SUMMARY

crizotinib

XALKORI 200 mg and 250 mg,

hard capsules

New indication

Adopted by the Transparency Committee on 19 April 2023

The legally binding text is the original French opinion version

Key points

Favourable opinion for reimbursement of XALKORI (crizotinib) in the treatment of paediatric patients (age ≥6 to <18 years) with recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumour (IMT).

Role in the care pathway?

In paediatric medicine, despite the low level of evidence related to the limited data and the resulting uncertainties with respect to its efficacy, the Committee considers that XALKORI (crizotinib) is a treatment option for recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumours (IMT) in children from 6 years of age.

According to the experts, XALKORI (crizotinib) could have a role in the paediatric management of:

– ALK-positive IMT that cannot be operated on using conservative surgery following the failure of anti-inflammatory drugs;
– metastatic ALK-positive IMT.

Transparency Committee's conclusions

Clinical Benefit

- Inflammatory myofibroblastic tumours (IMT) are very rare tumours, generally occurring in children and young adults. IMTs are usually benign but they can be locally aggressive and lead to a risk of metastases.
- This is a curative medicinal product.
- The efficacy/adverse effects ratio is high in paediatric medicine despite the uncertainties that persist in terms of its therapeutic contribution compared to the available alternatives given limited data and the absence of comparative data in the target paediatric population.
- XALKORI (crizotinib) is a treatment option for recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumours (IMT) in children from 6 years of age.

Public health benefit

Considering:

- the seriousness of the disease and its very low prevalence,
- the inadequately met medical need,
- the partial response to the identified need:
  - with an additional impact of XALKORI (crizotinib) on morbidity and mortality and on quality of life that has not been demonstrated to date, but for which the Committee highlights the paediatric development efforts in a very rare disease, which provide a framework for the off-label use of chemotherapy protocols;
  - with an expected, but not supported, additional impact on the patient's care pathway considering the possibility of treating patients with XALKORI (crizotinib) hard capsules at home, unlike chemotherapy treatments, which require full hospitalisation throughout treatment;

XALKORI (crizotinib) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of XALKORI (crizotinib) hard capsules, in the 250 mg and 200 mg strengths, is substantial in the treatment of paediatric patients (age ≥6 to <18 years) with recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumour (IMT).

The Committee issues a favourable opinion for inclusion of XALKORI (crizotinib) hard capsules, in the 250 mg and 200 mg strengths in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of paediatric patients (age ≥6 to <18 years) with recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumour (IMT) and at the MA dosages.

Recommended reimbursement rate for inclusion in the retail list of reimbursed proprietary medicinal products approved for use: 100%

Clinical Added Value

Considering:

- the data from phase 1-2 studies provided suggesting an anti-tumour activity of crizotinib in recurrent or refractory ALK-positive unresectable IMTs, in particular the results of the ADVL0912 study reporting the following in 12 paediatric patients treated at a dose of 280 mg/m² twice daily (MA dosage): 5 patients with a complete response, 6 patients with a partial response and 1 patient with stable disease, and a median response duration of 14.8 months (min./max.: 2.8-48.9 months);
- the inadequately met medical need in the treatment of recurrent or refractory ALK-positive unresectable IMTs in children due to the absence of a standard and/or authorised treatment in the event of IMT that cannot be operated on using conservative surgery or metastatic IMT;
- the expected, but not supported, improvement in care conditions compared to chemotherapy, with oral administration of crizotinib (hard capsules) at home;

and despite:

- the absence of comparative data in the target paediatric population, in whom the results do not enable any robust conclusion to be reached with respect to the therapeutic contribution of crizotinib compared to the available alternatives;
- the limited safety data in children in terms of the follow-up duration, with a median follow-up of less than 1 year in the studies provided;
- the potential onset of ocular toxicity and grade 3-4 neutropenia, which are known adverse reactions of crizotinib occurring more frequently in children and requiring reinforced monitoring in the paediatric population;

the Committee deems that XALKORI (crizotinib) hard capsules, in the 250 mg and 200 mg strengths, provides a minor clinical added value (CAV IV) in the care pathway for recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumour (IMT) in paediatric patients (age ≥6 to <18 years).