NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Histamine dihydrochloride with interleukin-2 for maintenance treatment of acute myeloid leukaemia

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using histamine dihydrochloride with interleukin-2 in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: April 2026

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using histamine dihydrochloride with interleukin-2 in the NHS in England.

For further details, see NICE's technology appraisal and highly specialised technologies guidance manual.

The key dates for this evaluation are:

- Closing date for comments: 22 May 2026
- Second evaluation committee meeting: TBC
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Histamine dihydrochloride with interleukin-2 should not be used as maintenance treatment for acute myeloid leukaemia (AML) in first remission in adults.

1.2 This recommendation is not intended to affect treatment with histamine dihydrochloride with interleukin-2 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

These are NICE's draft recommendations. If these recommendations become final, histamine dihydrochloride with interleukin-2 would not be required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because the available evidence does not suggest that histamine dihydrochloride with interleukin-2 offers benefit in this population.

Why the committee made these recommendations

People with AML that is in first remission may have a stem cell transplant. If they cannot or do not want to have a stem cell transplant, they can have oral azacitidine. Some people might have monitoring without treatment.

Clinical trial evidence suggests that histamine dihydrochloride with interleukin-2 increases how long people have before their AML comes back compared with monitoring without treatment. But it is unclear whether people who have histamine dihydrochloride with interleukin-2 live longer. The relevance of the clinical trial

evidence is uncertain because the trial was done more than 20 years ago and does not reflect current clinical practice or the population seen in the NHS.

Histamine dihydrochloride with interleukin-2 has not been directly compared in a clinical trial with oral azacitidine and indirect comparisons are highly uncertain.

Because of the uncertainties with the clinical evidence there are also uncertainties with the economic model. So it is not possible to determine the most likely cost-effectiveness estimates for histamine dihydrochloride with interleukin-2.

So, histamine dihydrochloride with interleukin-2 should not be used.

2 Information about histamine dihydrochloride with interleukin-2

Marketing authorisation indication

2.1 Histamine dihydrochloride (Brancaster Pharma) is indicated for ’adult patients with acute myeloid leukaemia in first remission concomitantly treated with interleukin-2 (IL-2). The efficacy of Histamine dihydrochloride 0.5 mg/0.5 mL solution for injection has not been fully demonstrated in patients older than age 60’.

Dosage in the marketing authorisation

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

Price

2.3 Histamine dihydrochloride costs £1,200 for 14 vials (equivalent to 1 week of treatment; company submission).

2.4 Interleukin-2 (aldesleukin) costs £636 per 18 million unit vial (BNF online accessed March 2026).

2.5 Costs may vary in different settings because of negotiated procurement discounts.

Sustainability

2.6 Information on the Carbon Reduction Plan for UK carbon emissions for Brancaster Pharma will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by Brancaster Pharma, 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 Acute myeloid leukaemia (AML) is a rapidly progressing cancer of the blood and bone marrow that is usually diagnosed in older people. The patient experts explained that AML has a substantial impact on all aspects of life, including being able to work and care for yourself or for others. They described the problems associated with currently available treatments, such as graft-versus-host disease from having a stem cell transplant. They noted that there are a number of currently available treatments but that they may not be suitable for some people, depending on their condition, genetics and general fitness. The clinical experts stated that even for people with AML who can have intensive chemotherapy, long-term survival is still around 50%. The committee concluded that AML significantly impacts quality and length of life.

Clinical management

Comparators

3.2 People with newly diagnosed AML who can have intensive chemotherapy are normally offered induction chemotherapy. If their AML reaches complete remission, they are offered consolidation chemotherapy. People with AML who have an FLT3 gene mutation may have midostaurin or quizartinib alongside induction and consolidation chemotherapy (see

