NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Temsirolimus for the treatment of relapsed or refractory mantle cell lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of temsirolimus within its licensed indications for the treatment of relapsed or refractory mantle cell lymphoma.

Background

Mantle cell lymphoma is a rare but frequently aggressive B-cell lymphoma in which the tumours are composed of cells from the 'mantle' zone of the lymph node. Mantle cell lymphoma represents five to six percent of all non-Hodgkin lymphoma cases. It is estimated to have an incidence of approximately 500 new cases per year in the United Kingdom, is more common in people over the age of 50, and is three times more common in men than in women.

Symptoms of mantle cell lymphoma include loss of appetite and weight loss, nausea and/or vomiting, indigestion, abdominal pain or bloating, discomfort due to an enlarged liver or spleen, pressure or pain in the lower back, or fatigue due to anaemia. The clinical course of mantle cell lymphoma is characterised by a high response to initial therapy but with a relative short time to progression. Median overall survival is three to five years after diagnosis and one to two years after relapse.

Clinical management of mantle cell lymphoma is often complex and the prognosis remains poor. Not all people with mantle cell lymphoma require immediate treatment. For those people who have slow disease progression, a period of 'watchful waiting" (during which the patient is closely monitored, before treatment is started) may be appropriate. However, the majority of people with mantle cell lymphoma have advanced stage disease at diagnosis and are treated immediately. There is great variability in the treatment of mantle cell lymphoma in clinical practice. A number of combination chemotherapies (with or without rituximab) are available for first line treatment and these may be given in combination with radiotherapy, interferon-alfa and corticosteroids for aggressive disease. High dose chemotherapy with stem cell transplantation may be used. Second line treatment may depend upon patient comorbidities, side effect profiles and prior chemotherapies. For some patients, the sequential use of standard chemotherapy regimens or aggressive combination chemotherapy regimens with rituximab may be treatment options. People experiencing multi-relapsed disease often become intolerant to combination chemotherapies, however presently there is no consensus on standard care for this group. A range of single agents may be

used, including fludarabine, chlorambucil, gemcitabine, etoposide, cladribine, thalidomide, vinblastine, alemtuzumab, and lenalidomide.

The technology

Temsirolimus (Torisel, Wyeth Pharmaceuticals) is a mammalian target of rapamycin (mTOR) signal transduction inhibitor which blocks a number of signal transduction pathways involved in cell cycle regulation.

Temsirolimus has a UK marketing authorisation for the treatment of adults with relapsed and/or refractory mantle cell lymphoma.

Intervention(s)	Temsirolimus
Population(s)	People with relapsed and/or refractory mantle cell lymphoma
Standard comparators	• single and combination treatment regimens that may include chemotherapy (such as gemcitabine or fludarabine), or immunomodulators (such as rituximab) • best supportive care
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. TA65, September 2003, Rituximab for aggressive non-Hodgkin's lymphoma. Technology Appraisal No. TA110, September 2006, Rituximab for the treatment of follicular lymphoma. Technology Appraisal No. TA137, February 2008, Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (review of technology appraisal guidance 37).