ינואר 2026

רופא/ה יקר/ה
רוקח/ת יקר/ה,

הנדון: **Prevymis 240 mg Film-Coated Tablets, Prevymis 480 mg Film-Coated Tablets**
<u>פרווימיס 240 מ"ג טבליות מצופות, פרווימיס 480 מ"ג טבליות מצופות</u>

Dosage form and Composition:
PREVYMIS 240 mg film-coated tablets: Each film-coated tablet contains 240 mg of letermovir.
PREVYMIS 480 mg film-coated tablets: Each film-coated tablet contains 480 mg of letermovir.

ההתוויה המאושרת לתכשירים:

PREVYMIS is indicated for prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult and paediatric patients weighing at least 15 kg who are CMV-seropositive recipients [R+] of an allogeneic haematopoietic stem cell transplant (HSCT).
Consideration should be given to official guidance on the appropriate use of antiviral agents.

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<u>עדכונים שבוצעו בעלון לרופא:</u>
(טקסט שהוסף לעלון לרופא מודגש בקו תחתון, טקסט שנמחק מהעלון לרופא מסומן בקו חוצה)

4.1 Therapeutic indications

PREVYMIS is indicated for prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult <u>and paediatric patients weighing at least 15 kg</u> who are CMV-seropositive recipients [R+] of an allogeneic haematopoietic stem cell transplant (HSCT).

Consideration should be given to official guidance on the appropriate use of antiviral agents.

4.2 Posology and method of administration

~~PREVYMIS~~<u>Letermovir</u> should be initiated by a physician experienced in the management of patients who have had an allogeneic haematopoietic stem cell transplant.

<u>Posology</u>

<u>Letermovir is also available as granules in sachet (20 mg and 120 mg).</u>

<u>Letermovir tablets and granules in sachet may be used interchangeably at the discretion of the physician.</u>

~~The recommended dose of PREVYMIS is one 480 mg tablet once daily.~~

~~PREVYMIS~~<u>Letermovir</u> should be started after HSCT. ~~PREVYMIS~~<u>Letermovir</u> may be started on the day of transplant and no later than 28 days post-<u>HSCT</u>~~transplant~~. ~~PREVYMIS~~<u>Letermovir</u> may be started before or after engraftment. Prophylaxis with ~~PREVYMIS~~<u>letermovir</u> should continue through 100 days post-<u> HSCT</u>~~transplant~~.

~~The safety and efficacy of letermovir use for more than 100 days has not been studied in clinical trials.~~ Prolonged ~~PREVYMIS~~<u>letermovir</u> prophylaxis beyond 100 days post-<u>HSCT</u>~~transplant~~ may be of benefit in some patients at high risk for late CMV reactivation (see section 5.1). <u>The safety and efficacy of letermovir use for more than 200 days has not been studied in clinical trials.</u>~~Use of letermovir prophylaxis for greater than 100 days requires a careful assessment of the benefit-risk balance.~~

<u>*Adult and paediatric patients weighing at least 30 kg who are HSCT recipients*</u>
<u>The recommended dose of letermovir is 480 mg once daily that can be administered either as one 480 mg tablet or as two 240 mg tablets.</u>

For patients who cannot swallow tablets, refer to the prescribing information for the letermovir granules for dosing information.

Dose adjustment in adult and paediatric patients weighing at least 30 kg who are HSCT recipients
If ~~PREVYMIS~~letermovir is co-administered with cyclosporine, the dose of ~~PREVYMIS~~letermovir should be decreased to 240 mg once daily (see sections 4.5 and 5.2).

- If cyclosporine is initiated after starting ~~PREVYMIS~~letermovir, the next dose of ~~PREVYMIS~~letermovir should be decreased to 240 mg once daily.
- If cyclosporine is discontinued after starting ~~PREVYMIS~~letermovir, the next dose of ~~PREVYMIS~~letermovir should be increased to 480 mg once daily.
- If cyclosporine dosing is temporarily interrupted due to high cyclosporine levels, no dose adjustment of ~~PREVYMIS~~letermovir is needed.

Paediatric patients weighing at least 15 kg to less than 30 kg who are HSCT recipients
The recommended dose of letermovir is 240 mg once daily that can be administered as one 240 mg tablet (see also section 5.2).
For paediatric patients who cannot swallow tablets, refer to the prescribing information for letermovir granules for dosing information.

Dose adjustment in paediatric patients weighing at least 15 kg to less than 30 kg who are HSCT recipients
If oral letermovir is co-administered with cyclosporine, the dose of letermovir should be decreased to 120 mg once daily (see also sections 4.5 and 5.2). For patients requiring a 120 mg dose, refer to the prescribing information for the letermovir granules for dosing information.

- If cyclosporine is initiated after starting letermovir, the next dose of letermovir should be decreased to 120 mg once daily.
- If cyclosporine is discontinued after starting letermovir, the next dose of letermovir should be increased to 240 mg once daily.
- If cyclosporine dosing is temporarily interrupted due to high cyclosporine levels, no dose adjustment of letermovir is needed.

…
Paediatric population
~~PREVYMIS is not indicated for children and adolescents under 18 years of age.~~
The safety and efficacy of ~~PREVYMIS~~letermovir in HSCT patients ~~below 18 years of age~~weighing less than 5 kg have not been established. No data are available ~~(see section 5.1)~~.

Method of administration
For oral use.
The tablet should be swallowed whole and may be taken with or without food. The tablet should not be divided, crushed, or chewed because these methods have not been studied.

