Applicant: Teva Pharmaceuticals (Pty) Ltd.	Product name: FILENGIA
Registration No.: 52/34/0364	**Dosage Form:** Each capsule contains 0,5 mg Fingolimod (as hydrochloride)

PATIENT INFORMATION LEAFLET:

SCHEDULING STATUS: S4

FILENGIA, 0,5 mg hard capsules

Fingolimod (as hydrochloride)

FILENGIA is sugar free

Read all of this leaflet carefully before you start taking FILENGIA.

- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor, pharmacist nurse or other healthcare provider.
- FILENGIA 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 FILENGIA IS AND WHAT IT IS USED FOR:

FILENGIA contains the active substance fingolimod. Fingolimod is a selective immunosuppressant and is used in adults to treat relapsing (returning) multiple sclerosis (MS) (characterised by repeated attacks (relapses) of nervous system symptoms that reflect inflammation within the central nervous system.

FILENGIA does not cure MS, but it helps to reduce the number of relapses and to slow down the progression of physical disabilities due to MS.

2. WHAT YOU NEED TO KOW BEFORE YOU USE FILENGIA:

Do not take FILENGIA:

- if you are hypersensitive (allergic) to fingolimod or any of the other ingredients of FILENGIA (listed in **section 6**)
- if you are taking or have recently taken medicine for irregular heartbeat such as quinidine, procainamide, disopyramide, amiodarone or sotalol
- if, in the last 6 months, you have had 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 (dysrhythmia), including patients in whom the electrocardiogram (ECG) shows prolonged QT interval before starting FILENGIA
- if you are pregnant or breastfeeding your baby
- if you can bear children and are not using effective contraception
- if you have a lowered immune response (due to an immunodeficiency syndrome, a disease or to medicines that suppress the immune system)
- if you have a severe active infection or active chronic infection such as hepatitis or tuberculosis
- if you have an active cancer
- if you have severe liver problems

Warnings and precautions:

Take special care with FILENGIA:

Tell your doctor before you start taking FILENGIA:

- if you have been told you have an abnormal electrocardiogram

- if you suffer from symptoms of slow heart rate (e.g., dizziness, nausea, or palpitations)
- if you have a history of sudden loss of consciousness or fainting (syncope)
- if you have severe breathing problems during sleep (severe sleep apnoea)
- if you are taking or have recently taken medicines that slow your heart rate (beta blockers (such as atenolol), calcium channel blockers (such as verapamil, diltiazem), ivabradine, digoxin, anticholinesteratic medicines or pilocarpine)
- if you have low levels of potassium or magnesium in your blood as this can increase your risk for heart rhythm disorder
- if you plan to get vaccinated
- if you have never had chickenpox or have not been vaccinated against varicella zoster virus
- if you have or have had visual disturbances or other signs of swelling in the central vision area (macula) at the back of the eye (a condition known as macular oedema, see below), inflammation or infection of the eye (uveitis), or if you have diabetes (which can cause eye problems)
- if you have liver problems
- if you have high blood pressure that cannot be controlled by medicines
- if you have severe lung problems

Slow heart rate (bradycardia) and irregular heartbeat:

FILENGIA causes the heart rate to slow down. As a result, you may feel dizzy or tired, or be consciously aware of your heartbeat, or your blood pressure may drop. If these effects are pronounced, tell your doctor, because you may need treatment right away. FILENGIA can also cause an irregular heartbeat, especially after the first dose. Irregular heartbeat usually returns to normal in less than one day. Slow heart rate usually returns to normal within one month.

Your doctor will ask you to stay at the surgery or clinic for at least 6 hours, with hourly pulse and blood pressure measurements, after taking the first dose of FILENGIA so that appropriate measures can be taken in the event of

side effects that occur at the start of treatment. You should have an electrocardiogram performed prior to the first dose of FILENGIA and after the 6-hour monitoring period. Your doctor may monitor your electrocardiogram continuously during that time. If after the 6-hour period you have a very slow or decreasing heart rate, or if your electrocardiogram shows abnormalities, you may need to be monitored for a longer period (at least 2 more hours and possibly overnight) until these have resolved. The same may apply if you are resuming FILENGIA after a break in treatment, depending on both how long the break was and how long you had been taking FILENGIA before the break.

