NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Duvelisib for treating relapsed or refractory chronic lymphocytic leukaemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of duvelisib within its marketing authorisation for treating relapsed or refractory chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is the most common type of chronic leukaemia and is a type of cancer that affects the white blood cells and tends to progress slowly over many years. It mostly affects people 60 years of age and over and is rare in people 40 years of age and younger. In England there were 3,157 new cases of CLL in 2017. The risk of developing CLL increases with age and is more common in men.[1]

In CLL, the material found inside some bones (bone marrow) produces too many white blood cells called lymphocytes that aren't fully developed and don't work properly. Over time this can cause a range of problems, such as an increased risk of picking up infections, persistent tiredness, swollen glands in the neck, armpits or groin, and unusual bleeding or bruising.[2] People with CLL may live with a considerable burden of symptoms impacting on their quality of life, whether or not they have received treatment. Approximately 5% to 10% of people diagnosed with CLL are considered to have 'high-risk' disease, characterised by the presence of cytogenetic mutations or abnormalities (that is, 17p deletion or TP53 mutation)[3]. The presence of 17p deletion or TP53 mutation can increase both the rate of cell growth and the resistance of the disease to treatment. The presence of an immunoglobulin heavy chain gene (IgHV) mutation may also affect clinical outcomes.

Treatment for relapsed or refractory CLL is complex and depends on several factors, including the extent of the disease, previous treatments, and the patient's age, symptoms and general state of health. The table below summarise the treatment options which are currently available as routine practice in the NHS in England for relapsed or refractory CLL.

Table 1. Treatment options for treated CLL in NHS practice

NICE technology appraisal	*Treatment option*	*Population*

TA561	venetoclax with rituximab	for people who have had at least 1 previous therapy
TA193	rituximab with fludarabine and cyclophosphamide	for people not refractory to fludarabine and who have not been previously treated with rituximab*
TA359	idelalisib with rituximab	for people whose disease has been treated but has relapsed within 24 months
TA429	ibrutinib monotherapy	for people who have had at least 1 previous therapy
Not applicable	bendamustine with or without rituximab (BR)	No marketing authorisation for this indication
*unless treated within the context of a clinical trial either at a lower dose than licensed or in combination with chemotherapy other than fludarabine and cyclosphosphamide.		

The technology

Duvelisib (Copiktra, Verastem) is a dual inhibitor of phosphatidylinositol 3 kinase (PI3K) δ and γ isoforms. The PI3K pathway promotes cell proliferation, growth, motility metabolism and survival. PI3K inhibitors have been shown to block growth and induce cell death. It is administered as oral capsules.

Duvelisib does not currently have a marketing authorisation in the UK for chronic lymphocytic leukaemia. It has been compared with ofatumumab in clinical trials in adults with chronic lymphocytic leukaemia and small lymphocytic lymphoma that has progressed during or relapsed after at least 1 previous therapy. CLL and small lymphocytic lymphoma (SLL) are considered as being the same condition. In CLL, cancer cells are found mostly in the blood and bone marrow. In SLL, cancer cells are found mostly in the lymph nodes.

Intervention(s)	Duvelisib
Population(s)	People with relapsed or refractory chronic lymphocytic leukaemia (CLL) after at least two prior therapies with or without the presence of 17p deletion or TP53 mutation
Comparators	• bendamustine with or without rituximab • venetoclax with rituximab • ibrutinib • rituximab with fludarabine and cyclophosphamide • idelalisib with rituximab

Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • time to next treatment • 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 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 a 17p deletion or TP 53 mutation • People with IgHV unmutated disease 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 in combination with rituximab for treating relapsed or refractory chronic lymphocytic leukaemia (2019) NICE technology appraisal guidance 561 Venetoclax for treating chronic lymphocytic leukaemia (2017) NICE technology appraisal guidance 487 Ibrutinib for previously treated chronic lymphocytic leukaemia and untreated chronic lymphocytic leukaemia with 17p deletion or TP53 mutation (2017) NICE technology appraisal guidance 429

	Idelalisib for treating chronic lymphocytic leukaemia (2015) NICE technology appraisal guidance 359 Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (2010) NICE technology appraisal guidance 193 **Terminated appraisals** Ofatumumab with chemotherapy for treating chronic lymphocytic leukaemia (terminated appraisal) NICE technology appraisal guidance 470 Idelalisib with ofatumumab for treating chronic lymphocytic leukaemia (terminated appraisal) NICE technology appraisal guidance 469. Ibrutinib with bendamustine and rituximab for treating relapsed or refractory chronic lymphocytic leukaemia after systemic therapy (terminated appraisal) (2017) NICE technology appraisal guidance 437 Appraisals in development (including suspended appraisals) Leukaemia (chronic lymphocytic, relapsed) - ofatumumab (maintenance) NICE technology appraisal guidance ID732. Publication date to be confirmed. Suspended February 2017 Idelalisib with bendamustine and rituximab for previously treated chronic lymphocytic leukaemia NICE technology appraisal guidance. Publication date to be confirmed. Suspended May 2018 **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150

	Related NICE Pathways: Blood and bone marrow cancers (2019) NICE pathway http://pathways.nice.org.uk/
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 and Social Care, NHS Outcomes Framework 2016-2017: Domain 1 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for duvelisib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory chronic lymphocytic leukaemia (CLL)?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate'?

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

Where do you consider duvelisib 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 duvelisib 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 duvelisib 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 duvelisib 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 technology/ies 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 July 2020
2. Chronic lymphocytic leukaemia. NHS Choices, accessed July 2020
3. Guidelines on the diagnosis, investigation and management of chronic lymphocytic leukaemia (2012). British Committee for Standards in Haematology. Accessed July 2020.