SUMMARY

tebentafusp
KIMMTRAK 100 µg/0.5 Ml,

concentrate for solution for infusion

First assessment

Adopted by the Transparency Committee on 4 January 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion for reimbursement as monotherapy for the treatment of human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

What therapeutic improvement?

Therapeutic improvement in the care pathway.

Role in the care pathway?

Around 50% of patients with uveal melanoma develop metastases.

Liver metastases are the most common (60%). Surgery may be considered to treat these metastases, but few patients are eligible for resection (< 10%).

The chemotherapy protocols indicated in the treatment of cutaneous melanoma including cisplatin, fotemustine, dacarbazine and temozolomide have been shown to be not very effective in the treatment of uveal melanoma.

Immunotherapies are used in the treatment of metastatic uveal melanoma by analogy with cutaneous melanoma (pembrolizumab, nivolumab, ipilimumab). However, these immunotherapies are not specific to the treatment of uveal melanoma, and the response rate obtained with these treatments is lower than that observed in the treatment of cutaneous melanoma.

The ASCO (2022) and NCCN (2022) guidelines recommend the use of tebentafusp in human leukocyte antigen (HLA)-A*02:01-positive patients with metastatic uveal melanoma. For the remaining patients who cannot benefit from tebentafusp, the ASCO (2022) guidelines indicate that,

at present, no recommendations can be made relative to the use of systemic treatments. For these patients, inclusion in clinical trials remains possible.

Role of KIMMTRAK (tebentafusp) in the care pathway:

KIMMTRAK (tebentafusp) as monotherapy is a first-line treatment for human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

In accordance with the SmPC, the Committee wishes to draw attention to the specific safety profile of KIMMTRAK (tebentafusp), in particular the risks of the occurrence of acute skin reactions and cytokine release syndrome (CRS) requiring monitoring for at least 16 hours following thethree infusions of tebentafusp in a hospital setting with immediate access to medicinal products and resuscitative equipment to manage CRS. The risk of sequelae associated with CRS may be higher in patients with pre-existing cardiovascular disorders and these patients should be closely monitored.

The summary of product characteristics (SmPC) and the risk management plan (RMP) must be complied with and special monitoring during and after treatment is required. In particular an ECG should be performed before and after infusion during the first 3 weeks of treatment with tebentafusp and subsequently as clinically indicated.

Committee's conclusions

Clinical Benefit

- Unresectable or metastatic uveal melanoma is a serious disease that is life-threatening in the short term (median survival of 10 to 12 months).
- The medicinal product KIMMTRAK (tebentafusp) is a curative medicinal product.
- The efficacy/adverse effect ratio of KIMMTRAK (tebentafusp) is substantial.
- There are no other alternatives.
- KIMMTRAK (tebentafusp) as monotherapy is a first-line treatment for human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

Public health benefit

Considering:

- the seriousness of the disease and its incidence,
- the unmet medical need,
- the partial response to the identified need given:
  - a demonstrated additional impact on morbidity and mortality of tebentafusp relative to the comparator treatment left to the investigator's choice, as a first-line treatment in HLA-A*02:01-positive adult patients with metastatic uveal melanoma, in view of the overall survival data in the IMCgp100-202 study (median OS increase of 5.7 months) and progression-free survival data (PFS increase of 0.4 months),
  - but a significativetoxicity marked, in particular, by the occurrence of acute skin reactions (94% of patients), cardiac disorders (15%) and cytokine release syndrome (89%),
  - the lack of robust data on quality of life supporting an improvement of quality of life among treated patients relative to the comparator treatment left to the investigator's choice,

- an impact on the organisation of care and the care pathway of patients given the need to administer the first three doses of KIMMTRAK (tebentafusp) in a specialised care unit close to an intensive care unit, and to conduct special ECG monitoring before and after administration during the first three weeks of treatment, and subsequently as clinically indicated,

KIMMTRAK (tebentafusp) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of KIMMTRAK 100 µg/0.5 mL (tebentafusp) concentrate for solution for infusion is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:

- the demonstration in a phase 3, comparative, randomised, open-label, multicentre study of the superiority of tebentafusp (IV route) versus the comparator treatment left to the investigator's choice (pembrolizumab in 82% of cases), as first-line treatment in HLA-A*02:01-positive adult patients with metastatic uveal melanoma, in terms of overall survival (OS), with a median increase of 5.7 months;

but considering on the other hand:

- the non-clinically relevant superiority of tebentafusp demonstrated versus the comparator treatment left to the investigator's choice, in terms of progression-free survival (PFS), with a median increase of 0.4 months;
- the safety profile marked by important risks of the occurrence of acute skin reactions (94%), cardiac disorders (15%) and cytokine release syndrome (89% of patients) requiring monitoring before and after the administration of tebentafusp;
- the absence of robust data on quality of life,

the Transparency Committee deems that KIMMTRAK 100 µg/0.5 mL (tebentafusp) concentrate for solution for infusion provides a moderate clinical added value (CAV III) as monotherapy for the treatment of human leukocyte antigen (HLA)-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.