Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Vumerity 231 mg
Delayed release capsules

Name and quantity of active ingredient:
Each delayed-release capsule contains:
diroximel fumarate 231 mg.

For a list of inactive ingredients and allergens in this medicine, see section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult 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.

1. What is this medicine intended for?

Vumerity is intended to treat adult patients with relapsing-remitting multiple sclerosis.

Therapeutic group: medicine that affects the nervous system.

2. Before using this medicine

Do not use this medicine if:
- you are sensitive (allergic) to diroximel fumarate or any of the other ingredients in this medicine
- you have moderately or severely impaired kidney function or if you have mildly, moderately or severely impaired liver function
- you have a human immunodeficiency virus (HIV) infection
- you have severe active infections or active chronic infections such as tuberculosis, hepatitis B and C
- you have severe stomach or digestive system disorders (conditions such as an ulcer in the intestines)
- the number of white blood cells is below threshold (leukocytes < 3.0 X 10^9/L and lymphocytes < 0.5 X 10^9/L)
- you have PML (progressive multifocal leukoencephalopathy) or if you are suspected of having the disease. Progressive multifocal leukoencephalopathy is an infection of the brain.
- Do not start Vumerity therapy if you are pregnant.
- Do not use Vumerity in children and adolescents under 18 years of age.

Special warnings about using this medicine

Before starting treatment with Vumerity, tell your doctor if any of the following conditions apply to you:
- you have other illnesses
- you have any allergies

Children and adolescents
This medicine is not intended for children and adolescents under 18 years of age.
There is no information about the safety and efficacy of using this medicine in children and adolescents under 18 years of age.

Adults and the elderly
The safety and efficacy of Vumerity have not been investigated in adults over 55 years of age.
Do not exceed the prescribed dosage. If you believe that the effect of the medicine is too weak or too strong, talk to your doctor or pharmacist.

Tests and follow-up
Using Vumerity can change the number of white blood cells in your blood and cause changes in your kidney and liver values. Before treatment with Vumerity, your doctor will do a blood test to check the number of white blood cells and check your kidney and liver function. Your doctor will repeat these tests regularly during treatment.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- medicines that contain fumaric acid esters (fumarates) and are used to treat psoriasis
- medicines that affect the body's immune system, including other medicines to treat multiple sclerosis such as fingolimod, natalizumab, or mitoxantrone
- medicines that affect the kidneys, including some antibiotics (used to treat infections)
- diuretics
- certain types of pain relievers (including over-the-counter products)
- lithium-containing medicines.
- Vaccines: Vaccination with live vaccines is not recommended during treatment with Vumerity, as this could lead to infection during treatment with Vumerity. If you need a vaccination you should ask your doctor for advice first.

Using this medicine and food
Vumerity can be taken with or without food. If Vumerity is taken with food, a high-fat and high-calorie meal should be avoided (see section 3, ‘How to use this medicine’ for information about taking this medicine with food).

Using this medicine and alcohol consumption
Vumerity should not be taken together with alcoholic beverages.

Pregnancy and breastfeeding

Pregnancy
If you are pregnant or breastfeeding, think you might be pregnant, or are planning to become pregnant, ask your doctor or pharmacist for advice before taking this medicine.

You must not start Vumerity therapy if you are pregnant. Only take Vumerity during pregnancy if you have discussed this in detail with your doctor and no better alternative has been found.

Breastfeeding
It is not known whether the components of Vumerity are excreted in breast milk. Only take Vumerity while you are breastfeeding if you have discussed this with your doctor.

Driving and using machines
It is not known whether Vumerity affects your ability to drive and use machines. Your doctor will tell you whether your illness allows you to drive and use machines safely.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

Take Vumerity medicine exactly as your doctor has told you.

Starting dose
The starting dose recommended for Days 1-7 is one capsule twice a day.
Take this starting dose for the first 7 days, then take the regular dose.

Regular dose
The recommended dose is 2 capsules, twice a day.

Do not exceed the recommended dose.

Your doctor may temporarily reduce your dose to 231 mg twice a day in the event of side effects such as flushing, rash, hot flashes, itching, or a burning sensation. Such a dose reduction should be as short as possible and not last longer than 4 weeks, otherwise your doctor should talk to you about changing the therapy. Do not reduce your dose on your own unless instructed to do so by your doctor.

- Talk to your doctor about taking the right dose that will reduce your side effects.
- You can take this medicine with or without food. Taking it with food (avoid high-calorie and high-fat foods) can help reduce the flushing side effect.
- If taking this medicine with food, avoid taking it with high-fat and high-calorie foods.
- A meal may contain up to 700 calories and up to 30 grams of fat.
- Swallow each capsule with a little water. Do not divide, crush, suck, or chew the capsule or sprinkle its content on food.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you**.**

If you forget to take this medicine at the scheduled time, do not take a double dose. You can take the missed dose if there are at least 4 hours between the morning and evening doses. Otherwise, take your next dose at the usual time and consult your doctor.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor.

