**Package leaflet: Information for the patient**

**PREVYMIS 240 mg concentrate for solution for infusion**
**PREVYMIS 480 mg concentrate for solution for infusion**
letermovir

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you are given this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, or nurse.
- If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**



## 1. What PREVYMIS is and what it is used for

PREVYMIS is an antiviral prescription medicine that contains the active substance letermovir.

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. What you need to know before you are given PREVYMIS

**You should not be given 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 - used for Tourette's syndrome
  - ergot alkaloids (such as ergotamine and dihydroergotamine) - used for migraine headaches.
- you take the following herbal product:
  - St. John's wort (*Hypericum perforatum*)

You should not be given PREVYMIS if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before you are given PREVYMIS.

**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

**Warnings and precautions**
If you are also taking a medicine for high cholesterol (see list of medicines in section "Other medicines and PREVYMIS" 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 medicinal products:
- Cyclosporine, tacrolimus, sirolimus
- Voriconazole

**Children and adolescents**
PREVYMIS is not for use in children and adolescents under 18 years old. This is because PREVYMIS has not been tested in this age group.

**Other medicines and PREVYMIS**
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. 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 take PREVYMIS if you take either of these 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
- carbamazepine, phenobarbital, 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

You can ask your doctor or pharmacist for a list of medicines that may interact with PREVYMIS.

**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. Breast-feeding is not recommended while taking PREVYMIS. This is because 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 Possible 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.

**PREVYMIS contains sodium**
PREVYMIS contains sodium. If you are on a low sodium diet, talk to your doctor before you are given this medicine.

Each 240 mg vial contains 23 mg sodium (main component of cooking/table salt). This is equivalent to 1.15% of the recommended maximum daily dietary intake of sodium for an adult.

Each 480 mg vial contains 46 mg sodium (main component of cooking/table salt). This is equivalent to 2.30% of the recommended maximum daily dietary intake of sodium for an adult.

**PREVYMIS contains cyclodextrin**
Each 240 mg dose (12 mL vial) of this medicine contains 1800 mg cyclodextrin.
Each 480 mg dose (24 mL vial) of this medicine contains 3600 mg cyclodextrin.

If you have a kidney disease, talk to your doctor before you receive this medicine.

## 3. How you are given PREVYMIS

The recommended dose of PREVYMIS is 480 mg once a day. If you also take cyclosporine, your doctor will decrease the dose of PREVYMIS to 240 mg once a day.
You will get PREVYMIS as an infusion (drip) into a vein and it will take about 1 hour.
You will get PREVYMIS once a day.

**If you are given more PREVYMIS than you should**
If you think you have been given too much PREVYMIS, tell your doctor straight away.

**If you miss your appointment to get PREVYMIS**
It is very important that you do not miss or skip doses of PREVYMIS.
- If you miss your appointment to get PREVYMIS, call your doctor straight away to reschedule your appointment.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Common:** may affect up to 1 in 10 people
- diarrhoea
- feeling sick (nausea)
- being sick (vomiting)

**Uncommon:** 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
- muscle spasms
- high blood creatinine - shown in blood tests
- feeling very tired (fatigue)
- swelling of hands or feet

**Reporting of side effects**
If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store PREVYMIS

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions. Store in original carton to protect from light.

Chemical and physical in-use stability has been demonstrated for 48 hours at 25 °C and for 48 hours at 2 to 8 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Any unused portion of the infusion solution should be discarded.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

## 6. Contents of the pack and other information

**What PREVYMIS contains**
The active substance is letermovir. Each vial contains 240 mg or 480 mg letermovir. Each mL of concentrate contains 20 mg/mL.
The other ingredients are: hydroxypropylbetadex (cyclodextrin), sodium chloride, sodium hydroxide (E524), water for injections.

**What PREVYMIS looks like and contents of the pack**
PREVYMIS 240 mg and 480 mg concentrate for solution for infusion is a clear, colourless liquid and may contain a few product-related small translucent or white particles.
The 240 mg and 480 mg concentrate for solution for infusion is packaged in clear, glass vials. Each

vial is packaged in a carton.

**Marketing Authorisation Holder**
Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

**Manufacturer**
Schering-Plough Labo NV
Industriepark 30 – Zone A
B-2220 Heist-op-den-Berg
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu.

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**The following information is intended for healthcare professionals only:**

Administration instructions for PREVYMIS concentrate for solution for infusion

PREVYMIS concentrate for solution for infusion vials are for single use only. Discard any unused portion.

Administration through a sterile 0.2 or 0.22 micron PES in-line filter
PREVYMIS concentrate for solution for infusion may contain a few product-related small translucent or white particles. Administration of PREVYMIS diluted solution always requires the use of a sterile 0.2 micron or 0.22 micron PES in-line filter, regardless of whether these product-related particles are visible in the vial or diluted solution.

Preparation
PREVYMIS concentrate for solution for infusion must be diluted prior to intravenous (IV) use. The preparation and administration instructions are the same for either dose.

