NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Burosumab for treating X-linked hypophosphataemia in adults

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of burosumab within its marketing authorisation for treating X-linked hypophosphatemia (XLH) in adults.

Background

X-linked hypophosphataemia (XLH) is a genetic disorder characterised by low levels of phosphate in the blood. Excess activity of a type of signalling peptide FGF23 results in phosphate being abnormally processed in the kidneys, which causes a loss of phosphate in the urine (phosphate wasting) and leads to soft, weak bones.

It is the most common form of hereditary hypophosphatemia and is equally common in both sexes. Clinical manifestations of XLH vary in severity, but patients most commonly present in childhood with bowed or bent legs, disproportionate short stature, bone pain, delayed walking, and dental anomalies.[1] Symptoms generally present at 12–15 months of age, however symptoms can be misdiagnosed as vitamin D deficient rickets, especially if there is no family history of XLH.[2] In adults, the main manifestations of XLH include bone pain, fractures and pseudofractures, joint stiffness and restricted movement (as a result of enthesopathy), neurological complications, including hearing problems, and, in severe cases, spinal cord compression. Many adults will eventually develop hyperparathyroidism. The burden of the disease can also impact mental health, which may lead to depression and anxiety. It is estimated that there are between 400 and 500 adults with XLH in England currently registered at clinics, with as many as 1,000 people including those who are not registered or are undiagnosed.

There are currently no treatments that target the underlying cause of XLH in adults. There is no consensus on the management of XLH in adults however options include +phosphate supplementation, vitamin D analogues such as alfacalcidol or calcitriol, or supportive care. Conventional therapy is taken 4-6 times a day which interferes with usual activities including work and can disturb sleep. Management of XLH differs across treatment centres, for example phosphate is not always offered to adults without fractures because of the risks of treatment-related complications such as hyperparathyroidism but most people with XLH receive treatment. Corrective surgery of skeletal deformities and joint replacements may be required.

The technology

Burosumab (Crysvita, Kyowa Kirin) is an anti-FGF23 human monoclonal antibody which improves phosphate homeostasis by targeting excess FGF23. Burosumab binds to FGF23 rendering it inactive, and thereby restores renal tubular reabsorption of phosphate and increases the production of 1,25-dihydroxyvitamin D which enhances intestinal absorption of calcium and phosphate. Burosumab is administered by subcutaneous injection.

Appendix B

Burosumab has a marketing authorisation in the UK for the treatment of X-linked hypophosphataemia in children (ages 1-17) with radiographic evidence of bone disease and in adults.

Intervention(s)	Burosumab
Population(s)	Adults with X-linked hypophosphatemia
Comparators	Established clinical management without burosumab (including vitamin D analogues and phosphate supplementation)
Outcomes	The outcome measures to be considered include: • fractures • pain (including bone pain, joint pain and joint stiffness) • motor skills • tooth loss and pain • neurological complications (including problems with hearing and balance, and spinal cord compression) • renal function • parathyroid hormone levels • alkaline phosphatase levels • mortality • adverse effects of treatment • health-related quality of life (for patients and carers).
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. 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 Technology Appraisals: Burosumab for treating X-linked hypophosphataemia in children and young people (2018) NICE highly specialised technology guidance 8.

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Cochrane Database of Systematic Reviews (2005): Recombinant growth hormone therapy for X-linked hypophosphatemia in children
2. XLH Network. Learn About XLH. Accessed September 2020 https://xlhnetwork.org/learn-about-xlh