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

If you have any further questions about using this medicine, consult your doctor or

pharmacist.

4. Side effects

Like with all medicines, using Vumerity may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Vumerity (diroximel fumarate) and the comparable product Tecfidera (dimethyl fumarate) are converted to the active ingredient monomethyl fumarate after oral ingestion. It is to be expected that the undesirable effects of Vumerity will be the same as those of Tecfidera.

Consult a doctor immediately if you notice any of the following serious side effects - you may need urgent medical attention:

1. **Serious allergic reactions:**
   - such as difficulty breathing, hives or swelling of the throat and/or tongue, rash, hot flashes, itching
   - Reddening, rash, hot flashes, itching, and a flushing sensation may occur, especially when starting treatment with Vumerity.
   - Redness of the face or body (flushing) is a very common side effect. Contact a doctor immediately if you develop redness on your face or body with a rash and any of the following symptoms:
     - swelling of the face, lips, mouth, or tongue
     - wheezing, difficulty breathing, or shortness of breath
     - dizziness or loss of consciousness

These symptoms could indicate a serious allergic reaction. Stop taking the treatment and contact a doctor immediately.

The frequency of serious allergic reactions is not known.

2. **Progressive multifocal leukoencephalopathy (PML)**

   The number of lymphocytes (a type of white blood cell) may be low for a long time. If your white blood cells are low for a long time, your risk of infections increases, including the risk of a rare brain infection called progressive multifocal leukoencephalopathy (PML). Symptoms of PML can be similar to those of multiple sclerosis flare-up. Symptoms can include: a new or worsening weakness on one side of the body; clumsiness; changes in eyesight, thinking, or memory; confusion or personality changes that last for several days. Talk to a person you trust or who cares for you and inform them about your treatment. You may have symptoms that you may not notice yourself.

3. **Shingles (herpes zoster infection)** - can occur at any time during treatment.
   Symptoms of shingles may include fever followed by numbness, itching and red spots or blisters on your face or trunk with severe pain.

Very common side effects - especially at the start of treatment (affect more than one in ten users)

- reddening of the face or body, rash, hot flashes, itching and/or burning sensations of the skin (flushing)
- itching
- loose stools (diarrhea)
- nausea
- stomach pain or cramps
- presence of ketones in urine

Common side effects (affect 1-10 in 100 users)

- indigestion, vomiting, inflammation of the stomach lining
- gastrointestinal complaints
- itchy skin
- rash
- itchy pink or red spots on the skin (erythema)
- burning sensation
- hot flashes

Common side effects that may show up in your blood or urine tests:

- low number of white blood cells (lymphopenia, leukopenia) in the blood
- albumin in the urine
- increased levels of liver enzymes (ALT, AST) in the blood

Uncommon side effects (affect 1-10 in 1,000 users)

- allergic reactions (hypersensitivity)

Side effects observed after taking Tecfidera

- Progressive multifocal leukoencephalopathy (PML) has occurred in patients with a persistent decrease in white blood cells after administration of Tecfidera.
- shingles (herpes zoster infections) (see 'Serious side effects' in section 3)
- runny nose
- circular hair loss (alopecia)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the carton and bottle. The expiry date refers to the last day of that month.

Storage conditions:

- Store this medicine below 25°C.
- Store in the original package.

6. Additional information

In addition to the active ingredient diroximel fumarate, this medicine also contains:

Inactive ingredients:
methacrylic acid-ethyl acrylate copolymer; crospovidone; microcrystalline cellulose; colloidal silicone dioxide; triethyl citrate; talc; magnesium stearate (non-bovine); hypromellose; titanium dioxide; potassium chloride; carrageenan; black iron oxide; shellac; dehydrated alcohol; propylene glycol; isopropyl alcohol; butyl alcohol; ammonia solution; potassium hydroxide and water.

What the medicine looks like and contents of the pack
Delayed-release capsules each containing 231 mg diroximel fumarate. The capsules are white and imprinted with **DRF 231 mg**.

Quantity per pack: 106 or 120 capsules. Not all pack sizes may be marketed.

Registration holder's name and address:
Medison Pharma Ltd., 10 Hashiloach St., POB 7090, Petach Tikva.

Manufacturer's name and address:
Biogen Inc., Cambridge MA 02142, USA.

- For nurse service and additional information call ***5274**

Approved in December 2021.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 168-83-36412-00

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