HAUTE AUTORITÉ DE SANTÉ

# TRANSPARENCY COMMITTEE
## SUMMARY
## 15 DECEMBER 2021

*The legally binding text is the original French opinion version*

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

**New indication**

### Key points

Favourable opinion for reimbursement as monotherapy for the treatment of children or adolescents aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL) as part of the consolidation therapy.

### What therapeutic improvement?

Therapeutic improvement compared to conventional chemotherapy.

## Role in the care pathway?

In patients with first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL), second-line therapy is not standardised but is generally based on re-induction polychemotherapy followed by a further consolidation phase. The objective is to achieve a second remission and to enable the patient to have access to allogeneic haematopoietic stem cell transplantation in the best possible haematological conditions and general health with, insofar as possible, negative minimum residual disease (MRD) before allogeneic transplantation. It is now established, in fact, that the efficacy of allogeneic transplantation (measured by the absence of post-transplant relapse) depends on the level of pre-transplant disease.

In the event of a high-risk relapse (definition based on the time to relapse and its location, see Annex 1), it is usually recommended to administer polychemotherapy protocols at higher doses than in standard-risk situations, inducing short and/or long-term toxicities before having access to allogeneic transplantation.

**Role of the medicinal product in the care pathway**

BLINCYTO (blinatumomab) represents a treatment to be favoured over conventional chemotherapy as a third block of consolidation therapy for the treatment of children or adolescents aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor ALL, having achieved complete remission after a first high-risk relapse.

The Committee highlights the fact that BLINCYTO (blinatumomab) can mainly be administered to patients at home, unlike chemotherapy treatments, which require full hospitalisation throughout treatment, particularly due to the risk of infectious complications associated with the haematological toxicity of chemotherapies.

## COMMITTEE'S CONCLUSIONS

**Considering all of this information and further to debate and voting, the Committee considers:**

## Clinical benefit

◗ Childhood Philadelphia chromosome negative B-precursor acute lymphoblastic leukaemia (ALL) is a serious blood disease. The disease is liable to be life-threatening in the short term, particularly in the event of high-risk relapse.

◗ The proprietary medicinal product BLINCYTO (blinatumomab) is a curative medicinal product.

◗ BLINCYTO (blinatumomab) demonstrated that it improved event-free survival (primary endpoint) in high-risk first relapsed children and adolescents compared to conventional chemotherapy as part of the 3rd block of consolidation therapy. However, to date it has not demonstrated any superiority in terms of overall survival (exploratory secondary endpoint). The safety profile of blinatumomab is marked by a lower haematotoxicity compared to chemotherapy, despite more frequent general and neurological disorders. The efficacy/adverse effects ratio is high.

◗ There are alternative therapies.

◗ BLINCYTO (blinatumomab) represents a treatment to be favoured over conventional chemotherapy as a third block of consolidation therapy for the treatment of children or adolescents aged 1 year or older with Philadelphia chromosome negative CD19 positive B-precursor ALL, having achieved complete remission after a first high-risk relapse.

**Public health impact**

Considering:

- the seriousness of the disease in high-risk first relapsed patients and its low incidence,
- the partially met medical need at this stage of the disease,
- the partial response to the identified need, due to the additional impact demonstrated on morbidity only compared to conventional chemotherapy and the absence of a demonstrated impact to date on mortality or quality of life, and in a context in which blinatumomab was associated with a lower haematotoxicity,
- an expected, but not demonstrated, additional impact on the patient's care pathway considering the possibility of treating patients with BLINCYTO (blinatumomab) mainly at home, unlike chemotherapy treatments, which require full hospitalisation throughout treatment,

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

**Considering all these elements, the Committee deems that the clinical benefit of BLINCYTO (blinatumomab) is substantial as monotherapy for the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL) as part of the consolidation therapy.**

**The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL) as part of the consolidation therapy and at the marketing authorization (MA) dosages.**

## Clinical Added Value

Considering:

- demonstration of a superiority of blinatumomab in comparison with conventional chemotherapy, as a third block of consolidation therapy before allogeneic transplantation, in terms of event-free survival following a median follow-up of 22 months (HR=0.36; 95% CI [0.19; 0.66]; p<0.001);
- the favourable safety profile of blinatumomab, marked by a lower haematotoxicity compared to chemotherapy, despite more frequent general and neurological disorders,
- the expected improvement in care conditions compared to chemotherapy given the possibility of administering blinatumomab to patients mainly at home,

but in view of:

- the absence of demonstration of an improvement in overall survival versus chemotherapy, secondary endpoint in the study,
- the absence of quality of life data,

**the Committee considers that BLINCYTO (blinatumomab) provides a moderate clinical added value (CAV III) compared to conventional chemotherapy in the treatment of children and adolescents aged 1 year or older with high-risk first relapsed Philadelphia chromosome-negative CD19 positive B-precursor ALL as part of the third block of consolidation therapy.**