NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Burosumab for treating X-linked hypophosphataemia

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of burosumab within its licensed indication for treating X-linked hypophosphataemia for national commissioning by NHS England.

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, and diagnosis can be sooner if there is a 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 approximately 250 children and young people with XLH in England, and up to 2,500 adults with the condition.

There are currently no treatments that target the underlying cause of XLH and medical management is aimed at improving growth, decreasing morbidity, and preventing skeletal deformities. XLH does not respond to vitamin D supplementation alone. The current standard of care for children is multiple daily doses of phosphate, in combination with active vitamin D analogues (alfacalcidol or calcitriol) to prevent secondary hyperparathyroidism that can be induced by phosphate administration. The effectiveness of this treatment is limited because phosphate levels cannot be maintained at appropriate levels to allow mineralisation of bone and improve skeletal outcomes, and high-dose oral phosphates have potential safety and tolerability issues. Frequent monitoring and dose adjustment is required. The management of XLH in adults is less consistent; phosphate is not always offered to adults because of the risks of treatment-related complications. Corrective surgery of skeletal deformities and joint replacements may be required.

The technology

Burosumab (brand name unknown, 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.

Burosumab does not currently have a marketing authorisation in the UK. It is being studied in clinical trials in children and adults with XLH. The phase III trial in children compares burosumab with phosphate and vitamin D treatment. The phase III trials in adults are either single arm (no comparator) or placebo-controlled.

Intervention(s)	Burosumab
Population(s)	Children and young people with X-linked hypophosphataemia
Comparators	Established clinical management without burosumab
Outcomes	The outcome measures to be considered include: • fractures • severity of rickets • pain (including bone pain, joint pain and joint stiffness) • motor skills • growth (including height) • tooth loss and pain • skull and spinal deformities • neurological complications (including increased intracranial pressure, craniosynostosis, problems with hearing and balance, and spinal cord compression) • radiographic response • renal function • parathyroid hormone levels • alkaline phosphatase levels • mortality • adverse effects of treatment • health-related quality of life (for patients and carers).

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, and on the delivery of the specialised services	• 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	Department of Health (2016) NHS Outcomes

Policy	Framework 2015-2016. Domains 1, 2, 4 and 5. Department of Health (2013) The UK strategy for rare diseases Nottingham University hospitals NHS trust (2016), Guideline for the Treatment of Hypophosphataemia in Adults NHS England, NHS standard contract 2013/2014: Paediatric medicine: endocrinology and diabetes NHS England, NHS standard contract 2013/2014: Specialised Endocrinology Services (Adult) NHS England, NHS standard contract 2013/2014: Metabolic Disorders (Adult)

References

1. Cochrane Database of Systematic Reviews (2005): Recombinant growth hormone therapy for X-linked hypophosphatemia in children
2. XLH Network. Familial hypophosphatemia. Accessed November 2017 http://xlhnetwork.org/xlh.pl?f=larry/website/VitaminD/Famhypo.html