NICE's technology appraisal guidance on midostaurin for untreated AML and NICE's technology appraisal guidance on quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive AML). After chemotherapy, some people may be able to have a stem cell transplant. People who cannot have or do not want a stem cell transplant may be offered oral azacitidine (see NICE's technology appraisal guidance on Oral azacitidine for maintenance treatment of AML after induction therapy). Midostaurin (although not after stem cell transplant) and quizartinib may be continued as maintenance treatment. Histamine dihydrochloride with interleukin-2 is indicated as a maintenance treatment in adults with AML in first remission. The company positioned histamine dihydrochloride with interleukin-2 for people under 60, whose AML is in first complete remission, with normal karyotype, and for whom a stem cell transplant is not suitable. This is a subgroup of the full population in the marketing authorisation. The company stated that midostaurin and quizartinib were not relevant comparators for histamine dihydrochloride with interleukin-2. This is because people who had had midostaurin or quizartinib in the induction and consolidation phases of treatment would continue them in the maintenance phase. They would not switch to a non-targeted treatment, such as histamine dihydrochloride with interleukin-2. The committee agreed that midostaurin and quizartinib were not relevant comparators. The company also stated that oral azacitidine was not a relevant comparator because it is normally offered to people over 55 years, in line with the clinical trial evidence for its use. The marketing authorisation for histamine dihydrochloride states that the efficacy has not been fully demonstrated in people over 60 years of age. The clinical experts suggested that histamine dihydrochloride with interleukin-2 may be more suitable for people under 60 years whose AML is in remission and at lower risk of relapse. For these people, the toxicities associated with stem cell transplant would likely outweigh the benefits. They explained that some of this population would currently be monitored with no active treatment. The clinical experts stated that uptake of oral

azacitidine in clinical practice is low. They thought that it would be a comparator for a subgroup of the population who would be eligible for histamine dihydrochloride with interleukin-2, but that it was difficult to define this group. They said that oral azacitidine may be used for people whose AML is at high risk of relapse but who cannot or do not want to have a stem cell transplant. The clinical experts noted that histamine dihydrochloride with interleukin-2 could be beneficial for some people because it has a fixed treatment duration, whereas oral azacitidine is an open-ended treatment. The NHS England Cancer Drugs Fund lead presented evidence showing that since 2022, 260 people had had oral azacitidine, and 38.8% of these were aged 60 years or under. The committee agreed that the data suggested that relatively few people with AML had had azacitidine since 2022, and that it was unclear for how long people have it. The committee agreed that it was difficult to clearly define subgroups of the population who would have oral azacitidine and who would have monitoring with no active treatment. It concluded that oral azacitidine and standard care (monitoring with no active treatment) were both relevant comparators.

Clinical effectiveness

Generalisability

3.3 The main clinical evidence for histamine dihydrochloride with interleukin-2 came from a randomised controlled trial by Brune et al. (2006). It compared histamine dihydrochloride plus interleukin-2 with standard care. The trial population was adults with AML that was in complete remission after induction and consolidation and for whom an allogeneic stem cell transplant was not suitable. Participants had an Eastern Cooperative Oncology Group score of 0 or 1. The study reported that in the intention-to-treat analysis, leukaemia-free survival was longer with histamine dihydrochloride with interleukin-2 at 324 days than with standard care at 264 days (hazard ratio [HR] 0.71, 95% confidence intervals [CI] 0.54 to 0.92, $p<0.01$). Overall survival was also reported to be longer with

histamine dihydrochloride with interleukin-2, although this was not statistically significant (HR 0.82, 95% CI 0.61 to 1.11, p=0.21). The EAG noted that recruitment to the study took place between 1998 and 2000 and there have been many changes to clinical practice since then. Molecular risk stratification is now used, new targeted therapies are now available, and there have been improvements in supportive care. The EAG highlighted that FLT3 status was not known at the time of the study. So it is unclear how many people with FLT3-positive AML are represented in the results, and the effect that that has on them. There was also no information about subsequent treatment in the study. Clinical experts highlighted that the subgroup of people with AML for whom an allogeneic stem cell transplant was not suitable between 1998 and 2000 would likely be different to people for whom a stem cell transplant is not suitable today. A stem cell transplant would be considered for more people today because there is a better understanding of cytogenetics, risk of relapse and the mortality risk of graft-versus-host disease. The committee agreed that there were considerable limitations in the generalisability of the trial data to the current population in the NHS who would be eligible for histamine dihydrochloride with interleukin-2.

