SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

TUVIGIN 0,5 mg (CAPSULES)

Read all of this leaflet carefully before you start using TUVIGIN 0,5 mg CAPSULES

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

- The **active substance** of TUVIGIN is 0,5 mg fingolimod.
- The **other ingredients of** 0,5 mg hard capsules are: gelatin, mannitol, magnesium stearate, titanium dioxide.

2. WHAT TUVIGIN IS USED FOR:

TUVIGIN is used in the treatment of relapsing (returning) multiple sclerosis (MS).

TUVIGIN does not cure MS, but it helps to reduce the number of relapses (returns) that occur and to slow the build-up of physical problems due to MS (disability progression).

How TUVIGIN works

TUVIGIN helps to fight against cells that cause inflammation from reaching the brain. This reduces nerve damage caused by MS.

- **BEFORE YOU TAKE TUVIGIN**

Do not take TUVIGIN if:

- you are allergic to fingolimod or any of the other ingredients of TUVIGIN listed above.

- you are pregnant or breastfeeding.
- if, in the last 6 months, you have had a heart attack, angina, stroke or warning of a stroke or certain types of heart failure.
- if you have certain types of irregular or abnormal heartbeat (arrhythmia), or your electrocardiogram (ECG) shows prolonged QT interval before starting Tuvigin.
- you are taking medicines for irregular heartbeat such as quinidine, procainamide, amiodarone or sotalol

Take special care with TUVIGIN

You will be observed hourly by a health care professional for at least 6 hours after taking the first dose of TUVIGIN so that your heart rate and blood pressure can be checked. You will be required to have an ECG (electrocardiogram) to check the health of your heart before you start TUVIGIN and a second ECG at the end of the 6-hour observation. In case of abnormal ECG recording or slow heart rate at the end of the 6-hour observation period, you may be observed overnight by a health care professional.

The same recommendation may apply if you start treatment after a break in TUVIGIN therapy, depending on how long the break is and how long you have been receiving treatment.

Checking the health of your heart is particularly important if any of the following applies to you. Your doctor may decide not to use TUVIGIN. If your doctor thinks that TUVIGIN is good for you, he/she may refer you first to a cardiologist (doctor specialised in heart disease). You may also be monitored overnight by a health care professional after taking the first dose of TUVIGIN.

Tell your doctor or pharmacist before using TUVIGIN:

- **If you are taking medicines for an irregular heartbeat such as quinidine, procainamide, amiodarone or sotalol (see *Taking other medicines with TUVIGIN*).**
- **If you have uncontrolled high blood pressure, if when you sleep you are severely affected by interruptions of breathing (sleep apnoea that is not treated). Your doctor may decide not to use TUVIGIN if you have or have had one of these conditions.**

- **If you suffer from a slow heart rate, if at the start of the treatment with TUVIGIN you are taking medicines that slow your heart rate or if you have a history of sudden loss of consciousness (fainting). Your doctor may decide not to use TUVIGIN or may refer you first to a cardiologist to switch you to medicines that do not slow your heart rate or to decide how you should be observed after you take the first dose of TUVIGIN.**

At the beginning of treatment, TUVIGIN can cause the heart rate to slow down. TUVIGIN can also cause an irregular heartbeat, especially after the first dose. Irregular heartbeat usually returns to normal within one day. Slow heart rate usually returns to normal within one month.
If your heart rate slows down after your first dose, you may feel dizzy or tired, or may become aware of your heartbeat. If your heart rate slows down too much or your blood pressure drops, you may need treatment right away. In this case you will be monitored overnight by a health care professional and the same observation process that took place for your first dose of TUVIGIN will also apply for the second dose of TUVIGIN.

- **If you have no history of chickenpox or have not been vaccinated against varicella zoster virus.** Your doctor will test your status of the antibody against the virus and may decide to vaccinate you (if you do not have antibodies to this virus). In this case you will start TUVIGIN treatment one month after the full course of the vaccination is completed.
- **If you have a lowered immune response** (due to a disease or medicines that suppress the immune system, see Taking other medicines with TUVIGIN). You may get infections including opportunistic infections more easily or an infection you already have may get worse.

