Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986
This medicine is sold with a doctor's prescription only

Finolim 0.5 mg
Capsules

Active ingredient
Each capsule contains: Fingolimod (as hydrochloride) 0.5 mg
For the list of the additional ingredients, see section 6.
Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, please refer to your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

Taking the first dose:
After taking the first dose of Finolim, observation by a health care professional is required for at least 6 hours.
This recommendation applies also if you are resuming treatment after an interruption.
The full instructions regarding taking the first dose are detailed in the section 'Special warnings regarding the use of this medicine'.

1. What is the medicine intended for?

The medicine is intended for the treatment of relapsing forms of multiple sclerosis (MS), to reduce the number of relapses and slow the development of physical problems (disability) caused by the disease.

Therapeutic group:
Selective Immunosuppressor.
Sphingosine-1-phosphate receptor modulator.

What is Multiple Sclerosis
Multiple sclerosis is a chronic disease that affects the central nervous system which includes the brain and the spinal cord. In MS, the inflammatory process destroys the protective sheath (called myelin) around the nerves in the central nervous system and prevents normal activity of the nerves (demyelination).

Relapsing-remitting MS is characterized by relapses of symptoms of the nervous system, which reflects inflammation in the central nervous system. Different patients may have different symptoms but typical symptoms are: difficulties in walking, numbness, vision problems or balance problems.
The relapse symptoms may disappear completely when the relapse is over but certain problems may remain.

How does the medicine work
The medicine helps protect the central nervous system from an attack by the immune system in the body by reducing the ability of certain white blood cells (lymphocytes) to move freely in the body and preventing them from reaching the brain and the spinal cord. This limits the damage to the nerves caused by multiple sclerosis. The medicine also reduces part of the body's immune response.

2. Before using the medicine

Do not use the medicine if:

- You have suffered from a heart attack, unstable angina, stroke or transient ischemic attack, or from certain types of heart failure during the last 6 months.
- You suffer or have suffered in the past from certain types of irregular or abnormal heartbeats (arrhythmia-rhythm disturbances) including patients in whose ECG a heart finding called prolonged QT was observed before starting treatment with Finolim.
- You have a heart rhythm problem requiring treatment with certain medicines.
- You are allergic (hypersensitive) to fingolimid or to any of the other ingredients the medicine contains, listed in section 6, 'Additional Information'. The symptoms of an allergic reaction may include: rash, itchy hives or swelling of the lips, tongue or face.

Talk to your doctor about these conditions, before you take the medicine.

Special warnings regarding the use of this medicine:

- **Taking the first dose:**

The medicine may cause your heart rate to slow, particularly after you take the first dose. You will undergo a test called electrocardiogram (ECG) test to examine the heart's electrical activity before you take the first dose of Finolim.
All patients will remain for observation by a healthcare professional for at least 6 hours after taking the first dose of Finolim.

After you take the first dose of Finolim:

- Your pulse and blood pressure need to be checked hourly.
- You must be under observation by a healthcare professional in order to see whether you have any serious side effects. If your heart rate slows down too much, you may experience symptoms such as:
  - Dizziness
  - Tiredness
  - A feeling that your heart is beating slowly or misses beats.
  - Chest pain
- If you have one or more symptoms of slow heart rate, they will generally occur during the first 6 hours after taking the first dose. The symptoms may occur up to 24 hours after you take the first dose.
- 6 hours after you take the first dose, you will undergo another ECG test. If the ECG shows any heart problems or if your heart rate is still too low or continues to decrease, you will continue to be under observation.
- If you have any serious side effects after taking the first dose, particularly those that require treatment with other medicines, you will stay at the medical center for observation overnight. You will also be under observation for any serious side effects for at least 6 hours after you take the second dose the next day.
- If you have certain types of heart problems, or if you are taking certain types of medicines that might affect your heart, you will stay at the medical center for observation by a healthcare professional overnight after taking the first dose.

Your slow heart rate will usually return to normal within one month after you start taking Finolim. Refer to your doctor immediately or to the nearest hospital emergency room if you have any symptoms of slow heart rate.

If you missed one or more doses of Finolim, you may need to be under observation by a healthcare professional when you take the next dose. Refer to your doctor if you missed a dose. Also see 'How to use this medicine?'.

