NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Burosumab for treating X-linked hypophosphataemia in adults

Draft 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 hormone 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 and fractures, joint stiffness and restricted movement (as a result of enthesopathy), neurological complications and, in severe cases, spinal cord compression. Many adults will eventually develop hyperparathyroidism. It is estimated that there are up to 2,500 adults with XLH in England.

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 because of the risks of treatment-related complications such as hyperparathyroidism. 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. KRN23 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. KRN23 is administered by subcutaneous injection.

Burosumab has a marketing authorisation in the UK for the treatment of X-linked hypophosphataemia in children (ages 1-17) but not in adults. It has been studied in adults with XLH in clinical trials that have a single arm (no comparator) or are placebo-controlled.

Intervention(s)	Burosumab
Population(s)	Adults with X-linked hypophosphatemia
Comparators	Established clinical management without burosumab
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 increased intracranial pressure, craniosynostosis, 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 Guidelines: None

	Related Public Health Guidance/Guidelines: None Related Quality Standards: None Related NICE Pathways: None
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

Questions for consultation

Is the adult population of adults with XLH in England accurate?

Are adults with XLH treated in a small number of specialist centres?

What proportion of adults with XLH were diagnosed in adulthood?

Which treatments are considered to be established clinical practice in the NHS for XLH?

Are the outcomes listed appropriate?

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

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 burosumab 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 burosumab 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 burosumab 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

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

