NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

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

Final scope

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 for whom treatment with single agent chemotherapy is being considered.

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 may include malaise, weight loss, fevers and night sweats, as well as local pain and restriction in movement associated with enlarged lymph nodes.

The optimum management of NHL depends on the precise identification of the type of lymphoma and an accurate staging of the disease. 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 region 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. Approximately half of all NHL is aggressive and up to 50% of aggressive NHL may become refractory to treatment over time. The incidence of NHL increases with age, and rises sharply in people over 50 years and more than 70% of all NHL is 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. People with aggressive NHL whose disease does not respond to first-line treatment may receive platinum-based chemotherapy with or without rituximab or single-agent chemotherapy (if they cannot be treated with combination chemotherapy) as second-line treatment options. High-dose chemotherapy with stem cell support may then be considered as a subsequent line of therapy, otherwise single-agent chemotherapy is usually given when disease relapses or becomes refractory to prior treatments. Treatment options for relapsed or refractory aggressive NHL include monotherapy with vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone or gemcitabine, but often these agents have limited efficacy.

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 with other chemotherapeutic agents (vinorelbine, oxaliplatin, ifosfamide, etoposide, mitoxantrone, gemcitabine or rituximab) in people with relapsed aggressive non-Hodgkin's lymphoma which is sensitive to treatment with anthracyclines. Patients were considered to be sensitive to anthracyclines in the clinical trial if their disease 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 whose disease is sensitive to treatment with anthracyclines and who would otherwise be treated with single-agent chemotherapy as a second or subsequent line of treatment.
Comparators	• vinorelbine • oxaliplatin • ifosfamide • etoposide • mitoxantrone • gemcitabine

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'.