Population and subgroup analysis

3.4 The company's target population for this evaluation was people under 60 years with AML in first complete remission, with normal karyotype, when an allogeneic stem cell transplant is not suitable. It based the supporting evidence for this population on Nilsson et al. (2020), which is a post-hoc subgroup analysis of Brune et al. (2006). There were 72 people included in the subgroup analysis. The results suggested that leukaemia-free survival was significantly increased for people in this subgroup who had histamine dihydrochloride with interleukin-2, compared with people who had no active treatment (HR 0.40, 95% CI 0.20 to 0.79, p=0.006). The results also suggested that histamine dihydrochloride with interleukin-2 improved overall survival compared with no active treatment (HR 0.43, 95% CI 0.18 to 1.01, p=0.04). The clinical expert stated that the

subgroup in Nilsson et al. was the most relevant subgroup to current clinical practice from the population in Brune et al. The EAG cautioned that this subgroup was not pre-specified, and there was a high risk of bias from selective reporting and data-driven identification of subgroup effects. So, they considered the results should be considered exploratory only. The committee also noted that it was unclear how karyotype had been determined in Nilsson et al. and whether it was the same way that it would be determined in current clinical practice. The committee noted that in the results for overall survival, the p-value suggested statistical significance but the confidence intervals crossed 1. The committee understood that this meant that overall survival may be better with histamine dihydrochloride with interleukin-2, but it was also possible that there was no difference between the groups. It noted that in the first 6 months of the Kaplan–Meier curves, there was no difference in leukaemia-free survival between the treatment arms, but there was a considerable difference in overall survival. The committee thought it was unusual that participants in the histamine dihydrochloride with interleukin-2 group would have a relapse of their AML without any of those participants dying. It would like the company to confirm it has investigated that this analysis is correct. There were small patient numbers and a high degree of censoring. This made interpreting the results uncertain, particularly the apparent plateaus in the Kaplan–Meier curves for leukaemia-free and overall survival. The committee noted that the summary of product characteristics (SmPC) for histamine dihydrochloride did not include data on overall survival for the subgroup. But, in its response to clarification, the company had stated that it had proposed to the Medicines and Healthcare products Regulatory Agency (MHRA) that the post-hoc subgroup results for leukaemia-free survival and overall survival, including Kaplan–Meier graphs, be included in the SmPC. The committee would like to understand why the MHRA did not accept the addition of information relating to overall survival to the SmPC, nor the Kaplan–Meier graphs. Taking all of this into account, the committee agreed that the results for overall survival in the subgroup were

not reliable. It concluded that the results from the post-hoc subgroup analysis were not sufficiently robust for decision making.

Indirect treatment comparison

3.5 The company did not consider oral azacitidine to be a relevant comparator (see section 3.2). But at the clarification questions stage of the evaluation, it did present an indirect treatment comparison (ITC) of histamine dihydrochloride with interleukin-2 and oral azacitidine. This used data from the QUAZAR AML-001 trial of oral azacitidine. The company compared the intention-to-treat population of QUAZAR AML-001 with the intention-to-treat population of Brune et al. (2006), and with the Nilsson et al. (2020) subgroup. It did not have data for the equivalent subgroup from QUAZAR AML-001. It used the results comparing the 2 intention-to-treat populations in the economic model. The hazard ratios for overall survival and leukaemia-free survival favoured oral azacitidine. The company considers the results to be confidential so they cannot be reported here. The EAG was concerned that the estimated treatment effect between the 2 treatments was highly uncertain because of limited population overlap between the 2 trials. It was also concerned that the Bucher et al. ITC was done without adjusting for population differences. It highlighted that the population in Brune et al. was younger and healthier than that in QUAZAR AML-001. In Brune et al. the mean age was 55 years in the histamine dihydrochloride with interleukin-2 group and 54 years in the control group, whereas in QUAZAR AML-001 the mean age was 68 years. It added that age could be a treatment effect modifier for histamine dihydrochloride with interleukin-2 and for oral azacitidine. It noted that, without population adjustments, the Bucher et al. ITC would be expected to result in a more favourable estimated treatment effect for histamine dihydrochloride with interleukin-2 versus oral azacitidine. This would be driven by the difference in age compared with a population-adjusted ITC. It also noted that the Brune et al. trial was done much earlier than QUAZAR AML-001, and the treatment landscape had changed significantly. This led to concerns with using the standard care arms as a common comparator.

The committee agreed that there were considerable issues with the generalisability of the Brune et al. study (see section 3.3) and the methods used to do the ITC. So, it concluded that the results from the ITC were highly uncertain.

