OPINION ON MEDICINAL PRODUCTS

difelikefalin

KAPRUVIA 50 µg/ml,

solution for injection

First assessment

Adopted by the Transparency Committee on 4 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of KAPRUVIA (difelikefalin) for the “treatment of moderate to severe pruritus associated with chronic kidney failure in adult haemodialysis patients.”

Transparency Committee’s conclusion

Actual Clinical Benefit

- Moderate to severe pruritus associated with chronic kidney disease in haemodialysis patients is an incapacitating chronic disease, impacting patients’ quality of life.
- The proprietary medicinal product KAPRUVIA (difelikefalin) is a symptomatic medicinal product.
- Considering the evidence of modest efficacy, the methodological limitations of the studies and long-term extrapolation of the findings in respect of this treatment, the efficacy/adverse effect ratio of difelikefalin is moderate.
- Off-label therapeutic alternatives are available, such as gabapentinoids, but their efficacy remains low and the safety profile is unacceptable.
- It is a first-line treatment.

➔ Public health benefit

Considering:

- the incapacitating nature of moderate to severe forms of pruritus associated with chronic kidney disease in haemodialysis patients;
- a high prevalence of this condition in the haemodialysis patient cohort ranging from 23.1% to 37% according to the studies;
- the medical need insufficiently met by off-label therapeutic alternatives;
- the partial response to the identified insufficiently met need due to a moderate or modest impact on morbidity and quality of life;
- the lack of evidence of an additional impact on the patient's care pathway;

KAPRUVIA (difelikefalin) is not likely to have an additional impact on public health for the treatment of moderate to severe pruritus associated with chronic kidney disease in haemodialysis patients.

Considering all of these elements, the Committee deems that the actual clinical benefit of KAPRUVIA (difelikefalin) is moderate in the marketing authorisation indication.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use for the marketing authorisation indication and dosages.

Clinical Added Value

Considering:

- the medical need for an effective therapeutic option with an acceptable safety;
- evidence of superiority of difelikefalin versus placebo in two phase III double-blind studies in a study cohort composed of adult haemodialysis patients suffering from moderate to severe pruritus (primary outcome measure: at least 3-point improvement of the WI-NRS score at W12 was respectively 51.0% versus 27.6% in the KALM-1 study and 54.0% versus 42.2% in the KALM-2 study);
- the acceptable safety profile according to the data from the studies available, particularly characterised by adverse gastrointestinal and neurological effects;

But in view of:

- the choice of a routinely used clinically relevant primary outcome measure, but the reproducibility and robustness of which are debatable;
- an effect size which can be described as modest;
- a greater proportion of patients from the placebo group achieving the primary outcome measures in the KALM-1 study (27.6%) demonstrating a placebo effect which may be non-negligible in dermatological conditions;
- the missing data management by sensitivity analyses: confirming the findings obtained in the KALM-1 study, but non-significant in the most conservative sensitivity analysis of the KALM-2 study,

the Committee deems that KAPRUVIA (difelikefalin) provides minor clinical added value (CAV IV) in the current therapeutic strategy which includes the relevant comparators (see clinically relevant comparators).