NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity

1 Recommendations

1.1 Blinatumomab is recommended as an option for treating Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia in adults with minimal residual disease (MRD) of at least 0.1%, only if:

- the disease is in first complete remission and
- the company provides blinatumomab according to the commercial arrangement (see section 2).

1.2 This recommendation is not intended to affect treatment with blinatumomab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Current treatment for acute lymphoblastic leukaemia that is in complete remission with MRD of at least 0.1% is continued chemotherapy followed by haematopoietic stem cell transplantation (HSCT) if possible. Some people with MRD can have HSCT without chemotherapy.

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Evidence from 2 clinical studies suggests that blinatumomab may help increase the time people have without their disease relapsing and may lead to more disease being cured. But there are no data directly comparing blinatumomab with continued chemotherapy, with or without HSCT. This means that the exact size of the benefit of blinatumomab compared with continued chemotherapy is uncertain.

Blinatumomab meets the extension-to-life criterion, but not the short-life expectancy criterion. Therefore, blinatumomab does not meet NICE's criteria to be considered a life-extending treatment at the end of life.

There is some uncertainty about the cost effectiveness of blinatumomab compared with continued chemotherapy in people with acute lymphoblastic leukaemia with MRD because of the way survival curves are fitted to the clinical data in the new semi-Markov model. Also, there is no evidence presented about the cost effectiveness of blinatumomab in people with acute lymphoblastic leukaemia that is in second complete remission. Because no cost-effectiveness evidence for the second complete remission group is presented, no recommendation for this group can be made. However, all plausible cost-effectiveness estimates of blinatumomab compared with continued chemotherapy are within the range that NICE normally considers a cost-effective use of NHS resources. Therefore, blinatumomab is recommended for routine use in the NHS for people with Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with MRD of at least 0.1% whose disease is in first complete remission.

2 Information about blinatumomab

Marketing authorisation indication	Blinatumomab (Blincyto, Amgen) is indicated as 'monotherapy for the treatment of adults with Philadelphia-chromosome-negative CD19 positive B-precursor acute lymphoblastic leukaemia in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%'.
Dosage in the marketing authorisation	Blinatumomab is administered by continuous intravenous infusion delivered at a constant rate using an infusion pump. A single cycle of blinatumomab treatment comprises continuous intravenous infusion at a dose of 28 micrograms/day for 28 days, followed by a 14-day treatment-free interval.
Price	The list price of blinatumomab is £2,017 per 38.5 microgram vial. The average cost of blinatumomab per cycle at the list price is £56,476 (company submission). The company has a commercial arrangement (simple discount patient access scheme). This makes blinatumomab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee (section 6) considered evidence submitted by Amgen, a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

New treatment option

3.1 People with acute lymphoblastic leukaemia in remission with Philadelphia-chromosome-negative CD19-positive B-precursor disease, and with minimal residual disease (MRD) would welcome a new treatment option. MRD in this document refers to detectable MRD of at least 0.1%. Acute lymphoblastic leukaemia is a rare, rapidly progressing form of cancer of the white blood cells. Outcomes for adults with acute lymphoblastic leukaemia are poor. Common symptoms include fatigue, breathlessness, infections, bleeding, bruising, fever and sweating. Although in more than 80% of people with acute lymphoblastic leukaemia, the disease will achieve complete remission, in up to 44% of adults the disease is

expected to relapse. Both patient and clinical experts explained that people with MRD experience symptoms, even if their disease is in remission, because they are often having treatment that has a lot of side effects. Although the degree of symptoms varies across patients, overall, they are not well and cannot work. The clinical experts noted that current treatment options (chemotherapy) are difficult for patients to tolerate and they could benefit from novel treatment options. Currently, no approved treatments exist specifically for MRD B-precursor acute lymphoblastic leukaemia that is in haematological complete remission. The committee concluded that people with MRD B-precursor acute lymphoblastic leukaemia would welcome a new treatment option that would improve symptoms and the chance of survival.

