SUMMARY

dabrafenib/trametinib

FINLEE 10 mg / SPEXOTRAS 0.05 mg/mL

dispersible tablet / powder for oral solution

First listing

Original French opinion adopted by the Transparency Committee on 10 July 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement in the following indications:

- **"Treatment of paediatric patients aged 1 year and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy and;**
- **Treatment of paediatric patients aged 1 year and older with high-grade glioma (HGG) with a BRAF V600E mutation who have received at least one prior radiation and/or chemotherapy treatment".**

Transparency Committee's conclusions

Clinical Benefit

Low-grade glioma

- Low-grade gliomas are rare, serious, indolent diseases with a major impact on patients' quality of life due to their functional consequences (particularly in terms of vision and motricity).
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high but needs to be confirmed by long-term follow-up data, particularly in terms of safety.
- There are medicinal alternatives.
- The FINLEE (dabrafenib)/SPEXOTRAS (trametinib) combination is a treatment option to be favoured compared to chemotherapy, in paediatric patients aged 1 year and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

- **Public health benefit**

Considering:

- the seriousness of the disease and its prevalence;
- the inadequately met medical need;
- the lack of response to the identified need considering:
  - an improvement in progression-free survival but with no demonstrated improvement in overall survival to date;
  - the lack of evidence of an impact on quality of life;
  - the absence of long-term safety data considering continuous administration of this treatment;
  - the lack of evidence of an impact on the patient's care pathway (no data were supplied by the pharmaceutical company enabling assessment of this endpoint);

FINLEE (dabrafenib) and SPEXOTRAS (trametinib) are unlikely to have an additional impact on public health.

High-grade glioma

- High-grade gliomas are life-threatening, particularly following a first line of radiation and chemotherapy treatment.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high.
- There are medicinal alternatives.
- It is a treatment option for paediatric patients aged 1 year and older with high-grade glioma (HGG) with a BRAF V600E mutation who have received at least one prior radiation and/or chemotherapy treatment.

Public health benefit

Considering:

- the seriousness of the disease and its prevalence;
- the inadequately met medical need;
- the lack of response to the identified need considering:
  - the lack of evidence of an impact on morbidity and mortality and on quality of life;
  - the lack of evidence of an impact on the patient's care pathway (no data were supplied by the pharmaceutical company enabling assessment of this endpoint);

FINLEE (dabrafenib) and SPEXOTRAS (trametinib) are unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of FINLEE (dabrafenib) 10 mg dispersible tablet and SPEXOTRAS (trametinib) 0.05 mg/mL powder for oral solution is substantial in the MA indications.

The Committee issues a favourable opinion for inclusion of FINLEE (dabrafenib) 10 mg dispersible tablet and SPEXOTRAS (trametinib) 0.05 mg/mL powder for oral solution in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the MA indications and at the MA dosages.

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

Clinical Added Value

Low-grade glioma

Considering:

- the comparative data versus chemotherapy demonstrating a superiority of the FINLEE (dabrafenib)/SPEXOTRAS (trametinib) combination compared to chemotherapy (carboplatin – vincristine) on a mainly radiological endpoint, progression-free survival (ranked secondary endpoint; reviewed by an independent review committee): PFS medians of 20.1 months in the D+T group and 7.4 months in the C+V group, i.e. a point estimate of the absolute difference of 12.7 months; HR = 0.31; $CI_{95\%}$ [0.17; 0.55]; p < 0.001;

and despite:

- the lack of experience in terms of the long-term safety profile in a context in which administration may be chronic, over several years, in these patients;
- the lack of formal conclusions that can be drawn from the exploratory results of the secondary endpoints, including quality of life, a relevant endpoint given the indolence of the disease;

the Committee deems that the combination of FINLEE (dabrafenib) 10 mg dispersible tablet and SPEXOTRAS (trametinib) 0.05 mg/mL powder for oral solution provides a minor clinical added value (CAV IV) compared to carboplatin plus vincristine chemotherapy in the treatment of paediatric patients aged 1 year and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy.

High-grade glioma

Considering:

- data from a non-comparative cohort, suggesting an overall response rate of 46.6% (n=23/41) with around a third of patients (29.3%; n=12) having a complete response after a median survival of 25.1 months;
- the medical need inadequately met by chemotherapies and the recommended targeted therapies, but with a dosage form ill-suited to paediatric use;

and despite:

- the lack of formal conclusions that can be drawn from the exploratory results of the secondary endpoints, including overall survival and quality of life;
- the lack of comparative data in the targeted paediatric population, but for which the Committee highlights the paediatric development efforts in this context;
- the absence of any formal conclusion that can be drawn based on the external comparison supplied in the dossier;

the Committee deems that the combination of FINLEE (dabrafenib) 10 mg dispersible tablet and SPEXOTRAS (trametinib) 0.05 mg/mL powder for oral solution provides a minor clinical added value (CAV IV) in the care pathway for paediatric patients aged 1 year and older with high-grade glioma (HGG) with a BRAF V600E mutation who have received at least one prior radiation and/or chemotherapy treatment.