- **If you have an infection, tell your doctor before you take TUVIGIN**. Any infection that you already have may get worse. Infections could be serious and sometimes life-threatening. Before you start taking TUVIGIN, your doctor will confirm whether you have enough white blood cells in your blood.
- **If you plan to receive a vaccine**. You should not receive certain types of vaccines (called live attenuated vaccines) during and for up to 2 months after treatment with TUVIGIN (see Taking other medicines with TUVIGIN).

- **If you have or have had visual disturbances or other signs of swelling in the central vision area at the back of the eye (a condition known as macular oedema), inflammation or infection of the eye (uveitis) or if you have diabetes.** Your doctor may want you to undergo an eye examination before you start TUVIGIN and at regular intervals after the start of TUVIGIN treatment.
- **If you have liver problems.** You will have a blood test to check your liver function before you start taking TUVIGIN.

  TUVIGIN may affect your liver function. If you notice yellowing of your skin or the whites of your eyes, abnormally dark urine or unexplained nausea, vomiting and tiredness during treatment, tell your doctor straight away.

If you get any of these symptoms or diseases, during your treatment with TUVIGIN, **tell your doctor straight away because it could be serious:**

•If you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms, because these may be the symptoms of a rare brain disorder caused by an infection and called progressive multifocal leukoencephalopathy (PML)

•If you think you have an infection, have fever, feel like you have the flu or have a headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion (these may be caused by a fungal infection and be symptoms of cryptococcal meningitis)

•A condition called posterior reversible encephalopathy syndrome (PRES) has been reported in MS patients treated with TUVIGIN. Symptoms may include sudden onset of severe headache, confusion, seizures and vision changes.

•A type of skin cancer called **basal cell carcinoma** (BCC) and **other cutaneous neoplasma** have been reported in MS patients treated with TUVIGIN. Symptoms of BCC may include skin nodules (e.g. shiny pearly nodules), patches or open sores that do not heal within weeks. Symptoms of other cutaneous neoplasms may include abnormal growth or changes of skin tissue (e.g. unusual moles) which may present as a change in colour or size over time.

Tell your doctor straight away, if you get any of the following symptoms or diseases **after you have stopped your treatment** with TUVIGIN because it could be serious:

- If you believe your MS is getting worse.

Older people (over 65 years old)

Experience with TUVIGIN in older people is limited. Talk to your doctor if you have any concerns.

Children and adolescents (under 18 years old)

TUVIGIN is not intended for use in children and adolescents, as it has not been studied in MS patients aged under 18.

Using TUVIGIN capsules with food and drink

You can take TUVIGIN with or without food.

Pregnancy and breastfeeding

You should avoid becoming pregnant while taking TUVIGIN or in the two months after you stop taking it because of the risks of harm to the baby. Talk to your doctor about the associated risks and about reliable methods of birth control that you should use during treatment and for 2 months after you stop treatment.

Tell your doctor if you are pregnant, think you might be pregnant, or are trying to become pregnant.

If you do become pregnant while taking TUVIGIN tell your doctor right away. You and your doctor will decide what is best for you and your baby. See also section – How to take Tuvigin – If you stop taking Tuvigin

You should not breastfeed your baby while you are taking TUVIGIN. TUVIGIN can pass into breast milk and there is a risk of serious side effects for a breastfed baby. Talk with your doctor before breastfeeding while you take TUVIGIN**.**

Ask your doctor or pharmacist for advice before taking any medicine**,** if you are pregnant or breastfeeding**.**

Driving and using machinery

Your doctor will tell you whether your illness allows you to drive vehicles and use machines safely. TUVIGIN is not expected to affect your ability to drive and use machines.

TUVIGIN contains mannitol and may have a laxative effect.

Taking other medicines with TUVIGIN

Always tell your healthcare professional if you are taking any other medicines, including complementary or traditional medicines.

