NICE National Institute for Health and Care Excellence

NICE guidance

Blinatumomab with chemotherapy for consolidation treatment of Philadelphia-chromosome-negative CD19-positive minimal residual disease-negative B-cell precursor acute lymphoblastic leukaemia

Technology appraisal guidance
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www.nice.org.uk/guidance/ta1049

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Blinatumomab with chemotherapy can be used as an option to treat Philadelphia-chromosome-negative CD19-positive B-cell precursor acute lymphoblastic leukaemia (ALL) in adults, if:

- the leukaemia is minimal residual disease-negative
- it is used at the start of consolidation treatment
- the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with blinatumomab with chemotherapy 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 healthcare professional consider it appropriate to stop.

What this means in practice

Blinatumomab with chemotherapy must be funded by the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Blinatumomab with chemotherapy must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that blinatumomab with chemotherapy provides benefits and value for money, so it can be used routinely across the NHS in this population.

NICE has produced tools and resources to support implementation of this guidance.

Why the committee made these recommendations

Usual consolidation treatment for Philadelphia-chromosome-negative CD19-positive B-cell precursor ALL that is minimal residual disease-negative is chemotherapy. For this

evaluation, the company asked for blinatumomab to be considered with chemotherapy and only for ALL that is minimal residual disease-negative at the start of consolidation treatment. This does not include everyone who it is licensed for.

Clinical trial evidence shows that blinatumomab with chemotherapy increases how long people live and how long they have before their ALL relapses compared with chemotherapy alone.

The cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, blinatumomab with chemotherapy can be used.

2 Information about blinatumomab

Marketing authorisation indication

2.1 Blinatumomab (Blincyto, Amgen) is indicated for 'the treatment of adult patients with Philadelphia chromosome negative CD19-positive B-cell precursor leukaemia ALL in the consolidation phase'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for blinatumomab.

Price

2.3 The list price of blinatumomab is £2,017 per 38.5-microgram vial (excluding VAT; BNF online, accessed February 2025).

2.4 The company has a commercial arrangement. This makes blinatumomab available to the NHS with a discount. The size of the discount is commercial in confidence.

3 Committee discussion

The evaluation committee considered evidence submitted by Amgen, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of the condition

3.1 B-cell precursor acute lymphoblastic leukaemia (ALL) is a rapidly progressing blood cancer which causes excess production of immature B-cell lymphocytes (known as lymphoblasts) in the bone marrow. B-cell precursor ALL is largely characterised by the expression of the surface antigen CD19 and the presence or absence of a chromosomal abnormality known as the Philadelphia (Ph) chromosome. People whose ALL is in haematological complete remission after initial treatment may still have residual cancer cells present at levels that are only detectable using sensitive molecular techniques. This is known as minimal residual disease (MRD). The committee understood that the presence of MRD (referred to as MRD-positive disease) is associated with poorer outcomes, but relapses also occur without MRD (referred to as MRD-negative disease). The committee noted the stakeholder submissions from 1 patient group, 1 patient expert and 2 clinical experts. The patient submissions described how ALL can impact the ability to carry out usual activities because of the physical symptoms of the condition (such as fatigue and pain) and toxicity related to current treatment. They explained how ALL has a substantial emotional impact on people with the condition and their families. The submissions also highlighted the financial burden of ALL because it often affects the ability to maintain employment for both the person with the condition and their caregivers. The committee discussed the population relevant to the decision problem for this evaluation: people with Ph-chromosome-negative CD19-positive B-cell precursor ALL that is MRD-negative in the frontline consolidation phase. It noted that there were no NICE-recommended treatments for this population and that most people would have chemotherapy (see section 3.2). The submissions described how the prognosis and quality of life for people with ALL is poor because the disease

often relapses after initial treatment. They highlighted that treatments which improve the efficacy of frontline chemotherapy and reduce the risk of relapse are needed. The committee noted that blinatumomab is currently used in a similar population with MRD-positive disease in line with NICE's technology appraisal guidance on blinatumomab for treating ALL in remission with minimal residual disease activity (TA589). It understood that the earlier use of blinatumomab for MRD-negative disease may prevent the disease worsening and becoming MRD-positive. The committee recognised the substantial impact that B-cell precursor ALL has on survival and quality of life. It further recognised that there is an unmet need for people with B-cell precursor ALL, and that the population eligible for treatment is estimated to be small.