Clinical management

The clinical importance of MRD is clearly established

3.2 The committee considered the treatment pathway for B-precursor acute lymphoblastic leukaemia. In the NHS, patients are monitored regularly for the presence of MRD during the 4 to 8 weeks after starting induction therapy when complete remission is first seen. The clinical experts explained that MRD status is a major predictive factor for patients whose disease is in haematological complete remission. MRD is a marker of chemotherapy resistance and is therefore a predictor of response to subsequent chemotherapy. They noted that there is no current therapy specifically to reduce MRD. The committee acknowledged that MRD is an important factor in predicting future treatment outcomes. It concluded that a treatment for MRD would be a valuable addition to the treatment pathway.

Haematopoietic stem cell transplantation (HSCT) is important in achieving cure, the main aim of treatment

3.3 The clinical experts stated that the main treatment goal for people with acute lymphoblastic leukaemia is to achieve cure through sustained

absence of MRD and maintained haematological complete remission. They explained that, in most people whose disease is cured, it is cured after HSCT. However, the use of HSCT may vary based on a patient's fitness, donor availability and their personal preferences. The committee understood that the aim of treatment for B-precursor acute lymphoblastic leukaemia is a cure. People with MRD may proceed to HSCT, but it is more likely to be successful in the absence of MRD. The committee concluded that HSCT has an important role in achieving a cure in people with acute lymphoblastic leukaemia.

People with untreated MRD are likely to need subsequent treatment for relapse

3.4 The committee noted that people with MRD are at high risk of relapse. The clinical experts explained that, if the disease relapses, the treatment options are continued chemotherapy, inotuzumab ozogamicin or blinatumomab, although continued chemotherapy is now rarely used at this stage. They also said that it is unlikely that people would have blinatumomab for a relapse if they had previously had it for MRD. The committee concluded that people with untreated MRD are likely to need subsequent treatment for relapse, and blinatumomab is a relevant option at this stage.

The definition and measurement of MRD is standardised

3.5 The clinical experts noted that MRD testing is standardised across treatment centres in England. One of the clinical experts stated that MRD presence is established across a quantifiable scale: at least 0.001% is the lowest end of detection possible with current technology. However, they noted that technology is rapidly progressing and there will be more sensitive technologies that will detect even smaller numbers of leukaemic cells in the future. The trial population presented by the company included MRD detected at a level of at least 0.1%. The committee was aware that the marketing authorisation applies to people with MRD of at least 0.1%; this is what is meant by MRD in this document. It agreed that MRD testing

is standard practice and was aware it could only make recommendations within the marketing authorisation.

Clinical evidence

Blinatumomab is clinically effective but the lack of direct comparative trial data means the size of this benefit is still unclear

3.6 The clinical evidence for blinatumomab came from 2 single-arm studies (BLAST and MT103-202). The committee understood that both studies included patients with acute lymphoblastic leukaemia in complete haematological remission with MRD. The company presented results from 116 patients from BLAST and 20 patients from MT103-202 (see table 1). All patients had at least 1 blinatumomab infusion. At the August 2015 data cut, the median follow-up in BLAST was 18 months. The survival data were immature. The committee noted a plateau in the Kaplan–Meier curves for overall and relapse-free survival. However, it was aware there were very few patients still at risk in this part of the curves, and no events were recorded after 41 months and 35 months for overall and relapse-free survival respectively. The MT103-202 study had a follow-up of about 4 years, included only 20 patients and did not record overall survival. The committee was concerned that the single-arm design of the studies meant that the results were potentially biased. It noted that there was no evidence on the effectiveness of blinatumomab directly compared with continued chemotherapy. As requested by the committee, in response to consultation, the company presented updated Kaplan–Meier graphs, using safety data from the latest data cut from June 2017. It presented overall survival data for people with Philadelphia-chromosome-negative, B-precursor acute lymphoblastic leukaemia and presence of MRD whose disease is in first, second or third complete remission. The committee agreed the updated clinical data is more reliable than the original submission. It concluded that blinatumomab is clinically effective, but the lack of direct comparative data means the size of this benefit is still unclear.

Table 1 Clinical effectiveness results for blinatumomab, full trial population

Outcome	BLAST (n=116, August 2015 data cut)*	MT103-202 (n=20)
Complete MRD response rate in 1 cycle	n=88 (77.9%)	n=16 (80.0%)
Median overall survival	36.5 months (19.2 months, not estimable)	N/A
Overall survival at 18 months	65% (95% CI 55 to 73)	N/A
Median relapse-free survival	18.9 months (95% CI 12.3 to 35.2)	not estimable (at 1,550 days of follow-up)
Relapse-free survival	53.0% (95% CI 44 to 62) at 18 months	52.6% (N/A) at 5.9 years
Abbreviations: CI, confidence interval; MRD, minimal residual disease; N/A, not applicable; n, number.		

