NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pexidartinib for treating symptomatic tenosynovial giant cell tumour

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pexidartinib within its marketing authorisation for treating symptomatic tenosynovial giant cell tumour.

Background

Tenosynovial giant cell tumours (TGCT) are a group of rare, benign tumours that involve the synovium (connective tissue in joints), bursae (fluid-filled sac around a joint) and tendon sheath (synovial membrane around a tendon). The tumours cause the synovium, bursae and tendon sheaths to grow and thicken. This can cause damage to the surrounding tissues of the body. The disease is progressive, and symptoms include pain, swelling and restricted movement of the joint. The tumours can affect large or small joints. The World Health Organization categorised the tumours into 2 distinct types:

- giant cell tumour of the tendon sheath (GCT-TS), a localised form that can be within or outside the joint, usually affecting smaller joints such as the hands and feet, and

- pigmented villonodular synovitis (PVNS), also called diffuse-type, which usually affects large joints such as the knee or hip.

However, these categories are under review.

The main treatment for TGCT is surgery to remove some or all of the synovium, although the tumour can recur, particularly in PVNS. Surgery also comes with the risk of complications. Radiation therapy may be used, either alone or as an adjunct to surgery. Imatinib or nilotinib may be options for extensive or recurrent TGCTs[2] although these treatments do not have marketing authorisations for this indication.

TGCT mainly affects adults between 20 and 50 years. The annual incidence has been estimated at between 11 and 43 in 1,000,000[1]. This would equate to between approximately 600 and 2400 cases per year in England. Around 780 tenosynovial giant cell tumours were registered in England in 2017. Of these around 270 people (200 with diffuse GCT and 70 with localised GCT-TS) are estimated to have GCT not amenable to improvement with surgery and would be eligible for pexidartinib.

The technology

Pexidartinib (Turalio, Daiichi Sankyo) is a small-molecule tyrosine kinase inhibitor that targets colony stimulating factor 1 receptor (CSF1R). By blocking this receptor, pexidartinib is expected to block the activity of macrophage colony-stimulating factor, preventing tumour growth and helping to delay the onset of symptoms of the disease. Pexidartinib is administered orally.

Pexidartinib does not currently have a marketing authorisation in the UK for treating TGCT. It has been studied in a clinical trial in people with symptomatic TGCT for

whom surgery would be associated with potentially worsening functional limitation or severe morbidity.

Intervention(s)	Pexidartinib
Population(s)	People with symptomatic TGCT for whom surgery is not appropriate
Comparators	Established clinical management without pexidartinib
Outcomes	The outcome measures to be considered include: • response rates • pain • stiffness • 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	If the evidence allows, the following subgroups will be considered. These include: • giant cell tumour of the tendon sheath • pigmented villonodular synovitis. Guidance will only be issued in accordance with the marketing authorisation. 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 marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related NICE Pathways: Musculoskeletal conditions
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is the population listed appropriate? In what circumstances would surgery be considered inappropriate to treat symptomatic TCGT?

Have all relevant comparators for pexidartinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for symptomatic tenosynovial giant cell tumour when surgery is not appropriate?

Are the outcomes listed appropriate?

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

Where do you consider pexidartinib will fit into the existing NICE pathway, musculoskeletal conditions?

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 pexidartinib 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 pexidartinib 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 pexidartinib 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 Giustini N et al (2018) Tenosynovial giant cell tumor: case report of a patient effectively treated with pexidartinib (PLX3397) and review of the literature. Clinical Sarcoma Research 8 (14).

2 Verspoor, Floortje GM (2018) Tenosynovial Giant Cell Tumours. The good, the bad and the ugly. [online; accessed 12 November 2019]