Economic model

Company's modelling approach and survival extrapolations

3.6 The company presented a partitioned survival model with 3 health states: pre-progression (leukaemia-free), post-progression and death. For the histamine dihydrochloride with interleukin-2 and oral azacitidine groups there were nested on- and off-treatment sub-states within the leukaemia-free health state. The company's model used a non-standard, blended approach. It based the overall cumulative probabilities for leukaemia-free survival and overall survival on weighted mean estimates for people who stopped treatment because of adverse events and people who did not. The EAG noted that the individual patient data used to produce the parametric models for leukaemia-free survival and overall survival already included 8.3% of people who had stopped treatment because of adverse events unrelated to relapse. So, it thought that discontinuation had been accounted for twice. The EAG preferred a standard, non-blended approach in which:

- leukaemia-free and overall survival were based directly on the standard parametric survival estimates, and
- treatment discontinuation only applied to partitioning between the on-treatment and off-treatment groups within the leukaemia-free state.

To extrapolate survival beyond the trial data, the company fitted parametric survival models to the survival data from Nilsson et al. (2020) for histamine dihydrochloride with interleukin-2 and standard care. The company jointly fitted models and selected the exponential models for both leukaemia-free survival and overall survival. Extrapolations for oral azacitidine were obtained by applying the hazard ratio from the ITC to the

selected parametric model for the histamine dihydrochloride with interleukin-2 group. The EAG thought that the proportional hazards assumption may not hold and that there was no clinical evidence to suggest that the treatment effect remains constant over time. So, it preferred to fit independent models. It also noted that the company's preferred models did not converge to zero within a plausible time frame. So, it selected alternative survival models. For leukaemia-free survival in its preferred analysis, the EAG selected the exponential model for the histamine dihydrochloride with interleukin-2 group and the log-normal model for the standard care group. For overall survival, it selected the Weibull model for both groups. This was based primarily on visual fit and long-term clinical plausibility, informed by discussions with clinical experts and a literature search. The EAG also highlighted a number of concerns with the survival extrapolations, because they were based on a small sample size with high censoring and limited follow up. So, assessing visual fit of the extrapolations to the observed data may be unreliable, particularly at the tails of the curves that were based on very small numbers. For oral azacitidine, the EAG noted that the company had derived the hazard ratios it used in the model from a mixture of stratified and unstratified hazard ratios. The EAG preferred to use a consistent approach, so it used the stratified overall-survival hazard ratio from QUAZAR AML-001 in its preferred analysis.

The committee considered that the subgroup data from Nilsson et al. was not reliable enough to be used in cost-effectiveness analysis (see section 3.5). It noted that the company's modelling approach suggested a substantial benefit in overall survival with histamine dihydrochloride with interleukin-2. This was because:

- the treatment effect for overall survival suggested by Nilsson et al. was large
- the median starting age in the model was 44 years, and

- the treatment effect was applied for the whole time horizon in the model.

This led to implausible survival assumptions in older people. The committee did not consider that such a large benefit in overall survival was plausible, based on the evidence it had seen. It concluded that there were substantial concerns with the survival modelling, particularly because it did not consider the subgroup results from Nilsson et al. to be reliable. The committee agreed that it would like to see the results for the full population in the marketing authorisation. The intention-to-treat population from Brune et al. (2006) may be more appropriate for modelling this.

Utility values

Source of utility values

3.7 The health-related quality-of-life data that was collected in Brune et al. (2006) was not available to the company. So, instead it used external data to inform health state utility values in the model. In its base case, the company used data from Tremblay et al. (2018), which was an economic evaluation study where the utility estimates were based on different literature sources. Some were based on EQ-5D-5L and some were from people in the US. The company also presented scenario analyses from the following alternative sources:

- Joshi et al. (2019), which used a composite time trade off method
- Stein et al. (2018), which used a discrete choice experiment method, and
- Russell-Smith et al. (2021), which was used in NICE's technology appraisal guidance on azacitidine for treating AML with more than 30% bone marrow blasts and used trial-based, disease-specific data from the EORTC QLQ-C30 questionnaire mapped to EQ-5D.

The EAG felt that it was unclear which source of utility values was most appropriate. The company assumed people having oral azacitidine would incur the same utility values as people having histamine dihydrochloride with interleukin-2. The committee noted that EQ-5D data had been collected in the QUAZAR AML-001 trial of oral azacitidine, and that this could be relevant to the population in the model for this evaluation. It thought that it was unfortunate that the health state utility values measured in the QUAZAR AML-001 trial for on and off treatment had been redacted in NICE's technology appraisal guidance on oral azacitidine. The committee concluded that it was uncertain which utility values should be used in the model, but this was not a key issue given the problems identified with the clinical data and survival modelling.

