**SUMMARY**

ivosidenib

# TIBSOVO 250 mg

**film-coated tablets**

First assessment

**Original French opinion adopted by the Transparency Committee on 20 September 2023**

**The legally binding text is the original French opinion version**

# Transparency Committee's conclusions

## Clinical Benefit

- Acute myeloid leukaemia (AML), particularly in patients who are ineligible for standard induction chemotherapy, is a serious disease that is life-threatening in the short term.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio of TIBSOVO (ivosidenib) in combination with azacitidine is high in adult patients with newly diagnosed acute myeloid leukaemia (AML) with an IDH1 R132 mutation who are ineligible for standard induction chemotherapy.
- This is a first-line treatment in view of the available therapies (see 2.2).

### Public health benefit

Considering:

- the seriousness of the disease and its incidence,
- the medical need, which is considered to be partially met,
- the partial response provided by TIBSOVO (ivosidenib) in combination with azacitidine, to the partially met medical need, due to demonstration of its superiority compared to azacitidine as monotherapy,
  - with an impact on morbidity and mortality due to demonstration of its superiority compared to azacitidine alone, particularly in terms of overall survival,
  - but without a demonstrated impact on quality of life (exploratory analysis), and the non-quantifiable impact on morbidity and mortality in view of the other available alternatives, in particular the venetoclax + azacitidine combination,
- the absence of any demonstrated impact on the organisation of care,

TIBSOVO (ivosidenib) in combination with azacitidine is unlikely to have an additional impact on public health.

**Considering all these elements, the Committee deems that the clinical benefit of TIBSOVO 250 mg (ivosidenib) film-coated tablets is substantial in the MA indication.**

**The Committee issues a favourable opinion for inclusion of TIBSOVO 250 mg (ivosidenib) film-coated tablets on both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and at the MA dosages. However, the Committee highlights the need for the IDH1 mutation test procedure associated with TIBSOVO (ivosidenib) to undergo assessment with a view to its funding.**

➔ **Recommended reimbursement rate for inclusion on the retail list of reimbursed proprietary medicinal products approved for use: 100%**

## Clinical Added Value

Considering:

- demonstration of a superiority of TIBSOVO (ivosidenib) in combination with azacitidine compared to azacitidine alone in a randomised, double-blind study, in terms of:
  - complete response rate (hierarchised secondary endpoint): OR = 4.76 (CI95% = [2.15; 10.50], p < 0.0001);
  - overall survival (hierarchised secondary endpoint): HR = 0.44 (CI95% = [0.27; 0.73], p = 0.0005). The median OS was 24.0 months (CI95% = [11.3; 34.1] in the Ivosidenib + azacitidine group versus 7.9 months (CI95% = [4.1; 11.3]) in the Placebo + azacitidine group, i.e. an absolute difference in median of 16.1 months;
- the overall safety profile, similar to that of azacidine alone and with a smaller proportion of serious adverse events compared to azacidine alone;
- the need to have access to treatment improving overall survival and quality of life in adult patients with newly diagnosed AML who are ineligible for standard induction chemotherapy;

and despite:

- the absence of any possible conclusion with respect to the primary endpoint of the study (event-free survival) as a result of methodological biases;
- the lack of a demonstrated impact on quality of life given the exploratory nature of the analysis;
- the risk of differentiation syndrome and the need for ECG monitoring due to the risk of QT prolongation;
- the lack of a direct comparison versus the venetoclax and azacitidine combination, although this was deemed to be acceptable given the concomitant development of TIBSOVO (ivosidenib) and VENCLYXTO (venetoclax);

**the Committee considers that TIBSOVO 250 mg (ivosidenib) film-coated tablets provides a moderate clinical added value (CAV III) compared to azacitidine as monotherapy in the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) with an IDH1 R132 mutation who are ineligible for standard induction chemotherapy.**