PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Dimethyl Fumarate Medomie 120 mg
Dimethyl Fumarate Medomie 240 mg

Delayed release capsules

The active ingredient and its quantity:
Each capsule contains: 120 mg or 240 mg dimethyl fumarate
Inactive ingredients and allergens: see section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for 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.

The medicine is not intended for children under the age of 18. No information is available regarding the safety and efficacy of Dimethyl Fumarate Medomie in this age group.

1. WHAT IS THE MEDICINE INTENDED FOR?

Dimethyl Fumarate Medomie is intended for treatment of adult patients with relapsing-remitting multiple sclerosis.

Therapeutic class: a medicine that affects the nervous system.

Multiple sclerosis is a chronic disease that affects the central nervous system, including the brain and the spinal cord. Relapsing-remitting multiple sclerosis is characterized by repeated attacks (relapses) of nervous system symptoms. The symptoms differ from patient to patient, but usually include difficulty walking, a sensation of loss of balance and visual difficulties (such as blurry vision or double vision). These symptoms may completely disappear when the attack passes, but some of the problems may remain.

How does Dimethyl Fumarate Medomie work?

It seems that Dimethyl Fumarate Medomie prevents the immune system from damaging the brain and the spinal cord. This may also prevent future deterioration of the disease.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the additional components the medicine contains.
- You are suspected or you have been tested and found to suffer from a rare brain infection called progressive multifocal leukoencephalopathy (PML).

Special warnings regarding the use of the medicine

The medicine may affect white blood cell counts, the kidneys and the liver. Before starting treatment with Dimethyl Fumarate Medomie, the doctor will order blood tests in order to count your white blood cells and will check that your kidneys and liver are working properly. The doctor will perform these tests periodically during treatment. If the number of white blood cells decreases during treatment, the doctor may consider adding additional analytical tests or stopping the treatment.

- Inform the doctor if:
  - **You suffer from a severe kidney disease**
  - **You suffer from a severe liver disease**
  - **You suffer from a gastrointestinal disease**
  - **You suffer from a severe infection (such as pneumonia)**

Shingles may occur during treatment with Dimethyl Fumarate Medomie. In certain cases, serious complications will occur. You should inform the doctor immediately if you suspect symptoms of shingles.

If you think your multiple sclerosis is worsening (for example, weakness or changes in vision) or if you notice new symptoms, talk to your doctor immediately since these may be the symptoms of a rare brain infection called progressive multifocal leukoencephalopathy (PML). PML is a serious condition which may lead to severe disability or death.

A serious but rare kidney disease (Fanconi Syndrome) has been reported for a medicine that contains dimethyl fumarate, in combination with other derivatives (esters) of fumaric acid, used for treatment of psoriasis (skin disease). If you notice that you urinate more, you are thirstier and drink more than usual, you feel that your muscles are weaker, you break a bone or you only suffer from pain, refer to your doctor as soon as possible in order for him to thoroughly examine your condition.

Children and adolescents

Do not use Dimethyl Fumarate Medomie in children and adolescents under the age of 18 years. The safety and efficacy of the medicine in this age group are not known.

Tests and follow-up

Before beginning and during use of the medicine, the doctor will refer you for a blood test and kidney and liver function tests.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:

- Medicines that contain fumarates (derivatives of fumaric acid) for treatment of psoriasis.
- Medicines that affect the body's immune system, including additional medicines for treatment of multiple sclerosis, such as fingolimod, natalizumab, teriflunomide, alemtuzumab, ocrelizumab, cladribine or medicines to treat cancer (rituximab or mitoxantrone).
- Vaccines – taking Dimethyl Fumarate Medomie together with certain types of vaccines (vaccines composed of live viruses) may cause infection and should therefore be avoided. The doctor will advise which other types of vaccine (vaccines composed of inactivated viruses) will be given.
- Medicines that affect the kidneys, such as certain antibiotics (for treatment of infections), diuretics, certain types of analgesics (such as ibuprofen and other similar medicines for treatment of inflammation and non-prescription medicines) and medicines that contain lithium.

