NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ibrutinib for treating Waldenström's macroglobulinaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ibrutinib within its marketing authorisation for treating Waldenström's macroglobulinaemia.

Background

Waldenström's macroglobulinaemia is a type of non-Hodgkin's lymphoma. Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Lymphomas are divided into two types: Hodgkin's lymphoma and non-Hodgkin's lymphoma. Non-Hodgkin's lymphomas can be categorised according to their grade (how fast they grow) or cell type affected (B-cell or T-cell), as well as by their clinical features. Lymphoplasmacytic lymphomas are a group of rare low grade (slow growing or indolent) non-Hodgkin's lymphomas. The most common of these is Waldenström's macroglobulinaemia.[1] Waldenström's macroglobulinaemia is caused by abnormal B cells which produce immunoglobulin M (IgM). IgM molecules are very large and can thicken the blood, reducing its flow through capillaries which can cause nerve damage in the hands and feet.[1, 2]

In 2013, 207 people were diagnosed with Waldenström's macroglobulinaemia in England.[3] It is more common in men and mainly affects people 70 years and older.[2] Because Waldenström's macroglobulinaemia develops slowly, most people have no symptoms until they are diagnosed. As a result, most people are diagnosed in the advanced stages of the disease.

There is currently no NICE guidance for Waldenström's macroglobulinaemia. The British Committee for Standards in Haematology (BCSH) guidelines recommend treatment with a combination regimen with rituximab and either cladribine, bendamustine, dexamethasone (plus cyclophosphamide) or fludarabine (with or without cyclophosphamide).[2] Chlorambucil monotherapy is also recommended for those people who cannot tolerate other treatments. Choice of treatment depends on a variety of clinical factors including grade of disease, kidney function, co-morbidities and whether a person is able to have stem cell transplantation. [2]

The technology

Ibrutinib (Imbruvica, Janssen) inhibits B-cell proliferation, and promotes cell death. It is administered orally.

Ibrutinib has a marketing authorisation for the treatment of adult patients with Waldenström's macroglobulinaemia who have received at least one prior

therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

Intervention(s)	Ibrutinib
Population(s)	Adults with Waldenström's macroglobulinaemia who have received at least 1 prior therapy Adults with Waldenström's macroglobulinaemia who are not eligible for chemo-immunotherapy

Comparators	For people who have received at least 1 prior therapy:
	• Established clinical management without ibrutinib including single agent and combination regimens with:
	  • bendamustine
	  • bortezomib
	  • chlorambucil
	  • cladribine
	  • cyclophosphamide
	  • dexamethasone
	  • fludarabine
	  • rituximab
	For people who are not eligible for chemo-immunotherapy:
	  • best supportive care
	  • watch and wait

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall response rate • duration of response/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. 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.
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 Guidelines: Cancer Service Guidance, Improving outcomes in haemato-oncology cancers, October 2003 (Update in development, anticipated publication date: January 2018): http://www.nice.org.uk/guidance/indevelopment/gid-cgwave0799 Clinical Guideline in Preparation, 'Non-Hodgkin's lymphoma: diagnosis and management of non-Hodgkin's lymphoma'. Earliest anticipated date of publication July 2016. Related NICE Pathways: NICE Pathway: Blood and bone marrow cancers, Pathway created: Updated 2015. http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers/blood-and-bone-marrow-cancers-overview
Related National Policy	NHS Commissioning Board, Apr 2013, 'Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages)'. http://www.england.nhs.uk/wp-content/uploads/2013/10/b04-p-a.pdf Department of Health, Jan 2011, 'Improving Outcomes: A Strategy for Cancer' Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framew

	ork.pdf

Questions for consultation

Have all relevant comparators for ibrutinib been included in the scope? Should haematopoietic stem cell transplantation be included as a comparator?

Which treatments are considered to be established clinical practice in the NHS for Waldenström's macroglobulinaemia? Should only people with symptomatic Waldenström's macroglobulinaemia be included in the population?

How would best supportive care be defined for people who are ineligible or intolerant to chemo-immunotherapy?

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

Where do you consider ibrutinib 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 ibrutinib is 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 ibrutinib 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 ibrutinib 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. Lymphoma Association (2011). Waldenström's macroglobulinaemia information sheet. Accessed July 2015.

2. Owen, R et al. (2014) Guidelines on the diagnosis and management of Waldenström macroglobulinaemia. British Journal of Haematology, 165:316-33.

3. Office of National Statistics (2014), Cancer Statistics Registrations, England (Series MB1), No. 44, 2013 http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-394268