PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Finolim 0.5 mg
Capsules

Active ingredient:
Each capsule contains: Fingolimod (as hydrochloride) 0.5 mg
Inactive 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 the doctor or pharmacist.

This medicine has been prescribed for the treatment of 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.

In addition to the leaflet, there is a patient safety information card for **Finolim 0.5 mg.** This card contains important safety information, that you need to know before starting the treatment and during the treatment with **Finolim 0.5 mg,** and act according to it.
Peruse the patient safety information card and the patient leaflet before starting to use the medicine. Keep the card for further perusal if necessary.

Taking the first dose:
After taking the first dose of **Finolim 0.5 mg**, observation by a healthcare professional is required for at least six hours.
This recommendation also applies if you are resuming treatment after interrupting treatment with **Finolim 0.5 mg**.
The full instructions regarding taking the first dose are detailed in the 'Special warnings regarding the use of the medicine' section.

1. What is the medicine intended for?

Finolim 0.5 mg is intended for the treatment of relapsing forms of multiple sclerosis, to reduce the number of relapses and slow the development of physical problems (disability) caused by the disease.

Therapeutic group:
Selective immune system suppressor.
Sphingosine-1-phosphate receptor modulator.

What is Multiple Sclerosis?
Multiple sclerosis (MS) is a chronic disease that affects the central nervous system that 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).

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

How does **Finolim 0.5 mg** work:

Finolim 0.5 mg helps protect the central nervous system from being attacked by the body's immune system 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. **Finolim 0.5 mg** 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 in the last 6 months.
- You suffer or have suffered in the past from certain types of irregular or abnormal heart rates (arrhythmia) including patients in whom a heart finding called QT interval prolongation was observed on their ECG prior to starting the treatment with **Finolim 0.5 mg**.
- You have a heart rate problem requiring treatment with certain medicines.
- You are allergic (hypersensitive) to fingolimod or to any of the additional ingredients the medicine contains, listed in section 6, 'Additional Information'. The symptoms of an allergic reaction may include: rash, urticaria (itching hives) or swelling of the lips, tongue or face.

Before you take the medicine, talk to your doctor about these medical conditions if you suffer from one of them, and also if you are not sure about it.

Special warnings regarding the use of the medicine:

- **Taking the first dose:**

Finolim 0.5 mg may cause your heart rate to slow, particularly after you take the first dose. You will undergo a test called electrocardiogram (ECG), to examine the heart's electrical activity before taking the first dose of **Finolim 0.5 mg**.
All patients will remain for observation by a healthcare professional for at least 6 hours after taking the first dose of Finolim 0.5 mg.

After you take the first dose of **Finolim 0.5 mg:**

- Your pulse and blood pressure should be checked hourly.
- You should be under observation by a healthcare professional to see whether you have any serious side effects. If your heart rate slows down too much, you may have 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 have another ECG. 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 of **Finolim 0.5 mg**, particularly those that require treatment with other medicines, you will stay at the medical facility for observation overnight. In addition, you will be under observation for any serious side effects for at least 6 hours after you take the second dose on 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 facility for observation by a healthcare professional overnight after taking the first dose.

Your slow heart rate will return to normal, usually within one month after you started taking **Finolim 0.5 mg**. **Refer to your doctor** or go to the nearest hospital emergency room **immediately** if you have any symptoms of slow heart rate.

If you missed one or more doses of Finolim 0.5mg, 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 of **Finolim 0.5 mg**. See also 'How to use the medicine?'.

Inform the doctor about all of your medical conditions before taking Finolim 0.5 mg, including, if you suffer or suffered in the past from one of the following medical conditions:

- Irregular or abnormal heart rate (arrhythmia).
- History of stroke or transient ischemic attack.
- Heart problems, including heart attack or angina pectoris.
- History of repeated fainting (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. The doctor may perform a blood test for the chickenpox virus. You may have to receive the full course of the chickenpox vaccinations and then wait a month before you start treatment with **Finolim 0.5 mg**.
- Eye problems, particularly an eye inflammation called uveitis.
- Diabetes.
- Breathing problems, including during sleep.
- Liver problems.
- High blood pressure.
- Skin cancer of the basal cell carcinoma (BCC) type or melanoma.
- Please consult your doctor before becoming pregnant. You should avoid becoming pregnant while taking **Finolim 0.5 mg** and also during the two months after you stop taking the medicine because of the risk of harming the fetus. See the 'Pregnancy and breastfeeding' section below.

Elderly patients (over the age of 65)
The experience with **Finolim 0.5 mg** treatment in 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 the age of 18.

Tests and follow-up

Before starting the treatment:

- Blood tests: white blood cells test, liver functions test (see 'Side effects' section).
- Vision test (see 'Side effects' section).
- Pregnancy test - see 'Pregnancy and breastfeeding' section.
- The doctor may perform a blood test for the chickenpox virus.
- For the tests required when taking the first dose of **Finolim 0.5 mg** - see the 'Taking the first dose' section above.

