

NCPE Assessment

Summary

Blinatumomab (Blincyto®)

25052

24 September 2026

Applicant: Amgen Inc

Blinatumomab monotherapy as part of consolidation therapy for the treatment of adult patients with newly diagnosed Philadelphia chromosome-negative CD19-positive B-cell precursor acute lymphoblastic leukaemia (BCP-ALL).

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of blinatumomab (Blincyto®) as part of consolidation therapy for the treatment of adult patients with newly diagnosed Philadelphia chromosome-negative CD19-positive B-cell precursor acute lymphoblastic leukaemia who are minimal residual disease (MRD)-negative. This is a subpopulation of the licensed indication. Following assessment of the Applicant's submission, the NCPE recommends that blinatumomab (Blincyto®) be considered for reimbursement, for this indication, if cost-effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Amgen Inc) Health Technology Assessment of blinatumomab (Blincyto®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In April 2026, Amgen Inc submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of blinatumomab (Blincyto®) monotherapy as part of consolidation therapy for the treatment of adult patients with newly diagnosed Philadelphia chromosome-negative CD19-positive B-cell precursor acute lymphoblastic leukaemia (BCP-ALL). Amgen Inc is seeking reimbursement of blinatumomab on the Oncology Drug Management System.

Blinatumomab is a bispecific T-cell engager molecule that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T-cells. Blinatumomab is indicated as an add-on treatment to consolidation therapy, which consists of four cycles of multi-agent chemotherapy (such as vincristine, daunorubicin, cytarabine, etoposide, methotrexate, corticosteroids, and (peg)-asparaginase). Blinatumomab is administered as a continuous intravenous infusion at a fixed dose of 28 mcg/day in patients weighing ≥ 45 kg. In patients weighing < 45 kg, blinatumomab is administered at a dose of $15\text{mcg}/\text{m}^2/\text{day}$ based on body surface area. A single cycle of blinatumomab is 28 days of continuous infusion followed by a 14-day treatment-free interval. Patients may receive up to four cycles of blinatumomab.

The Applicant's place in therapy for blinatumomab, as part of consolidation therapy, is for first-line treatment in patients with Philadelphia chromosome-negative CD19-positive BCP-ALL who are minimal residual disease (MRD)-negative (defined as $\text{MRD} < 10^{-4}$ or 0.01%). This is considered a subpopulation of the product licence, which does not differentiate by MRD status. The Review Group note that blinatumomab is currently reimbursed as monotherapy in patients with Philadelphia chromosome-negative CD19-positive BCP-ALL who are MRD-positive. In the population of patients who are MRD-negative, blinatumomab is indicated as an add-on treatment to consolidation chemotherapy. Standard of care (SOC) consolidation therapy is considered a comparator to blinatumomab in combination with SOC consolidation chemotherapy (henceforth referred to as blinatumomab + SOC).

1. Comparative effectiveness of blinatumomab

The clinical trial programme, supporting the regulatory approval of blinatumomab for the indication under assessment, is an ongoing phase III, randomised, open-label trial. The E1910 trial has four treatment phases: induction, intensification, consolidation, and maintenance.

All participants were assigned to 'induction' chemotherapy at enrolment where participants received two cycles of induction treatment. Participants who achieved complete response (CR) or CR with incomplete peripheral blood count recovery received 'intensification' chemotherapy (one 28-day cycle). In the original trial protocol, after 'intensification' chemotherapy, all participants (MRD-positive and MRD-negative) were randomised to receive 'consolidation' therapy, either blinatumomab in combination with SOC consolidation chemotherapy (blinatumomab + SOC arm) or SOC consolidation chemotherapy (SOC arm). However, following a protocol amendment, all participants who were MRD-positive were assigned to the blinatumomab + SOC arm, while all participants who were MRD-negative continued to be randomised to either blinatumomab + SOC or SOC arms. This resulted in an imbalance in the number of participants who were MRD-positive between the two treatment arms (blinatumomab + SOC arm: 40 participants; SOC arm: 22 participants). After completing 'consolidation' therapy, all participants in blinatumomab + SOC and SOC arms received 'maintenance' therapy. Participants in the blinatumomab + SOC arm can receive allogeneic haematopoietic stem cell transplant (alloSCT) after at least two cycles of blinatumomab, while participants in the SOC arm can receive alloSCT at any cycle. The primary endpoint was overall survival (OS) in participants who are MRD-negative following induction and intensification chemotherapy. Relapse-free survival (RFS) was measured in the same population as a secondary endpoint. Post-hoc analyses were conducted to measure OS and PFS in the full trial population (MRD-negative and MRD-positive, data not presented).

