SUMMARY

fedratinib

INREBIC 100 mg

hard capsules

Reassessment at pharmaceutical company's request

Adopted by the Transparency Committee on 25 September 2024

Summary of opinion

Favourable opinion for maintenance of reimbursement in "the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with ruxolitinib."

Transparency Committee's conclusions

Clinical Benefit

- Myelofibrosis is a serious disease that is life-threatening.
- This is a symptomatic medicinal product.
- Its efficacy/adverse effect ratio remains moderate, given:
  - evidence of superiority compared to the "best available therapy" in terms of spleen volume reduction and symptom response rate,
  - its safety profile, marked, in particular, by the risk of the development of Wernicke's encephalopathy,
  - the absence of long-term safety data.
- INREBIC (fedratinib) remains a treatment option in a context of a substantial medical need in patients previously treated with ruxolitinib.

Public health benefit

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the partial response to the identified need:
  - INREBIC (fedratinib) could provide a response to the need due to evidence of superiority compared to the "best available therapy" in terms of spleen volume reduction and symptom

response rate, but whose impact on morbidity and quality of life remains to be demonstrated, owing to the limitations in terms of the transposability of the results and the risk of the development of Wernicke's encephalopathy. There is no evidence of an impact on mortality to date.

- the lack of evidence of an impact on the organisation of care.

INREBIC (fedratinib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of INREBIC (fedratinib) 100 mg hard capsules remains moderate in the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with ruxolitinib.

The Committee issues a favourable opinion for maintenance of inclusion of INREBIC (fedratinib) 100 mg hard capsules in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use within the scope of the reassessment and at the MA dosages.

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

Clinical Added Value

Considering:

- evidence of a superiority of fedratinib compared to the “best therapy available” (BAT) in patients previously treated with ruxolitinib, in terms of ≥ 35% spleen volume reduction in the FREEDOM-2 trial, with a statistically significant difference of 29.6% ($CI_{95\%}$ = [19.9; 39.4], p<0.0001, ITT population) between the two groups, at the end of cycle 6 compared to baseline,
- evidence of a superiority of fedratinib compared to BAT in patients previously treated with ruxolitinib, in terms of the percentage of patients with an at least 50% reduction in total symptom score on the MFSAF form, at the end of cycle 6 compared to baseline, with a statistically significant difference of 17.1% ($CI_{95\%}$ =[4.8; 29.4], p=0.0033, ITT population) between the two groups,

but:

- the safety profile of INREBIC (fedratinib) marked by gastrointestinal and haematological (anaemia, thrombocytopenia) adverse events and the occurrence of potential serious cases of Wernicke’s encephalopathy during studies, requiring monitoring before and after treatment with INREBIC (fedratinib),
- the absence of long-term safety data,
- the impossibility of determining the role of INREBIC (fedratinib) compared to OMJJARA (momelotinib),

the Committee considers that INREBIC (fedratinib) provides no clinical added value (CAV V) in the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who have been treated with ruxolitinib.