NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Duvelisib for treating relapsed follicular lymphoma after at least 2 systemic therapies

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of duvelisib within its marketing authorisation for treating follicular lymphoma after at least two systematic therapies.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system, and involve abnormal production of lymphocytes (a type of white blood cell). They are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin lymphomas are a heterogeneous group of conditions ranging from 'indolent' (low-grade) to 'aggressive' (high-grade) depending on the rate at which the abnormal lymphocytes divide. Indolent lymphomas are slow growing. Follicular lymphoma, which affects B cells, is the most common type of indolent non-Hodgkin lymphoma[1]. People with follicular lymphoma typically present with painless, swollen lymph nodes in the neck, armpit or groin.

Lymphomas are commonly staged I (best prognosis) to IV (worse prognosis). The stage of the lymphoma reflects how many groups of lymph nodes are affected, where they are in the body, and whether other organs such as the bone marrow or liver are affected. More people are diagnosed with advanced (stage III or IV) non-Hodgkin lymphoma than early stage disease (stage I and II): 50% are diagnosed with advanced disease, 29% are diagnosed with early stage disease, and in the remainder of cases the stage at diagnosis is not known[2].

Between 2015 and 2017, an average of approximately 12,100 people per year were diagnosed with non-Hodgkin lymphoma in England[2]. Follicular lymphoma makes up 18% of all cases of non-Hodgkin lymphoma[3]. Survival rates for follicular lymphoma depend on the stage at which they are diagnosed. Early stage (stage I or II) 5-year survival rate is 90%, advanced stage (stage III or IV) is 80%[4].

Treatment for follicular lymphoma also depends on stage at diagnosis. Early stage follicular lymphoma is likely to be treated with localised radiotherapy to the affected areas, whereas advanced stage is likely to be treated with rituximab, in combination with chemotherapy if symptoms are present.

NICE technology appraisal guidance 513 recommends in cases where the person has a Follicular Lymphoma International Prognostic Index (FLIPI) score of 2 or more that obinutuzumab in combination with chemotherapy should be used at first-line treatment. NICE technology appraisal guidance 629 recommends follicular lymphoma that did not respond or progressed up to 6 months after treatment with rituximab should be treated with obinutuzumab with bendamustine followed by obinutuzumab maintenance. NICE technology appraisal guidance 627 recommends lenalidomide with rituximab within its marketing authorisation, as an option for

previously treated follicular lymphoma (grade 1 to 3A) in adults. Rituximab in combination with chemotherapy may also be used as an option for the induction of remission in people with relapsed stage III or IV follicular non-Hodgkin's lymphoma. Idelalisib, which is in the same class of drugs as duvelisib, was considered by NICE as a treatment for follicular lymphoma after 2 prior lines of treatment, however it was not recommended. Consolidation with autologous or allogenic stem cell transplantation can also be offered for people with follicular lymphoma, in second or subsequent remission (complete or partial), who meet the eligibility criteria.

The technology

Duvelisib (Copiktra, Verastem Oncology) is a small-molecule, selective dual inhibitor of phosphatidylinositol 3 kinase (PI3K) δ and γ isoforms. PI3K is an enzyme involved in cellular activities such as cell growth, proliferation and survival. Mutations in the gene that encodes PI3K can cause cancer. Therefore, inhibition of the misfunctioning enzyme could reduce this effect.

Duvelisib does not currently have a marketing authorisation in the UK for treating follicular lymphoma. It has been studied in clinical trials as a monotherapy in adults with rituximab-refractory indolent non-Hodgkin lymphoma who have not had previous treatment with a PI3K inhibitor or BTK inhibitor. Duvelisib is administered orally.

Intervention(s)	Duvelisib
Population(s)	People with relapsed follicular lymphoma, previously treated with at least two systemic therapies
Comparators	Established clinical management without duvelisib. Treatment choice will depend on previous treatments, and how effective those treatments were. • Obinutuzumab with bendamustine followed by obinutuzumab maintenance. • Lenalidomide with rituximab • Rituximab in combination with chemotherapy • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall 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. 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. The availability of any managed access arrangement for the intervention 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**: Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab (2020). NICE Technology Appraisal 629 (replaces TA472). Review date 2023. Lenalidomide with rituximab for previously treated follicular lymphoma (2020). NICE Technology Appraisal 627. Review date 2023. Idelalisib for treating refractory follicular lymphoma (2019). NICE Technology Appraisal 619. Review date 2022. Rituximab for the first-line treatment of stage III-IV follicular lymphoma (2012). NICE Technology Appraisal 243. Review decision August 2014: static guidance list. Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma (2011). NICE technology appraisals guidance 226. Review decision August 2014: static guidance list. Rituximab for the treatment of relapsed or refractory stage III

	or IV follicular non-Hodgkin's lymphoma: Review of technology appraisal guidance 37 (2008). NICE Technology Appraisal 137. Review decision March 2011: static guidance list. **Terminated appraisals** Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab (terminated appraisal) (2010). NICE Technology Appraisal 206. **Appraisals in development (including suspended appraisals)** Duvelisib for treating relapsed chronic lymphocytic leukaemia [ID1083]. NICE technology appraisal guidance. Publication date to be confirmed. Lymphoma (non-Hodgkin's) - bendamustine (with rituximab) [ID434]. NICE technology appraisals guidance. Publication date to be confirmed (Suspended). Lymphoma (follicular non-Hodgkin's - advanced) - bortezomib [ID407]. NICE technology appraisals guidance. Publication date to be confirmed (Suspended). **Related Guidelines:** Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guideline 52. Review date to be confirmed. Haematological cancers: improving outcomes (2016) NICE guideline 47. Review date to be confirmed. **Related NICE Pathways:** Non-Hodgkin's Lymphoma (2020) NICE pathway Treating follicular lymphoma (2020) 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). Chapters 105 and 106 (specialist cancer services, adults and children). Department of Health and Social Care, NHS Outcomes Framework 2016-2017, Dec 2016. Domains 1, 2, 4 and 5. NHS England, National Cancer Drugs Fund List, June 2020. Department of Health and Social Care, Improving Outcomes: A strategy for cancer, fourth annual report, Dec 2014. Department of Health and Social Care, Commissioning cancer services, July 2011.

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 follicular lymphoma after at least 2 systematic therapies?

How should best supportive care be defined?

How would the use of duvelisib change the subsequent treatments available for managing follicular lymphoma, including stem cell transplantation?

Are the outcomes listed appropriate?

Are there any 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 pathways, Non-Hodgkin's Lymphoma and Treating Follicular Lymphoma?

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 Research UK (2018) How doctors group non-Hodgkin lymphomas. Accessed May 2020

2 Cancer Research UK (2017) Non-Hodgkin lymphoma incidence statistics. Accessed May 2020

3 Cancer Research UK (2019) Follicular lymphoma. Accessed May 2020

4 Cancer Research UK (2018) Survival. Accessed May 2020