NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Glasdegib with chemotherapy for untreated acute myeloid leukaemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of glasdegib within its marketing authorisation for untreated 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). 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.[3] There were an estimated 2,638 new diagnoses of AML in England in 2016.[1] The incidence rate increases with age. In the UK in 2013-2015, around 41% of new cases were in people aged 75 years and over.[2]

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). Intensive chemotherapy treatment for untreated AML includes:

- liposomal cytarabine–daunorubicin (NICE TA552)
- midostaurin with standard daunorubicin and cytarabine induction therapy and high-dose cytarabine consolidation therapy, for people with acute FLT3-mutation-positive myeloid leukaemia (NICE TA523)
- gemtuzumab ozogamicin with daunorubicin and cytarabine for de novo CD33-positive acute myeloid leukaemia (NICE TA545)
- standard cytarabine and daunorubicin

There are alternative treatment options for people for whom intensive chemotherapy is considered not suitable. This group may include people with comorbidities and/or poor performance status, for example, people who are aged 75 or older and people aged under 75 with heart, lung, liver or kidney or an elevated Eastern Cooperative Oncology Group score. Non-intensive chemotherapy treatments for untreated AML include:

- low dose cytarabine and azacytidine

- 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 TA218)
- azacitidine is not recommended for treating AML with more than 30% bone marrow blasts in people of 65 years or older who are not eligible for HSCT (NICE TA399).

The technology

Glasdegib (Daurismo, Pfizer) is a small-molecule inhibitor of the hedgehog (Hh) signaling pathway with potential antineoplastic activity. It acts by inhibiting the smoothened (SMO) receptor, thereby disrupting the Hh signalling pathway. It is administered orally.

Glasdegib does not have a marketing authorisation in the UK for treating acute myeloid leukaemia. It is currently being studied in a clinical trial of adults with untreated acute myeloid leukaemia:

- as an add-on treatment to daunorubicin and cytarabine compared with placebo in combination with daunorubicin and cytarabine
- as an add-on treatment to azacytidine compared with placebo in combination with azacitidine, for people in whom intensive induction chemotherapy is not appropriate.

Intervention(s)	Glasdegib in combination with chemotherapy
Population	Adults with previously untreated acute myeloid leukaemia
Comparators	If intensive chemotherapy is appropriate: • established clinical management without glasdegib (including but not limited to cytarabine [standard or liposomal] and daunorubicin) • midostaurin (only for people with acute FLT3-mutation-positive myeloid leukaemia) • gemtuzumab ozogamicin (only for de novo CD33-positive acute myeloid leukaemia) If intensive chemotherapy is not appropriate: • established clinical management without glasdegib (including but not limited to azacitidine [only for people with acute myeloid leukaemia with 20–30% blasts and multilineage dysplasia] and low dose cytarabine)

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 and NICE Pathways	**Related Technology Appraisals** 'Liposomal cytarabine-daunorubicin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal guidance TA552. Review date December 2021. 'Gemtuzumab ozogamicin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal guidance TA545. Review date November 2021. 'Midostaurin for untreated acute myeloid leukaemia.' (2018) NICE Technology Appraisal guidance 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 'Decitabine for the treatment of acute myeloid leukaemia' (2012) NICE Technology Appraisal TA270 **Appraisals in development (including suspended appraisals)** 'Guadecitabine for untreated acute myeloid leukaemia' [ID1411]. Suspended. 'Venetoclax with a hypomethylating agent or low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable' Proposed NICE technology appraisal [ID1564]. Publication date to be confirmed. 'Talacotuzumab for untreated acute myeloid leukaemia' Proposed NICE technology appraisal [ID1262]. Publication date to be confirmed. **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	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for glasdegib been included in the scope?

- For previously untreated AML, in whom would intensive induction chemotherapy be used? What intensive treatments are currently used in NHS clinical practice?
- For previously untreated AML, in whom would non-intensive induction chemotherapy be used? What non-intensive treatments are currently used in NHS clinical practice?
- For previously untreated AML, what consolidation treatments are currently used in NHS clinical practice? Would these differ depending on whether intensive or non-intensive induction chemotherapy is appropriate?

Are the outcomes listed appropriate?

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

Where do you consider glasdegib 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 glasdegib 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 glasdegib 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 glasdegib 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Office for National Statistics. Cancer Registration Statistics, England, 2016. Accessed April 2019.
2. Cancer Research UK (2016) Acute myeloid leukaemia (AML) incidence statistics. Accessed March 2019.
3. Cancer Research UK (2016) Acute myeloid leukaemia (AML) statistics. Accessed April 2019.