Inform the doctor of all your medical conditions before taking Finolim, including if you had or currently have:

- Irregular or abnormal heartbeat (arrhythmia)
- History of stroke or transient ischemic attack
- Heart problems, including heart attack or angina pectoris
- History of recurring fainting spells (loss of consciousness)
- Fever or infection, or if you cannot fight infections because of a disease or if you are taking or have taken in the past medicines that weaken your immune system
- You have recently been vaccinated or are due to be vaccinated
- Chickenpox or if you have been vaccinated against chickenpox. Your doctor may perform a blood test for chickenpox. You may have to receive the full course of the chickenpox vaccinations and then wait one month before you start treatment with Finolim.
- Eye problems, particularly an eye inflammation called uveitis.
- Diabetes
- Breathing problems, including when you are asleep
- Liver problems
- High blood pressure
- Types of skin cancer called basal cell carcinoma (BCC) or melanoma
- Please consult your doctor before becoming pregnant. You should avoid becoming pregnant while taking Finolim and/or during the two months after you stop taking the medicine because of the risk of harm to the fetus. See 'Pregnancy and breastfeeding' section below.

Elderly patients (over the age of 65)
The experience with elderly people is limited and therefore the medicine should be used with caution in patients aged 65 and over.

Children and adolescents
The medicine is not intended for children and adolescents under 18 years of age.

Tests and follow-up
See reference to the tests below also in the 'Side effects' section.

<u>Before starting the treatment:</u>

- White blood cells test, vision test, blood test to check liver functions.
- Your doctor may perform a blood test for chickenpox.
- For the tests required when taking the first dose of Finolim - see the 'Taking the first dose' section above.

<u>During the treatment:</u>

- Blood pressure tests, skin test, vision test 3 to 4 months after starting treatment, blood test to check liver functions.
- You should consult about routine cervical screening (Pap smear).

Drug interactions
The use of Finolim concurrently with other medicines may cause serious side effects.
If you are taking, or have recently taken any other medicines, including non-prescription medicines, vitamins and nutritional supplements, please inform your doctor or pharmacist. Especially if you are taking:

- **Medicines that prolong the QT interval** such as citalopram, chlorpromazine, haloperidol, methadone, erythromycin, since starting treatment with Finolim causes a decrease in heart rate and may prolong the QT interval.
- **Ketoconazole** - a medicine to treat fungal infections. A patient using Ketoconazole and Finolim concurrently should be closely monitored since there is a greater risk of side effects.

- **Vaccinations** - if you need to receive a vaccine, refer first to your doctor for advice. During the treatment and for up to 2 months after treatment with Finolim, you cannot receive some vaccines containing a live virus (live attenuated vaccines) since they may trigger the infection that the vaccine is supposed to prevent. Other vaccines may not work as usual if administered during this period.
- **Antineoplastic medicines, medicines that suppress or modulate the immune system** (including corticosteroids) - are liable to increase the risk of suppressing the immune system and the risk of a further effect on the immune system should be taken into consideration if these medicines are administered concurrently with Finolim. When the treatment is changed from medicines with a prolonged effect on the immune system such as natalizumab, teriflunomide or mitoxantrone, the duration and method of action of these medicines should be taken into consideration in order to prevent an additional and unintentional effect of immunosuppression when starting treatment with Finolim.
- **Medicines that slow down heart rate and atrioventricular conduction** such as beta blockers, digoxin or calcium channel blockers such as diltiazem or verapamil. Before starting treatment with Finolim, consult the doctor who prescribed these medicines for you about the possibility of replacing them with medicines that do not slow the heartbeat and the **atrioventricular** conduction.

Use of Finolim and food
The medicine can be taken with or without food.

Pregnancy and Breastfeeding
Inform your doctor before taking Finolim, if you are pregnant or planning to become pregnant. The medicine may harm your fetus.
Inform your doctor immediately if you become pregnant during treatment with Finolim or if you become pregnant within two months from stopping the treatment.

- You should stop taking the medicine two months before you try to become pregnant.
- If you could become pregnant, you must use effective contraceptive means during the treatment with the medicine and for at least two months after stopping the treatment.

Inform your doctor before taking the medicine, if you are breastfeeding or planning to breastfeed.
It is not known whether the medicine passes into breastmilk. Consult your doctor on the best way to feed your baby if you are taking Finolim.