At the interim analysis with a median follow-up time of 4.5 years, participants who were MRD-negative in the blinatumomab + SOC arm experienced a statistically significant improvement in OS compared with those in the SOC arm (hazard ratio [HR] 0.44, 95% confidence interval [CI] 0.25 to 0.76; $p = 0.003$). A statistically significant improvement in RFS was also observed in the blinatumomab + SOC arm compared with the SOC arm (HR 0.53,

95% CI 0.32 to 0.88; $p = 0.013$). Prespecified sensitivity analyses of OS and RFS censored at alloSCT showed a statistically significant improvement in OS but not RFS. The Kaplan Meier (KM) estimates of OS at five years were 82.4% (95% CI 73.7% to 88.4%) in the blinatumomab + SOC arm and 62.5% (95% CI 52.0% to 71.3%) in the SOC arm. For PFS, the KM estimates at five years were 77.05% (95% CI 67.8% to 83.8%) in the blinatumomab + SOC arm and 60.5% (95% CI 50.1% to 69.4%) in the SOC arm. Limitations of the E1910 trial include that OS and RFS data are immature (median OS and RFS were not reached in either arm at the interim analysis); the open-label trial design may introduce bias and health-related quality of life (HRQoL) data were not collected.

2. Safety of blinatumomab

For the population of patients who were MRD-negative, adverse events (AEs) were reported by 111 participants (100%) and 110 participants (98.2%) in the blinatumomab + SOC and SOC arms, respectively. Grade ≥ 3 treatment-emergent AEs (TEAEs) that occurred in $\geq 20\%$ of participants were neutrophil count decreased (blinatumomab + SOC arm: 87.4% versus SOC arm: 94.6%), platelet count decreased (70.3% versus 77.7%), white blood cell count decreased (54.1% versus 66.1%), lymphocyte count decreased (34.2% versus 27.7%), anaemia (31.5% versus 41.1%), and febrile neutropenia (20.7% versus 28.6%). The SmPC includes special warnings for AEs of special interest including cytokine release syndrome and neurologic events as well as the potential for infections, infusion-related reactions, tumour lysis syndrome, neutropenia and febrile neutropenia, pancreatitis, and progressive multifocal leukoencephalopathy, for which patients should be monitored closely.

3. Cost effectiveness of blinatumomab

Methods

A partitioned-survival model was submitted, comprising three mutually exclusive health states: relapse-free, post-relapse, and death. The Applicant also applied an additional cure assumption, in the cost-effectiveness model (CEM) whereby patients remaining relapse-free for five years switch to general population utility (quality of life) and are not subject to any costs. The treatment effects captured by the CEM were the delay in disease progression and death.

RFS and OS data from the E1910 trial were extrapolated separately by treatment arm using mixture-cure parametric survival analysis. The Weibull mixture-cure model was used for OS and the lognormal mixture cure model for RFS in the Applicant base case, which the Review Group consider reasonable. The Applicant applied a constraint on RFS by capping the per-cycle risk of RFS events to never be lower than the per-cycle risk of OS, to correct for overestimation due to missed relapse events. The Review Group consider this constraint inappropriate as it does not adequately address possible interval censoring of relapse in the trial data and has implications for transitions from the post-relapse state given the partitioned-survival model structure. In the NCPE-adjusted base case a constraint is instead applied to RFS to ensure logical consistency, so that the percentage of patients who are relapse-free is never higher than the proportion of patients who are alive.

No appropriate utility data was identified in the systematic literature review, and HRQoL data were not collected in E1910. Data from the BLAST and TOWER trials were used to inform the utility values for the relapse-free and post-relapse health states, respectively. However, the Review Group noted that differences in patient populations across BLAST, TOWER, and E1910 may introduce bias and uncertainty to the estimated utility values used in the CEM. The Applicant assumed that patients who remained relapse-free for five years were consider “cured” and were assumed to have the same utility values as the general population. Clinical opinion to the Review Group indicated that chemotherapy-related toxicities, psychological distress, and cardiovascular side effects may negatively impact patients’ HRQoL in the long-term. Therefore, in the NCPE-adjusted base case, a long-term disutility, which was calculated as 97.8% of the age- and sex-matched general population utility, was applied to patients who were considered “cured” in the CEM. This 97.8% was estimated by dividing the relapse-free utility value of 0.850 by the age-and sex-matched general population utility value of 0.869.

The model also included costs associated with drug acquisition, hospitalisation, intravenous administration, maintenance treatment, alloSCT, subsequent treatments, and management of AEs. The Review Group considered that the Applicant had overestimated the subsequent treatment costs, as well as costs and associated disutility of post-relapse alloSCT, by

assuming that patients who die would incur these costs and outcomes. The NCPE-adjusted base case corrected for this overestimation.