Tell your doctor if you are taking any of the following medicines:

- **Medicines for an irregular heartbeat** such as, quinidine, procainamide, amiodarone or sotalol.
- **Medicines that slow down heartbeat** such as beta-blockers (such as atenolol), calcium channel blockers (such as verapamil or diltiazem) or ivabradine or digoxin. Your doctor may decide not to use TUVIGIN or may refer you first to a cardiologist to change your medicines due to a possible added effect on slowing down heartbeat on the first days you start TUVIGIN.
- **Medicines that suppress or modulate the immune system including other medicines used to treat MS** such as beta-interferon, glatiramer acetate, natalizumab, or mitoxantrone, dimethyl fumarate, teriflunomide, alemtuzumab or corticosteroids due to a possible added effect on the immune system
- **Vaccines.** If you need to receive a vaccine, seek your doctor's advice first. During and for up to 2 months after treatment with TUVIGIN, administration of some vaccines containing live virus (live attenuated vaccines) may result in infection that the vaccination should prevent, while others may not work well. Check with your doctor or pharmacist.

Tell your doctor or a pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3. HOW TO TAKE TUVIGIN

Always use **TUVIGIN** exactly as your doctor or pharmacist has instructed. **Do not exceed the recommended dose.**

Do not share medicines prescribed for you with others.

How much TUVIGIN to take

The dose is one capsule per day (0,5 mg of fingolimod).

How and when to take TUVIGIN

Take TUVIGIN once a day, with half a glass of water. TUVIGIN can be taken with or without food.

Taking TUVIGIN at the same time each day will help you remember when to take your medicine.

How long to take TUVIGIN

Do not stop taking TUVIGIN or change your dose without talking with your doctor.

If you have questions about how long to take TUVIGIN, talk to your doctor or your pharmacist.

If you take more TUVIGIN than you should or if you have taken a first dose of TUVIGIN by mistake.

If you take too much TUVIGIN at one time, or if you have taken a first dose of TUVIGIN by mistake, contact your doctor or pharmacist right away.

Your doctor may decide to observe you with heart rate and blood pressure measurements every hour, to run ECGs and he may decide to monitor you overnight. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take TUVIGIN

If you forget a dose, take the next dose as planned. Do not take a double dose to make up for a forgotten dose.

If you have been taking TUVIGIN for less than 2 weeks and you forgot to take a dose for one day, contact your doctor right away. Your doctor may decide to observe you at the time you take the next dose.

If you stop taking TUVIGIN

Do not stop taking TUVIGIN or change your dose without talking with your doctor.

After TUVIGIN treatment is stopped, symptoms of MS can return and may become worse compared to before or during treatment. Tell your doctor if you have worsening of MS symptoms after stopping TUVIGIN.

TUVIGIN will stay in your body for up to 2 months after you stop taking it. Your white blood cell count (lymphocyte count) may also remain low during this time and the side effects described in this leaflet may still occur.

If you are a woman, see *Pregnancy and breast feeding*.

If you have stopped TUVIGIN for 1 day or more during the first 2 weeks of TUVIGIN treatment, if you stop for more than 7 days during weeks 3 and 4 of treatment, or if you stop taking TUVIGIN for more than 2 weeks after your first month of TUVIGIN treatment, the initial effect on your heart rate may occur again. When you restart TUVIGIN

treatment, your doctor may decide to monitor your heart rate and blood pressure every hour, to run ECG's or to keep you under monitoring overnight.

4. SIDE EFFECTS

TUVIGIN capsules can have side effects.

