NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Venetoclax with obinutuzumab for untreated chronic lymphocytic leukaemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of venetoclax with obinutuzumab within its marketing authorisation for untreated chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). It causes anaemia, swollen lymph nodes, spleen enlargement, 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.

In England there were 3,157 new cases of CLL in 2017[1]. The risk of developing CLL increases with age and is more common in men[1].

Treatment options for untreated CLL depend on factors such as stage of disease, performance status and co-morbidities.

Table 1. Treatment options for untreated CLL in NHS practice

NICE technology appraisal	Treatment option for untreated CLL	Population
Without a 17p deletion (del[17p]) or TP53 mutation		
TA174	rituximab with fludarabine and cyclophosphamide (FCR)	people for whom fludarabine in combination with cyclophosphamide is considered appropriate
TA216	bendamustine with or without rituximab (BR)	people who cannot have fludarabine combination chemotherapy
No TA published*	chlorambucil, with or without rituximab	
TA343	obinutuzumab with chlorambucil	people for whom fludarabine-based therapy and bendamustine is unsuitable
TA344	ofatumumab with chlorambucil	
With a del(17p) or TP53 mutation		
TA359	idelalisib with rituximab	people for whom chemo-immunotherapy is unsuitable
TA429	ibrutinib alone	

TA487	venetoclax for use in the Cancer Drugs Fund	people for whom B-cell receptor pathway inhibitors are unsuitable
*use of chlorambucil, with or without rituximab, is detailed in TA343.		

The technology

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

Venetoclax with obinutuzumab does not have a UK marketing authorisation for untreated CLL. It is being studied in clinical trials in comparison with standard chemo-immunotherapy (FCR and BR) and obinutuzumab with chlorambucil, in adults with untreated CLL.

Venetoclax monotherapy has a marketing authorisation in the UK for treating CLL in adults. Venetoclax with rituximab has a UK marketing authorisation for treating relapsed or refractory CLL.

Intervention	Venetoclax with obinutuzumab
Population	People with untreated chronic lymphocytic leukaemia
Comparators	Without a del(17p) or TP53 mutation: • fludarabine, cyclophosphamide and rituximab (FCR) • bendamustine with or without rituximab (BR), for people for whom fludarabine-based therapy is unsuitable • chlorambucil with or without rituximab, for people for whom fludarabine-based therapy is unsuitable • obinutuzumab with chlorambucil, for people for whom fludarabine-based therapy and bendamustine is unsuitable • ofatumumab with chlorambucil, for people for whom fludarabine-based therapy and bendamustine is unsuitable. With a del(17p) or TP53 mutation: • ibrutinib alone, for people for whom chemo-immunotherapy is unsuitable • idelalisib with rituximab.

Outcomes	The outcome measures to be considered include: • overall survival • progression- free survival • response 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	If the evidence allows the following subgroups will be considered: • people with untreated CLL without del(17p) or TP53 mutation • people with untreated CLL for whom fludarabine-based therapy is unsuitable. 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: Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (2019) NICE technology appraisal 561. Review date February 2022. Venetoclax for treating chronic lymphocytic leukaemia (2017) NICE technology appraisal 487. To be updated when the CDF data collection period has ended

	(expected December 2020). Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (2017) NICE technology appraisal 429. Review date January 2020. Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal 359. On static list Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia (2015) NICE technology appraisal 344. On static list Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia (2015) NICE technology appraisal 343. On static list Bendamustine for the first-line treatment of chronic lymphocytic leukaemia (2011) NICE technology appraisal 216. On static list. Rituximab for the first-line treatment of chronic lymphocytic leukaemia (2009) NICE technology appraisal 174. On static list. Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia (2007). NICE technology appraisal 119. On static list. Terminated appraisals Ofatumumab with chemotherapy for treating chronic lymphocytic leukaemia (terminated appraisal) (2017). NICE technology appraisal 470. Idelalisib with ofatumumab for treating chronic lymphocytic leukaemia (terminated appraisal) (2017). NICE technology appraisal 469. Ibrutinib for untreated chronic lymphocytic leukaemia without a 17p deletion or TP53 mutation (terminated appraisal) (2017). NICE technology appraisal 452. Appraisals in development (including suspended appraisals) Venetoclax with ibrutinib and obinutuzumab for untreated chronic lymphocytic leukaemia NICE technology appraisals guidance ID1270. Suspended. Related Guidelines:

	Haematological cancers: improving outcomes (2016). NICE guideline 47 Review date to be confirmed. Related quality standards: Haematological cancers (2017). NICE quality standard 150. Related NICE Pathway: Blood and bone marrow cancers
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) Chapter 105. Department of Health (2016) NHS Outcomes Framework 2016 to 2017: Domain 1.

Questions for consultation

Have all relevant comparators for venetoclax with obinutuzumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated chronic lymphocytic leukaemia?

Are the outcomes listed appropriate?

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

Where do you consider venetoclax with obinutuzumab 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 with obinutuzumab 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 with obinutuzumab 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 with obinutuzumab 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 https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/process).

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. Cancer registration statistics, England: 2017 (2019). Office for National Statistics. Accessed May 2019.

