NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Evaluation

Histamine dihydrochloride with interleukin-2 for maintenance treatment of acute myeloid leukaemia [ID1627]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of histamine dihydrochloride with interleukin-2 within its marketing authorisation for maintenance treatment of acute myeloid leukaemia.

Background

Acute myeloid leukaemia (AML) is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid cells (blasts). The abnormal cells build up in the bone marrow and blood and interfere with normal blood cell production. AML progresses quickly over weeks or months and is fatal if not treated. AML is classified into different types. In most types of AML, the leukaemia cells are immature white blood cells. In other less common types, too many immature platelets or immature red blood cells form leukaemia cells. Anaemia, bleeding problems and serious infections are common symptoms of AML. People with AML also feel fatigued, which can affect daily life.There were 2,945 new diagnoses of acute myeloid leukaemia in England between 2017 to 2018.[1] The incidence rate increases with age with the highest rates being in the 85 to 89 age group. The 5-year survival rate for AML is 15%.[2]

The presence of specific genetic mutations may influence how AML progresses. One of most common mutations in AML is a mutation in the fms-like tyrosine kinase 3 (FLT3) gene. This mutation is associated with a poor prognosis, with people having a lower chance of achieving remission and shorter overall survival.[3]

The aim of treatment for AML is to cure it. For people who are fit enough, intensive treatment is available. It is conducted in 2 phases: induction therapy to achieve remission, followed by consolidation therapy to reduce the risk of relapse. Further treatment may be required with stem cell transplantation in suitable patients. Following the intensive treatment stage, people who are in complete remission may be offered long-term maintenance therapy. Although 80% of adult AML patients achieve complete remission after initial induction chemotherapy, many patients will eventually relapse.[4] The aim of maintenance therapy is to prevent the cancer returning when it is in remission. Treatment options for maintenance therapy include:

- quizartinib for people with FLT3-ITD-positive AML (Technology Appraisal guidance 1013)
- oral azacitidine for people who cannot have or do not want a haematopoietic stem cell transplant (Technology Appraisal guidance 827)
- midostaurin for people with FLT3-positive AML (Technology Appraisal guidance 523).

- sorafenib in people with FLT3-ITD positive AML and have received allogeneic haematopoietic stem cell transplant [5]

The technology

Histamine dihydrochloride (Ceplene, Brancaster Pharma) does not currently have a marketing authorisation in the UK for maintenance therapy in adults with AML.

Histamine dihydrochloride has been studied in a clinical trial as maintenance therapy in combination with interleukin-2 compared with no treatment for people with acute myeloid leukaemia in the first complete remission.

Intervention(s)	Histamine dihydrochloride with interleukin-2 as maintenance therapy
Population(s)	People with acute myeloid leukaemia who are in first remission
Subgroups	If the evidence allows the following subgroups will be considered: • people who are eligible or ineligible for allogeneic stem cell transplant • people with or without an FLT3 mutation • people with or without an FLT3-ITD mutation
Comparators	Established clinical management without histamine dihydrochloride with interleukin-2 including but not limited to: • oral azacitidine for people who cannot have or do not want a haematopoietic stem cell transplant • midostaurin for people with an FLT3-mutation • sorafenib, after a stem cell transplant, for people with an FLT3-ITD mutation • quizartinib for people with an FLT3-ITD mutation • cytarabine alone or in combination with other antineoplastic agents • best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • minimal residual disease • remission rate • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability and cost of biosimilar products of should be taken into account. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive acute myeloid leukaemia (2024). NICE technology appraisal guidance 1013 Ivosidenib with azacitidine for untreated acute myeloid leukaemia with an IDH1 R132 mutation (2024) NICE technology appraisal guidance 979 Oral azacitidine for maintenance treatment of acute myeloid leukaemia after induction therapy(2022). NICE technology appraisal guidance 827. Venetoclax with low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 787 Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 765 Liposomal cytarabine–daunorubicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 552

	Midostaurin for untreated acute myeloid leukaemia (2018). NICE technology appraisal guidance 523. Gemtuzumab ozogamicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 545 **Related Guidelines:** Haematological cancers: improving outcomes (2016). NICE guideline 47. Review date to be confirmed. Suspected cancer: recognition and referral (2015). NICE guideline NG12. Updated July 2017. **Related quality standards:** Haematological cancers (2017). NICE quality standard 150. **Related NICE Pathway:** Blood and bone marrow cancers **Related NICE guidelines in development:** Iodine (131I)–apamistamab for treating relapsed or refractory acute myeloid leukaemia before an allogeneic haematopoietic stem cell transplant [ID6355] Publication date to be confirmed.

References

1. BMJ Acute myeloid leukaemia; Summary BMJ 2024. Accessed April 2025

2. Cancer Research UK Survival for acute myeloid leukaemia (AML). Accessed April 2025 Accessed April 2024

3. Daver, N., Schlenk, R. F., Russell, N. H., & Levis, M. J. (2019). Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia, 33(2), 299-312.

4. Patel, A., Agha, M., Raptis, A., Hou, J. Z., Farah, R., Redner, R. L., Im, A., Dorritie, K. A., Sehgal, A., Rossetti, J., Saul, M., Normolle, D., Lontos, K., & Boyiadzis, M. (2021). Outcomes of Patients With Acute Myeloid Leukemia Who Relapse After 5 Years of Complete Remission. Oncology research, 28(7), 811–814.

5. NHS England Clinical Commissioning Policy: Sorafenib maintenance for adults with FLT3-internal tandem duplication (FLT3-ITD) acute myeloid leukaemia (AML) undergoing allogeneic haematopoietic stem cell transplantation 2023. Accessed April 2024