Clinical management

Treatment pathway and comparators

3.2 The company submission outlined that people with MRD-negative disease would have blinatumomab plus chemotherapy as part of their consolidation treatment, but would not have both treatments at the same time. The treatment schedule would be expected to include up to 4 cycles of blinatumomab and 4 cycles of chemotherapy (standard care) in line with the key clinical trial (see section 3.3). People would likely have each treatment in the following sequence: 2 cycles of blinatumomab, 3 cycles of chemotherapy, 1 cycle of blinatumomab, 1 cycle of chemotherapy and 1 cycle of blinatumomab. The committee noted that the clinical expert submission suggested that blinatumomab is generally well tolerated compared with chemotherapy. The committee discussed the company's positioning of blinatumomab plus chemotherapy as a treatment option for adults with Ph-chromosome-negative CD19-positive B-cell precursor ALL that is MRD-negative in the frontline consolidation phase. It noted that this positioning was narrower than the license extension for blinatumomab which does not restrict usage by MRD status or to the start of the consolidation phase. The committee understood that the treatment pathway for adults with Ph-chromosome-negative B-cell precursor ALL typically follows the UKALL14 trial protocol for people aged 25 to 65 years. The protocol includes a steroid pre-phase followed by 4 main treatment phases: induction, intensification, consolidation and maintenance. The

final scope for the evaluation included established clinical management without blinatumomab plus chemotherapy as the comparator. This included chemotherapy (with or without corticosteroids) and a stem cell transplant. The company and EAG agreed that consolidation chemotherapy was the most suitable comparator. This was based on clinical opinion that a stem cell transplant would typically be reserved for high-risk disease (such as disease with adverse cytogenetics) in the population of relevance to this evaluation. The company and EAG's clinical experts also considered that a stem cell transplant would likely happen before consolidation treatment (after induction or intensification phases) and so blinatumomab would not displace a stem cell transplant if it was recommended. The committee understood that very few people with MRD-negative disease would have a stem cell transplant before their disease had relapsed because of the risk of treatment-related mortality. It agreed with the company's approach to model stem cell transplant as part of the treatment pathway in line with the key clinical trial (see section 3.3). The committee concluded that the company's positioning of blinatumomab plus chemotherapy is appropriate. It further concluded that chemotherapy is the most relevant comparator for blinatumomab plus chemotherapy.

Clinical effectiveness

E1910 trial

3.3 The clinical evidence came from E1910 which is an ongoing, phase 3, open-label, randomised controlled trial. E1910 included 77 centres in the USA, Canada and Israel. The population included adults aged between 30 and 70 years with newly diagnosed Ph-chromosome-negative B-cell precursor ALL. In E1910, people had 2 cycles of induction chemotherapy followed by 1 cycle of intense chemotherapy if their disease was in haematological complete remission. Remission and MRD status were then assessed, with MRD negativity defined as less than or equal to 0.01%. People with MRD-negative disease were then randomised to have blinatumomab plus chemotherapy (4 cycles of each treatment) or chemotherapy alone (4 cycles) as part of consolidation treatment. Consolidation chemotherapy included the following treatments:

- Cycles 1, 2 and 4: cytarabine, etoposide, methotrexate, pegaspargase (for

people aged 55 years or over in cycle 1 only) and rituximab (for people whose ALL was CD20-positive).

- Cycle 3: cyclophosphamide, cytarabine, daunorubicin, dexamethasone, 6-mercaptopurine, methotrexate, rituximab (for people whose ALL was CD20-positive) and vincristine.