*Results presented for primary company analyses, which are not censored at HSCT

Blinatumomab can only be recommended within its marketing authorisation

3.7 Blinatumomab's marketing authorisation includes adult patients with acute lymphoblastic leukaemia in first or second complete remission and which is Philadelphia-chromosome-negative with MRD of at least 0.1%. The study population in BLAST was wider than the population outlined in the marketing authorisation. Although most patients had disease that was in first or second complete remission, it also included patients whose disease was in third complete remission. Also, it included patients with Philadelphia-chromosome-positive and Philadelphia-chromosome-negative disease. In the MT103-202 study, all patients had disease that was in complete remission, but it also included both Philadelphia-chromosome-positive and negative disease. The committee concluded that it could only make recommendations within the population outlined in the marketing authorisation.

The indirect comparison is appropriate but is not generalisable to the wider marketing authorisation population

3.8 The committee was aware that there were no data directly comparing blinatumomab with continued chemotherapy. The company therefore did an indirect comparison of blinatumomab and continued chemotherapy which was used in the economic model. The comparator data came from

Study 20120148, a retrospective study with data on patients with Philadelphia-chromosome-negative B-precursor acute lymphoblastic leukaemia in complete haematological remission and MRD. The study collected data on overall and relapse-free survival but not on adverse effects. It was used as a matched control for BLAST. Because of differences between the populations in BLAST and the historical comparator, the company used a subset of the original study populations. The committee was aware that the population in the indirect comparison was narrower than the marketing authorisation and excluded the following groups:

- patients who could not have HSCT or tolerate chemotherapy
- patients whose disease is in second complete remission (CR2).

The clinical experts suggested that survival outcomes for the excluded groups of people were poor and that they could potentially benefit from treatment with blinatumomab. This was because some patients who had blinatumomab have had good outcomes even without subsequently having HSCT. The committee concluded that the indirect comparison was appropriate, given the absence of randomised controlled trial data, but that the results are not generalisable to the full population outlined in the marketing authorisation.

The indirect comparison method is appropriate but subject to uncertainty

3.9 The company used a propensity score model to compare the primary analysis set from BLAST and the direct comparator Study 20120148. This method produced weights that were applied to the control study (Study 20120148). The aim was to estimate the response to chemotherapy that would be expected in a population with the same characteristics as the population in the BLAST primary analysis set. The ERG noted that the chosen method of applying weights to balance the datasets was appropriate given the lack of randomised controlled trials. The company used 2 different methods to produce weights: 'average

treatment effect' and 'average treatment effect on the treated'. For both methods, the company used stabilised and non-stabilised weights. It used stabilised weights to produce the average treatment effect on the treated estimates in the clinical effectiveness analysis. However, non-stabilised weights were used to produce the treatment effect on the treated estimates that were used in the cost-effectiveness analysis. As part of the clarification response, the company provided data to show that there was no substantial difference in the results produced from both methods of applying weights. The results are confidential and cannot be reported here. The committee concluded that the method used to compare the 2 studies was appropriate but subject to uncertainty.

Cost-effectiveness model

The company's original model was not suitable for decision making

3.10 The company's original model was a partitioned survival model based on relapse-free survival and overall survival, with 3 health states: (1) relapse free; (2) post relapse and (3) dead. The main partitioned survival structure had 2 linked sub-models which were intended to estimate additional costs and utility decrements associated with HSCT received before or after disease has relapsed. The pre-relapse sub-model was not causally related to relapse-free or overall survival, whereas the post-relapse sub-model was partially related to relapse-free survival. The ERG noted that the causal effect of transplant on outcome was not adequately modelled. The clinical experts also explained that MRD status highly correlates with HSCT outcomes: HSCT is less likely to be successful in people with MRD. However, the committee acknowledged that the model did not show how many patients with or without MRD have HSCT. The clinical expert further noted that there is unpublished but more mature and up-to-date data on survival outcomes after HSCT that could be included. The clinical experts highlighted that the original model was not reflective of current practice or the treatment pathway (see section 3.2). They clarified that the treatment pathway has recently changed and now includes inotuzumab ozogamicin

