SUMMARY

letermovir

PREVYMIS 240 and 480 mg

film-coated tablets and concentrate for solution for infusion

Indication extension

Original French opinion adopted by the Transparency Committee on 14 February 2024

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- CMV infection is a serious infectious complication of SOT and is one of the leading causes of morbidity and mortality in this situation.
- This is a preventive medicinal product.
- The efficacy/adverse effects ratio of PREVYMIS (letermovir) is high in the prophylaxis of CMV disease in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-].
- This is a first-line treatment in view of the therapies available.

- **Public health benefit**

Considering:

- the seriousness of the disease and its incidence;
- the medical need to have access to new antiviral treatments with improved efficacy, safety, drug interaction and resistance profiles,
- the response to the identified medical need with an additional impact expected on morbidity and mortality due to an efficacy non-inferior to that of valganciclovir and a better safety and resistance profile;
- the absence of an organisational impact or a demonstrated impact on the care pathway;

PREVYMIS (letermovir) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PREVYMIS (letermovir) is substantial in the prophylaxis of CMV disease in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-].

The Committee issues a favourable opinion for inclusion of PREVYMIS (letermovir) in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the prophylaxis of CMV disease in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-] and at the MA dosages.

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%.**

Clinical Added Value

Considering:

- the partially met medical need in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-] in the context of prophylaxis of CMV disease;
- the demonstrated non-inferiority of letermovir compared to valganciclovir in terms of the proportion of patients with CMV disease at week 52 post-transplant (primary endpoint) in whom the donor is CMV-seropositive [D+/R-]: 10.4% (30/289) versus 11.8% (35/297), i.e. an adjusted difference = -1.4% (95% CI = [-6.5; 3.8]);
- a relatively favourable safety profile due to a lower risk of leukopenia and neutropenia (risk factors for infection with CMV and other pathogens) compared to valganciclovir;
- a genetic resistance barrier of letermovir that appears to be convincing (low resistance rate) and an absence of cross-resistance with other anti-CMV antiviral agents, in particular DNA polymerase inhibitors, leaving open the possibility of considering the use of other antiviral agents at a later stage without the risk of therapeutic failure;

but:

- the lack of demonstration of a superiority of letermovir compared to valganciclovir in terms of the proportion of patients with CMV disease at week 52 post-transplant in whom the donor is CMV-seropositive [D+/R-];
- the lack of demonstration of an improvement in the time to onset of CMV disease with letermovir compared to valganciclovir, after follow-up for 52 weeks post kidney transplant;

the Committee deems that PREVYMIS (letermovir) provides a minor clinical added value (CAV IV) in the care pathway for the prophylaxis of CMV disease in CMV-seronegative adults who have received a kidney transplant from a CMV-seropositive donor [D+/R-].