- Inspect vial contents for discolouration and particulate matter prior to dilution. PREVYMIS concentrate for solution for infusion is a clear, colourless solution and may contain a few product-related small translucent or white particles.
- Do not use the vial if the solution is cloudy, discoloured or contains matter other than a few small translucent or white particles.
- Do not use PREVYMIS concentrate for solution for infusion with IV bags and infusion set materials containing polyurethane or the plasticizer diethylhexyl phthalate (DEHP). Materials that are phthalate-free are also DEHP-free.
- Do not shake PREVYMIS vial.
- Add one single-dose vial of (either 12 mL (240 mg dose) or 24 mL (480 mg dose)) of PREVYMIS concentrate for solution for infusion to a 250 mL pre-filled IV bag containing either 0.9% sodium chloride or 5% dextrose, and mix the diluted solution by gentle inversion. Do not shake.
- Once diluted, the solution of PREVYMIS is clear, and ranges from colourless to yellow. Variations of colour within this range do not affect the quality of the product. The diluted solution should be inspected visually for particulate matter and discolouration prior to administration. Discard if the diluted solution is cloudy, discoloured, or contains matter other than a few small translucent or white particles. If a vial is added to a 250 mL IV diluent bag, the final concentration ranges of letermovir would be 0.9 mg/mL (for 240 mg dose) and 1.8 mg/mL (for 480 mg dose).

Administration

- The diluted solution must be administered through a sterile 0.2 micron or 0.22 micron PES in-line filter.
- Do not administer the diluted solution through a filter other than a sterile 0.2 micron or 0.22 micron PES in-line filter.
- Administer as an intravenous infusion only. Do not administer as an intravenous push or bolus.
- After dilution, administer PREVYMIS via intravenous infusion via peripheral or central venous catheter using a total time of approximately 60 minutes. Administer the entire contents of the IV bag.

Compatible intravenous solutions and other medicinal products

- PREVYMIS concentrate for solution for infusion is compatible with 0.9% sodium chloride and 5% dextrose solutions.
- Compatible medicinal products are listed below.
- This medicinal product must not be mixed with other medicinal products except those listed below.
- PREVYMIS should not be co-administered through the same intravenous line (or cannula) with other medicinal products and diluent combinations except those listed below.

**List of compatible medicinal products when PREVYMIS and medicinal products* are prepared in 0.9% sodium chloride**

- Ampicillin sodium
- Ampicillin sodium/Sulbactam sodium
- Anti-thymocyte globulin
- Caspofungin
- Daptomycin
- Fentanyl citrate
- Fluconazole
- Human insulin
- Magnesium sulfate
- Methotrexate
- Micafungin

*Refer to the prescribing information to confirm compatibility of simultaneous co-administration.

**List of compatible medicinal products when PREVYMIS and medicinal products* are prepared in 5% dextrose**

- Amphotericin B (lipid complex)[†]
- Anidulafungin
- Cefazolin sodium
- Ceftaroline
- Ceftriaxone sodium
- Doripenem
- Famotidine
- Folic acid
- Ganciclovir sodium
- Hydrocortisone sodium succinate
- Morphine sulfate
- Norepinephrine bitartrate
- Pantoprazole sodium
- Potassium chloride
- Potassium phosphate
- Tacrolimus
- Telavancin
- Tigecycline

*Refer to the prescribing information to confirm compatibility of simultaneous co-administration.

[†]Amphotericin B (lipid complex) is compatible with PREVYMIS. However, Amphotericin B (liposomal) is incompatible (see section 6.2).

Compatible intravenous bags and infusion set materials

PREVYMIS is compatible with the following intravenous bags and infusion set materials. Any intravenous bags or infusion set materials not listed below should not be used.

*Intravenous bag materials*
Polyvinyl chloride (PVC), ethylene vinyl acetate (EVA) and polyolefin (polypropylene and polyethylene)

*Infusion set materials*
PVC, polyethylene (PE), polybutadiene (PBD), silicone rubber (SR), styrene–butadiene copolymer (SBC), styrene-butadiene-styrene copolymer (SBS), polystyrene (PS)

*Plasticizers*
Tris (2-ethylhexyl) trimellitate (TOTM), butyl benzyl phthalate (BBP)

*Catheters*
Radiopaque polyurethane

Incompatible medicinal products
PREVYMIS concentrate for solution for infusion is physically incompatible with amiodarone hydrochloride, amphotericin B (liposomal), aztreonam, cefepime hydrochloride, ciprofloxacin, cyclosporine, diltiazem hydrochloride, filgrastim, gentamicin sulfate, levofloxacin, linezolid, lorazepam, midazolam HCl, mycophenolate mofetil hydrochloride, ondansetron, palonosetron.

Incompatible IV bags and infusion set materials
PREVYMIS is incompatible with diethylhexyl phthalate (DEHP) plasticizers and polyurethane-containing IV administration set tubing.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.