Driving and use of machinery
Your doctor will tell you whether your illness allows you to drive a vehicle, including riding a bicycle, and use machinery safely. The medicine is not expected to affect your ability to drive and use machinery.
However, after taking the first dose of Finolim, you must remain for observation by a health care professional for at least 6 hours. During this time and potentially also afterward, your ability to drive and to use machinery might be impaired.

3. How to use this medicine?

Always use the medicine according to the doctor's instructions. Check with your doctor or pharmacist if you are unsure about the dosage and manner of treatment with the medicine.

Dosage
The capsules are intended to be taken orally.
The dosage and manner of treatment will be determined by the doctor only.
The standard dosage is usually:
One capsule per day (of 0.5 mg).
Do not exceed the recommended dose.

Take Finolim once a day, with a glass of water.

Taking Finolim at the same time each day will help you remember when to take the medicine.
There is no information regarding opening the capsule and dispersing its contents.

If you accidentally took a higher dosage
If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine
If you forgot a dose of Finolim, refer to your doctor immediately. You may have to be under observation by a healthcare professional for at least 6 hours when you take the next dose. If you need to be under observation by a healthcare professional when you take the next dose of Finolim, you will undergo:

- ECG test before taking the dose
- Pulse and blood pressure measurement hourly after taking the dose
- ECG test 6 hours after taking the dose

Stopping treatment
Adhere to the treatment as recommended by your doctor.
Even if your state of health improves, do not stop the treatment with this medicine without consulting your doctor.
If you stop taking the medicine, the MS symptoms may return and worsen - see section 'Severe worsening of the multiple sclerosis after stopping Finolim' in the Side Effects chapter.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine.
Wear glasses if you need them.

If you have further questions concerning the use of the medicine, consult the doctor or pharmacist.

4. Side effects

As with any medicine, the use of Finolim may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

The medicine may cause serious side effects, including:

- **Slow heart rate (bradycardia or bradyarrhythmia) when you start taking Finolim**

The medicine may cause your heart rate to slow, particularly after you take the first dose. See details in the section ‘Special warnings regarding the use of this medicine’, in the subsection 'Taking the first dose'.

- **Infections**

The medicine may increase your risk of serious infections that could be life-threatening and cause death. Do not receive **live** vaccines during the treatment with Finolim and for two months after you stop taking Finolim. Talk to your doctor before receiving vaccines during the treatment and for two months after the treatment with Finolim. If you receive a live vaccine, you may receive the infection that the vaccine was supposed to prevent. Vaccinations may be less effective when they are given during the treatment period with Finolim.

The papillomavirus (HPV) - Because of the risk of infection with the papillomavirus you should consult your doctor about routine cervical screening (Pap smear).

The medicine reduces the number of white blood cells (lymphocytes) in the blood. The level of the white blood cells will return to normal generally within two months from stopping the treatment. Your doctor may send you for a blood test to examine your white blood cells before you start taking the medicine. Refer to your doctor immediately if you have any symptoms of infection during the treatment and for two months after the last dose of Finolim:

- Fever
- Tiredness
- Body aches
- Chills
- Nausea
- Vomiting
- Headache accompanied by fever, stiff neck, sensitivity to light, nausea or confusion (these may be symptoms of meningitis, infection of the membranes surrounding the brain and spinal cord).

- **Progressive Multifocal Leukoencephalopathy (PML)**

PML is a rare infection in the brain which usually leads to death or severe disability. If PML occurs, this is usually in people with a weaked immune system but it has also occurred in people without a weakened immune system. The PML symptoms worsen in days up to weeks. Refer immediately to your doctor if you experience new or worse PML symptoms, which continue for a few days, including:

- Weakness of one side of the body
- Loss of coordination in arms and legs
- Decreased strength
- Balance problems
- Changes in vision
- Changes in thinking or memory
- Confusion
- Personality changes

- **A vision problem called macular edema**

Macular edema may cause some of the same vision symptoms as an MS attack (inflammation of the optic nerve). You may not discern any symptoms of macular edema. If macular edema occurs, it usually starts during the first 3 to 4 months after starting treatment with the medicine. Your doctor should check your vision before you start the treatment and 3 to 4 months after starting treatment, or any time you observe changes in vision during the treatment. Your risk of macular edema is higher if you have diabetes or if you have had an eye infection called uveitis.

