg daily, taken either as 300 mg once daily or 150 mg twice daily
- Zidovudine 300 mg twice daily
- Nevirapine 200 mg once daily

After this lead-in dosing period, the nevirapine dose will be increased to 200 mg twice a day (as contained in **MIVIRDO**), if there are no serious gastrointestinal problems or hypersensitivity (allergic) reactions.

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

If you take more MIVIRDO tablets than you should:

In the event of an overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control centre.

If you forget to take MIVIRDO:

It is important that you do not miss any doses. Try not to miss a dose. If you notice within 8 hours take a dose and then continue as before. If you only notice after 8 hours take the next regular dose at the scheduled time.

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

Effects when treatment with MIVIRDO is stopped:

You should not stop treatment unless your doctor instructs you to. When your **MIVIRDO** supply starts to run low, get more from your healthcare provider or pharmacy. This is very important because the amount of virus in your blood may increase if the medicine is

stopped for even a short time. The virus may develop resistance to **MIVIRDO** and become harder to treat.

5. POSSIBLE SIDE-EFFECTS

MIVIRDO can have side-effects.

Get emergency medical help if you have any of the following signs of an allergic reaction:

- **skin rash**
- **fever**
- **swelling of the face, tongue or throat**
- **severe tiredness or aches and pains or generally feeling ill**

Lactic acidosis (excess lactic acid in the blood) is manifested by:

- Feeling very weak or tired.
- Unusual (not normal) muscle pain.
- Trouble breathing.
- Stomach pain with nausea and vomiting.
- Feeling cold, especially in your arms and legs.
- Feeling dizzy or lightheaded.
- Fast or irregular heartbeat.

Call a doctor at once if you notice any of these serious side-effects:

- headache

- chest pain

Other side-effects include:

Frequent:

Dizziness, headache, tiredness, rash, nausea, vomiting, diarrhoea, abdominal pain, muscle and joint pain, fever, increase in certain liver enzymes, inflammation of the liver (hepatitis), hair loss, loss of appetite, cough and nasal symptoms

Less frequent:

Anxiety, depression, abnormal thinking, confusion, inability to sleep, abnormal dreams, irritability, forgetfulness. chest pains, fever like symptoms, chills, generalised pain, taste disturbances, vomiting, abdominal pain, diarrhoea, anorexia, liver disorders, skin rash and hives, blood disorders, tiredness, fits, nail and skin disorders, sweating, frequently passing urine, redistribution/accumulation of body fat, inflammation of the pancreas

Not all side-effects reported for **MIVIRDO** are included in this leaflet. Should your general health worsen while taking **MIVIRDO**, please consult your doctor, pharmacist or other health care professional for advice.

If you notice any side-effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF MIVIRDO:

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.

Store at or below 30 °C.

Store in the original container. Keep the container in the outer carton.

The bottle must be kept tightly closed.

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).

7. PRESENTATION OF MIVIRDO:

MIVIRDO is packed in high density propylene (HDPE) bottle pack comprising of white opaque wide mouth HDPE bottle with a white opaque polypropylene (PP) screw closure in 60's and 100's pack* in a cardboard carton.

*Not all packs may be marketed

8. IDENTIFICATION OF MIVIRDO:

MIVIRDO tablets are blue coloured, capsule shaped, biconvex, film-coated tablets, debossed with "M" and "104" on one side and plain on other side.

9. REGISTRATION NUMBER/REFERENCE NUMBER:

45/20.2.8/0388

10. NAME AND ADDRESS OF REGISTRATION HOLDER:

Viatris Healthcare (Pty) Ltd

4 Brewery Street

Isando

Gauteng, 1601

11. DATE OF PUBLICATION:

To be advised