or blinatumomab for treating relapses (see section 3.4). The committee noted that while the model implicitly incorporated HSCT within the relapse-free survival and the overall survival curves, it did not show how many patients had HSCT. Without this direct link, it was not clear what proportion of patients had HSCT, and what their outcomes after HSCT were. Given the importance of HSCT to the likelihood of cure (see section 3.3), the committee was aware that this made it difficult to assess the reliability and clinical plausibility of the original model. At the first committee meeting, it concluded that it would have liked to have seen a cost-effectiveness model including:

- a revised cost-effectiveness analysis reflecting the current treatment pathway in the NHS and comparing blinatumomab with continued chemotherapy. The revised economic model should:
  - include costs, health-related quality-of-life estimates and outcomes associated with the current treatment pathway for people with relapsed or refractory acute lymphoblastic leukaemia
  - include the proportion of people with and without MRD after blinatumomab treatment and how many have HSCT
  - incorporate an explicit causal link between the probability of HSCT and relapse-free survival and overall survival in both groups
  - explicitly model a cure for people whose disease is expected to be cured and include scenario analyses considering different cure fractions and cure points
  - factor in the different positions in the treatment pathway at which HSCT might be given.
- the latest available evidence on survival outcomes after HSCT
- the latest trial data cut.

In response to consultation, the company submitted a new model (see section 3.13).

The cure point assumption in the original model should be reconsidered because it is not clinically plausible

3.11 The company's original model did not have a fixed cure point. Instead, the model predicted the timepoint at which patients were assumed to be cured and had mortality rates similar to those of the general population with some additional excess mortality risk after a cure. This approach resulted in different cure points between the relapse-free survival and the overall survival extrapolations. The committee concluded that having a large gap between the resulting cure points (company model) is not clinically plausible. It was aware that the assumptions around the cure fraction or cure point were a key driver in the cost-effectiveness analysis. Therefore, at the first committee meeting, the committee concluded they would have liked to have seen a clinically plausible, explicitly modelled cure for the patients whose disease is expected to be cured. In response to consultation, the company submitted a new model with explicitly modelled cure states (see section 3.14).

Health-related quality of life

The company's post-relapse utility value is too high

3.12 The company used a post-relapse utility value of 0.69 in the model, which was lower than the one seen in the BLAST study (0.819). However, the ERG's clinical experts noted that both values are too high for relapsed patients and were not clinically plausible. The ERG ran exploratory analyses with lower utility values (0.50 and 0.25), which had a small effect on the incremental cost-effectiveness ratio (ICER). The committee concluded that the post-relapse quality-of-life estimates included in the company model were too high but were not a key driver of the results.

Company's new cost-effectiveness evidence and revised base case

The company submitted a revised partitioned survival model

3.13 In response to consultation, the company submitted a revised partitioned survival model, which used the same structure and parameters as the original model (see section 3.9). It included 3 key changes

- inotuzumab ozogamicin is included as a salvage treatment for relapsed disease
- the proportions of patients having blinatumomab or inotuzumab ozogamicin as salvage therapy for relapsed disease were estimated based on clinical expert opinion. In the continued chemotherapy arm, patients having first salvage therapy are split equally between blinatumomab and inotuzumab ozogamicin and
- the cost calculations for blinatumomab as salvage therapy for relapsed disease have been amended.

The revised partitioned survival model did not include the remaining amendments requested by the committee (see section 3.10). Therefore, the committee concluded that the revised partitioned survival model was not suitable for decision making.