Use of the medicine and food

The medicine should be taken with food. This may help reduce some of the very common side effects (see section 4 – "Side effects").

Use of the medicine and alcohol consumption

Avoid drinking concentrated alcoholic beverages (above 30% alcohol by volume) in large amounts (more than a shot) close to the time of taking Dimethyl Fumarate Medomie. Wait an hour between taking the medicine and drinking the beverage, since drinking alcohol within a short period of taking the medicine may increase side effects in the stomach, such as gastritis, especially in people prone to it.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, inform the doctor as soon as possible. You and the doctor will discuss together whether you should continue this treatment.

Pregnancy

Do not take Dimethyl Fumarate Medomie if you are pregnant unless you have discussed this with the doctor.

Breastfeeding

It is not known whether the active ingredient (dimethyl fumarate) passes into breastmilk. Do not use this medicine while breastfeeding. The doctor will help you decide whether to stop breastfeeding or stop taking Dimethyl Fumarate Medomie after considering the possible benefit of breastfeeding for your baby against the possible benefit of the treatment for you.

Driving and operating machinery

The effect of Dimethyl Fumarate Medomie on driving and operating machinery is not known. The use of Dimethyl Fumarate Medomie is not expected to affect the ability to drive and operate machinery. Consult your doctor on whether your disease allows you to perform these activities.

Important information about some of the ingredients of the medicine

This medicine contains less than 23 mg of sodium per capsule, and is therefore essentially considered "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation. The dosage and treatment regimen will be determined only by the doctor. The standard dosage is usually: the starting dosage is 120 mg twice daily for 7 days, and then the regular dosage is 240 mg twice daily.

Do not exceed the recommended dose.

- The medicine should be swallowed whole with water and food.
- Do not halve, crush, dissolve, suck or chew the capsule, since this may increase some side effects.
- Taking Dimethyl Fumarate Medomie with food can help reduce some of the very common side effects (see section 4).

If you have accidentally taken a higher dosage refer to a doctor.

If you have taken an overdose or if a child has accidentally swallowed this medicine, refer immediately to a doctor or to a hospital emergency room and take the package of the medicine with you. You may experience similar side effects to those listed below in section 4.

If you forget to take the medicine at the required time and there are at least 4 hours until the time for the next dose, you can take the missed dose. Otherwise, take only the next dose at the usual time. **Do not take a double dose.**

Follow the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Dimethyl Fumarate Medomie may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

<u>Severe side effects:</u>

- Dimethyl Fumarate Medomie may cause a low lymphocyte (a type of white blood cell) count. A low white blood cell count may increase the risk of infection, including a risk of a rare brain infection called progressive multifocal leukoencephalopathy (PML).
- **Progressive multifocal leukoencephalopathy (PML) –** may lead to severe disability or death. Progressive multifocal leukoencephalopathy has been found to occur after 1 to 5 years of treatment, and therefore the doctor needs to continue monitoring your white blood cell count during treatment, and you should continue monitoring for any potential symptom of PML as explained below. The risk of progressive multifocal leukoencephalopathy may be higher if you haven taken in the past a medicine that weakens the immune system.
- The symptoms of progressive multifocal leukoencephalopathy may be similar to a multiple sclerosis attack. The symptoms may include new or worsening weakness on one side of the body, clumsiness, changes in vision, thinking or memory or confusion, personality changes, speech and communication difficulties, that last more than a few days.
- If you think that your multiple sclerosis is worsening or if you notice new symptoms while you are being treated with Dimethyl Fumarate Medomie, it is very important that you talk to the doctor as soon as possible. In addition, speak to your partner or medical team and let them know about your treatment. The symptoms may appear without you being aware of them yourself.

Refer to the doctor <u>immediately</u> if you suffer from one or more of these symptoms.

