Report BLINCYTO® Blinatumomab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: blinatumomab **Brand Name:** BLINCYTO® **Originator/licensee:** Amgen Europe B.V. **Classification:** NI **ATC code:** L01XC19 **Orphan Status:** **Eu:** Yes **Us:** Yes **Mechanism of action:** Blinatumomab is a bispecific T-cell engager antibody construct. It activates endogenous T-cells by connecting CD3 in TCR complex with CD19 on benign and malignant B-cells. Blinatumomab, by the formation of a cytolytic synapse between the T-cell and the tumor cell, also increases the proliferation of T-cells and results in elimination of CD19+ cells [1].	**Authorized Indication:** **EMA:** blinatumomab is indicated as monotherapy for the treatment of pediatric pts aged 1 year or older with high-risk first relapsed Ph chromosome negative CD19+ B-precursor ALL as part of the consolidation therapy [2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 20/5/2021 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AEs:** Adverse Events **ALL:** Acute Lymphoblastic Leukemia **BG:** Blinatumomab Group **CCG:** Consolidation Chemotherapy Group **CD19:** Cluster of Differentiation 19 **CHMP:** Committee for Medicinal Products for Human Use **EFS:** Event-Free Survival **HR:** Hazard Ratio **HLA:** Human Leukocyte Antigen **IQR:** interquartile range **IV:** Intravenous Infusion **M.A.:** Marketing Authorization **OS**: oral **P.O.:** Positive Opinion **Ph:** Philadelphia **pts:** patients **SAEs:** Serious Adverse Events **TCR:** T-cell receptor **vs:** versus	**Summary of clinical EFFICACY** **Study NCT02393859:** is a multicenter, open label, randomized, phase III clinical trial. Eligible pts were children older than 28 days and younger than 18 years with Ph-chromosome negative, high-risk first-relapse B-ALL in morphologic complete remission (M1 marrow <5% morphologic blasts) or M2 marrow (blasts ≥5% and <25%) at randomization, who previously received an induction therapy and two blocks of consolidation therapy. Pts were randomly assigned (1:1) to receive a third consolidation course with either blinatumomab (15mcg/m^2/d for four weeks by continuous IV) or consolidation chemotherapy. The primary end-point was EFS (i.e. relapse, death, second malignancy, or failure to achieve complete remission). The median follow-up time for EFS was 22.4 months (IQR, 8.1-34.2). Events were reported in 31.5% pts from the BG and in 57.4% pts from CCG. The EFS HR was 0.33 (95% CI, 0.18-0.61) in favor of blinatumomab. The 24-month Kaplan-Meier estimate of EFS rate was 66.2% (95% CI, 50.1%-78.2%) in the BG and 27.1% (95% CI, 13.2%-43.0%) in the CCG [3]. **Summary of clinical SAFETY** The incidence of AEs of grade ≥3 was 57.4% in BG and 82.4% in CCG. The most common events were: thrombocytopenia (18.5% in BG vs. 35.3% in CCG), stomatitis (18.5% in BG vs. 31.4 % in CCG), neutropenia (16.7% in BG vs. 31.4% in CCG) and anemia (14.8% in BG vs. 41.2% in CCG). The incidence of SAEs was 24.1% in the BG and 43.1% in CCG; the most common reported events were neurologic symptoms and seizure (each 3.7%) in the BG and febrile neutropenia (17.6%) in CCG. No fatal AEs were reported [3]. **Ongoing studies:** • ***For the same indication:*** Yes • ***For other indications:*** Yes **Discontinued studies (for the same indication):** Yes --- **References:** 1.https://www.ema.europa.eu/en/documents/product-information/blincyto-epar-product-information_en.pdf 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/blincyto-2 3. https://jamanetwork.com/journals/jama/article-abstract/2776881?utm_campaign=articlePDF&utm_medium=articlePDFlink&utm_source=articlePDF&utm_content=jama.2021.0987 4.https://gallery.farmadati.it/Home.aspx 5.https://www.aieop.org/web/famiglie/schede-malattia/leucemia-linfoblastica-acuta/#:~:text=STRATEGIA%20TERAPEUTICA,quindi%20della%20ricaduta%20della%20malattia. 6.https://www.airc.it/cancro/informazioni-tumori/guida-ai-tumori-pediatrici/leucemia-linfoblastica-acuta-bambino 7.https://www.annalsofoncology.org/article/S0923-7534(19)31639-4/pdf 8.http://www.io.nihr.ac.uk/wp-content/uploads/2017/12/9916-Blinatumomab-for-ALL-V1.0-NON-CONF.pdf 9.https://clinicaltrials.gov/ct2/show/NCT03914625?recrs=abdf&type=Intr&cond=Acute+Lymphoblastic+Leukemia&intr=Blinatumomab&age=0&phase=12&draw=2&rank=9	**Cost of therapy:** The cost for one vial of blinatumomab (38,5 mcg 10 ml) is € 4,209.40*. One cycle of therapy (15mcg/m^2/28 days) costs around € 46,303.4/m^2 [4]. **Retail price including VAT* **Epidemiology** The incidence of ALL in pediatric age, which represents 3/4 of all leukemias, is about 30 cases/year/million of subjects aged 0-17 years. In Italy about 400 new cases/year are estimated. The peak of incidence is between 2 and 5 years of age, and it is slightly higher in males than in females: this difference is more marked during adolescence and for T-cell ALL [5-6]. **POSSIBLE PLACE IN THERAPY** The treatment for ALL in children is generally carried out in three main stages: 1. induction stage with: - chemotherapy (which includes large cumulative doses of corticosteroids, vincristine, L-asparaginase and consequent CNS-directed therapy); - targeted therapies (monoclonal antibodies, e.g. rituximab, blinatumomab); 2. consolidation stage, using IV chemotherapy; 3. maintenance stage, using OS chemotherapy [7-8]. **OTHER INDICATIONS IN DEVELOPMENT:** No **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** Yes [9]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** No *Service reorganization: No *Possible off label use: Yes

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