The new semi-Markov model submitted by the company is suitable for decision making

3.14 In response to consultation, the company also submitted a semi-Markov model. The model structure was comprised of 4 health states: first complete haematological remission (CR1); pre-relapse HSCT; relapse and dead. The model compares blinatumomab and continued chemotherapy, both followed by pre-relapse HSCT for some patients, followed by post-relapse salvage therapy using inotuzumab ozogamicin for the blinatumomab arm and either inotuzumab ozogamicin or blinatumomab for the continued chemotherapy arm. Most of the parameters used in the new semi-Markov model are the same as the

ones used in the updated partitioned survival model. The new semi-Markov model produces outcomes that depend on treatment offered, MRD response and the patient's current health state. This leads to different results compared with the company's partitioned survival model. The ERG explained that the new semi-Markov model incorporates most of the assumptions preferred by the committee (see section 3.10), but it was also subject to certain limitations:

- HSCT costs were applied to some patients who relapsed but were not related to downstream salvage treatment
- there was a small number of events and patients at risk
- the rationale for curve selection was not consistent
- concerns about model-predicted relapse-free survival and overall survival (see section 3.17).

The committee considered the new semi-Markov model and concluded that it was suitable for decision making.

The most plausible cure point is likely to be below 5 years.

3.15 The committee considered how the cure points are modelled in the new semi-Markov model. The ERG explained that the cure point is not fixed but defined in each cure state. People with acute lymphoblastic leukaemia who have pre-relapse HSCT have a cure point later than that applied to the CR1 state. The cure point for CR1 was 5 years. The cure point for patients entering the pre-relapse HSCT state was 5 years after entry into that state (that is, the time spent in CR1 plus 5 years). Patients who experienced relapse and did not die within 5 years of relapse were assumed to be cured 5 years after they entered the relapse state. These patients would have a cure point of more than 5 years but less than 15 years from entering the model. In this way, the model considered patients who remained relapse-free and proceed to transplant to be cured at a later timepoint than those who remain relapse-free but never proceed to HSCT. The clinical experts said that in clinical practice people with

acute lymphoblastic leukaemia are considered cured if their disease has not relapsed within 2 years. The committee concluded that the cure point is likely to be less than 5 years and possibly 3 years would be most plausible.

The new semi-Markov model uses an inappropriate method for handling competing risks

3.16 The company's new semi-Markov model faces an issue with competing risks. Competing risks happen when patients in the model can experience 1 or more events which 'compete' with the event of interest. The new semi-Markov model estimates each transition state by using patient time-to-event data, it then keeps events of interest and removes events not of interest. The ERG explained that this approach does not handle competing risks appropriately. Specifically, the problem with removing events not of interest is that it may lead to a pattern of removal that is not independent anymore. Because of this, the model estimates may be biased and inaccurate. The ERG believes that the company's approach is likely to have increased the risk of each event. The committee concluded that there is uncertainty in the model because of the method used for handling competing risks.

Overall survival in the new semi-Markov model

The overall survival extrapolations are subject to uncertainty

3.17 The committee considered the overall survival from the new semi-Markov model. The company presented a graph comparing the Kaplan–Meier curves from BLAST and the historical control and the new semi-Markov model predictions for overall survival including blinatumomab and inotuzumab ozogamicin as salvage treatments for relapsed disease. The company used data from the TOWER study (phase III, randomised study of blinatumomab compared with standard care in patients with acute lymphoblastic leukaemia) to inform the post-relapse survival estimation in the new semi-Markov model. The survival curves projected by the model

fit the survival curves of the BLAST data and the historical control closely. The parametric curves estimated that the proportion of patients that would be relapse-free at 5 years was 40% and 18.1% for blinatumomab and standard care, respectively. However, the ERG ran exploratory analyses and presented the same comparison but excluding blinatumomab and inotuzumab ozogamicin as salvage treatments for relapsed disease. The ERG used the restricted Gompertz overall survival function for the standard chemotherapy group after relapse fitted to data from TOWER to model overall survival for patients whose disease had relapsed. The results showed that the new semi-Markov model no longer gives a good fit to the Kaplan–Meier curves in either treatment group. The ERG explained that the predictions from this version of the model should match the Kaplan–Meier curves because both the parametric curves and the Kaplan–Meier data excludes blinatumomab and inotuzumab ozogamicin for treating relapsed disease. Instead, predicted overall survival was underestimated in both treatment groups, but more so in the standard chemotherapy comparator group. The clinical expert pointed out that if there is any benefit because of the newly introduced treatments, there should be an increase in overall survival curves for both blinatumomab and standard care. The committee concluded that the overall survival extrapolations in both arms were subject to uncertainty.

