NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Pixantrone dimaleate monotherapy for the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pixantrone dimaleate monotherapy within its licensed indication for the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma in people who have had at least two prior therapies.

Background

Lymphomas are cancers of the lymphatic system, which is a part of the body's immune system. They are broadly divided into Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL). NHL can be divided into low grade (also called 'indolent') and high grade (aggressive) lymphomas. Low-grade lymphomas grow slowly and are associated with a long median survival. Aggressive lymphomas grow quickly and have a short natural history, with only a 50-60% cure rate. Symptoms of NHL include malaise, weight loss, fevers and night sweats, as well as local pain and restriction in movement associated with enlarged lymph nodes.

Precise identification of the type of lymphoma and accurate staging of the disease is crucial both for choosing the optimum treatment and for monitoring disease progression. The stage of NHL 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. One of the most common systems for classifying NHL identifies four stages. In stage I, only one group of lymph nodes in one organ of the body is affected. In stage II, the disease has spread to two lymph groups on the same side of the diaphragm. Stage III disease includes lymph nodes affected on both sides of the diaphragm, and stage IV of the disease usually involves multiple internal organs, for example, the liver, bone marrow, or blood.

NHL accounts for approximately 4% of all cancers diagnosed in the UK, with 9431 new cases of NHL registered in England and Wales in 2006, and 4011 registered deaths in 2007. The incidence of NHL increases with age, with rates increasing sharply in people over 50 years and more than 70% of all cases are diagnosed in people over 60 years.

First-line treatment options for aggressive NHL include combination chemotherapy regimens based on alkylating agents, without or with steroids (chemo-immunotherapy). NICE technology appraisal guidance 65 recommends rituximab in combination with a regimen of cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) for the first-line treatment of people with CD20-positive diffuse large-B-cell (aggressive) lymphoma at clinical stages II, III or IV. Subsequent therapy options include single-agent chemotherapy, rituximab monotherapy, or high-dose chemotherapy with stem cell support. Treatment options for relapsed or refractory aggressive NHL include single agent chemotherapy such as vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone, gemcitabine, or rituximab, but often these agents have limited efficacy. If required, granulocyte colony-stimulating factor (G-CSF) can be used adjunctively with chemotherapy.

The technology

Pixantrone dimaleate (Pixuvri, Cell Therapeutics) is an aza-anthracenedione analogue and inhibitor of topoisomerase II. It is administered intravenously.

Pixantrone dimaleate does not currently have UK marketing authorisation for the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma. It is being studied as monotherapy in clinical trials compared to other chemotherapeutic agents (vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone, gemcitabine or rituximab) in people with relapsed aggressive non-Hodgkin's lymphoma who have received at least two prior therapies and whose disease is sensitive to treatment with anthracyclines. Patients were considered to be sensitive to anthracyclines in the clinical trial if they had previously responded to anthracycline or anthracenedione and had relapsed after a response duration of at least 6 months.

Intervention(s)	Pixantrone dimaleate
Population(s)	Adults with relapsed or refractory aggressive non-Hodgkin's lymphoma who have received at least 2 prior therapies and are sensitive to treatment with anthracyclines.
Comparators	• vinorelbine • oxaliplatin • ifosfamide • etoposide • mitoxantrone • gemcitabine • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 65, September 2003, 'Rituximab for aggressive non-Hodgkin's lymphoma'. Appraisal on static list since 2006. Related Guidelines: Clinical Guideline No. CSGHO, October 2003, 'Improving outcomes in haemato-oncology cancer'.

Questions for consultation

Have the most appropriate comparators for the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma been included in the scope? Are the comparators listed routinely used in clinical practice in the UK?

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

Do you consider pixantrone dimaleate in the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma 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 pixantrone dimaleate in the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma 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.

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)