SUMMARY

trastuzumab deruxtecan

ENHERTU 100 mg

powder for concentrate for solution for infusion

Indication extension

Original French opinion adopted by the Transparency Committee on 24 May 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- Gastric cancer and adenocarcinoma of the gastroesophageal junction (GEJ) are serious, life-threatening diseases.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high in adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received at least two prior trastuzumab-based treatment lines. The transposability of the results to the French population (different aetiology profile) cannot be confirmed, however.
- This is a third or later-line therapy in adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received at least two prior trastuzumab-based treatment lines. It has no role in other situations, i.e. as second-line therapy, in the absence of comparative clinical data.

Public health benefit

Considering:

- the seriousness of gastric cancer and adenocarcinoma of the GEJ,
- the medical need, which is considered to be inadequately met,
- the low impact demonstrated on mortality,
- the absence of conclusive quality of life data,
- the absence of data enabling assessment of the impact on the organisation of care (hospitalisations avoided, transfer of care to consultations),

ENHERTU (trastuzumab deruxtecan) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of ENHERTU (trastuzumab deruxtecan) is:

- **substantial "as monotherapy in adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received at least two prior trastuzumab-based treatment lines";**
- **insufficient in the other situations of the MA indication extension - i.e. as second-line therapy - to justify public funding cover.**

The Committee issues a favourable opinion for inclusion of ENHERTU (trastuzumab deruxtecan), in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "as monotherapy in adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received at least two prior trastuzumab-based treatment lines" and at the MA dosages.

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other clinical situations of the MA extension, i.e. as second-line therapy.

Clinical Added Value

➔ **Within the reimbursement scope:**

Considering:

- demonstration of a superiority in the phase 2 DESTINY-Gastric01 study of T-DXd treatment compared to treatment of the physician's choice (TPC) in terms of:
  - ORR (primary endpoint) with a differential of + 37.0% ($CI_{95\%}$ = [41.9; 60.5] in the T-DXd group and $CI_{95\%}$ = [6.4; 26.2] in the TPC group; p < 0.0001) in favour of T-DXd,
  - OS (ranked secondary endpoint) with a differential of + 4.1 months (HR = 0.59, $CI_{95\%}$: [0.39; 0.88]; p=0.0097) in favour of T-DXd,
- the inadequately met medical need insofar as the efficacy of LONSURF (trifluridine / tipiracil) is limited with short median PFS and OS durations;

and despite:

- the lack of demonstration of any superiority of T-DXd treatment compared to the LONSURF comparator (trifluridine / tipiracil);
- questions concerning the transposability of the results of the DESTINY-Gastric01 study, conducted in Asia only;
- an excess haematotoxicity (neutropenia, anaemia, leukopenia, lymphopenia and thrombocytopenia);
- the risk of diffuse interstitial lung disease/pneumonitis, identified as an important risk in the RMP;
- the absence of a demonstrated impact on quality of life (exploratory endpoint).

the Committee deems that ENHERTU (trastuzumab deruxtecan) provides a minor clinical added value (CAV IV) in the current care pathway as third or later-line treatment, which includes LONSURF (trifluridine / tipiracil).

➔ **Within the scope included in the MA but not retained for reimbursement:**

Not applicable.

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