Results

An incremental analysis of the costs and benefits of blinatumomab + SOC versus SOC was presented by the Applicant (Table 1).

Table 1: Applicant base case incremental cost-effectiveness results^{a,b}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
SOC	128,642	8.43	-	-	-
Blinatumomab + SOC	289,899	11.92	161,256	3.49	46,204

SOC: standard of care; **QALY:** quality adjusted life year; **ICER:** incremental cost-effectiveness ratio

^a Corresponding probabilistic ICER using 1,000 iterations=€47,196/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. A discount rate of 4% was applied to costs and outcomes.

^b A commercial in confidence patient access scheme (CIC PAS) has been proposed for blinatumomab, not included here

The Review Group assessment identified a number of limitations in the Applicant's base case which were addressed in the NCPE adjusted base case. These included: adjusting subsequent treatment costs, adjusting post-relapse alloSCT cost and disutility by the proportion of patients who experienced fatal progression events in the E1910 trial (to ensure these are not applied to patients in the death state), applying a utility decrement for "cured" patients, and capping the percentage of patients who are relapse-free to never be higher than the proportion of patients who are alive. The NCPE-adjusted base case is presented in Table 2.

Table 2: NCPE-adjusted base case incremental cost-effectiveness results^{a,b}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
SOC	107,635	8.46	-	-	-
Blinatumomab + SOC	276,936	11.79	169,302	3.33	50,811

NCPE: National Centre for Pharmacoeconomics; **SOC:** standard of care; **QALY:** quality adjusted life year; **ICER:** incremental cost-effectiveness ratio

^a Corresponding probabilistic ICER using 1,000 iterations=€52,553/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. A discount rate of 4% was applied to costs and outcomes.

^b A commercial in confidence patient access scheme (CIC PAS) has been proposed for blinatumomab, not included here

Sensitivity analysis

The probabilities of cost-effectiveness for blinatumomab + SOC versus SOC, in the Applicant and NCPE-adjusted base cases was 0% at the threshold of €20,000 per quality-adjusted life year (QALY). At the threshold of €45,000 per QALY, the probability of cost-effectiveness was

44.7% in the Applicant base case and 31.1% in the NCPE-adjusted base case. Deterministic one-way sensitivity analyses indicated that the most influential parameters in the model, for both the Applicant and the NCPE-base case, related the proportion of patients in the relapse-free health state receiving alloSCT in either treatment arm. Results of the probabilistic analysis, which were estimated for 1,000 simulations, are stable and similar to the results of the deterministic analysis.

Using the NCPE adjusted base case, a reduction in the blinatumomab price-to-wholesaler (PtW) of about 19.8% would be required to reach the €45,000 per QALY threshold. A reduction of about 66.2% would be required to reach the €20,000 per QALY threshold.

4. Budget impact of blinatumomab

The PtW for one pack of blinatumomab (38.5mg powder for concentrate and solution for infusion) is €2,663.13 (including VAT). The estimated total cost, per patient, per treatment course of blinatumomab is €224,364 (including VAT). National Cancer Registry Ireland data indicated that an average of 22 new cases of acute lymphoblastic leukaemia (ALL) were diagnosed in Ireland annually. Allowing for population growth, this corresponds to 22 newly diagnosed ALL cases in Year one rising to 24 cases in Year five of the budget impact model. Of these, the Applicant assumed 78% to have B-cell lineage, and 93% to have BCP-ALL specifically, 85% are Philadelphia chromosome-negative, and 78.32% are MRD-negative. This resulted in eleven patients eligible for treatment in Year one increasing to twelve patients in Year five, and a cumulative five-year total of 56 patients. In a world without blinatumomab all patients are currently treated with SOC consolidation therapy. In a world with blinatumomab, which is an add-on therapy to the current SOC, 90% of patients who are MRD-negative are estimated to receive blinatumomab in Year one, rising to 100% in Years four and five. The cumulative five-year gross and net drug budget impact is €11.99 million (including VAT). The Review Group consider many of the inputs uncertain including the proportion of patients estimated to have B-cell lineage, BCP-ALL, and who are MRD-negative and Philadelphia chromosome-negative.

5. Patient Organisation Submission

No patient organisation submissions were received during the course of the assessment.

6. Conclusion

The NCPE recommends that blinatumomab, as part of consolidation therapy for the treatment of adult patients with newly diagnosed Philadelphia chromosome-negative CD19-positive BCP-ALL- who are MRD-negative, be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments *.

*Next steps: The NCPE Assessment Report and recommendation, will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found [here](#).