

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

This medicine is marketed upon physician's prescription only

PREVYMIS[®] 240 mg film-coated tablets
PREVYMIS[®] 480 mg film-coated tablets

Each film-coated tablet of **PREVYMIS 240 mg** contains:
letermovir 240 mg

Each film-coated tablet of **PREVYMIS 480 mg** contains:
letermovir 480 mg

For the list of the inactive ingredients see section 6. "FURTHER INFORMATION". See also subsection 2. "Important information about some of the ingredients of the medicine".

Read all of this leaflet carefully before you start using the medicine.

- This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

1. WHAT PREVYMIS IS INTENDED FOR?

PREVYMIS is indicated for prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult CMV-seropositive recipients [R+] of an allogeneic haematopoietic stem cell transplant (HSCT).

Therapeutic group: Antivirals for systemic use, direct acting antivirals, ATC code: J05AX18.

PREVYMIS is an antiviral medicine that contains the active substance letermovir. The medicine is given upon physician's prescription only.

PREVYMIS is a medicine for adults who have recently had a bone marrow transplant. The medicine helps stop you from getting ill from CMV ('cytomegalovirus').

CMV is a virus that a lot of people have without knowing. Normally, CMV just stays in their body and it does not hurt them. However, if your immune system is weak after you get a bone marrow transplant, you may be at high risk of becoming ill from CMV.

2. BEFORE USING PREVYMIS

Do not use PREVYMIS if:

- you are allergic to letermovir or any of the other ingredients of this medicine (listed in section 6).
- you take either of these medicines:
 - pimozide - antipsychotic
 - ergot alkaloids (such as ergotamine and dihydroergotamine) - used for migraine headaches.

- you take the following herbal product:
 - St. John's wort (*Hypericum perforatum*) for treatment of depression symptoms.

If you are taking PREVYMIS with cyclosporine, do not take the following medicines:

- dabigatran - used for blood clots
- atorvastatin, simvastatin, rosuvastatin, pitavastatin – for high cholesterol

Special warnings regarding use of PREVYMIS

If you are also taking a medicine for high cholesterol (see list of medicines in section “Interactions with other medicines” below) you must tell your doctor immediately if you have unexplained muscle aches or pains especially if you feel unwell or have a fever. Your medicine or dose may then need to be changed. See the package leaflet for your other medicine for further information.

Additional blood tests may be needed to monitor the following medicines:

- Cyclosporine, tacrolimus, sirolimus
- Voriconazole

Children and adolescents

PREVYMIS is not indicated for children and adolescents under 18 years of age.

No data is available for the safety and efficacy of this medicine in children and adolescents under 18 years of age.

Interactions with other medicines

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines, including non-prescription medicines and nutritional supplements.

This is because **PREVYMIS** may affect the way other medicines work, and other medicines may affect how **PREVYMIS** works. Your doctor or pharmacist will tell you if it is safe to take **PREVYMIS** with other medicines.

There are some medicines you **must not take** with **PREVYMIS** (see list under “Do not use **PREVYMIS** if:”).

There are some additional medicines you **must not take** with **PREVYMIS** and cyclosporine (see list under “If you are taking **PREVYMIS** with cyclosporine, do not take the following medicines:”).

Also tell your doctor if you are taking any of the following medicines. This is because your doctor may have to change your medicines or change the dose of your medicines:

- alfentanil - for severe pain
- fentanyl - for severe pain
- quinidine - for abnormal heart rhythms
- cyclosporine, tacrolimus, sirolimus - used to prevent transplant rejection
- voriconazole - for fungal infections
- statins, such as atorvastatin, fluvastatin, rosuvastatin, simvastatin, pravastatin, pitavastatin - for high cholesterol
- glyburide, repaglinide - for high blood sugar
- phenobarbital – used as a sedative or hypnotic
- carbamazepine, phenytoin - for fits or seizures
- dabigatran, warfarin - used to thin the blood or for blood clots
- midazolam – used as a sedative
- amiodarone - used to correct irregular heartbeats
- oral contraceptive steroids-for birth control
- omeprazole, pantoprazole – for stomach ulcers and other stomach problems
- nafcillin - for bacterial infections

- rifabutin, rifampicin - for mycobacterial infections
- thioridazine - for psychiatric disorders
- bosentan - for high blood pressure in the vessels in the lungs
- efavirenz, etravirine, nevirapine, lopinavir, ritonavir - for HIV
- modafinil - for wakefulness

Using the medicine and food

Take **PREVYMIS** with or without food.

Pregnancy

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine. **PREVYMIS** is not recommended in pregnancy. This is because it has not been studied in pregnancy and it is not known if **PREVYMIS** will harm your baby while you are pregnant.

