NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ibrutinib for treating Waldenström's macroglobulinaemia (CDF review of TA491)

Final scope

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. 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. Symptoms are highly variable, but the most common ones include severe fatigue, night sweats, lack of concentration, frequent/persistent infections, breathlessness, sinus problems, and unexplained weight loss.

Approximately 330 people are diagnosed with Waldenström's macroglobulinaemia in England annually.[1] 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.

NICE technology appraisal 491 currently recommends ibrutinib for use within the Cancer Drugs Fund for treating Waldenström's macroglobulinaemia in adults who have had at least 1 prior therapy. There is currently no other NICE guidance on treating Waldenström's macroglobulinaemia. The British Committee for Standards in Haematology (BCSH) guidelines recommends treatment with a combination regimen with rituximab and either cladribine, bendamustine, dexamethasone (plus cyclophosphamide) or fludarabine (with or without cyclophosphamide). 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. Patients treated with existing treatments generally have a partial response which lasts for a time before the disease relapses.

The technology

Ibrutinib (Imbruvica, Janssen) is an inhibitor of a protein called Bruton's tyrosine kinase, which stops B-cell (lymphocyte) proliferation and promotes cell death.

Ibrutinib has a marketing authorisation in the UK for treating adult patients with Waldenström's macroglobulinaemia who have received at least one prior therapy, or as first line treatment for patients in whom chemo-immunotherapy is unsuitable.

Intervention(s)	Ibrutinib
Population(s)	Adults with Waldenström's macroglobulinaemia who have received at least one prior therapy
Comparators	• rituximab and bendamustine • rituximab, dexamethasone and cyclophosphamide • rituximab and fludarabine with or without cyclophosphamide • cladribine with or without rituximab • rituximab • chlorambucil
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • 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	Terminated appraisals: Ibrutinib with rituximab for treating Waldenstrom's macroglobulinaemia (terminated appraisal) (2019) NICE technology appraisal TA608 Appraisals in development (including suspended appraisals): Zanubrutinib for treating Waldenström's macroglobulinaemia NICE technology appraisals guidance [ID1427] Expected publication date November 2021 Related Guidelines: Haematological cancers: improving outcomes (2016). NICE guideline NG47 Non-Hodgkin's lymphoma: diagnosis and management (2016). NICE guideline NG52 Related NICE Pathways: NICE Pathway: Blood and bone marrow cancers, updated 2021.
Related National Policy	Department of Health, Dec 2014, 'Improving Outcomes: A Strategy for Cancer - Fourth Annual Report' Department of Health, NHS Outcomes Framework 2021.

References

1. WMUK (2015), What is WM? Accessed December 2015.

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