

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Venetoclax for treating chronic lymphocytic leukaemia associated with a 17p deletion or TP53 mutation

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of venetoclax within its marketing authorisation for treating chronic lymphocytic leukaemia associated with a 17p deletion or TP53 mutation.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). It causes anaemia, swollen lymph nodes, spleen enlargement, unexplained weight loss and increased susceptibility to infection. People with CLL may live with a considerable burden of symptoms impacting on their quality of life, whether or not they have received treatment.

CLL is a common form of leukaemia, with an estimated 2770 new diagnoses in England each year¹. The risk of developing CLL increases with age and is more common in men². Approximately 5% to 10% of people diagnosed with CLL are considered to have 'high-risk' disease characterised by the presence of cytogenetic mutation or abnormalities (that is, 17p deletion or TP53 mutation)³. The presence of 17p deletion or TP53 mutation influences the rate of cell growth as well as the resistance of the disease to treatment. People with high risk disease with the 17p deletion or TP53 mutation have a median survival of 2 to 3 years³.

Active treatment options are limited for people with CLL associated with a 17p deletion or TP53 mutation because chemotherapy (such as fludarabine plus cyclophosphamide and rituximab, bendamustine, and chlorambucil) generally causes further deletions and mutations to occur.

NICE technology appraisal guidance 359 has recommended idelalisib in combination with rituximab for adults with CLL associated with a 17p deletion or TP53 mutation. NICE is also currently developing guidance for ibrutinib [ID749] and idelalisib in combination with ofatumumab [ID817] for CLL associated with a 17p deletion or TP53 mutation. Ibrutinib is currently available through the Cancer Drugs Fund but only for treated CLL.

The technology

Venetoclax (brand name unknown, AbbVie) is an oral inhibitor of the B-cell lymphoma 2 protein that regulates cell death.

Venetoclax does not currently have a marketing authorisation in the UK for treating chronic lymphocytic leukaemia associated with a 17p deletion or TP53 mutation. It has been studied in a single arm clinical trial in adults with untreated and treated chronic lymphocytic leukaemia associated with a 17p deletion.

Intervention(s)	Venetoclax
Population(s)	People with chronic lymphocytic leukaemia associated with a 17p deletion or TP53 mutation
Comparators	<ul style="list-style-type: none"> • ibrutinib (subject to ongoing NICE appraisal, funded by the CDF only for treated CLL) • idelalisib in combination with rituximab • idelalisib in combination with ofatumumab (subject to ongoing NICE appraisal, <i>not</i> funded by the CDF in the interim) • best supportive care (including but not limited to regular monitoring, blood transfusions, infection control and psychological support)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes and nationally available simple discount agreements for the intervention or comparator technologies will be taken into account.</p>

<p>Other considerations</p>	<p>If the evidence allows the following subgroups will be considered. These include:</p> <ul style="list-style-type: none"> • people who have not had treatment for chronic lymphocytic leukaemia (untreated CLL) • people who have had treatment for chronic lymphocytic leukaemia (treated CLL). <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>'Idelalisib for treating chronic lymphocytic leukaemia' (2015). NICE technology appraisal 359. Review date September 2018.</p> <p>Appraisals in development:</p> <p>'Ibrutinib for treating chronic lymphocytic leukaemia' NICE technology appraisal guidance [ID749]. Publication expected June 2016.</p> <p>'Idelalisib in combination with ofatumumab for chronic lymphocytic leukaemia' NICE technology appraisal guidance [ID817]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>'Improving outcomes in haematological cancer' (2003). NICE cancer service guidance.</p> <p>Related NICE Pathways:</p> <p>Blood and bone marrow cancers (2015), NICE pathway available at:</p> <p>http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers</p>

Related National Policy	<p>NHS England Manual for prescribed specialised services 2013/2014. Specialist cancer services (adults) [section 105, page 234]:</p> <p>http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1–5.</p> <p>https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</p>
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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 and treated chronic lymphocytic leukaemia associated with a 17p deletion or TP53 mutation?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other 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.

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 (2012) Chronic lymphocytic leukaemia incidence statistics. Accessed December 2015.
2. Cancer Research UK (2015) Chronic lymphocytic leukaemia risks and causes. Accessed October 2015.
3. Patient (2015) Chronic lymphocytic leukaemia prognosis. Accessed October 2015.