Maintenance chemotherapy was offered for 2.5 years from the start of the intensification cycle for people who completed consolidation treatment. There were 112 people in the intervention group and 112 people in the comparator group. Participants in the trial could proceed to a stem cell transplant either after 2 cycles of blinatumomab in the intervention group or at any time during consolidation treatment in the comparator group. The trial includes a follow up of 10 years from the start of the induction treatment. The company reported overall survival and relapse-free survival data from the primary analysis data cut (June 2023) with a median follow up of 4.5 years for both arms. In the intention-to-treat population, blinatumomab plus chemotherapy increased overall survival compared with chemotherapy alone (hazard ratio 0.44; 95% confidence interval 0.25 to 0.76, p=0.001). Blinatumomab plus chemotherapy also increased relapse-free survival compared with chemotherapy alone (hazard ratio 0.53; 95% confidence interval 0.32 to 0.88, p=0.006). The committee noted that median overall survival and relapse-free survival were not reached in either treatment arm. It concluded that blinatumomab plus chemotherapy significantly improved overall survival and relapse-free survival compared with chemotherapy alone.

Generalisability of E1910 to younger and older adults

3.4 The committee understood that the chemotherapy regimen in E1910 was very similar to that in the UKALL14 protocol, typically followed for adults aged between 25 and 65 years in clinical practice (see section 3.2). It recalled that the inclusion criteria in E1910 included adults aged between 30 and 70 years at enrolment. The committee noted that the license extension for blinatumomab includes all adults and does not restrict usage by age. The company explained that the lower age cut-off in the trial was selected because of practical considerations around the trial design rather than any underlying biological

rationale. The EAG clinical experts considered that they would expect blinatumomab to be effective in adults aged under 30 years. They suggested that if blinatumomab was to be recommended for people 30 years and over this would lead to inequality of access for adults under 30 years. The committee discussed whether the chemotherapy regimen for adults aged between 18 and 25 years would be similar to that in the UKALL14 protocol. The clinical experts explained that current treatment for this age group is very similar to the UKALL14 protocol and, in some cases, identical. They considered that there was no clinical or biological reason why the trial results for blinatumomab would not be generalisable to adults under 30 years. The clinical experts highlighted that subgroup analyses from the trial suggested that blinatumomab was most effective in younger adults. The committee noted that the results for this subgroup analysis were uncertain because of the small numbers of people in the subgroup. It discussed that because disease prognosis is linked to age, it would expect outcomes for people under 30 to be better in both the intervention and comparator groups. The clinical expert explained that the upper age limit of the trial was 70 years, but that in clinical practice people aged 55 years and over may have treatment in line with an age-adapted protocol (based on the UKALL60+ trial). They explained that the UKALL60+ trial included multiple treatment arms and some of these were likely similar to those in the UKALL14 trial but that there may be some differences. The committee understood that the number of people with B-cell precursor ALL who would follow this age-adapted protocol would likely be small. The clinical lead for the Cancer Drugs Fund (CDF) confirmed that all adults having intensive chemotherapy would be potentially eligible for blinatumomab as part of consolidation treatment. The committee concluded that the chemotherapy regimen in E1910 was reflective of clinical practice for most adults in the target population, including those aged between 18 to 25 years. It considered that the effect of blinatumomab plus chemotherapy in adults aged under 30 years would likely be similar to the observed data from the trial.

Differences in MRD thresholds

3.5 MRD tests investigate the presence of detectable cancer cells in the bone marrow or blood typically at a level above (MRD-positive) or below (MRD-negative) a certain threshold when disease is in remission. The committee recalled that the threshold in E1910 for MRD-negative disease was less than or

equal to 0.01%, but that the license extension for blinatumomab did not specify MRD status. It noted that the recommendations in TA589 include a threshold of at least 0.1% for MRD-positive disease based on the key clinical trial (BLAST) and the marketing authorisation for blinatumomab in that indication. The EAG clinical experts considered that if blinatumomab was recommended in this evaluation based on the MRD threshold in E1910, this would leave some people with MRD-positive disease ineligible for treatment. This is because although they have ALL with detectable MRD, it would not have reached the threshold specified for treatment in TA589. The committee understood that this would mean people with an MRD level between 0.01% and 0.1% would have to wait for their ALL to progress until they would be eligible for blinatumomab. The clinical lead for the CDF explained that this issue could be addressed by NHS England in the commissioning criteria for blinatumomab to prevent any of the population being left ineligible for treatment based on their MRD level. The committee discussed the threshold used in E1910 to define MRD-negative disease. The clinical experts confirmed that there is evidence to suggest that an MRD above 0.01% is associated with a high rate of relapse. They explained that, in some cases, MRD status cannot be evaluated because of a lack of an identifiable MRD marker or technical issues relating to the sensitivity of MRD tests. The clinical lead for the CDF highlighted that they were unaware of such issues affecting the prescribing of blinatumomab for people with MRD-positive disease as per TA589. The committee concluded that the threshold in E1910 for defining MRD-negative disease (less than or equal to 0.01%) was appropriate. It recognised that NHS England could address any gaps in eligibility for treatment that arise as a result of the recommendations for blinatumomab in TA589 and in this appraisal.

