

SUMMARY

ivosidenib

TIBSOVO 250 mg,**film-coated tablet****Indication extension**

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

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

- ➔ Cholangiocarcinoma is a rare tumour with an estimated annual incidence in France of 2965 new cases excluding intrahepatic cholangiocarcinoma, and 1328 to 1825 new cases of intrahepatic cholangiocarcinoma. Diagnosis is frequently delayed on account of the clinical signs present at an advanced stage of the disease. The prognosis is hence poor, in particular for intrahepatic cholangiocarcinoma.
- ➔ This is a curative medicinal product.
- ➔ The efficacy/adverse effects ratio is moderate :
 - on account of the small effect size observed in the CLarIDHy phase 3 study (median difference of 1.3 months in progression-free survival versus placebo with no evidence of a gain in overall survival);
 - a safety profile particularly marked by grade ≥ 3 AEs affecting 51.2% of the patients of the ivosidenib group versus 37.3% of the patients of the placebo group.
- ➔ This is a second- and further-line treatment.

➔ Public health benefit

In view of:

- the seriousness of the condition and its prevalence,
- the insufficiently met medical need,
- the partial response to the identified need with:
 - evidence of an additional impact on morbidity on account of the evidence of superiority versus placebo in terms of progression-free survival with an effect size deemed to be low and the lack of evidence of an impact on overall survival,

- the lack of evidence of an impact on quality of life;
- the lack of evidence of an additional impact on delivery of care and on the care pathway;

TIBSOVO (ivosidenib) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of TIBSOVO (ivosidenib) 250 mg, film-coated tablet, is:

- moderate only for adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation whose disease has progressed after least one line of systemic treatment and who are ineligible for FOLFOX chemotherapy;
- insufficient in other contexts to justify public funding.

The Committee approves the inclusion of TIBSOVO (ivosidenib) 250 mg film-coated tablet, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients within the selected scope and at the MA dosages.

The Committee disapproves the inclusion of TIBSOVO (ivosidenib) 250 mg film-coated tablet, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients for other contexts.

Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 100%

Clinical Added Value

→ Within the reimbursement scope:

In view of:

- the evidence of superiority of TIBSOVO (ivosidenib) versus placebo in terms of progression-free survival (HR = 0.37 CI_{95%}: [0.25; 0.54], p <0.0001), with an absolute difference in the medians of 1.3 months in a randomised double-blind phase III study;

and despite:

- the modest deemed gain on this outcome measure and the lack of evidence on a gain in overall survival;
- a toxicity profile marked by severe AEs observed in 35% of the patients of the ivosidenib group and in 23.7% of the patients in the placebo group, and a risk of QT interval prolongation;
- the lack of evidence of an improvement in quality of life;
- the inability to define the precise place of this treatment in relation to the FOLFOX regimen in the absence of robust comparative data;

the Committee deems that TIBSOVO (ivosidenib) 250 mg, film-coated tablet, provides minor clinical added value (CAV IV) for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation whose disease has progressed after least one line of systemic treatment and who are ineligible for FOLFOX chemotherapy.

TIBSOVO 250 mg, 20 December 2023

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