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

Serious side effects include:

Frequent:

- Bronchitis with symptoms such as cough with phlegm, chest pain, fever
- Gastroenteritis with symptoms such as vomiting, nausea, diarrhoea, fever
- Shingles (herpes zoster) with symptoms such as blisters, burning, itching or pain of the skin, typically on the upper body or the face. Other symptoms may be fever and weakness in the early stages of infection, followed by numbness, itching, and red patches , with severe pain
- Slow heartbeat (bradycardia)

Less frequent:

- Pneumonia with symptoms such as fever, cough, difficulty breathing
- Macular oedema (swelling in the central vision area of the retina at the back of the eye) with symptoms such as shadows or blind spot in the center of the vision, blurred vision, problems seeing colours or details
- Melanoma, a type of skin cancer usually developing from an unusual mole (nevus). Possible signs of melanoma include moles which may change size.shape, elevation or colour over time, or new moles. The moles may itch,bleed or ulcerate.
- A condition called posterior reversible encephalopathy syndrome (PRES). Symptoms may include sudden onset of severe headache, confusion, seizures and vision changes.
- Tumor related to infection with human herpes virus 8 (Kaposi's sarcoma)

- Serious irregularity in heart beat that is temporary and that usually returns to normal during the 6-hour observation period

Frequency not known:

- A rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML). The symptoms of PML may be similar to MS (e.g. weakness or visual changes).
- Cryptococcal infections (a type of fungal infection), including cryptococcal meningitis with symptoms such as headache accompanied by stiff neck, sensitivity to light, nausea, and/or confusion.
- After TUVIGIN treatment is stopped, symptoms of MS can return and may become worse compared to before or during treatment.

If you experience any of these, **tell your doctor straight away**.

Other frequent side effects are

- Infection from flu virus with symptoms such as tiredness, chills, sore throat, joint or muscles aching, fever
- Headache
- Diarrhoea
- Back pain
- Blood testing showing higher levels of liver enzymes
- Cough
- Feeling of pressure or pain in the cheeks and forehead (sinusitis)
- Ringworm, a fungal infection of the skin (tinea versicolor),
- Basal Cell Carcinoma (a type of skin cancer)
- Nausea
- Dizziness
- Severe headache often accompanied by nausea, vomiting and sensitivity to light (signs of migraine)
- Weakness
- Itchy, red, burning rash (signs of eczema)
- Itchy skin

- Blood fat (triglycerides) level increased
- Breathlessness
- Abnormal lung function test results starting after one month of treatment, remaining stable after that and reversible after treatment discontinuation.
- Blurred vision (see also the paragraph on macular oedema above and under section “Before you take TUVIGIN”)
- Hypertension. TUVIGIN may cause a mild increase in blood pressure
- Low level of white blood cells (lymphopenia, leukopenia)
- Muscle pain
- Joint pain

If any of these affects you severely, **tell your doctor.**

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

5. STORING AND DISPOSING OF TUVIGIN

- Store at or below 25 °C, protect from moisture.
- TUVIGIN 0,5 mg capsules must always be stored in the blister to protect from moisture and only be removed immediately before use. The blisters should be kept in the carton until required for use.
- **STORE ALL MEDICINES OUT OF THE REACH OF CHILDREN.**
- Do not use after the expiry date shown on the box.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

6. PRESENTATION OF TUVIGIN

7 or 14 capsules per blister made of PVC/PVDC with aluminium foil (Duplex), consisting of a transparent laminated plastic film made of polyvinyl chloride (PVC) and polyvinylidene chloride (PVDC). The aluminium foil is silver and the PVC/PVDC is clear, colourless and transparent. The outer container is a printed cardboard box.

Pack sizes are 7, 28 or 98. Not all pack sizes might be marketed.

7. IDENTIFICATION OF TUVIGIN

The capsule has a white opaque body and bright yellow cap; radial imprint with black ink, “FTY 0.5 mg” on the cap and two radial bands imprinted on the capsule body with yellow ink, containing white to almost white powder. Capsule size: 3.

8. REGISTRATION NUMBER:

TUVIGIN 0,5 mg capsules: 46/34/0023

9. NAME AND ADDRESS OF REGISTRATION HOLDER

Sandoz SA (Pty) Ltd

72 Steel Road

Spartan

Kempton Park

South Africa

10. DATE OF PUBLICATION

Date of registration: 14 September 2012

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