Economic model

Company's modelling approach

3.6 The company presented a partitioned survival model with 3 mutually exclusive health states: relapse-free, post-relapse and death. The modelled intervention and comparator reflected E1910. The model perspective on costs was that of the NHS and Personal Social Services and the cycle length was 1 week with no half-cycle correction. The time horizon was 50 years, and costs and outcomes were

discounted at a rate of 3.5% per year. The model assumes that people whose disease remains relapse-free after 5 years are cured. This cure time point acts as a cap on costs and quality-adjusted life years (QALYs) as follows:

- the utilities for people in the relapse-free health state rebound to age-and sex-matched general population norms
- no ALL-related costs are incurred after this time point (including subsequent drug treatment, stem cell transplant and end of life care costs)
- QALY losses with having a stem cell transplant after relapse and end of life care are not applied.

The committee understood that the company's model did not include a causal link between having a stem cell transplant (before or after relapse) and its impact on overall survival and relapse-free survival. It noted that the EAG would have preferred for the company to have presented a model which reflected the differential impact of a stem cell transplant on subsequent event risks. This is because it may lead to curative outcomes for some people. However, the committee understood that this structural limitation was likely to have been mitigated by the similarly low number of people across both treatment arms in E1910 who had a stem cell transplant (the company considers the actual figures to be confidential and so they cannot be reported here). The EAG also noted that the number of people available to inform transitions between the health states with and without a stem cell transplant would be small and any resulting model predictions would likely be highly uncertain. Therefore, the committee concluded that the company's model was acceptable for decision making.

Modelling overall survival and relapse-free survival

3.7 The company fitted mixture-cure models to the observed overall survival and relapse-free survival data from E1910. This was to extrapolate survival outcomes beyond the trial data and because the company's clinical experts considered that ALL that remains in remission for around 3 to 5 years would likely be cured. In addition to using mixture-cure models, the company's model included a 5-year cure time point for people whose disease remained relapse-free (see

section 3.6). The mixture-cure model included a cured group and an uncured group. The cured group assumed age- and sex-matched general population mortality, while the uncured group followed a standard parametric survival trajectory. A standardised mortality ratio was applied to the general population mortality for both groups (see section 3.8). The company selected the Weibull mixture-cure model to model overall survival for people on blinatumomab plus chemotherapy and on chemotherapy alone. It also selected the log-normal mixture-cure model to model relapse-free survival for people on blinatumomab plus chemotherapy and on chemotherapy alone. The EAG considered that the long-term overall survival and relapse-free survival projections were uncertain because of the limited sample size and relatively short follow up in E1910. The EAG's clinical experts considered that the log-normal and exponential mixture-cure models underestimated overall survival in the chemotherapy arm and were not clinically plausible. The committee noted that the EAG scenarios exploring the remaining alternative mixture-cure models for overall survival and relapse-free survival had a minimal impact on the incremental cost-effectiveness ratio (ICER). It further noted that the EAG considered the company's survival analysis methods to be appropriate and retained the same models in the EAG base case. The committee concluded that there was uncertainty around the modelled survival extrapolations, but that the choice of model was unlikely to have a large impact on the cost-effectiveness results. It considered that the company's approach was appropriate for decision making.

