NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Cedazuridine-decitabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of cedazuridine-decitabine within its marketing authorisation for untreated acute myeloid leukaemia when intensive chemotherapy is not suitable.

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). AML progresses quickly over weeks or months and is fatal if not treated. Anaemia, bleeding problems and serious infections are common symptoms of acute myeloid leukaemia. People with AML also feel fatigued which can impact on daily life.

The incidence rates of AML have remained stable in the UK, over the last decade.[1] There were 3,089 new diagnoses of AML on average each year in the UK from 2016 to 2018.[1] The incidence rate increases with age[1].

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 chemotherapy to reduce the number of blast cells, followed by consolidation chemotherapy to reduce the risk of recurrence. For people with good general health, the treatment options are intensive chemotherapy and allogeneic haematopoietic stem cell transplant (HSCT).

Over half of patients with AML are ineligible for intensive chemotherapy and stem cell transplants because of factors such as age or comorbidities. Other treatment options for these people include low dose azacitidine, cytarabine, liposomal cytarabine–daunorubicin and venetoclax.

NICE technology appraisal guidance 218 recommends azacitidine for adults who are not eligible for HSCT and have AML with 20% to 30% blasts and multilineage dysplasia, according to the World Health Organization classification.

NICE technology appraisal guidance 765 recommends venetoclax with azacitidine for untreated AML in adults when intensive chemotherapy is unsuitable.

NICE technology appraisal guidance 787 recommends venetoclax with low dose cytarabine for untreated AML in adults when intensive chemotherapy is unsuitable, if they have over 30% bone marrow blasts.

The technology

Cedazuridine-decitabine (Inqovi. Otsuka Pharmaceutical) does not currently have a marketing authorisation in the UK for AML. It has been studied in clinical trials compared with decitabine (a hypomethylation agent) in adults with untreated AML when intensive chemotherapy is not suitable. It is also being studied in clinical trials with no active comparator in adults with untreated AML when intensive chemotherapy is not suitable.

Intervention(s)	Cedazuridine-decitabine
Population(s)	Adults with untreated acute myeloid leukaemia (AML) when intensive chemotherapy is unsuitable.
Comparators	• azacitidine alone for adults who are not eligible for HSCT and have AML with 20% to 30% blasts and multilineage dysplasia • low dose cytarabine • venetoclax with low dose cytarabine if people have over 30% bone marrow blasts • venetoclax with azacytidine • ivosidenib with azacitidine (for people with IDH1-positive AML, subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • disease-free survival • response rates, including remission • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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 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:** Oral azacitidine for maintenance treatment of acute myeloid leukaemia after induction therapy (2022) NICE technology appraisal guidance 827. Review date not stated. Venetoclax with low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 787. Review date 2025. Venetoclax with azacitidine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable (2022) NICE technology appraisal guidance 765. Review date 2025. Gilteritinib for treating relapsed or refractory acute myeloid leukaemia (2020) NICE technology appraisal guidance 642. Review date 2023. Liposomal cytarabine–daunorubicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 552. Review date 2021. Decitabine for untreated acute myeloid leukaemia (terminated appraisal) (2018) NICE technology appraisal guidance 548. Review date not stated. Gemtuzumab ozogamicin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 545. Review date 2021. Midostaurin for untreated acute myeloid leukaemia (2018) NICE technology appraisal guidance 523. Review date 2021. Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts (2016) NICE technology appraisal guidance 399. Review date 2019. Decitabine for the treatment of acute myeloid leukaemia (terminated appraisal) (2012) NICE technology appraisal guidance 270. Review date not stated.

	Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia (2011) NICE technology appraisal guidance 218. Review date not stated. **Related technology appraisals in development:** Talacotuzumab for untreated acute myeloid leukaemia. NICE technology appraisal guidance [ID1262] Publication to be confirmed. **Related NICE guidelines:** COVID-19 rapid guideline: delivery of systemic anticancer treatments (2020) NICE guideline NG161. Review date not stated. Haematological cancers: improving outcomes (2016) NICE guideline NG47. Review date not stated. **Related quality standards:** Haematological cancers (2017) NICE quality standard 150
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 105 – Specialist cancer services (adults) NHS England (November 2018) Clofarabine for refractory or relapsed acute myeloid leukaemia (AML) as a bridge to stem cell transplantation (all ages). Clinical Commissioning Policy. Reference 170080P NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a Department of Health Cancer research and treatment Department of Health (2016) NHS Outcomes Framework 2016 to 2017: Domains 3, 4 and 5. Department of Health (2014) The national cancer strategy: 4th annual report

Questions for consultation

Have all relevant comparators for cedazuridine-decitabine been included in the scope?

Should best supportive care be a comparator? If yes, for which population and how should it be defined?

Is low dose cytarabine a relevant comparator?

Where do you consider cedazuridine-decitabine will fit into the existing care pathway for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable?

Would cedazuridine-decitabine be considered as a treatment option for people with untreated IDH1-positive AML?

Would cedazuridine-decitabine be a candidate for managed access?

Do you consider that the use of cedazuridine-decitabine can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Are the outcomes listed appropriate?

Are there any appropriate subgroups?

Do you consider cedazuridine-decitabine to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which cedazuridine-decitabine will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK: Acute myeloid leukaemia (AML) statistics. Accessed April 2023.