NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Ridaforolimus for the first-line maintenance treatment of metastatic soft tissue or bone sarcoma

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ridaforolimus within its licensed indication for the first-line maintenance treatment of metastatic soft tissue or bone sarcoma.

Background

Sarcomas are a heterogeneous group of cancers thought to have a common embryological origin, and can be broadly divided into those arising in the soft tissue and those arising in the bone. Soft tissue sarcomas develop from cells in the soft, supporting tissues in the body including muscle, fat and blood vessels and often occur in the limbs, head and neck area, and the abdomen. There are many types of soft tissue sarcoma. Common types of soft tissue sarcoma include leiomyosarcomas, which arises from smooth muscle tissue, and liposarcomas, which develops from fat cells. Bone sarcomas (which are primary bone cancers) can arise in any part of the skeleton, including the cartilage and joints. There are many types of bone sarcoma. Osteosarcoma and Ewing's sarcoma are the most common bone sarcomas, most often arising in the long bones of the arms and legs. Other types of bone sarcoma include, but are not limited to, chondrosarcoma (originating in the cartilage) and spindle cell sarcoma.

Soft tissue and bone sarcomas account for less than 1% of all cancers. In 2007, there were 2067 people diagnosed with soft tissue or bone sarcoma in the UK of which 500 to 600 had advanced or metastatic disease. Bone sarcoma occurs less frequently than soft tissue sarcoma, comprising roughly one quarter of all sarcomas. The incidence of soft tissue sarcoma increases with age, although a third of people diagnosed are under 50 years of age. Osteosarcoma and Ewing's sarcoma are often diagnosed in people under the age of 20. Chondrosarcoma and spindle cell sarcoma are often diagnosed in middle age.

Metastatic cancer refers to a cancer that has spread from the original tumour site to a distant part or parts of the body. If identified before metastasis occurs, the 5-year survival for sarcoma 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%. Initial treatment for localised soft tissue and bone sarcoma includes a combination of surgery to remove the tumour (which in the case of bone sarcoma may involve limb sparing surgery or amputation), and chemotherapy. If surgical intervention is not appropriate, chemotherapy

alone may be used. Radiotherapy may be curative or palliative, depending on the type of sarcoma.

The standard first-line chemotherapy for the treatment of metastatic soft tissue sarcoma is doxorubicin and ifosfamide, used either as monotherapy or in combination regimens. For bone sarcoma several chemotherapy regimens can be used depending on the type of tumour. For example, standard multi-agent first-line treatments for osteosarcoma include cisplatin and doxorubicin, or high dose methotrexate and ifosfamide. First-line treatment for Ewing's sarcoma may include vincristine, ifosfamide, doxorubicin, etoposide and actinomycin D.

Maintenance therapy (therapy taken immediately after first line chemotherapy until disease progression) is not currently part of routine care for patients with soft tissue or bone sarcoma.

The technology

Ridaforolimus (Brand name unknown; Merck Sharp & Dohme and ARIAD Pharmaceuticals) is a protein inhibitor which stops cell growth and division, and also inhibits the formation of new blood vessels in the tumours and surrounding tissue. It is administered orally until disease progression.

Ridaforolimus does not have a UK marketing authorisation for the treatment of soft tissue and bone sarcoma. It is currently being studied in a clinical trial as maintenance therapy compared with placebo in people aged 13 years or older with metastatic soft tissue or bone sarcoma whose disease has responded to treatment with at least 4 cycles of standard first-line chemotherapy.

Intervention(s)	Ridaforolimus
Population(s)	People aged 13 years or older with metastatic soft tissue or bone sarcoma, following response to treatment with first-line chemotherapy
Comparators	Standard management without ridaforolimus
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. 185, Feb 2010, 'Trabectedin for the treatment of advanced soft tissue sarcoma', Review Date Feb 2013 Technology Appraisal in Preparation, 'Mifamurtide for the treatment of osteosarcoma', Earliest anticipated date of publication TBC. Related Guidelines: Cancer service guidance, March 2006, Improving outcomes for people with sarcoma.

Questions for consultation

Should the populations for soft tissue sarcoma and bone sarcoma be considered separately?

How should standard management without ridaforolimus be defined? Are there any other comparators for the maintenance treatment of metastatic soft tissue or bone sarcoma which should be included?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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.

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)