Standardised mortality ratio

3.8 In the company's base case, a standardised mortality ratio (SMR) of 1.09 was applied to the age- and sex-matched general population mortality for the cured and uncured populations of the mixture-cure models. This was to account for any residual complications from ALL or after having a stem cell transplant. The committee understood that an SMR of 1.09 had been selected by the company because it was used in previous NICE appraisals for diffuse large B-cell lymphoma. It noted that the company's clinical experts considered that SMRs of 3.0 and 4.0 used in previous NICE appraisals for B-cell precursor ALL were too high for the target population in this appraisal. This was because these previous appraisals focused on populations who either went on to have a stem cell transplant or had relapsed or refractory disease and so were not comparable to

the target population in E1910. The EAG considered that there was uncertainty around the magnitude of the SMR applied. But its clinical experts supported the use of a low SMR in the MRD-negative population because they are unlikely to have a stem cell transplant before relapse. The committee noted that the EAG had explored further scenarios applying higher SMRs of 2.0 and 3.0 which had a small-to-moderate impact on the ICER. The EAG considered that these SMRs are likely to be overestimates for the target population and so retained the same SMR of 1.09 in its base case. The clinical expert considered that an SMR lower than 3 would be clinically appropriate for the appraisal population. The committee acknowledged that a lower SMR was appropriate for the population under consideration. It considered that it would have been helpful for the company to have presented either a structured elicitation or clinical expert opinion to justify why a value of 1.09 had been selected for the SMR. It concluded that in the absence of an alternatively suitable value, an SMR of 1.09 was the most appropriate for decision making.

Utility values

3.9 The E1910 trial did not collect any health-related quality of life data. The company's approach to selecting utility values for each of the health states in the model aligned with TA589. To inform the relapse-free utility value, it used EQ-5D data from people whose ALL changed from MRD-positive to MRD-negative in the BLAST trial. This trial included people with Ph-chromosome-negative B-cell precursor ALL which was MRD-positive and in complete remission. A utility decrement was applied in the relapse-free health state for people on blinatumomab to account for the disutility associated with how it is given (by continuous intravenous infusion). To inform the post-relapse utility, it used EQ-5D data from people having standard care salvage chemotherapy in the TOWER trial (with matching between participants in TOWER and BLAST). This trial included people with relapsed or refractory Ph-chromosome-negative B-cell precursor ALL. An end of life care disutility was applied to people who died within 5 years of model entry, informed by the BLAST trial. The EAG considered that the utility value of 0.692 applied in the post-relapse health state was implausibly high. It highlighted that the same issue had been raised by the EAG in TA589. The committee agreed that the post-relapse utility was higher than it would expect for people with relapsed disease. It noted that the company and EAG had

presented exploratory scenarios using lower post-relapse utilities of 0.50 and 0.25 which resulted in small reductions in the ICER. Because of this, the EAG retained the same utility values in its base-case analysis. The committee recognised that there was uncertainty around the post-relapse utility value but that it was not a driver of the cost-effectiveness results. It concluded that the utility values were reasonable for decision making.

Severity

3.10 NICE's methods on conditions with a high degree of severity did not apply.

Cost effectiveness

Acceptable ICER

3.11 NICE's manual on health technology evaluations notes that, above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee discussed the uncertainty around the modelled long-term survival extrapolations, choice of SMR and post-relapse utility value. It recalled that the EAG had explored these uncertainties in various scenario analyses that mostly had a relatively small effect on the ICER. The committee noted the significant survival benefit and substantial QALY gain with blinatumomab plus chemotherapy compared with chemotherapy alone. It understood that blinatumomab would likely reduce disease progression in people with MRD-negative disease and that there was an unmet need for treatments which improve the efficacy of frontline consolidation chemotherapy. So, it concluded that an acceptable ICER would be around £30,000 per QALY gained.

Cost-effectiveness estimates

3.12 The exact ICERs are confidential and cannot be reported here because they include the confidential discount for blinatumomab and other treatments in the pathway. The company's base-case ICERs were around £30,000 per QALY gained. The committee's preferred modelling assumptions included:

- using the Weibull mixture-cure model to model overall survival for both treatment arms (see section 3.7)
- using the log-normal mixture-cure model to model relapse-free survival for both treatment arms (see section 3.7)
- applying an SMR of 1.09 to the general population mortality for both cured and uncured groups of the mixture-cure models (see section 3.8)
- applying a utility value of 0.692 in the post-relapse health state (see section 3.9).