During the treatment:

- Blood pressure tests, skin test, vision test 3 to 4 months after starting treatment, blood test for liver functions (see 'Side effects' section).
- You should consult about routine cervical screening (Pap screen) - see 'Side effects' section.

Drug interactions:

The use of **Finolim 0.5 mg** together 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 tell the 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 0.5 mg** causes slowing of the heart rate and may prolong the QT interval.
- **Ketoconazole** - a medicine to treat fungal infections. A patient using **Finolim 0.5 mg** and Ketoconazole concurrently needs to 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 0.5 mg**, you cannot receive certain vaccines containing a live virus (live attenuated vaccines), since they may trigger the infection that the vaccination is supposed to prevent. Other vaccines as well may not act as usual if administered during this period.
- **Antineoplastic medicines, medicines that suppress or modulate the immune system** (including corticosteroids) – are expected to increase the risk of suppressing the immune system and the risk of a further effect on the immune system should be taken into account if these medicines are administered concurrently with **Finolim 0.5 mg.** 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 account in order to prevent an added and unintentional effect of immunosuppression when starting treatment with **Finolim 0.5 mg**.
- **Medicines that slow the heart rate and the atrioventricular conduction** such as beta blockers, digoxin or calcium channel blockers such as diltiazem or verapamil. Before starting treatment with **Finolim 0.5 mg**, consult with the doctor who prescribed these medicines for you about the possibility of switching to medicines that do not slow the heart rate and the atrioventricular conduction.

Use of Finolim 0.5 mg and food
The medicine can be taken with or without food.

Pregnancy and breast-feeding:
<u>Pregnancy</u>
The medicine may harm your fetus.
Inform your doctor before taking **Finolim 0.5 mg**, if you are pregnant or are planning to become pregnant.
Tell your doctor immediately if you become pregnant during treatment with **Finolim 0.5 mg** or if you become pregnant within two months after stopping the treatment.

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

See also 'Severe worsening of multiple sclerosis after stopping **Finolim 0.5 mg'** in the 'Side Effects' section**.**

<u>Breastfeeding</u>
Inform your doctor before taking the medicine, if you are breastfeeding or if you are planning to breastfeed.
It is not known whether **Finolim 0.5 mg** passes into breastmilk. Consult with your doctor on the best way to feed your baby if you are taking **Finolim 0.5 mg**.

Driving and use of machinery:

The doctor will tell you whether your illness allows you to drive a vehicle, ride a bicycle, and use machinery safely. **Finolim 0.5 mg** is not expected to have an effect on your ability to drive and use machinery.
However, after taking the first dose of **Finolim 0.5 mg,** you need to remain under observation by a healthcare professional for at least 6 hours. During this time and potentially also afterward, your ability to drive and use machinery might be impaired.

Important information about some of the medicine's ingredients:
Finolim 0.5 mg contains about 36 mg sodium per capsule.
This amount constitutes about 1.8% of the recommended maximum daily intake of sodium for adults, which is 2 g.

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

Dosage:
The dosage and manner of treatment will be determined by the doctor only.
The standard dosage is usually: one capsule daily (0.5 mg fingolimod).
Do not exceed the recommended dose.

Method of administration:
The capsules are to be taken orally.
Take **Finolim 0.5 mg** once a day, with a glass of water.
Taking the medicine at the same time each day will help you remember when to take the medicine.
Always swallow **Finolim 0.5 mg** capsules whole, without opening them.

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

If you forgot to take the medicine:
If you forgot a dose of **Finolim 0.5 mg**, refer to a doctor immediately. You may need 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 0.5 mg**, you will undergo:

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

Stopping the treatment:
Adhere to the treatment as recommended by the doctor.
Even if your state of health improves, do not stop the treatment with the medicine without consulting the doctor.
If you stop taking the medicine, the multiple sclerosis symptoms may return and worsen - see section 'Severe worsening of multiple sclerosis after stopping **Finolim 0.5 mg**' in the Side Effects chapter.

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

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

4. Side Effects

As with any medicine, the use of **Finolim 0.5 mg** 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 0.5 mg**

The medicine may cause your heart rate to slow, particularly after you take the first dose. Refer immediately to your doctor or to the nearest hospital emergency room, if you have any symptoms of slow heart rate. 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. You should not receive **live** vaccines during the treatment with **Finolim 0.5 mg** and for two months after you stop taking **Finolim 0.5 mg**. Talk to your doctor before receiving a vaccine during the treatment and for two months after the treatment with **Finolim 0.5 mg**. If you receive a live vaccine, you may receive the infection that the vaccine was supposed to prevent. Vaccinations may be less effective when given during the treatment with **Finolim 0.5 mg**.

Human papillomavirus (HPV) - infections, including papilloma, dysplasia, warts and papillomavirus-related cancer, have been reported in patients treated with **Finolim 0.5 mg**. Your doctor will consider whether you should receive a papillomavirus vaccination before starting the treatment. Because of the risk of infection with the papillomavirus, you should consult with your doctor about routine cervical screening (Pap test).