If you have, or if you are at risk for, an irregular or abnormal heartbeat, if your electrocardiogram is abnormal, or if you have heart disease or heart failure, FILENGIA may not be appropriate for you.

If you have a history of sudden loss of consciousness or decreased heart rate, FILENGIA may not be appropriate for you. You will be evaluated by a cardiologist (heart specialist) to advise how you should start treatment with FILENGIA, including overnight monitoring.

If you are taking medicines that can cause your heart rate to decrease, FILENGIA may not be appropriate for you. You will need to be evaluated by a cardiologist, who will check whether you can be switched to alternative medicine that does not decrease your heart rate in order to allow treatment with FILENGIA. If such a switch is impossible, the cardiologist will advise how you should start treatment with FILENGIA, including overnight monitoring.

If you have never had chickenpox or have not been vaccinated against varicella zoster virus:

If you have never had chickenpox, your doctor will check your immunity against the virus that causes it (varicella zoster virus). If you are not protected against the virus, you may need a vaccination before you start treatment with FILENGIA. If this is the case, your doctor will delay the start of treatment with FILENGIA until one month after the full course of vaccination is completed.

Infections:

FILENGIA lowers the white blood cell count (particularly the lymphocyte count). White blood cells fight infection. While you are taking FILENGIA (and for up to 2 months after you stop taking it), you may get infections more easily. Any infection that you already have may get worse. Infections could be serious and life-threatening. 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 may be symptoms of meningitis), contact your doctor straight away, because it could be serious and life-threatening. If you believe your MS is getting worse (e.g., weakness or visual changes) or if you notice any new symptoms, talk to your doctor straight away, because these may be the symptoms of a brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML). PML is a serious condition that may lead to severe disability or death.

Human papilloma virus (HPV) infection, including papilloma, dysplasia, warts and HPV-related cancer, has been reported in patients treated with FILENGIA. Your doctor will consider whether you need to have a vaccination against HPV before starting treatment. If you are a woman, your doctor will also recommend HPV screening.

Macular oedema:

Before you start FILENGIA, if you have or have had visual disturbances or other signs of swelling in the central vision area (macula) at the back of the eye, inflammation or infection of the eye (uveitis) or diabetes, your doctor may want you to undergo an eye examination.

Your doctor may want you to undergo an eye examination 3 to 4 months after starting FILENGIA treatment.

The macula is a small area of the retina at the back of the eye which enables you to see shapes, colours, and details clearly and sharply. FILENGIA may cause swelling in the macula, a condition that is known as macular oedema. The swelling usually happens in the first 4 months of FILENGIA treatment.

Your chance of developing macular oedema is higher if you have diabetes or have had an inflammation of the eye called uveitis. In these cases, your doctor will want you to undergo regular eye examinations in order to detect macular oedema.

If you have had macular oedema, talk to your doctor before you resume treatment with FILENGIA.

Macular oedema can cause some of the same vision symptoms as an MS attack (optic neuritis). Early on, there may not be any symptoms. Be sure to tell your doctor about any changes in your vision. Your doctor may want you to undergo an eye examination, especially if:

- the centre of your vision gets blurry or has shadows;
- you develop a blind spot in the centre of your vision;
- you have problems seeing colours or fine detail.

Liver function tests:

If you have severe liver problems, you should not take FILENGIA. FILENGIA may affect your liver function. You will probably not notice any symptoms but if you notice yellowing of your skin or the whites of your eyes, abnormally dark urine, unexplained nausea and vomiting, abdominal pain, anorexia or fatigue, tell your doctor straight away.

If you get any of these symptoms after starting FILENGIA, tell your doctor straight away.

Before, during and after treatment with FILENGIA your doctor will request blood tests to monitor your liver function. If your test results indicate a problem with your liver, you may have to interrupt treatment with FILENGIA.

High blood pressure:

As FILENGIA causes a slight elevation of blood pressure, your doctor may want to check your blood pressure

regularly.

Lung problems:

FILENGIA has a slight effect on the lung function. Patients with severe lung problems or with smoker's cough may have a higher chance of developing side effects.