The committee understood that its preferred assumptions were in line with both the company's and EAG's base cases. It noted that the EAG had made minor adjustments to the model which included:

- correction of remaining model errors and other minor issues
- adjustment of relapse-free survival events to account for the proportion of events which were deaths
- including healthcare resource use (HCRU) costs after consolidation treatment in the relapse-free and post-relapse health states and removing the 5-year cap on HCRU costs in the post-relapse health state
- removing the 5-year cap for costs associated with subsequent treatments (second-line drug treatments and a stem cell transplant) and QALY losses with a stem cell transplant after relapse.

The committee considered that the EAG amendments to the model were appropriate and noted that these had a minimal impact on the company's base-case ICER. Using its preferred assumptions and including the EAG amendments to the model, the committee's preferred ICERs for

blinatumomab plus chemotherapy compared with chemotherapy were around £30,000 per QALY gained. It concluded that blinatumomab plus chemotherapy could be considered a cost-effective use of NHS resources.

Other factors

Equality

3.13 A stakeholder commented that the E1910 trial applies an upper age limit but that the standard approach is to individualise treatment decisions on biological, personal and clinical parameters. They considered that the evaluation should reflect clinical practice and not necessarily restrict to a clinical trial-defined criteria when determining treatment benefit. The committee recalled that the lower age limit in E1910 had also been raised as an equality consideration because the EAG considered that it may lead to inequality of access to blinatumomab for younger adults (see section 3.4). It agreed that, because its recommendation does not restrict access to treatment based on a person's age, these potential equality issues had been addressed. The committee noted that the clinical expert submission reiterated concerns about the difference in MRD thresholds between TA589 and this appraisal which may result in an MRD-positive population being left ineligible for blinatumomab (see section 3.5). The clinical expert submission highlighted that this population has a high probable risk of relapse and would be left ineligible for treatment with no biological or clinical basis for their exclusion. The committee recalled that NHS England stated it could address this issue as a result of the committee's recommendation of blinatumomab in this appraisal. It noted that the clinical expert submission and comments from a stakeholder provided further context to its previous considerations around MRD testing (see section 3.5). This included that older adults and certain biological subgroups may not have equal access to standard MRD monitoring because of a lack of an identifiable MRD marker. The clinical expert submission explained these people should be eligible for alternative MRD assessment approaches to ensure equitable access to MRD-indicated treatment. A stakeholder commented that a small proportion of people may not be evaluable for MRD testing for reasons such as sample failure or lack of an applicable assay. They considered that this subgroup should not be discriminated against based on

technical factors related to MRD testing. The committee considered that issues around the accessibility and technical nature of MRD testing could not be addressed in a technology appraisal. It concluded that there were no outstanding equality issues relevant to the recommendations.

Uncaptured benefits

3.14 The committee considered whether there were any uncaptured benefits of blinatumomab. It did not identify additional benefits of blinatumomab not captured in the economic modelling. So, the committee concluded that all additional benefits of blinatumomab had already been taken into account.

Conclusion

Recommendation

3.15 The clinical-effectiveness evidence showed that blinatumomab plus chemotherapy improved key outcomes in people with Ph-chromosome-negative CD19-positive B-cell precursor ALL that is MRD-negative in the frontline consolidation phase. The committee concluded that the ICERs that included its preferred assumptions and model amendments were within the range that NICE considers an acceptable use of NHS resources (see section 3.12). So, blinatumomab plus chemotherapy is recommended for routine commissioning.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.4 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 Philadelphia-chromosome-negative CD19-positive minimal residual disease-negative B-cell precursor acute lymphoblastic leukaemia and the healthcare professional responsible for their care thinks that blinatumomab with chemotherapy is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

This topic was evaluated as a single technology evaluation by the highly specialised technologies evaluation committee. The highly specialised technologies evaluation committee and the 4 technology appraisal committees are standing advisory committees of NICE.

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

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

Chair

Paul Arundel
Chair, highly specialised technologies evaluation committee

NICE project team

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

Anita Sangha
Technical lead

Alan Moore
Technical adviser

Louise Jafferally
Project manager

Ross Dent
Associate director

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