- **Severe allergic reactions –**
  The frequency of severe allergic reactions cannot be estimated from the available information (unknown).
- Flushing of the face or body is a very common side effect; however, if you suffer from flushing accompanied by red rash or hives **and one** of the following symptoms:
  - Swelling of the face, lips, mouth and tongue *(angioedema)*
  - Wheezing, difficulty breathing and shortness of breath *(dyspnoea, hypoxia)*
  - Dizziness or loss of consciousness *(hypotension)*

These may indicate a severe allergic reaction *(anaphylaxis)*. **Discontinue use and refer to the doctor immediately.**

<u>Additional side effects:</u>

Very common side effects – effects that occur in more than one out of ten users:

Flushing of the face or sensation of heat, burning or itch, diarrhea, nausea, abdominal pain or abdominal cramps. Taking Dimethyl Fumarate Medomie with food can help reduce these side effects.

Ketones may appear in a urine test.

Consult the doctor about how to treat these side effects. The doctor may reduce the dosage. Do not reduce the dosage without an explicit instruction from the doctor.

Common side effects – effects that occur in up to 1 out of 10 users:

Inflammation of the intestinal wall (gastroenteritis), burning sensation, hot flashes, vomiting, indigestion (dyspepsia), inflammation of the stomach wall (gastritis), digestive disturbances, rash, redness of the skin (pink or red patches – erythema), itching of the skin, heat sensation, hair loss (alopecia).

Side effects that appear in blood or urine tests:

- Decrease in white blood count (leukopenia, lymphopenia). A decrease in the amount of white blood cells may indicate that the body is less able to fight infections. If you suffer from a serious infection (such as pneumonia), refer to the doctor immediately.
- Protein (albumin) in the urine.
- Increased levels of liver enzymes (ALT, AST) in the blood.

Uncommon side effects – effects that occur in 1-10 out of 1,000 users:

- Allergic reaction (hypersensitivity).
- Decreased level of platelets in the blood.

Side effects with unknown frequency – effects whose frequency has not yet been determined:

- Inflammation of the liver and an increase in the levels of liver enzymes (ALT or AST along with bilirubin).
- Shingles (herpes zoster) accompanied by symptoms such as blisters, burning sensation, itching or skin pain, usually on one side of the upper body or face, and other symptoms such as fever and weakness in the early stages of infection, followed by numbness, itching and red patches with severe pain.
- Rhinorrhoea.

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

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:
https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Storage conditions:

Store at a temperature lower than 25°C.

The medicine can be used for up to 30 days after first opening the bottle, but no later than the expiry date that appears on the package.

6. Additional information

- **In addition to the active ingredient the medicine also contains:**
  Microcrystalline cellulose, methacrylic acid ethyl copolymer (1:1) dispersion 30%, croscarmellose sodium, talc, methacrylic acid methyl methacrylate copolymer (1:1), colloidal silicon dioxide, triethyl citrate and magnesium stearate.
  The capsule shell contains gelatin and titanium dioxide and is imprinted with black ink.
- **What does the medicine look like and what are the contents of the package?**
  - Dimethyl Fumarate Medomie 120 mg – a white gelatin capsule with "120 mg" printed in black ink. A bottle containing 14 capsules.
  - Dimethyl Fumarate Medomie 240 mg – a white gelatin capsule with "240 mg" printed in black ink. A bottle containing 60 capsules.

Marketing authorization holder and address: Medomie Pharma Ltd., P.O.B. 816, Givatayim 5358305

Name and address of the manufacturer: MSN Laboratories Private Limited, Telangana, 509228 India

Revised in December 2023 in accordance with the Ministry of Health guidelines.

Registration numbers of the medicines in the National Drug Registry of the Ministry of Health:

Dimethyl Fumarate Medomie 120 mg: 170-06-36832-99
Dimethyl Fumarate Medomie 240 mg: 170-07-36833-99