Posterior reversible encephalopathy syndrome (PRES):

A condition called posterior reversible encephalopathy syndrome (PRES) has been reported in MS patients treated with FILENGIA. Symptoms may include sudden onset of severe headache, confusion, seizures and vision changes. Tell your doctor straight away if you experience any of these symptoms during your treatment with FILENGIA, because it could be serious.

Blood count:

The desired effect of FILENGIA treatment is to reduce the amount of white blood cells in your blood. This will usually go back to normal within 2 months of stopping treatment. If you need to have any blood tests, tell the doctor that you are taking FILENGIA. Otherwise, it may not be possible for the doctor to understand the results of the test, and for certain types of blood test your doctor may need to take more blood than usual.

Before you start FILENGIA, your doctor will confirm whether you have enough white blood cells in your blood and may want to repeat a check regularly. In case you do not have enough white blood cells, you may have to interrupt treatment with FILENGIA.

Skin cancer:

Skin cancers have been reported in MS patients treated with FILENGIA. Talk to your doctor straight away if you notice any skin nodules (e.g., shiny pearly nodules), patches or open sores that do not heal within weeks. Symptoms of skin cancer may include abnormal growth or changes of skin tissue (e.g., unusual moles) with a change in colour, shape or size over time. Before you start FILENGIA, a skin examination is required to check whether you

have any skin nodules. Your doctor will also carry out regular skin examinations during your treatment with FILENGIA. If you develop problems with your skin, your doctor may refer you to a dermatologist, who after consultation may decide that it is important for you to be seen on a regular basis.

Exposure to the sun and protection against the sun:

Fingolimod weakens your immune system. This increases your risk of developing cancers, in particular skin cancers. You should limit your exposure to the sun and

UV rays by:

- wearing appropriate protective clothing.
- regularly applying sunscreen with a high degree of UV protection.

Unusual brain lesions associated with MS relapse:

Some cases of unusually large brain lesions associated with MS relapse have been reported in patients treated with FILENGIA. In case of severe relapse, your doctor will consider performing MRI to evaluate this condition and will decide whether you need to stop taking FILENGIA.

Switch from other treatments to FILENGIA:

Your doctor may switch you directly from beta interferon, glatiramer acetate or dimethyl fumarate to FILENGIA if there are no signs of abnormalities caused by your previous treatment. Your doctor may have to do a blood test in order to exclude such abnormalities. After stopping natalizumab you may have to wait for 2-3 months before starting treatment with FILENGIA. To switch from teriflunomide, your doctor may advise you to wait for a certain time or to go through an accelerated elimination procedure. If you have been treated with alemtuzumab, a thorough evaluation and discussion with your doctor is required to decide if FILENGIA is appropriate for you. Should you require combined treatment with a corticosteroid and FILENGIA, your doctor will need to carefully consider the concomitant treatment if required for a prolonged period.

Children and adolescents:

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

Other medicines and FILENGIA:

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

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

- Medicines that suppress or modulate the immune system, including other medicines used to treat MS, such as beta interferon, glatiramer acetate, natalizumab, mitoxantrone, teriflunomide, dimethyl fumarate or alemtuzumab. You must not use FILENGIA together with such medicines as this could intensify the effect on the immune system (see also **Do not take FILENGIA**).
- 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 FILENGIA, you should not receive certain types of vaccine (live attenuated vaccines) as they could trigger the infection that they were supposed to prevent. Other vaccines may not work as well as usual if given during this period.
- Medicines that slow the heartbeat for example beta blockers (such as atenolol), calcium channel blockers (such as verapamil, diltiazem), ivabradine, digoxin, anticholinesteratic medicines or pilocarpine. Use of FILENGIA together with such medicines could intensify the effect on heartbeat in the first days after starting FILENGIA.
- Medicines for irregular heartbeat, such as quinidine, procainamide, disopyramide, amiodarone or sotalol. You must not use FILENGIA if you are taking such a medicine because it could intensify the effect on irregular heartbeat (see also **Do not take FILENGIA**).
- Other medicines:
  - protease inhibitors, anti-infectives such as ketoconazole, azole antifungals, clarithromycin or telithromycin.
  - carbamazepine, rifampicin, phenobarbital, phenytoin, efavirenz or St. John's Wort.

FILENGIA with food and drink:

FILENGIA can be taken with or without food.

Pregnancy, breastfeeding and 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 healthcare provider for advice before taking FILENGIA.

