

Prevymis (letermovir)



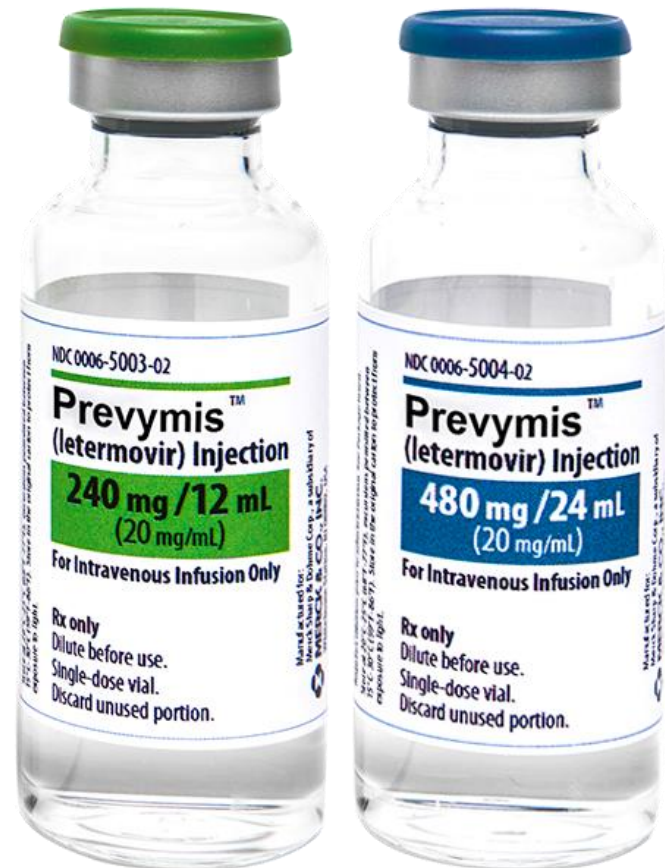
NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Previmis
- **Generic name:** Letermovir
- **Pharmacological class:** CMV DNA terminase complex inhibitor
- **Strength and Formulation:** 240mg, 480mg tabs; 240mg/12mL, 480mg/24mL; solution for IV infusion after dilution (contains hydroxypropyl betadex)
- **Manufacturer:** Merck & Co
- **How supplied:** Tabs—14, 28; Single-dose vial (30mL)—1
- **Legal Classification:** Rx

PREVYMIS



Indications

- Prophylaxis of **cytomegalovirus (CMV)** infection and disease in adult CMV-seropositive recipients of an allogeneic hematopoietic stem cell transplant (HSCT)

Dosage & Administration

■ **Tablets**

- Swallow whole
- Start between Days 0 and 28 post-transplantation (before or after engraftment) and continue through Day 100 post-transplant
- 480mg once daily
- Concomitant cyclosporine: 240mg once daily

Dosage & Administration

■ Injection

- Give as IV infusion over 1hr; **do not** give as IV bolus
- Start between Days 0 and 28 post-transplantation (before or after engraftment) and continue through Day 100 post-transplant
- 480mg once daily
- Concomitant cyclosporine: 240mg once daily
- Switch to oral therapy as soon as able to take oral meds

Considerations for Special Populations

- **Pediatric:** <18yrs: not established
- **Pregnancy:** Insufficient human data to establish drug-associated risk
- **Nursing mothers:** Unknown whether drug is present, affects human milk production, or has effect on breastfed child
- **Renal impairment:** CrCl <50mL/min: closely monitor serum creatinine (for IV)
- **Hepatic impairment:** Severe (Child-Pugh C): not recommended

Contraindications

- Concomitant pimozide, ergot alkaloids
- Concomitant pitavastatin, simvastatin when co-administered with cyclosporine

Warnings/Precautions

- Monitor for CMV reactivation after therapy completion

Interactions

- **See Contraindications**
- Specific interactions with cyclosporine: see full labeling
- May be potentiated by OATP1B1/3 inhibitors
- Potentiates CYP3A substrates (eg, midazolam, alfentanil, fentanyl, quinidine), OATP1B1/3 substrates: see full labeling for dose adjustment

Interactions

- Concomitant amiodarone, phenytoin, voriconazole, sirolimus, tacrolimus, omeprazole, pantoprazole: monitor frequently and adjust dose if necessary
- Monitor INR with warfarin
- Concomitant glyburide, repaglinide, rosiglitazone: monitor glucose levels; avoid repaglinide if co-administered with cyclosporine

Interactions

- Concomitant rifampin, pitavastatin, simvastatin: **not recommended**
- Concomitant atorvastatin (max 20mg daily): monitor closely; **avoid** if co-administered with cyclosporine
- Concomitant fluvastatin, lovastatin, pravastatin, rosuvastatin: monitor and reduce statin dose if necessary; avoid lovastatin if co-administered with cyclosporine

Adverse Reactions

- Nausea
- Diarrhea
- Vomiting
- Peripheral edema
- Cough
- Headache
- Fatigue
- Abdominal pain
- Lab abnormalities

Mechanism of Action

- Letermovir inhibits the CMV DNA terminase complex which is required for viral DNA processing and packaging
- Letermovir affects the production of proper unit length genomes and interferes with virion maturation

Clinical Studies

- Prevyms was evaluated in a Phase 3 multicenter, double-blind, placebo-controlled trial (P001) in adult CMV-seropositive recipients of an allogeneic hematopoietic stem cell transplant (HSCT)
 - Patients were randomized to oral or IV Prevyms 480mg once daily or placebo

Clinical Studies

- CMV DNA monitoring was performed weekly until post-transplant Week 14 and then bi-weekly until post-transplant Week 24
 - Follow-up was conducted through Week 48
- Of the total 565 treated patients, 70 were excluded due to CMV viremia occurring prior to study drug initiation

Clinical Studies

- The **primary efficacy endpoint** was the incidence of clinically significant CMV infection through Week 24 post-transplant (prophylaxis failure)
- **Clinically significant CMV infection** was defined as occurrence of either CMV end-organ disease or initiation of anti-CMV pre-emptive therapy based on documented CMV viremia

Clinical Studies

- A smaller proportion of patients **failed prophylaxis** in the letermovir group vs placebo (38% vs 61%)
- Fewer patients failed therapy due to **clinically significant CMV infection** by Week 24 in the letermovir group vs placebo (18% vs 42%)

Clinical Studies

- The rate of **study discontinuation** before Week 24 was slightly higher in the letermovir group vs placebo (17% vs 16%)
- The stratum-adjusted **treatment difference** (letermovir – placebo) was -23.5 (95% CI: -32.5, -14.6; $P < .0001$)
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

<https://www.empr.com/prevymis/drug/34775/>