NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Palovarotene for preventing heterotopic ossification associated with fibrodysplasia ossificans progressiva

Draft scope

Draft remit/evaluation objective

To evaluate the benefits and costs of palovarotene within its marketing authorisation for preventing heterotopic ossification associated with fibrodysplasia ossificans progressiva for national commissioning by NHS England.

Background

Fibrodysplasia ossificans progressiva (FOP; also known as myositis ossificans progressiva) is a very rare, severely disabling and life-shortening genetic disorder. FOP is usually diagnosed in the first decade of life when children develop painful inflammatory swellings of soft tissue (muscle and connective tissue such as tendons and ligaments) called 'flare ups'. The appearance of inflammatory swelling is usually spontaneous but can also be provoked by any injury to the muscles such as trauma, surgery or viral infection. Over time these areas of soft tissue inflammation are gradually replaced by heterotopic ossification (extra-skeletal bone). The abnormal bone formation results in progressive movement restriction in the affected areas. Most people with FOP need to use a wheelchair by early adulthood and need lifelong assistance in performing activities of daily living. They may also have difficulty speaking and eating because of bone deposits in the mandibular joint (jaw) that make it difficult to fully open the mouth, which in turn may lead to malnutrition. Extra-skeletal bone formation around the rib cage can restrict expansion of the lungs and result in breathing difficulties. The median life expectancy for people with FOP in the UK is around 40 years.[1]

There are estimated 50-80 people living with FOP in the UK.[2,3]

There are currently no curative treatment options for the condition; anti-inflammatory medicines provide symptomatic relief but do not reduce the frequency of heterotopic ossification episodes. Usually corticosteroids are used to reduce inflammation at the mandibular joint during acute flare-ups and non-steroidal anti-inflammatory medication is used between flare-ups. Preventative management also involves measures to reduce the number and impact of falls (e.g. improvement in household safety, use of protective headgear), respiratory decline (e.g., incentive spirometry), and viral infections.

The technology

Palovarotene is an oral, once-daily, retinoic acid receptor-γ (RAR-γ) agonist, which binds to bone morphogenetic protein (BMP) receptors to prevent

abnormal bone formation in people with FOP. BMPs function in the regulation of cellular activities involved with the thickening and scarring of connective tissue (fibrosis).

Palovarotene does not currently have a marketing authorisation in the UK for preventing heterotopic ossification associated with FOP. It is being studied in a single arm clinical trial to prevent heterotopic ossification in people aged 4 and older with FOP.

Intervention	Palovarotene
Population	People with clinically diagnosed fibrodysplasia ossificans progressiva
Comparators	Established clinical management without palovarotene
Outcomes	The outcome measures to be considered include: • amount of new heterotopic ossification • rate of soft tissue swelling (flare-ups) • changes in movement and physical function (including active range of motion) • overall survival • adverse effects of treatment • health-related quality of life.
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• cost effectiveness using incremental cost per quality-adjusted life year • patient access schemes and other commercial

	agreements • the nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	• Guidance will only be issued in accordance with the marketing authorisation. • Guidance will take into account any Managed Access Arrangements.
Related NICE recommendations and NICE Pathways	None
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 3, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 2013/14 NHS Standard Contract for Specialised Rheumatology Services (Adult) https://www.england.nhs.uk/wp-content/uploads/2013/06/a13-spec-rheumatology.pdf

Questions for consultation

Have all relevant comparators for palovarotene been included in the scope?

Which treatments are considered to be established clinical management in the NHS for preventing heterotopic ossification associated with fibrodysplasia ossificans progressiva?

Are cytochrome P450 inhibitors or inducers or kinase inhibitors like imatinib used to treat fibrodysplasia ossificans progressiva in the NHS?

Are the outcomes listed appropriate?

How is new heterotopic ossification measured?

How is fibrodysplasia ossificans progressiva diagnosed in the NHS?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

Are there any differences in the treatment of fibrodysplasia ossificans progressiva in children compared with adults?

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 palovarotene 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 Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

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)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-

guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

References

1. FOP Friends (2021) What is FOP? Accessed November 2021.

2. Estimate by Ipsen.

3. Liljesthrom et al. (2020) Epidemiology of the Global Fibrodysplasia Ossificans Progressiva (FOP) Community. Journal of Rare Diseases Research and Treatment. 5(2): 31-36.