The new semi-Markov model is appropriate for decision making but results are not generalisable to the full marketing authorisation

3.18 The company modelled the cost effectiveness of blinatumomab using data from BLAST, the historical control and TOWER. However, this did not include patients whose disease was in second complete remission (CR2). The committee recalled that this was a narrower population than the marketing authorisation (see section 3.8). At consultation, the company stated that there are few people with acute lymphoblastic leukaemia in CR2, and the number of people is declining and it should be included in committee's decision making. The committee considered all the evidence within the marketing authorisation. Because the committee did not see

cost-effectiveness evidence on acute lymphoblastic leukaemia in CR2, it could not make recommendation for this indication. It further concluded that it could only make recommendations based on the evidence presented to it.

Cost-effectiveness results

Blinatumomab is cost effective compared with continued chemotherapy

3.19 The committee recalled its preferred assumptions (see section 3.10). The committee concluded that its preferred analysis would include a 3-year cure timepoint. Based on the ERG's exploratory analysis, the scenarios with a 3-year cure point produce an ICER that falls between £21,874 and £25,551 per QALY gained, although the committee were aware that there was uncertainty in these estimates. The ERG also reproduced the analyses to include the confidential commercial arrangement for inotuzumab ozogamicin, and the ICERs were within the range that NICE usually considered an acceptable use of NHS resources (the exact ICERs are confidential and cannot be reported here). The committee could make recommendation based only on the evidence presented. Because the committee did not see evidence on people with acute lymphoblastic leukaemia in CR2, it was unable to make a recommendation for this indication. Based on the evidence presented to it, the committee concluded the most plausible ICERs were within the range that NICE usually considers an acceptable use of NHS resources.

Innovation

Blinatumomab is innovative but there are no benefits not captured by the QALY

3.20 The committee considered blinatumomab to be innovative because it represents a step change in the treatment of CD19-positive B-precursor acute lymphoblastic leukaemia with presence of MRD. No evidence was presented to suggest that there were additional benefits that were not

captured in the QALY calculations. The committee concluded that there were no benefits that would not be captured in the QALY calculations.

End of life

Blinatumomab does not meet the end-of-life criteria

3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. The company proposed that blinatumomab met the criteria for life-extending treatments for people with a short life expectancy (normally less than 24 months). The company's new evidence was not substantially different from the initial evidence submitted. The committee considered the median and mean survival and the proportion of patients alive at 2 years for the continued chemotherapy arm from the company and the ERG's model. The clinical experts suggested that for patients with MRD, the proportion of people alive at 2 years would be around 20%. The committee noted all the estimates of life expectancy from clinical evidence and the model. It agreed that the mean estimates from the company's model were much longer than the median estimates. The mean and median survival outcomes are confidential and cannot be reported here. The committee concluded that overall the short life expectancy criterion was not met. The committee also discussed whether a survival benefit of over 3 months can be expected for blinatumomab compared with continued chemotherapy. Based on all the evidence presented to it, the committee concluded that the extension-to-life criterion was met. The committee concluded that blinatumomab did not meet NICE's criteria for being considered a life-extending treatment at the end of life.

Conclusion

Blinatumomab is recommended for routine use for people with acute lymphoblastic leukaemia in first complete remission

3.22 The committee concluded that the most plausible ICERs for blinatumomab were within the range that NICE usually considers an acceptable use of NHS resources. Blinatumomab could not be considered an end-of-life treatment because the short life expectancy criterion was not met. It also noted that blinatumomab is clinically effective. However, the committee did not see any evidence to assess cost effectiveness in the second complete remission population. Therefore, the committee recommended blinatumomab as an option for treating Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia in adults with MRD of at least 0.1%, only if:

- the disease is in first complete remission and
- the company provides blinatumomab according to the commercial arrangement (see section 2).

4 Implementation

Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.1 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.2 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has acute lymphoblastic leukaemia in first complete remission with MRD of at least 0.1% activity and the doctor responsible for their care thinks that blinatumomab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Review of guidance

5.1 The guidance on this technology will be considered for review 3 years after publication. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Professor Stephen O'Brien
Chair, appraisal committee
May 2019

6 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Lyudmila Marinova
Technical lead

Alex Filby
Technical adviser

James Maskrey
Project manager

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