PREVYMIS® ▼ (letermovir)

PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics before prescribing

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD (Tel: 01992 467272), UK.
By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION
PREVYMIS 240 mg film-coated tablets:
each film-coated tablet contains 240 mg of letermovir.
PREVYMIS 240 mg concentrate for solution for infusion: each vial contains 240 mg (12 mL per vial) of letermovir. Each mL contains 20 mg of letermovir.

USES
Prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult CMV-seropositive recipients [R+] of an allogeneic haematopoietic stem cell transplant (HSCT).

DOSAGE AND ADMINISTRATION
Therapy to be initiated by a physician experienced in the management of patients who have had an allogeneic haematopoietic stem cell transplant. Tablets and concentrate for solution for infusion may be used interchangeably, no dose adjustment necessary.

Recommended dosage: 480 mg once daily.
Start treatment after HSCT. Treatment may start on the day of transplant and no later than 28 days post-transplant. Start before or after engraftment. Prophylaxis should continue to 100 days post-transplant. Safety and efficacy >100 days: Not studied. Some patients at high risk for late CMV reactivation may benefit from prolonged letermovir prophylaxis >100 days post-transplant. Carefully assess the benefit-risk balance for use >100 days.
Dosage adjustment: When co-administered with ciclosporin, decrease the dosage of PREVYMIS to 240 mg once daily:

- If ciclosporin is initiated after starting letermovir, decrease the next dose of letermovir to 240 mg once daily.
- If ciclosporin is discontinued after starting letermovir, increase the next dose of letermovir to 480 mg once daily.
- If ciclosporin dosing is temporarily interrupted due to high ciclosporin levels, no dose adjustment is required

Film-coated tablets: Oral use. Swallow whole with or without food. Do not divide, crush or chew.
Concentrate for solution for infusion: Intravenous use only. Do not administer as an intravenous push or bolus. Requires dilution prior to administration. Administer by intravenous infusion via peripheral or central venous catheter using a total time of approximately 60 minutes.

Special populations: *Elderly*: no dose adjustment required. *Hepatic impairment*: no dose adjustment required for patients with mild to moderate hepatic impairment. Not recommended for patients with severe hepatic impairment (Child-Pugh Class C). *Combined hepatic and renal impairment*: not recommended in patients with moderate hepatic impairment combined with moderate or severe renal impairment. *Renal impairment*: no dose adjustment recommended for patients with mild, moderate, or severe renal impairment. No recommendation for patients with ESRD. PREVYMIS concentrate for solution for infusion contains hydroxypropylbetadex. The anticipated clinical exposure to hydroxypropylbetadex with intravenously administered letermovir is expected to be approximately 3600 mg/day for a letermovir dose of 480 mg. In patients with moderate or severe renal impairment (creatinine clearance < 50 mL/min), accumulation of hydroxypropylbetadex could occur. Closely monitor serum creatinine levels in these patients. *Paediatric population < 18 years*: no data available.

CONTRA-INDICATIONS
Hypersensitivity to active substance or excipients. Concomitant administration with pimozide and ergot alkaloids. When combined with ciclosporin: concomitant use with dabigatran, atorvastatin, simvastatin, rosuvastatin or pitavastatin.

PRECAUTIONS

Risk of adverse reactions or reduced therapeutic effect due to interactions with certain medicinal products. See table 1 in SmPC. Use caution with CYP3A substrates with narrow therapeutic ranges (e.g., alfentanil, fentanyl, and quinidine). Close monitoring and/or dose adjustment of co-administered CYP3A substrates is recommended. Increased monitoring of ciclosporin, tacrolimus, sirolimus is recommended the first 2 weeks after initiating and ending letermovir as well as after changing route of administration. Therapeutic drug monitoring recommended for voriconazole and phenytoin.

Interaction potential and clinical consequences may be different depending on whether administered orally or IV, and whether ciclosporin is concomitantly used. When changing the route of administration, or if changing immunosuppressant, recommendation concerning co-administration should be revisited. General information about differences in exposure between different letermovir treatment regimens: -The estimated letermovir plasma exposure is different depending on the dose regimen used. Therefore, the clinical consequences of drug interactions for letermovir will be dependent on which letermovir regimen is used and whether or not letermovir is combined with ciclosporin. -The combination of ciclosporin and letermovir may lead to more marked or additional effects on concomitant medicinal products as compared to letermovir alone. Refer to SmPC for complete information on drug interactions.

Pregnancy: No data on use in pregnant women. Do not use during pregnancy and in women of childbearing potential not using contraception. *Breast-feeding:* It is unknown whether letermovir is excreted in human milk. The decision whether to discontinue breast-feeding or the drug, should balance the benefit of breast-feeding against that of treatment for the woman.

Excipients: PREVYMIS Tablets contain lactose monohydrate; patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product. PREVYMIS 240 mg concentrate for solution for infusion contains 23 mg (or 1.0 mmol) sodium per dose. Take into consideration for patients on a controlled sodium diet.

SIDE EFFECTS

Refer to SmPC for complete information on side-effects.

Common (≥ 1/100 to < 1/10): The most commonly reported adverse reactions occurring in at least 1% of subjects in the PREVYMIS group and at a frequency greater than placebo were: nausea (7.2%), diarrhoea (2.4%), and vomiting (1.9%).

The most frequently reported adverse reactions that led to discontinuation of PREVYMIS were nausea (1.6%), vomiting (0.8%), and abdominal pain (0.5%).

Uncommon (≥ 1/1,000 to < 1/100): hypersensitivity, decreased appetite, dysgeusia, headache, vertigo, abdominal pain, muscle spasms, alanine aminotransferase increased, aspartate aminotransferase increased, fatigue, oedema peripheral, blood creatinine increased

PACKAGE QUANTITIES AND BASIC NHS COST

240 mg film-coated tablets - pack of 28 tablets (7x4): £3,723.16

240 mg concentrate for solution for infusion - 1 vial: £146.27

Marketing Authorisation number

240 mg film-coated tablets

EU/1/17/1245/001

240 mg concentrate for solution for infusion

EU/1/17/1245/003

Marketing Authorisation Holder

Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

Legal category: POM

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