Appendix ?

CONFIDENTIAL until minded referral announced (remove before consultation)

Scope: **Mifamurtide for osteosarcoma**

Document cover sheet
Remove before consultation

Timing	Action	Who	Initials	Date
pre-referral				
	Pre-referral draft scope forwarded to TA for comment	TL	PK	12/10/07
	Pre-referral draft scope updated following TA review	TL/TA	JR	23/10/07
	Pre-referral draft scope updated following CD review	TL/TA	JR	12/12/07
	Pre referral draft scope updated with **tracked changes** following consultation and scoping workshop	TL	PK	26/02/08
post-referral				
	Scope reviewed and updated if necessary	TL/IS		
If necessary	second consultation on scope	TL		
	scope updated following consultation	TL		
7 weeks before invitation to participate	Scope sign off report completed	TL/TA/ PM		
5 weeks before invitation to participate	Final scope signed off	AD		

Appendix ?

CONFIDENTIAL until minded referral announced (remove before consultation)

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Mifamurtide for osteosarcoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of mifamurtide within its licensed indications as an adjunct to multi-agent chemotherapy for the treatment of osteosarcoma

Background

Osteosarcoma is the most common type of primary bone cancer. It occurs predominantly in children and young adults, with 80% of tumours occurring in the long bones of the arms and legs. In older patients, it may arise secondary to radiation or Paget's disease.

The exact causes of osteosarcoma are unknown, possible risk factors could be genetic, radiotherapy for other cancers, previous damage to bones and certain bone diseases. Symptoms usually include pain, redness, swelling and heat as the tumour grows. Often it can cause the bone to fracture by weakening it. In addition, other symptoms include tingling or numbness if the tumour squeezes a nerve.

In England and Wales there were 445 cases of primary bone cancer registered in 2002, with 279 deaths in 2004. Osteosarcoma accounts for around one-third of all primary bone cancers, with an estimated UK incidence of around 150 patients per year. Around 30 children a year develop osteosarcoma in the UK. It is more common in teenagers and young adults and more common in boys than girls.

Osteosarcoma is can be divided into high grade or low grade according to its appearance under a microscope. High grade osteosarcomas are the most common. Staging is commonly based on histological grade, extension through the bone surface and the presence of detectable metastases. According to this system osteosarcomas can be placed in the following stages:

- Stage 1 – low-grade tumour
    - Stage 1A completely found within the hard coating of the bone (intracompartmental).
    - Stage 1B extending outside the bone into the soft tissue spaces, which contain nerves and blood vessels (extracompartmental).

- Stage 2 – high-grade tumour
    - Stage 2A completely found within the hard coating of the bone (intracompartmental)
    - Stage 2B extending outside the bone into the soft tissue spaces, which contain nerves and blood vessels (extracompartmental)
- Stage 3 – the cancer can be low-grade or high-grade and has spread to other parts of the body, or to other bones not directly connected to the bone where the tumour started.

Although it does not form part of the staging system, anatomical location for the tumour is also prognostically important.

The high-grade non-metastatic type of osteosarcoma accounts for 80-90% of all cases. The overall 5-year survival of patients diagnosed with osteosarcoma between 1992 and 1996 was 57%. The five-year survival rates for specific stages of the disease are 90% for low grade and still localised disease (stage 1), 55% for high grade and still localised disease (stage 2) and less than 10%.for metastatic disease (stage 3). There has been no major improvement in survival or treatment in the last two decades.

Current management comprises surgery and chemotherapy. The primary aim of surgical resection and chemotherapy is patient survival. Chemotherapy may be used preoperatively to facilitate excision (induction) and postoperatively (adjuvant therapy). Most standard regimens include doxorubicin and cisplatin and may also include methotrexate and ifosfamide. Limb salvage is often possible but preservation of function is always a secondary to the aim of cure.

The technology

Mifamurtide (Mepact, IDM Pharma Inc.) is an immune adjuvant macrophage stimulant. It is under investigation as an additive therapy for patients with osteosarcoma, following surgical resection and in combination with post-operative multi-agent chemotherapy. It is administered as an intravenous infusion. It does not currently have a marketing authorisation.

Intervention(s)	Mifamurtide in combination with post-operative multi-agent chemotherapy
Population(s)	People with osteosarcoma who have had surgical resection
Standard comparators	Post-operative multi-agent chemotherapy alone

Outcomes	The outcome measures to be considered include: • overall survival • disease free survival • 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. If the evidence allows, and if included in the marketing authorisation, the following groups will be included • people with osteosarcoma related to Paget's disease • people with metastatic osteosarcoma • people with relapsed osteosarcoma
Related NICE recommendations	Related Guidelines: Cancer service guidance March 2006, 'Improving outcomes for people with sarcoma'