NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Trabectedin for the treatment of advanced metastatic soft tissue sarcoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of trabectedin within its licensed indication for the treatment of advanced metastatic soft tissue sarcoma.

Background

Soft tissue sarcomas (STSs) are a heterogeneous group of cancers which develop from cells in the soft, supporting tissues in the body including muscle, fat and blood vessels. Most sarcomas occur within the limbs, other sites being the head and neck area, the abdomen. STS can sometimes also be associated with specific organs such as the womb (uterus). STS is a comparatively rare cancer, with a UK incidence of around 1300 people per year making up less than 1% of all cancers. It affects people of all ages. It is estimated that each year there are 500–600 UK patients with advanced metastatic STS. If identified before metastasis occurs, the 5-year survival for STS can be up to 90%. However once metastasised, median survival is estimated to be 8–12 months and 5-year survival falls to around 10–15%.

There are many types of STS; common types include leiomyosarcoma which arises from smooth muscle tissue and liposarcoma which develops from fat cells. The histological grade of the cell, rather than the tissue of origin, is more predictive of prognosis, as are the site and size of the tumour.

Initial treatment for localised disease is surgery, and may be curative. Where metastases occur, surgical invention may be possible for some patients alongside radiotherapy and sometimes chemotherapy. If surgical intervention is not appropriate chemotherapy alone may be used. The standard chemotherapy treatments for metastatic STS are doxorubicin and ifosfamide monotherapy or in combination regimens. Doxorubicin is usually administered as an out-patient and ifosfamide which may be given as an in-patient or as an out-patient, depending on the dosage. In general the different types of STS are managed in the same way though there are important exceptions, such as gastrointestinal stromal tumours (GIST) or rhabdomyosarcomas, for which different treatment protocols are followed.

The technology

Trabectedin (Yondelis, PharmaMar) is an alkylating anticancer agent which causes damage to DNA, disrupting cell processes and leading to cell death. It

also inhibits the expression of multi-drug resistance. Originally a natural extract, trabectedin is now produced synthetically.

Trabectedin has a marketing authorisation for the treatment of patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents. The therapeutic indications section of the summary of product characteristics (SPC) specifies that efficacy data are based mainly on liposarcoma and leiomyosarcoma patients. The SPC also states that trabectedin must not be used for children and adolescents until safety and efficacy in these groups has been established.

Trabectedin is administered by intravenous infusion over 24 hours.

Intervention(s)	Trabectedin
Population(s)	Adults with advanced metastatic soft tissue sarcoma after failure of anthracyclines and ifosfamide, or whom these agents are unsuitable.
Current standard comparators	Best supportive care
Outcomes	Outcomes to be considered include: • overall survival • progression-free survival • response rates (including disease stabilisation) • 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 a NHS and Personal Social Services Perspective.

Other considerations	If evidence allows different histological types of STS with improved response to trabectedin or other non-standard chemotherapy regimens will be considered as subgroups. Details of the components of best supportive care should be clearly described. Guidance will be issued in accordance with the marketing authorisation. Trabectedin may be continued if disease stabilisation is achieved in the absence of disease progression Special consideration should be given as to whether the appraisal of trabectedin in GIST and rhabdomyosarcomas should be carried out given that these conditions follow different treatment protocols.
Related NICE recommendations	Related Guidelines: NICE Cancer service guidance, March 2007. Improving outcomes for people with sarcoma.