4.5 Interaction with other medicinal products and other forms of interaction
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Additional effects of other products on letermovir relevant when combined with cyclosporine

Inhibitors of OATP1B1 or 3
Co-administration of ~~PREVYMIS~~letermovir with medicinal products that are inhibitors of OATP1B1/3 transporters may result in increased letermovir plasma concentrations. If ~~PREVYMIS~~letermovir is co-administered with cyclosporine (a potent OATP1B1/3 inhibitor), the recommended dose of ~~PREVYMIS~~letermovir is 240 mg once daily in adult and paediatric patients weighing at least 30 kg (see Table 1 and sections 4.2 and 5.2). If oral letermovir is co-administered with cyclosporine in paediatric patients weighing less than 30 kg, the dose should be decreased (see sections 4.2 and 5.2). Caution is advised if other OATP1B1/3 inhibitors are added to letermovir combined with cyclosporine.
-Examples of OATP1B1 inhibitors include gemfibrozil, erythromycin, clarithromycin, and several protease inhibitors (atazanavir, simeprevir).

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Table 1: Interactions and dose recommendations with other medicinal products. Note that the table is not extensive but provides examples of clinically relevant interactions. See also the general text on DDIs above.

Unless otherwise specified, interaction studies have been performed <u>in adults</u> with oral letermovir without cyclosporine. Please note that the interaction potential and clinical consequences may be different depending on whether cyclosporine is concomitantly used. When changing immunosuppressant, the recommendation concerning co-administration should be revisited.

Concomitant medicinal product	**Effect on concentration† ~~M~~<u>m</u>ean ratio (90% confidence interval) for AUC, C_{max} (likely mechanism of action)**	**Recommendations concerning co-administration with ~~PREVYMIS~~<u>letermovir</u>**
…		
Immunosuppressants		
cyclosporine (50 mg single dose)/ letermovir (240 mg daily)	↑ cyclosporine AUC 1.66 (1.51, 1.82) C_{max} 1.08 (0.97, 1.19) (CYP3A inhibition)	If ~~PREVYMIS~~<u>letermovir</u> is co-administered with cyclosporine, the dose of ~~PREVYMIS~~<u>letermovir</u> should be decreased to 240 mg once daily <u>in adults</u> (see sections 4.2 and 5.1) <u>and paediatric patients weighing at least 30 kg (see section 4.2). If oral letermovir is coadministered with cyclosporine in paediatric patients weighing less than 30 kg, the dose should be decreased (see section 4.2)</u>. Frequent monitoring of cyclosporine whole blood concentrations should be performed during treatment, and at discontinuation of ~~PREVYMIS~~<u>letermovir</u> and the dose of cyclosporine adjusted accordingly#.
cyclosporine (200 mg single dose)/ letermovir (240 mg daily)	↑ letermovir AUC 2.11 (1.97, 2.26) C_{max} 1.48 (1.33, 1.65) (OATP1B1/3 inhibition)	
…		

4.8 Undesirable effects

Summary of the safety profile

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<u>In P040, 218 adult HSCT recipients received letermovir or placebo from Week 14 (~100 days) through Week 28 (~200 days) post-HSCT and were followed for safety through Week 48 post-HSCT (see section 5.1). The adverse reactions reported were consistent with the safety profile of letermovir as characterised in study P001.</u>

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<u>Paediatric population</u>

<u>The safety assessment of letermovir in paediatric patients from birth up to 18 years old was based on a Phase 2b clinical trial (P030). In P030, 63 HSCT recipients were treated with letermovir through Week 14 post-HSCT. Their age distribution was as follows, i.e., 28 adolescents, 14 children aged 7 to less than 12 years, 13 aged 2 to less than 7 years, and 8 less than 2 years old (5 of them less than 1 year old). The adverse reactions were consistent with those observed in clinical studies of letermovir in adults.</u>

בוצעו עדכונים ונוסף מידע בסעיפים המפורטים מטה:

5.1 Pharmacodynamic properties
5.2 Pharmacokinetic properties
5.3 Preclinical safety data

בעלון לרופא בוצעו עדכונים נוספים שאינם נכללים בהודעה זו. בעלון מופיעה הפניה לצורת מינון נוספת שנרשמה אך טרם החל שיווקה, Prevymis 20 mg granules, Prevymis 120 mg granules.
למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא המאושר על ידי משרד הבריאות.
העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.

Prevymis 240 mg Film-Coated Tablets ו-Prevymis 480 mg Film-Coated Tablets מופצות ע"י חברת נובולוג בע"מ.

דיווח על תופעות לוואי לתכשירים רשומים הינו חשוב ומאפשר המשך מעקב אחר מאזן התועלת/סיכון של התכשיר. ניתן לדווח על תופעות לוואי למשרד הבריאות באמצעות לחיצה על הקישור "דיווח על תופעות לוואי עקב טיפול תרופתי" שנמצא בדף הבית של אתר משרד הבריאות (www.health.gov.il) המפנה לטופס המקוון לדיווח על תופעות לוואי, או ע"י כניסה לקישור: https://sideeffects.health.gov.il . כמו כן ניתן לדווח על תופעות לוואי לחברת MSD ישראל באמצעות פנייה טלפונית ל-09-9533333.

בברכה,
מזל כהן דאר
רוקחת ממונה
MSD ישראל

References:
Prevymis 240 mg Film-Coated Tablets, Prevymis 480 mg Film-Coated Tablets SPC updated 01/2026