SUMMARY

maralixibat

LIVMARLI 9.5 mg/mL

oral solution

Inclusion on list

Adopted by the Transparency Committee on 9 October 2024

Summary of opinion

Favourable opinion for reimbursement in the "treatment of progressive familial intrahepatic cholestasis (PFIC) in patients 3 months of age and older".

Transparency Committee's conclusions

Clinical Benefit

- Progressive familial intrahepatic cholestasis (PFIC types 1 to 6 depending on the genetic mutation) is a rare genetic disease that directly or indirectly affects the canalicular transport of bile acids and/or the transport of phospholipids; it evolves towards progressive cholestasis with liver damage. PFIC, particularly type 1, 2 and 3, can cause severe pruritus, growth disorders and irreversible liver damage. PFIC significantly impairs the quality of life of patients, their families and their caregivers. This severe disease generally progresses quickly towards liver failure, requiring liver transplantation. In the absence of treatment, they cause the patient's death.
- This is a symptomatic (pruritus) and preventive (complications) medicinal product.
- The efficacy/adverse effects ratio is high.
- This is a second-line treatment in view of the therapies available.

Public health benefit

Considering:

- the seriousness of PFIC and its rarity,
- the partially met medical need,
- the partial response to the identified need given:
  - evidence of an additional impact on morbidity in terms of reduction of pruritus and bile acid levels in PFIC type 1, 2, 3, 4 and 6, with limited follow-up, and the lack of evidence of an impact on mortality and quality of life,
  - an expected additional impact on the care and life pathway of patients and on the organisation of care (development of hepatocellular carcinoma, recourse to surgery or liver transplantation), but which has not yet been demonstrated,

LIVMARLI (maralixibat) is likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of LIVMARLI 9.5 mg/mL (maralixibat) oral solution is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of LIVMARLI 9.5 mg/mL (maralixibat) oral solution in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the indication and at the MA dosages.

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

Clinical Added Value

Considering:

- the demonstrated superiority of maralixibat versus placebo after 26 weeks on reduction of the pruritus severity score in a paediatric population with type 2 PFIC (with the exception of subtype BSEP3) with a clinically relevant effect size (primary endpoint), as well as statistically significant results for clinically relevant ranked secondary endpoints, i.e. the reduction in serum bile acid levels in this same population, and the results for these same endpoints in a broader population of paediatric patients with PFIC type 3, 4 and 6,
- the absence of a significant difference between maralixibat and placebo for the fourth secondary endpoint relative to the proportion of pruritus responders in the main cohort, interrupting the analysis of the subsequent ranked secondary endpoints,
- uncertainties concerning the long-term efficacy of maralixibat, particularly with respect to recourse to surgery and prevention of the development of hepatocellular carcinoma,
- the lack of robust assessment of the impact on quality of life of maralixibat, which is regrettable in this disease with a marked impact on the quality of life of patients and their families,
- the safety profile of LIVMARLI (maralixibat), which appears to be favourable in the paediatric population, with limited follow-up however,
- the benefit of an oral solution form of LIVMARLI (maralixibat) suitable for administration in children from 3 months of age,
- the concomitant development with BYLVAY (odevixibat), not enabling direct comparison with maralixibat in the phase 3 study,

the Committee deems that LIVMARLI 9.5 mg/mL (maralixibat) oral solution provides a moderate clinical added value (CAV III), in PFIC type 1 and 2 (with the exception of subtype BSEP3) in the same way as BYLVAY (odevixibat) and in the other types of PFIC, in the current care pathway, which includes the relevant comparators.