SUMMARY

Trifluridine/tipiracil

LONSURF 15 mg/6.14 mg and 20 mg/8.19 mg,

film-coated tablets

Indication extension

Adopted by the Transparency Committee on 4 September 2024

Summary of opinion

Favourable opinion for reimbursement within a restricted scope: patients with metastatic colorectal cancer (ECOG score 0-1) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, an anti-VEGF biologic therapy, and, in the event of a RAS wild type gene, an anti-EGFR agent.

Transparency Committee's conclusions

Clinical Benefit

- Metastatic colorectal cancer is a serious, life-threatening disease.
- This is a specific curative treatment for metastatic colorectal cancer.
- The efficacy/adverse effects ratio is modest due to:
  - uncertainties identified on interpreting the results of the trial with, in particular, more than a quarter of patients in the comparator arm not having received bevacizumab during previous treatment lines despite this being recommended in clinical practice,
  - the safety profile of this combination (incidence of severe events (grades ≥ 3) recorded in almost three quarters of patients (72.4%).
- There are medicinal therapeutic alternatives at this stage of the disease (see section 5.2).
- This is a third or later-line treatment.

Public health benefit

Considering:

- the seriousness of the disease and its incidence,
- the partially met medical need,
- the partial response to the identified need given:

- evidence of an additional impact for the combination of bevacizumab with LONSURF on morbidity and mortality compared to LONSURF as monotherapy, although a potential additional benefit compared to regorafenib was not assessed. The impact on quality of life has not been demonstrated to date.
- the lack of evidence of an impact on the organisation of care,

LONSURF (trifluridine/tipiracil) in combination with bevacizumab, is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of LONSURF in combination with bevacizumab is moderate in the restricted indication: patients with metastatic colorectal cancer (ECOG score 0-1) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, an anti-VEGF biologic therapy, and, in the event of a RAS wild type gene, an anti-EGFR agent.

In the rest of the MA scope, the clinical benefit is insufficient to justify public funding.

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

Clinical Added Value

Considering:

- data from a comparative study having demonstrated a superiority of the bevacizumab/LONSURF combination versus LONSURF monotherapy in terms of overall survival and progression-free survival (difference in median of around 3 months for each of the endpoints),
- limitations with respect to interpretation of the results of this study due to the fact that more than a quarter of the patients (28%) in the comparator group had not been treated with bevacizumab during previous treatment lines, despite this already being recommended in clinical practice,
- the absence of data in the population with an ECOG score > 1,
- the impossibility of drawing a conclusion with respect to quality of life (exploratory endpoint),
- comparative data from the SUNLIGHT study showing a benefit of adding bevacizumab to LONSURF but, in no case, the contribution of the latter in this context,
- the absence of robust comparative data versus regorafenib,

the Committee considers that, as the dossier currently stands, LONSURF in combination with bevacizumab provides no clinical added value (CAV V) in the current care pathway.