Refer to the doctor immediately if you have one or more of the following symptoms:

- Blurring or shadows in the center of your vision
- Blind spot in the center of your vision
- Sensitivity to light
- Abnormal seeing of colors (shades)

Additional serious side effects:

- **Swelling and narrowing of the blood vessels in your brain.** A condition called PRES (Posterior Reversible Encephalopathy Syndrome) has occurred on rare occasions in patients taking fingolimod. The PRES symptoms usually improve when the patient stops taking the medicine. However, without treatment, they could lead to a stroke. Refer to the doctor immediately if you have one or more of the following symptoms:
  - Sudden severe headache.
  - Sudden confusion

- Sudden loss of sight or other changes in your vision
- Seizures

- **Liver damage.** The medicine may cause liver damage. Your doctor should perform blood tests in order to check your liver before you start taking Finolim and periodically during the treatment. Refer to your doctor immediately if you have one or more of the following symptoms of liver damage:
  - Nausea
  - Vomiting
  - Stomachache
  - Tiredness
  - Loss of appetite.
  - Yellowing of the skin or the whites of the eyes
  - Dark urine
- **Breathing problems.** Some people taking Finolim have shortness of breath. Refer to your doctor immediately if you have new or worsened breathing problems
- **Severe worsening of the multiple sclerosis after stopping Finolim.**

  When treatment with Finolim is discontinued, multiple sclerosis symptoms might return and worsen in comparison with what was before or during treatment. Many people with worsening of MS symptoms that occurred after discontinuation of the treatment did not return to the level of functioning they had before stopping the treatment. This worsening occurs usually within 12 weeks after stopping the treatment but might occur later. Talk with your doctor always before you stop taking Finolim for any reason whatsoever. Inform your doctor if the MS symptoms get worse after you stop the treatment.

- **High blood pressure.** Your doctor should check your blood pressure during the treatment with Finolim.
- **Types of skin cancer called basal cell carcinoma (BCC) and melanoma.** Inform your doctor if there are any changes in your skin appearance including changes in a mole, a new dark area on your skin, a sore that does not heal or growths on your skin such as a bump that might be shiny, of skin color, pearly white or pink Your doctor should examine your skin to see if there are any changes during the treatment with Finolim. You need to limit the time you stay in sunlight and in ultraviolet (UV) light. Wear protective clothing and use sunscreen with a high protection factor.
- **Allergic reactions.** Refer to your doctor if you have symptoms of an allergic reaction, including rash, itchy hives or swelling of the lips, tongue or face.

<u>Very common side effects (appear in more than one user out of ten):</u>

- Headache
- Abnormal liver test results
- Diarrhea
- Cough
- Flu
- Inflammation in the sinuses (Sinusitis)
- Backache
- Abdominal pain
- Pain in the arms or legs

<u>Common side effects (appear in 1-10 users out of 100):</u>

- Inflammation of the bronchi (bronchitis)
- Shingles (herpes zoster)
- Ringworm (Tinea versicolor)
- Migraine
- Nausea
- Weakness

- Hair loss
- Actinic keratosis - a precancerous growth
- Increase in blood triglycerides levels
- Blurred vision
- Low lymphocyte count (lymphopenia)
- Low white blood cell count (leukopenia)
- Skin papilloma - a benign growth on the skin

Additional reported side effects include seizures, dizziness, pneumonia, eczema and itching.

If a side effect appears, if one of the side effects worsens, or you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting Side Effects
Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects or by entering the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed place out of the reach and sight of children and/or infants, to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Storage conditions**: Do not store above 30°C. Store in the original package. Protect from moisture.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Sodium chloride, gelatin, titanium dioxide (E171), yellow iron oxide (E172), sodium lauryl sulphate, Colorcon S-1-17823 black
What does the medicine look like and what does the package contain?
White-yellow colored capsules. 'SCM 0.5 mg' is printed on the capsules. Contents of the package: 7 or 28 capsules in blisters. Not all package sizes may be marketed.

Registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301
Manufacturer: Stem Cell Medicine Ltd, P.O. Box 45388 Jerusalem

Medicine registration number in the National Medicines Registry of the Ministry of Health:
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