Breast-feeding

If you are breast-feeding or are planning to breast-feed, tell your doctor before taking this medicine. It is not known if **PREVYMIS** gets in your breast milk and will be passed to your baby.

Driving and using machines

PREVYMIS may have minor influence on your ability to drive and use machines (see section 4 Side Effects below). Some patients have reported fatigue (feeling very tired) or vertigo (feeling like you are spinning) during treatment with **PREVYMIS**. If you experience any of these effects, do not drive or use machines until the effect wears off.

Important information about some of the ingredients of the medicine

PREVYMIS contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE PREVYMIS

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure regarding the dosage and treatment regimen.

How much to take

The dosage and treatment regimen will be determined by the doctor only. Usually, the recommended dose of **PREVYMIS** is one 480 mg tablet once a day. If you also take cyclosporine, your doctor will decrease the dose of **PREVYMIS** to one 240 mg tablet once a day.

- Take **PREVYMIS** at the same time every day.
- Take it with or without food.

Do not exceed the recommended dose.

How to take

- Swallow the tablet whole with some water. No information is available regarding breaking/crushing/chewing of tablets.

If you take more PREVYMIS than you should

If you take more **PREVYMIS** than you should, call your doctor straight away.

If you forget to take PREVYMIS

It is very important that you do not miss or skip doses of **PREVYMIS**.

- If you forget a dose, take it as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose. Take your next dose at the usual time.
- Do not take two doses of **PREVYMIS** at the same time to make up for a missed dose.
- If you are not sure what to do, call your doctor or pharmacist.

Do not stop taking PREVYMIS

Do not stop taking **PREVYMIS** without talking to your doctor first. Do not run out of **PREVYMIS**. This will give the medicine the best chance to keep you from becoming ill from CMV after you get a bone marrow transplant.

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 on the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicines, this medicine can cause side effects, although not everybody gets them.

Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Common side effects: may affect up to 1 in 10 people

- diarrhoea
- feeling sick (nausea)
- being sick (vomiting)

Uncommon side effects: may affect up to 1 in 100 people

- allergic reaction (hypersensitivity) – the signs may include wheezing, difficulty breathing, rashes or hives, itchiness, swelling.
- loss of appetite
- changes in taste
- headache
- feeling like you are spinning (vertigo)
- stomach ache
- abnormalities in laboratory tests of liver function (i.e. raised levels of liver enzymes)
- muscle spasms
- high blood creatinine - shown in blood tests
- feeling very tired (fatigue)
- swelling of hands or feet

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: <https://sideeffects.health.gov.il>.

5. HOW TO STORE PREVYMIS?

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. 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 pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions:** This medicine does not require any special temperature storage conditions. It is recommended to store at room temperature. Store in the original package in order to protect from moisture.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. FURTHER INFORMATION

What PREVYMIS contains

In addition to the active ingredient **PREVYMIS** also contains:

Tablet core

Microcrystalline cellulose (E460), croscarmellose sodium (E468), povidone 25 (E1201), colloidal anhydrous silica (E551), magnesium stearate (E470b).

Film-coating

Hypromellose (E464), titanium dioxide (E171), lactose monohydrate, triacetin (E1518), iron oxide yellow (E172), iron oxide red (only for 480 mg tablets) (E172), carnauba wax (E903). See section 2 'Important information about some of the ingredients of the medicine'.

What PREVYMIS looks like and contents of the pack

PREVYMIS 240 mg film-coated tablets

PREVYMIS 240 mg film-coated tablet is a yellow oval tablet, debossed with "591" on one side and corporate logo on the other side. The tablet is 16.5 mm long and 8.5 mm wide. The 240 mg tablets are packaged into a carton containing four (4) 7-count Polyamide/Aluminium/PVC – Aluminium blister cards for a total of 28 tablets.

PREVYMIS 480 mg film-coated tablets

PREVYMIS 480 mg film-coated tablet is a pink oval, bi-convex tablet, debossed with "595" on one side and corporate logo on the other side. The tablet is 21.2 mm long and 10.3 mm wide. The 480 mg tablets are packaged into a carton containing four (4) 7-count Polyamide/Aluminium/PVC – Aluminium blister cards for a total of 28 tablets.

Marketing Authorisation Holder and Importer

Merck Sharp & Dohme (Israel-1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

Revised in October 2023 according to MOHs guidelines.

Drug registration no. listed in the official Registry of the Ministry of Health:

PREVYMIS 240 mg film-coated tablets: 166-13-35974

PREVYMIS 480 mg film-coated tablets: 166-14-35993