Before you start treatment with FILENGIA your doctor may ask you to do a pregnancy test in order to ensure that you are not pregnant. You should avoid becoming pregnant while taking FILENGIA or in the two months after you stop taking it because there is a risk of harm to the baby. Talk to your doctor about reliable methods of birth control that you should use during treatment and for 2 months after you stop treatment.

Pregnancy:

You should not take FILENGIA if you are pregnant.

If you become pregnant while taking FILENGIA tell your doctor right away. You and your doctor will decide what is best for you and the baby.

Breastfeeding:

You should not take FILENGIA if you are breastfeeding your baby. FILENGIA 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 FILENGIA.

Fertility:

Data from preclinical studies do not suggest an effect on male and female fertility with FILENGIA.

Driving and using machines:

At initiation of treatment, you will have to stay at the doctor's surgery or clinic for 6 hours after taking the first dose of FILENGIA. Your ability to drive and use machines may be impaired during and potentially after this time

period.

It is not always possible to predict to what extent FILENGIA may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or use machines until you are aware of the measure to which FILENGIA affects you.

3. HOW TO TAKE FILENGIA:

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

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

The usual dose of FILENGIA is one 0,5 mg capsule once a day by mouth.

Do not exceed the recommended dose.

Take one FILENGIA capsule (0,5 mg of fingolimod) once a day with a glass of water. FILENGIA capsules should always be swallowed intact, without opening them. FILENGIA can be taken with or without food.

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

Your doctor will tell you how long your treatment with FILENGIA will last. If you have the impression that the effect of FILENGIA is too strong or too weak, tell your doctor or pharmacist.

If you take more FILENGIA 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 FILENGIA:

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

If you stop taking FILENGIA:

Do not stop taking FILENGIA or change your dose without talking to your doctor first.

FILENGIA 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. After stopping FILENGIA you may have to wait for 6-8 weeks before starting a new MS treatment.

If you have stopped FILENGIA for 1 day or more during the first 2 weeks of FILENGIA treatment, if you stop for more than 7 days during weeks 3 and 4 of treatment, or if you stop taking FILENGIA for more than 2 weeks after your first month of FILENGIA treatment, the initial effect on your heart rate may occur again. When you restart FILENGIA 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. Do not restart FILENGIA after stopping it for more than two weeks without seeking advice from your doctor.

Your doctor will decide whether and how you need to be monitored after stopping FILENGIA. Tell your doctor straight away if at any time you think your MS is getting worse after you have stopped treatment with FILENGIA. This could be serious.

4. POSSIBLE SIDE EFFECTS:

FILENGIA can have side effects.

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

If any of the following happens, stop taking FILENGIA 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 (dizziness)

These are all very serious side effects. If you have them, you may have had a serious reaction to FILENGIA. 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:

Frequent side effects:

- Bronchitis with symptoms such as cough with phlegm, chest pain, fever
- Gastroenteritis with symptoms such as vomiting, nausea, diarrhoea, fever
- Herpes virus infection (shingles or 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 or red patches with severe pain
- a type of skin cancer called basal cell carcinoma (BCC) which often appears as a pearly nodule, although it can also take other forms
- depression and anxiety are known to occur with increased frequency in the MS population and have also been reported in paediatric patients treated with FILENGIA
- slow heartbeat (bradycardia), irregular heart rhythm

Less frequent side effects:

- pneumonia with symptoms such as fever, cough, difficulty breathing
- malignant melanoma (a type of skin cancer which usually develops from an unusual mole). 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
- lymphoma (a type of cancer that affects the lymph system)

- squamous cell carcinoma: a type of skin cancer which may present as a firm red nodule, a sore with crust, or a new sore on an existing scar
- tumour related to infection with human herpes virus (Kaposi's sarcoma)
- reduction in blood platelets which increases risk of bleeding or bruising
- convulsion, fits (more frequent in children and adolescents than in adults)
- a condition called posterior reversible encephalopathy syndrome (PRES). Symptoms may include sudden onset of severe headache, confusion, seizures and/or vision disturbances
- 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 centre of the vision, blurred vision, problems seeing colours or details
- electrocardiogram anomaly (T-wave inversion)

Side effects with unknown frequency:

