SUMMARY

maribavir

LIVTENCITY 200 mg,

film-coated tablets

First assessment

Adopted by the Transparency Committee on 15 February 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion for reimbursement in “the treatment of cytomegalovirus (CMV) infection and/or disease that are refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet in adult patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT)”.

Role in the care pathway?

LIVTENCITY (maribavir) is a last-resort option for the treatment of CMV infection and/or disease that are refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet in adult patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT).

The use of this anti-CMV antiviral agent should only be considered as a last resort, i.e. when the available options are not feasible for reasons of toxicity (particularly haematological or nephrological), drug interaction or virological failure (viral strain refractory or resistant to conventional treatments). A second anti-CMV antiviral agent may be combined with maribavir in the event of life-threatening disease.

The Committee specifies that, despite an overall favourable effect observed in the SOLSTICE study, the benefit in terms of virological improvement appears to be inferior in the refractory population without resistance to prior treatment compared to that in the refractory population with resistance.

Due to its low diffusion, maribavir is not recommended in the event of neurological or ocular damage due to CMV infection and/or disease. In the latter case, a combination containing ganciclovir and foscarnet will be favoured.

Special recommendations

The Committee recommends the performance of resistance genotyping (testing for UL97 resistance) before initiating treatment with maribavir, particularly in patients previously treated with ganciclovir/valganciclovir and liable to present a maribavir resistance mutation. Treatment should be discontinued if resistance to maribavir is detected (see Section 4.4 Special warnings and precautions for use in the SmPC). The performance of genotyping does not prevent treatment from being initiated.

Transparency Committee's conclusions

Clinical Benefit

- CMV infection is a serious infectious complication of HSCT and SOT and is one of the leading causes of morbidity and mortality in these situations.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio is high.
- There are no therapeutic alternatives.
- LIVTENCITY (maribavir) is a last-resort medicinal product reserved for adult patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) and with CMV infection and/or disease refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet.

Public health benefit

Considering:

- the seriousness of the disease and its incidence;
- the unmet need in adult patients who have undergone HSCT or SOT and with CMV infection and/or disease refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet;
- the fact that LIVTENCITY (maribavir) could provide a response to the identified medical need in terms of confirmed CMV viremia clearance at week 8 and maintenance of the response at week 16;
- the expected impact on the care and life pathway of patients (oral administration, availability in the community setting);

LIVTENCITY (maribavir) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of LIVTENCITY (maribavir) 200 mg film-coated tablets is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of LIVTENCITY (maribavir) 200 mg film-coated tablets in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication and at the marketing authorisation dosages.

Recommended reimbursement rate for inclusion in the retail list of reimbursed proprietary medicinal products approved for use: 65%

Clinical Added Value

Considering:

- **the unmet medical need in adult patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) and with CMV infection and/or disease refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet;**

- **the effect size of LIVTENCITY (maribavir) in terms of confirmed CMV viremia clearance rate at week 8 of 33% and maintenance of the response at week 16 of 10% (SOLSTICE study);**
- **the effect of maribavir as a salvage therapy in patients initially treated with conventional anti-CMV therapies and who achieved confirmed CMV viremia clearance after 8 complete weeks of treatment in 50% of cases (N = 11);**
- **an acceptable safety profile but marked by adverse events such as mild to moderate dysgeusia, generally resolving spontaneously, and the risk of increases in plasma levels of certain immunosuppressants in the event of co-administration;**

But:

- **a benefit that appears to be inferior in terms of virological improvement in the refractory population without resistance to prior treatment;**
- **the low percentage of patients in whom the response was maintained at week 16 following a complete 8-week treatment and the absence of data concerning the duration of treatment beyond 8 weeks;**
- **the fact that the majority of the population included had asymptomatic CMV infection (91.8%), which limits the transposability to the curative treatment of patients with CMV disease (3.7% in the study);**
- **the risk of the emergence of resistance among patients with RAS to anti-CMV treatment or maribavir at baseline (PRS or MRS population), with 20% of them having developed RAS to maribavir after 8 weeks of treatment with maribavir;**

the Transparency Committee deems that LIVTENCITY (maribavir) 200 mg film-coated tablets provides a minor clinical added value (CAV IV) in the current care pathway for patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) and with CMV infection and/or disease refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet.

In conclusion, the target population of LIVTENCITY (maribavir), which corresponds to adult patients who have undergone HSCT or SOT and with CMV infection and/or disease refractory (with or without resistance) to one or more prior therapies (including ganciclovir, valganciclovir, cidofovir or foscarnet) cannot be precisely defined, but it can be estimated to be a maximum of in the region of 2,150 patients per year.

However, based on the current epidemiological context, these figures represent the upper limit of the target population of LIVTENCITY (maribavir) since this antiviral agent must only be used in the event of CMV infection and/or disease that are refractory (with or without resistance) and when the use of the other available options is not feasible.