Finolim 0.5 mg reduces the number of white blood cells (lymphocytes) in your blood. The level of the white blood cells will usually return to normal within two months after stopping the treatment. Your doctor may send you for a blood test to check 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 with **Finolim 0.5 mg** and for two months after the last dose of **Finolim 0.5 mg**:

- 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 brain infection which usually leads to death or severe disability. If PML occurs, it usually occurs in people with a weakened immune system, but has also occurred in people without a weakened immune system. The PML symptoms worsen within days up to weeks. Refer to your doctor immediately if you have new or worsened PML symptoms, which continue for several days, including:

- Weakness of one side of the body
- Loss of coordination in the 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 with macular edema. If macular edema occurs, it usually starts during the first 3 to 4 months after starting treatment with **Finolim 0.5 mg**. Your doctor should perform a vision test before starting the treatment and 3 to 4 months after starting the treatment, or any time you observe changes in vision during the treatment with **Finolim 0.5 mg**. Your risk of macular edema is higher if you have diabetes or if you have had an eye inflammation called uveitis.

  Refer to a 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)

- **Swelling and narrowing of blood vessels in your brain**
  A condition called PRES (Posterior reversible encephalopathy syndrome) has occurred rarely in patients taking **Finolim 0.5 mg**. The PRES symptoms usually improve when you stop taking the medicine. However, without treatment, they could lead to a stroke. Refer to your doctor immediately if you have one or more of the following symptoms:
  - Sudden severe headache
  - Sudden confusion
  - Sudden loss of vision or other changes in your vision
  - Seizures

- **Liver damage**
  Finolim 0.5 mg may cause liver damage. Your doctor should perform blood tests in order to check your liver functions before you start taking **Finolim 0.5 mg** 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
  - Stomach pain
  - Tiredness
  - Loss of appetite
  - Yellowing of the skin or the whites of the eyes
  - Dark urine

- **Breathing problems**
  Some people taking **Finolim 0.5 mg** have shortness of breath. Refer to your doctor immediately if you have new or worsened breathing problems.
  .
- **Severe worsening of multiple sclerosis after stopping Finolim 0.5 mg**
  When stopping treatment with **Finolim 0.5 mg**, multiple sclerosis symptoms might return and worsen compared to before and during treatment. Many people with worsening of MS symptoms that occurred after stopping the treatment, do not return to the level of functioning they had before stopping the **Finolim 0.5 mg** treatment. This worsening occurs usually within 12 weeks after stopping the medicine but might occur later. Before you stop taking **Finolim 0.5**

mg for any reason whatsoever, always talk with your doctor. Tell your doctor if the MS symptoms worsen after you stop the treatment.

- **MS relapse-related abnormal brain lesions** (tumefactive demyelinating lesions)
  Rare cases of MS relapse-related abnormally large brain lesions have been reported in patients treated with **Finolim 0.5 mg.** In case of a severe relapse, your doctor will consider performing an MRI test to evaluate the situation and will decide whether you should stop taking the medicine.

- **High blood pressure.** Your doctor should check your blood pressure during the treatment with **Finolim 0.5 mg**.

- **Skin cancer of the basal cell carcinoma (BCC) and melanoma type.**

Tell your doctor if there are any changes in the appearance of your skin, 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, skin-colored, pearly white or pink. Your doctor should examine your skin to see if there are any changes during the treatment with **Finolim 0.5 mg**. You should 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.

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

- Headache
- Abnormal liver tests
- Diarrhea
- Cough
- Flu
- Inflammation of the sinuses (sinusitis)
- Back pain
- Abdominal pain
- Pain in the arms or legs

Common side effects (appear in 1-10 users out of 100):

- Inflammation of the bronchi (bronchitis)
- Shingles (herpes zoster)
- Ringworm (Tinea versicolor)
- Migraine
- Nausea
- Weakness
- Hair loss
- Actinic keratosis - a precancerous growth
- Increase in blood triglyceride 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.

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Autoimmune hemolytic anemia - the autoimmune form of anemia (decreased amount of red blood cells), in which red blood cells are destroyed.
- Thrombocytopenia - reduction of blood platelets which increases the risk of bleeding or bruising.
- Kaposi's sarcoma - a tumor related to a human herpesvirus 8 infection.
- 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.
- Joint pain.
- Muscle pain.
- Squamous cell carcinoma (SCC) - a type of skin cancer that may appear as a firm red nodule, a sore with crust, or a new sore on an existing scar.
- Merkel cell carcinoma (a type of skin cancer) - possible signs include a painless, bluish-red or skin-colored nodule, frequently on the face, head or neck. Merkel cell carcinoma can also appear as a mass or a firm, painless nodule. Long-term sun exposure and a weak immune system can affect the risk of developing Merkel cell carcinoma.
- Lymphoma - a type of cancer that affects the lymphatic system.

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the 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 babies, 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) stated 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, purified water, 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
Hard white-yellow-colored capsules. 'SCM 0.5 mg' is printed on the capsules.
Contents of the package: 7 or 28 capsules in blister packs.
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: 158-49-34966-00

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