HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
08 JANUARY 2020

blinatumomab
BLINCYTO 38.5 micrograms powder for concentrate and solution for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.

What therapeutic improvement?

Slight therapeutic improvement compared to historical treatment.

Role in the care pathway?

In a situation of a Philadelphia chromosome negative ALL which is refractory or in second relapse, treatments are poorly standardised; allogeneic hematopoietic stem cell transplantation (HSCT) is recommended if not received after the first relapse and if complete remission can be obtained. Palliative supportive care can be proposed. A second transplant is sometimes considered.

The anti-CD 19 CAR-T tisagenlecleucel (KYMRIAH) has recently been granted an MA in the treatment of paediatric and young adult patients up to 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse, and it is recommended

by the Committee as a first-line treatment in paediatric and young adult patients up to 25 years of age with B-cell ALL that is refractory, in relapse post-transplant or in second or later relapse, while at the same time highlighting the uncertainties that remain concerning the efficacy and safety of KYMRIAH and the complexity of the treatment process.

Role of the medicinal product in the care pathway

BLINCYTO (blinatumomab) represents an alternative to chemotherapy-based salvage therapies in the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic HSCT.

The Committee highlights the fact that BLINCYTO can be administered at patients' homes in a home hospitalisation context, unlike chemotherapy-based salvage therapies, which require hospitalisation, partly due to the risk of infectious complications related to the haematotoxicity of chemotherapies.

Given the lack of comparative data to KYMRIAH (tisagenlecleucel), the role of BLINCYTO compared to KYMRIAH is not known. However, in patients with a general health status and life expectancy compatible with the administration of CAR-T treatment, the Committee considers that KYMRIAH should be favoured. The Committee reiterates that the efficacy and safety of KYMRIAH in patients previously treated with BLINCYTO has not been established (see Committee opinion for KYMRIAH dated 12 December 2018). In addition, KYMRIAH is not recommended if the patient has presented a relapse with CD19-negative leukaemia following previous treatment with an anti-CD19 therapy.

Finally, as in adult patients, on the basis of currently available data, the role of BLINCYTO compared to allogeneic HSCT, either as a "bridge" to allogeneic transplantation or to delayed allogeneic transplantation, or as a substitute for allogeneic transplantation, particularly in non-eligible patients, is not known.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Paediatric Philadelphia chromosome negative B-cell precursor acute lymphoblastic leukaemia (Phi- B-cell ALL) is a serious blood disease. The disease is liable to be life-threatening in the short term in case of refractory disease, or relapse after at least two prior therapies or relapse after prior allogeneic HSCT.
◗ It is a curative treatment.
◗ The efficacy/adverse effects ratio is high.
◗ There are therapeutic alternatives.
◗ BLINCYTO (blinatumomab) represents an alternative to chemotherapy-based salvage therapies in the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic HSCT (see paragraph 08 for more details).

◗ **Public health impact**

Considering:
- the seriousness of Phi- B-cell ALL in patients with refractory disease or in relapse after at least two prior therapies or in relapse after prior allogeneic HSCT,
- its low incidence,
- the partially met medical need at this stage of the disease,
- the lack of response to the identified need, due to the lack of any expected additional impact of BLINCYTO on morbidity and mortality (data derived from a non-comparative study) compared to historical treatment,
- the lack of elements enabling assessment of the impact on the care pathway and/or life of patients, and on the organisation of care,

BLINCYTO (blinatumomab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BLINCYTO (blinatumomab) is substantial in the indication "as monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation".

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 "as monotherapy for the treatment of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation" and dosages.

Clinical Added Value

Considering:

- **efficacy data demonstrating a complete remission percentage of around 38% during the first two cycles of blinatumomab treatment, maintained in around 18% of patients after a median follow-up of 24 months in a non-comparative study,**
- **uncertainties with respect to the effect size compared to historical treatments, in the absence of any direct comparison,**
- **the known efficacy and safety profile of blinatumomab in adults,**

the Transparency Committee considers that BLINCYTO provides a minor clinical added value (CAV IV) in terms of efficacy compared to historical treatments comprising chemotherapy-based salvage treatments, of paediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B-cell precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation.