NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Palovarotene for preventing heterotopic ossification associated with fibrodysplasia ossificans progressiva

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of palovarotene within its marketing authorisation for preventing heterotopic ossification associated with fibrodysplasia ossificans progressiva.

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). Heterotopic ossification in the soft tissue surrounding the joints drives the disability in FOP, as it causes loss of joint function, stiffness and, over time, 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 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 is around 56 years.[1]

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

There are currently no disease modifying 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 (brand name unknown, Ipsen) 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 confirmed by genetic testing
Comparator	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) • respiratory function • overall survival • adverse effects of treatment (including growth and final height) • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	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	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

References

1. Kaplan et al (2010) Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva. Journal of Bone and Joint Surgery. 92: 686–691.

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.