NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

NBTXR-3 for treating soft tissue sarcoma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of NBTXR-3 within its CE marked indication for neoadjuvant treatment of soft tissue sarcoma.

Background

Sarcomas are a rare and diverse group of cancers that arise from cells that make up the connective tissue structure. They can be broadly divided into soft tissue and bone sarcomas. 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 include leiomyosarcomas, which arise from smooth muscle tissue, and liposarcomas, which develop from fat cells.

Soft tissue sarcomas account for about 1% of all cancers[1]. About 3,330 people are diagnosed with a soft tissue sarcoma every year[2]. In general, patients with a soft tissue sarcoma diagnosis tend to be younger than the majority of people with other types of cancer, around 16% of bone or soft tissue sarcomas are diagnosed in patients less than 30 years old and 37% in patients less than 50[2]; incidence increases with age[1]. Extremity and superficial trunk sarcomas are the most common site for soft tissue sarcomas and make up 60% of all adult cases[1].

All people with limb, limb girdle or trunk soft tissue sarcoma should undergo definitive surgical resection (NICE Cancer Service Guidance 9: improving outcomes for people with sarcoma). The tumour is removed with a margin of normal tissue with the aim of removing all cancer cells and lowering the chance of relapse. Patients with tumours that, because of size or position, are considered borderline resectable may have pre-operative treatment with radiotherapy or chemotherapy[3]. The choice of pre-operative treatment is dependent on the histology of the tumour and the performance status of the patient[3].

The technology

NBTXR-3 (Brand name unknown, Nanobiotix) is a nanoparticle formation of hafnium oxide. The NBTXR-3 nanoparticles are implanted into tumours by injection and work by amplifying the effect of radiotherapy to generate more free radicals, which destroy tumour cells.

NBTXR-3 does not currently have a CE mark for treating soft cell sarcoma. It has been studied in a clinical trial in combination with radiotherapy compared

with radiotherapy alone as a neoadjuvant treatment in adults with locally advanced, unresectable soft tissue sarcoma of the extremity or trunk wall.

Intervention(s)	NBTXR-3 in combination with radiotherapy
Population(s)	People with locally advanced soft tissue sarcoma for whom neoadjuvant radiotherapy is suitable
Comparators	• Radiotherapy
Outcomes	The outcome measures to be considered include: • response rate • tumour volume changes • resection margins • relapse rate • overall 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 CE marking. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the CE marking granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Olaratumab in combination with doxorubicin for treating advanced soft tissue sarcoma' (2017). NICE Technology Appraisal 465. Review date August 2020. 'Trabectedin for the treatment of advanced soft tissue sarcoma' (2010). NICE Technology Appraisal 185. Guidance on Static List.

	Appraisals in development (including suspended appraisals) 'ridaforolimus for the maintenance treatment of metastatic soft tissue or bone sarcoma' NICE technology appraisals guidance ID415. Publication date to be confirmed. Related Guidelines: 'Improving outcomes for people with sarcoma' (2006). NICE guideline CSG9 Review date March 2019. Related Quality Standards: Sarcoma (2015) NICE quality standard 78 Related NICE Pathways: Sarcoma (2017) NICE pathway
Related National Policy	NHS England (2016) Manual for prescribed specialised services 2016/17 Chapters 90, 94, 105. NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Soft Tissue Sarcoma (Adult) Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,4 and 5 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

Questions for consultation

Is the population defined appropriately?

- Would NBTXR-3 be suitable for all people with locally advanced soft tissue sarcoma for whom neoadjuvant therapy is suitable?
- What defines the need for neoadjuvant radiotherapy?

Have all relevant comparators for NBTXR-3 been included in the scope?

- Is neoadjuvant chemotherapy a relevant comparator in people for whom treatment with NBTXR-3 is suitable? Is it used in combination with radiotherapy?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom NBTXR-3 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider NBTXR-3 will fit into the existing NICE pathway, Sarcoma?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which NBTXR-3 will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider NBTXR-3 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 NBTXR-3 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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/article/pmg19/chapter/1-Introduction).

References

1 NHS England 2014 '2013/14 NHS Standard Contract for Cancer: Soft Tissue Sarcoma (Adult). B12/S/a'

2 Sarcoma UK (2015) 'Understanding Sarcoma' [Accessed September 2017]

3 Dangoor A., Seddon B., Gerrand C., Grimer R., Whelan J., Judson I. (2016) UK guidelines for the management of soft tissue sarcomas Clinical Sarcoma Research 6:20.