Disutility for self-administration of injections

3.8 The clinical experts highlighted that histamine dihydrochloride is self-administered with a standard syringe using a timer to control the injection over 5 to 15 minutes. They stated that over the course of 18 months of treatment with histamine dihydrochloride and interleukin-2, a person would need to self-administer around 840 injections. In its preferred analysis, the EAG included a 0.124 utility decrement to account for the number and administration requirements associated with the injections. This was based on a study of people with type 2 diabetes, because it had not identified any evidence in people with AML. The committee agreed that self-administration of a large number of injections of histamine dihydrochloride and interleukin-2 could be difficult for people and so it was appropriate to include a disutility. It noted that a utility decrement of 0.124 seemed high but also that injectable medicines for diabetes are often available in a prefilled pen. They may therefore be easier to administer than injections of histamine dihydrochloride and interleukin-2, which are supplied in glass vials and need to be prepared at home before administration. The committee also noted that the potential adverse events associated with injecting the medicine include fainting because of a drop in blood pressure. In addition the requirement to inject twice a day,

means it would be difficult for people to leave home for extended periods. The committee concluded that it was appropriate to include a disutility for administration of histamine dihydrochloride with interleukin-2 in the model, but it would welcome more evidence on the most appropriate disutility.

Costs

Drug and administration costs

3.9 The EAG made some changes to the costs included in the model. These were:

- including relative dose intensity, premedication and administration costs for oral azacitidine
- including wastage for interleukin-2
- including an additional dispensing cost per 3-week treatment cycle for histamine dihydrochloride with interleukin-2, based on the dispensing instructions in the SmPC
- revising the proportion of people having each standard care treatment based on clinical opinion.

The committee noted that everyone in the histamine dihydrochloride with interleukin-2 arm of the model was assumed to self-administer most of the injections, and no accessories were costed. The committee discussed the difficulties associated with using glass vials and syringes, and having to use a timer to inject histamine dihydrochloride subcutaneously over 5 to 15 minutes. It considered it implausible that everyone could administer all injections over an 18-month period at home, with no wastage. The NHS England Cancer Drugs Fund lead noted that there could be a high burden on the NHS if some people could not self-administer. This is because of the number of injections needed during an 18-month treatment period, particularly compared with oral azacitidine, which is a tablet taken at home. The committee agreed that costs should be included in the model for wastage and disposal (using sharps bins) related to histamine dihydrochloride and interleukin-2 self-administration. It also agreed that

costs should also be included to account for some people having the treatment administered in a hospital setting. The committee also noted that people would need a medical fridge to store interleukin-2 at home, and these costs were not included in the model. It also had concerns that the costs of training people to self-administer the injections were only included as part of the cost for administration of the first dose of histamine dihydrochloride with interleukin-2. But, it was plausible that multiple nurse-led training sessions could be needed. The committee noted the environmental impact of the waste from such a high number of injections. Overall, the committee concluded that the costs of administering histamine dihydrochloride with interleukin-2 were not adequately captured in the model.

Severity

3.10 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to quality adjusted life years (QALYs), called a severity modifier, if technologies are indicated for conditions with a high degree of severity. The EAG provided absolute and proportional QALY shortfall estimates in line with NICE's technology appraisal and highly specialised technologies guidance manual. For the standard care arm in the company's base case and EAG's preferred analysis, the absolute QALY shortfall was above 12. In both the company base case and EAG's preferred analysis, the absolute QALY shortfall for the oral azacitidine comparison was below 12, and the proportional QALY shortfall was below 0.85. So, the committee concluded that the severity weight of 1.2 applied to the QALYs was appropriate for the comparison with standard care only. The committee acknowledged that the absolute and proportional QALY shortfalls would need to be recalculated if the company were to be provide the additional analyses requested.

Cost-effectiveness estimates

Acceptable incremental cost-effectiveness ratio

3.11 NICE's technology appraisal and highly specialised technologies guidance manual notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £25,000 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 noted the high level of uncertainty, specifically that:

- there were considerable limitations in the generalisability of the trial data to the current NHS population (see section 3.3)
- the post-hoc subgroup analysis was not robust enough for decision making (see section 3.4)
- the results from the ITC were highly uncertain (see section 3.5)
- there were substantial concerns with the survival modelling (see section 3.6)
- it was uncertain which utility values should be used in the model (see section 3.7)
- it was uncertain how much of a utility decrement for self-administration of injections should be included in the model (see section 3.8), and
- the costs of administering histamine dihydrochloride with interleukin-2 were not adequately captured in the model (see section 3.9).