- risk of a brain infection called progressive multifocal leukoencephalopathy (PML). The symptoms of PML may be similar to an MS relapse. Symptoms might also arise that you might not become aware of by yourself, such as changes in mood or behaviour, memory lapses, speech and communication difficulties, which your doctor may need to investigate further to rule out PML. Therefore, if you believe your MS is getting worse or if you or those close to you notice any new or unusual symptoms, it is very important that you speak to your doctor as soon as possible
- 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
- Merkel cell carcinoma (a type of skin cancer). Possible signs of Merkel cell carcinoma include flesh-coloured or bluish-red, painless nodule, often on the face, head or neck. Merkel cell carcinoma can also present as a firm painless nodule or mass. Long-term exposure to the sun and a weak immune system can affect the risk of developing Merkel cell carcinoma
- after FILENGIA treatment is stopped, symptoms of MS can return and may become worse compared to before or during treatment

- ischaemic and haemorrhagic strokes. Possible symptoms may include trouble walking, speaking and understanding, as well as paralysis or numbness of the face, arm or leg
- acute disseminated encephalomyelitis (ADEM)-like events where rapid appearance of encephalitis-like symptoms such as fever, fatigue, headache, nausea and vomiting can occur
- an autoimmune form of anaemia (decreased amount of red blood cells) where red blood cells are destroyed (autoimmune haemolytic anaemia)
- haemophagocytic syndrome (HPS), a life-threatening syndrome where the body's immune system does not work normally. Symptoms include enlargement of the spleen, liver and lymph nodes
- peripheral arterial occlusive disease, a condition that may narrow arteries and reduce blood flow to the legs or arms

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:

- infection from flu virus with symptoms such as tiredness, chills, sore throat, aching in the joints or muscles, fever
- feeling of pressure or pain in the cheeks and forehead (sinusitis)
- ringworm, a fungal infection of the skin (tinea versicolor)
- low level of white blood cells (lymphocytes, leucocytes)
- headache, migraine
- blurred vision
- high blood pressure
- cough, breathlessness
- diarrhoea
- itchy, red, burning rash (eczema)

- hair loss
- back pain
- muscle pain
- joint pain
- weakness
- increased blood fat (triglycerides) level
- increased liver enzymes showing in blood tests
- weight loss

Less frequent side effects:

- depressed mood
- nausea
- low level of certain white blood cells (neutrophils)
- swelling of your lower legs or hands (peripheral oedema)

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: *http://www.sahpra.org.za/health-oroducts-vigilance/* 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 FILENGIA.

5. HOW TO STORE FILENGIA:

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Store at or below 25 °C.

Keep the capsule in the blister in the outer carton until required for use.

Do not use after the expiry date stated 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).

6. CONTENTS OF THE PACK AND OTHER INFORMATION:

What FILENGIA contains:

The active substance is fingolimod (as hydrochloride).

The other ingredients are pregelatinised starch, sodium laurilsulphate, gelatin, titanium dioxide (E171), yellow iron oxide (E172) and printing ink consisting of black iron oxide (E172), potassium hydroxide, propylene glycol, shellac and strong ammonia solution.

What FILENGIA looks like and contents of the pack:

Hard gelatin capsule (size 4), filled with white to off-white powder with small agglomerates. Capsule body: white opaque with TV 7820 imprinted. Capsule cap: yellow with TV 7820 imprinted.

The capsules are packed into:

Aluminium – aluminium blister packs

Forming foil: Aluminium soft temper (OPA/Alum/PVC)

Lidding foil: Aluminium foil, heat sealable

Pack sizes: 7, 10, 28, 30, 98 in blisters.

or

Aluminium – aluminium blister packs (peel)

Forming foil: Aluminium soft temper (OPA/Alum/PVC)

Lidding foil: Aluminium foil, peelable (Paper/PET/Alum)

Pack sizes: 7 x 1, 10 x 1, 28 x 1, 30 x 1, 98 x 1 and 100 x 1 in perforated unit-dose blisters.

Not all pack sizes may be marketed.

Applicant: Teva Pharmaceuticals (Pty) Ltd.	Product name: FILENGIA
Registration No.: 52/34/0364	**Dosage Form:** Each capsule contains 0,5 mg Fingolimod (as hydrochloride)

Holder of Certificate of Registration:

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