NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Venetoclax with a hypomethylating agent or low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable [ID1564]

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of venetoclax within its marketing authorisation for untreated acute myeloid leukaemia in people for whom 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 of AML has increased by 8% in the UK over the last decade. There were 2,662 new diagnoses of AML in England in 2016.[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).

There are alternative treatment options for people for whom intensive chemotherapy is considered not suitable. This group may include people with. Treatments include low dose cytarabine and azacitidine. NICE technology appraisal guidance TA218 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 TA399 does not recommend azacitidine for treating AML with more than 30% bone marrow blasts in people who are not eligible for HSCT.

The technology

Venetoclax (Venclyxto, AbbVie) is a selective blocker of B-cell lymphoma-2 (BCL-2) a protein that allows cancer cells to stay alive. Venetoclax is administered orally.

Venetoclax does not currently have a marketing authorisation in the UK for AML. It is being studied in clinical trials in combination with low dose cytarabine or azacitidine in adults with untreated AML for whom intensive chemotherapy is not suitable.

Venetoclax has a marketing authorisation in the UK for chronic lymphocytic leukaemia.

Intervention(s)	Venetoclax in combination with a hypomethylating agent or low dose cytarabine.
Population(s)	People with untreated acute myeloid leukaemia (AML) for whom intensive chemotherapy is unsuitable.
Comparators	Established clinical management without venetoclax, for example: • low dose cytarabine • azacitidine • hydroxycarbamide
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. 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 and NICE Pathways	**Related Technology Appraisals** 'Gemtuzumab ozogamicin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal TA545. Review date November 2021. 'Liposomal cytarabine-daunorubicin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal guidance TA552. Review date December 2021. 'Midostaurin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal TA523. Review date June 2021. 'Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts.' (2016) Technology Appraisal TA399. Review date July 2019. 'Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia.' (2011) NICE Technology Appraisal TA218. Static list 2014. **Terminated appraisals** 'Decitabine for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal TA548 **Appraisals in development (including suspended appraisals)** None **Related Guidelines** Haematological cancers: improving outcomes. (2016) NICE guideline NG47 Review date to be confirmed. **Related Quality Standards** Haematological cancers (2017) Quality standard QS150. **Related NICE Pathways** Blood and bone marrow cancers (2015) NICE pathway.
Related National Policy	Department of Health Cancer research and treatment Department of Health (2014) The national cancer strategy: 4th annual report The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 29.

	Department of Health (2016) NHS Outcomes Framework 2016 to 2017: Domains 3, 4 and 5.

Questions for consultation

Have all relevant comparators for venetoclax been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated acute myeloid leukaemia (AML) ineligible for intensive chemotherapy?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom venetoclax is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider venetoclax will fit into the existing NICE pathway, Blood and bone marrow cancers.

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 venetoclax 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.

Do you consider venetoclax 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)?

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

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

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Cancer Research UK (2016) Acute myeloid leukaemia (AML) statistics. Accessed March 2019.

