SUMMARY

avapritinib

AYVAKYT 25 mg

film-coated tablets

Indication extension

Original French opinion adopted by the Transparency Committee on 10 July 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement in "the treatment of adult patients with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment".

Transparency Committee's conclusions

Clinical Benefit

- Indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment is a rare disease with almost normal survival but sometimes significant disability.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio is moderate, given the modest difference observed between the avapritinib group and the placebo group, in terms of mean change from baseline to week 24 in ISM-SAF total symptom score (TSS) (-6 points in ISM-SAF TSS measured on a 110-point scale),
- This is a new method for the treatment of adult patients with indolent systemic mastocytosis (ISM) with moderate to severe symptoms inadequately controlled on symptomatic treatment.

Public health benefit

Considering:

- the seriousness of the disease and its prevalence,
- the partially met medical need,

- the partial response to the identified need given demonstration of a superiority versus placebo, in terms of mean change from baseline to week 24 in ISM-SAF TSS (-6 points in ISM-SAF TSS measured on a 110-point scale), but with limitations concerning the clinical relevance of this modest difference,
- the time-limited nature of the efficacy and safety data available (median treatment duration of 18 months in the study),
- the lack of evidence of an additional impact on morbidity and mortality and on quality of life,
- the lack of evidence of an impact on the organisation of care,

AYVAKYT (avapritinib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of AYVAKYT 25 mg (avapritinib) film-coated tablets is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion of AYVAKYT 25 mg (avapritinib) film-coated tablets in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the MA indication and at the MA dosages.

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 30%**

Clinical Added Value

Considering:

- demonstration of the superiority of AYVAKYT (avapritinib) compared to placebo, administered in combination with the best supportive care on:
  - the mean change from baseline to week 24 in ISM-SAF TSS, the primary endpoint (the absolute difference = -6.43 points, $CI_{95\%}$= [-10.90, -1.96], p =0.003),
  - the five ranked secondary endpoints, in particular the percentage of patients achieving a ≥ 50% reduction in ISM-SAF TSS (24.8% in the avapritinib 25 mg group versus 9.9% in the placebo group, OR = 3.10, $CI_{95\%}$= [1.24; 8,64]), p=0.005),

and despite:

- the limited clinical relevance of the difference observed between the avapritinib group and the placebo group, in terms of mean change from baseline to week 24 in ISM-SAF TSS, the primary endpoint (-6 points in ISM-SAF TSS measured on a 110-point scale),
- the lack of any established correlation between the secondary endpoints concerning biomarkers and the clinical response (serum tryptase level, reduction in KIT D816V mutant allele fraction and reduction in bone marrow mast cell infiltrate),
- the absence of comparison during the additional follow-up period of almost one year (part 3 of the study),
- the exploratory nature of the quality of life data,
- the safety profile, mainly marked by the occurrence of anaphylactic reactions, which are also frequent manifestations of indolent systemic mastocytosis.
- the limited safety data in terms of the follow-up duration, with a median follow-up of less than 2 years.

the Committee deems that AYVAKYT (avapritinib) 25 mg film-coated tablets provides a minor clinical added value (CAV IV) in the current care pathway, which includes the relevant comparators.