The committee agreed that it could not conclude on an acceptable ICER before its concerns about the evidence had been addressed. But it thought it was unlikely that an acceptable ICER would be above £25,000 per QALY gained.

Uncertainty in the cost-effectiveness estimates

3.12 The committee noted that, before it could establish a plausible cost-effectiveness estimate for histamine dihydrochloride with interleukin-2, more evidence and analysis was needed. It asked the company to provide analyses for the whole population in the marketing authorisation, and asked for the following:

- including the full population in the marketing authorisation in the economic model (the intention-to-treat population from Brune et al. (2006) may be more appropriate for modelling this, see section 3.6); this should include reconsidering the survival extrapolations and severity modifier calculations (see section 3.10)
- including scenarios for different sources of utility values (see section 3.7)
- exploring alternative disutility values for the self-administration of injections (see section 3.8), and
- including additional costs of drug administration in the model (see section 3.9).

Managed access

Recommendation with managed access

3.13 Having concluded that histamine dihydrochloride with interleukin-2 could not be recommended for routine use in the NHS, the committee then considered if it could be recommended for use during a managed access period for treating AML. The company did not make a proposal for managed access to be considered. The committee considered whether a recommendation with managed access could be made. The committee noted that:

- there was a high level of uncertainty in the evidence and in the modelling that was unlikely to be resolvable through a period of managed access

- it had not been able to choose a preferred ICER so it was unclear whether there was plausible potential to satisfy the criteria for routine use
- the trial was over 20 years old and there were no ongoing trials that could provide evidence during a period of managed access
- real world data was unlikely to be able to provide useful data on the comparative benefits of histamine dihydrochloride with interleukin-2 in the relevant population.

The committee concluded that histamine dihydrochloride with interleukin-2 did not meet the criteria to be considered for a recommendation with managed access. Based on the committee's conclusions, the NHS England Cancer Drugs Fund lead agreed that managed access was unlikely to be suitable.

Other factors

Equality

3.14 A stakeholder highlighted that AML is more common in men and older adults. Age and sex are protected characteristics under the Equality Act 2010. The committee noted that the marketing authorisation for histamine dihydrochloride with interleukin-2 stated that the efficacy had not been demonstrated in people over 60 years and that it could not evaluate histamine dihydrochloride with interleukin-2 outside of its marketing authorisation. A stakeholder highlighted that people from ethnic minorities are under-represented on donor registries so are less likely to receive an allogeneic stem cell transplant. Race is a protected characteristic under the Equality Act 2010. The committee understood that an alternative treatment to stem cell transplant could be particularly beneficial for people from ethnic minorities because of reduced donor availability for these groups. But it agreed that the uncertainties in the evidence would need to be addressed before it could recommend histamine dihydrochloride with interleukin-2 for people with AML. A stakeholder also highlighted that

histamine dihydrochloride with interleukin-2 may be more difficult for disabled people to self-administer. Disability is a protected characteristic under the Equality Act 2010. The committee agreed that a positive recommendation for histamine dihydrochloride with interleukin-2 could therefore exacerbate access issues for disabled people.

Uncaptured benefits

3.15 The committee considered whether there were any uncaptured benefits of histamine dihydrochloride with interleukin-2. The company stated that there could be quality-of-life benefits for carers of people with AML, because carers may experience a substantial burden and psychological morbidity over the course of treatment. The committee noted that carer quality of life had not been included in the economic model. The committee concluded that it was plausible there was a quality-of-life impact for carers of people with AML. But it was not presented with enough evidence for this to be taken into account in its decision making.

Conclusion

Recommendation

3.16 The committee could not choose a preferred ICER because of the substantial uncertainty in the evidence. So, it concluded that it could not recommend histamine dihydrochloride with interleukin-2 for maintenance treatment of AML.

4 Evaluation committee members and NICE project team

Evaluation committee members

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

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

Megan John

Chair, technology appraisal committee D

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 or principal technical adviser.

Kirsty Pitt

Technical lead

Victoria Kelly

Technical adviser

Kate Moore

Project manager

Ross Dent

Associate director

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