HST checklist

Burosumab for treating XLH in adults [ID3822]

**MA wording:** CRYSVITA is indicated for the treatment of X-linked hypophosphataemia, in children and adolescents aged 1 to 17 years with radiographic evidence of bone disease, and in adults.

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|  | Criterion Met |
|  | Criterion partially met |
|  | Criterion not met |

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| **Criterion** |  |
| **The target patient group for the technology in its licensed indication is so small that treatment will usually be concentrated in very few centres in the NHS** | The MA currently covers the entire adult population of XLH. A voluntary survey of 14 XLH treatment centres commissioned by NHS England recorded approximately 280 people with genetically confirmed, symptomatic XLH receiving treatment. At the scoping workshop, an additional 70 patients were estimated from the Manchester treatment centre that did not respond to the NHS survey. The clinical experts noted that prevalence is increasing because of better diagnosis and that some patients would not always receive treatment. The NHS survey also cautioned that the survey did not represent all activity for XLH patients because some would only seek treatment for pseudofractures or intermittent treatment. The adult population is therefore a minimum of 350 patients currently receiving treatment, the clinical experts estimated that the true prevalence could be up to 1,000 people including those not currently receiving treatment or are undiagnosed. The company proposed targeting only patients with debilitating symptoms and clinical complications, however the full population within the licensed indication was considered as the target patient group.Note - after the stakeholder listening event: clinician and patient experts confirmed expected patient numbers currently receiving treatment within the marketing authorisation including a prevalence study estimating approximately 784 patients in total with XLH in England. Clinicians and patient experts also considered a targeted subgroup of the population. | **Not Met** |
| **The target patient group is distinct for clinical reasons** | XLH is a clinically distinct genetic condition that needs to be treated differently to other bone metabolic disorders. However, the company considered that only patients with debilitating symptoms and clinical complications would require treatment with burosumab. The company estimated that approximately 50% of patients would be eligible, based on estimates from an early access programme. However, the clinical experts noted that the MA covers all adults with XLH and that there is no clinical distinction or rationale for treating only patients with debilitating symptoms or clinical complications, therefore all adult patients would be treated within the MA. The proposed optimisation would not be distinct for clinical reasons as clinical experts considered all patients with XLH would be treated based on the genetic indication.Note - after the stakeholder listening event: clinicians presented a draft care pathway under development. They considered severe cases to be distinct although there are no single diagnostic criteria such as a clinical event or genetic subtype for differentiating those that have debilitating symptoms and clinical complications that would support restricting use to this subgroup. | **Partially met** |
| **The condition is chronic and severely disabling** | XLH is a lifelong chronic condition, but the disease activity is variable throughout a person’s lifetime. For some patients, XLH is a severely disabling progressive condition and can cause impairments to fracture healing, mobility, bone pain, neurological complications and depression and anxiety. However, the clinical experts explained that symptoms, complications and lifelong disability are most severe and partially determined during bone growth throughout childhood (burosumab is available through HST8 for children). Some patients do not seek treatment, are treated intermittently during pseudofractures, or have skeletal crises only in later life and this is dependent on disease activity.Note - after the stakeholder listening event: clinicians and patient experts presented evidence highlighting that adults have different manifestations of the disease than children. They considered those that those with chronic and severely disabling disease were distinct. | **Partially met** |
| **The technology is expected to be used exclusively in the context of a highly specialised service** | NHS England reported at the scoping workshop that burosumab would be given in a specialised service environment not a highly specialised service. There are currently 15-20 metabolic bone disorders regional specialist centres with 15 responding to the NHS survey and scoping workshop.Note - after the stakeholder listening event: burosumab would be administered through a multidisciplinary team. Clinicians suggested a hub and spoke system based on 3-4 regional networks. | **Not Met** |
| **The technology is likely to have a very high acquisition cost** | The dose used in the clinical trials for adults with XLH is weight-based and therefore the cost of burosumab is expected to be higher for adults than for children, however the dosing schedule is less frequent. The acquisition cost is estimated to be approximately similar to the price used in HST8. | **Met** |
| **The technology has the potential for lifelong use** | Assuming that there are no differences in the clinical response or side effects in the long-term, the technology has the potential for lifelong use. However long-term clinical evidence is limited (maximum study length is 96 weeks). There is also the potential for benefit from short term use in the case of improved fracture healing. The logic of the mechanism of action would suggest permanent lifelong use for all people with XLH to maintain bone mass and decrease chances of skeletal events. | **Met**  |
| **The need for national commissioning of the technology is significant** | There is currently no consensus on how adults with XLH should be treated and no disease modifying treatment beyond symptom management and supplementation. Further, current treatment options may elevate FGF23, which can worsen enthesopathy and lead to secondary hyperparathyroidism. | **Met** |