Provision of galsulfase (Naglazyme®) for long term enzyme replacement therapy in mucopolysaccharidosis VI (N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux-Lamy syndrome) in Wales

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Recommendation:
Galsulfase (Naglazyme®) is recommended as an option for use within NHS Wales for the treatment of patients with long term enzyme replacement therapy in mucopolysaccharidosis VI (N-acetylgalactosamine 4-sulfatase deficiency; Maroteaux-Lamy syndrome)

Background

Galsulfase (Naglazyme®) for treating mucopolysaccharidosis VI (MPS VI) was assigned orphan medicine status in 2001 by the European Medicines Agency and licensed in 2006. The All Wales Medicines Strategy Group (AWMSG) issued a statement of advice for galsulfase in 2013; due to the absence of a submission from the market authorisation holder galsulfase cannot be endorsed for the treatment of MPS VI. Galsulfase was commissioned and routinely available until January 2023, via the Welsh Health Specialised Services Committee (now the Joint Commissioning Committee, JCC). However, following a review, commissioning was withdrawn due to an absence of positive advice from either the National Institute for Health and Care Excellence (NICE) or AWMSG. Galsulfase does not meet the criteria for NICE appraisal and is commissioned by NHS England. Galsulfase is the only licensed medicines for MPS VI. JCC has approached AWTTC to provide advice for galsulfase, highlighting the unmet need which exists for patients with MPS VI. Clinicians have confirmed the need for patient access to galsulfase in Wales. They highlight that a number of studies conclude that galsulfase has a beneficial effect in MPS VI as demonstrated by improvements in survival (Quartel 2019), symptom severity (Lampe et al 2019), and a reduction in progress of the disease (Horowitz et al 2021) (if the medicine is administered as soon as possible following diagnosis) in addition to improvements in ambulation and in respiratory function (Harmatz 2006).

The condition and clinical guidelines

MPS VI is a genetic disorder caused by deficiency in *N*-acetylgalactosamine-4-sulfatase (Tomatsu et al, 2021). Patients are usually diagnosed in the first 6-24 months of life. Life expectancy for those with MPS VI is 20-30 years but patients have been treated into their early sixties (MPS Society). The condition impacts stature, joint mobility, eyes, heart and lungs. MPS VI is classified according to severity of symptoms and progress of the disease can vary from slow to rapidly progressing (Akyol et al, 2019). Paediatric patients in Wales may be referred to the outreach clinics of the Birmingham or Manchester lysosomal storage disorder clinics for multi-disciplinary treatment care (seen every 6 months), alternatively, they may be seen by the individual specialities within Wales. Adult patients would be managed in Wales.

Galsulfase is a recombinant form of human lysosomal enzyme N-acetylgalactosamine 4-sulfatase, an enzyme that is deficient in patients with MPS VI.

Enzyme replacement therapy (ERT) with galsulfase aims to transiently restore N-acetylgalactosamine 4-sulfatase activity, thereby preventing the accumulation of glycosaminoglycans in lysosomal compartments of cells, which causes the clinical manifestations of MPS VI. Results suggest if galsulfase is administered before the age of 16 years, patients have improved growth velocity (Guigliani et al 2014, Hendriksz 2013, Decker 2010, Harmatz 2017). Experts report that MPS VI is sometimes diagnosed in adulthood and for these patients ERT has had beneficial cardiorespiratory changes, therefore galsulfase would be offered to adults as well as to children. Guidelines developed by a global group of experts in 2019 found 89% consensus for the initiation of long term ERT with galsulfase at a dose of 1mg/kg/week by intravenous infusion for patients with MPS, as soon as possible following diagnosis (Akyol et al, 2019).

The only other disease modifying therapy for treating MPS VI is haematopoietic stem cell therapy (HSCT); whilst available as an alternative to ERT, for most patient's clinical opinion suggests the risks outweigh the benefits.

Incidence

Patient support groups estimate an incidence of about 1:600,000, and during a 10-year period between 1989-1999 there were 9 new diagnoses in the UK. [Confidential information removed]

Clinical effectiveness

In the 2006 pivotal study 39 MPS VI patients aged seven years or older were randomised to receive either galsulfase (n=19) or placebo (n=20) for 24 weeks (Harmatz et al 2006). The European Medicines Agency concluded that galsulfase treatment appeared to show limited clinical benefits for MPS VI patients. A Cochrane review of the study concluded (given a risk of bias in the study design and implementation) that it was uncertain whether there was a difference between groups in the 12 minute walking test (the primary endpoint) or in the three minute stair climb, however galsulfase may reduce urinary glycosaminoglycan levels.

Galsulfase has since been validated in clinical trials and long-term post-marketing surveillance studies. Results suggest that early intervention is important and if galsulfase is administered before the age of 16 years patients have improved growth velocity, although comparative data in patients who have not received ERT are limited (Guigliani et al 2014, Hendriksz 2013, Decker 2010, Harmatz 2017). Clinicians report sibling patients with MPS VI where one has started treatment at an earlier stage than the older sibling and the younger patient has shown improved clinical symptoms with fewer complications, and similar results have been reported in studies (e.g. Furujo et al 2017, McGill et al, 2010). Clinical studies show galsulfase results in reductions in urinary glycosaminoglycans, improvements in mobility (six minute walking tests, number of stairs climbed per minute) (e.g. Harmatz et al 2006) and lung function (Giugliani et al 2014). Long term treatment may stabilise the course of MPS VI (Lampe et al 2019) and may improve survival (Quartel 2019).

Cost-effectiveness

An AWTTC literature review did not identify any published cost-utility analyses of galsulfase for the treatment of MPS VI. Notably, the Australian Pharmaceutical Benefits Advisory Committee and Canadian Agency for Drugs and Technologies in Health both grant access to galsulfase (the former through the Life Saving Drugs Program, (Australian Government LSDP for MPS VI) while identifying that the potential for improvement on the 12-minute walking test is associated with a very high cost (CADTH 2016), and concluding that this would likely produce an 'unacceptably high' incremental cost-effectiveness ratio (PBAC, 2007). Currently, there is insufficient information in the public domain to undertake a robust de-novo AWTTC cost-utility analysis to inform a cost-effectiveness decision by AWMSG. The marketing authorisation holder confirms they do not have sufficient resource or available data to inform a cost-utility analysis.

Budget impact

Dosing of galsulfase is weight-based. The average cost per patient per year, based on the list price and assuming an average weight of 30 kg and the recommended dose of 1mg/kg/week, is £306,384. [Confidential information removed]. Galsulfase is supplied by a home healthcare provider in Wales.