NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Olipudase alfa for treating acid sphingomyelinase deficiency (Niemann-Pick disease type B and AB)

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of olipudase alfa within its marketing authorisation for treating acid sphingomyelinase deficiency (Niemann-Pick disease type B and AB) for national commissioning by NHS England.

Background

Niemann-Pick disease is a group of inherited autosomal recessive metabolic disorders. Niemann-Pick types A, B and AB (also collectively known as Acid Sphingomyelinase Deficiency[1]) are caused by mutations in the SMPD1 gene. This gene mutation leads to a deficiency in an enzyme called acid sphingomyelinase, which breaks down a naturally occurring fatty substance called sphingomyelin. The deficiency in this enzyme leads to accumulation of sphingomyelin in cells throughout the body. In Niemann-Pick types A, B and AB, build-up of sphingomyelin occurs in the liver, spleen and lungs.

Signs and symptoms of Niemann-Pick type A develop within the first few months of life and include feeding difficulties; prolonged jaundice; enlargement of the liver and spleen and progressive loss of early motor skills, including ataxia. Signs and symptoms of Niemann-Pick type B usually occur in childhood and include fatigue and exercise intolerance, enlargement of organs, usually starting with the liver or spleen; poor growth; puberty delay; susceptibility to respiratory infections; bleeding problems and bone pain. Life expectancy for people with Niemann-Pick type B is highly variable depending on the severity of symptoms. Some people present with a type AB variant, with symptoms consistent with both type A and B. Symptoms of type AB can range from moderate to severe[2].

It is estimated that around 1 to 2 people are diagnosed with Niemann-Pick type A, B or AB per year. Most are diagnosed in childhood, although it may be difficult to diagnose according to type in young infants. It is estimated that around 40 to 50 people are living with Niemann-Pick type A, B or AB in England, with most of these people having type B disease.

There are currently no specific treatments or cure for Niemann-Pick type B or AB. However, people with Niemann-Pick type B or AB will benefit from supportive or palliative treatments. This includes treatments for managing the symptoms of the disease, including blood transfusions, respiratory support, medication for lipid control and analgesia. Some people with late-stage liver disease caused by the disorder may be offered a liver transplant.

The technology

Olipudase alfa (brand name unknown, Sanofi) does not currently have a marketing authorisation in the UK for Niemann-Pick disease type A or B. It has been studied in clinical trials in adults compared with placebo and in a single arm trial in children.

Intervention(s)	Olipudase alfa
Population(s)	People with acid sphingomyelinase deficiency (also known as Niemann-Pick disease type B or type AB)
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • change in spleen volume • change in lung function • change in liver function and volume • change in physical observations (including observations or measurements from examination of the skin, head, eyes, ears, nose and throat; lymph nodes; heart, vital signs, lungs and abdomen; bone marrow; extremities and joints) • change in weight, height and onset of puberty in children and young people • change in neurological observations (including observations or measurements from examination of coordination; cranial nerves; extrapyramidal features; fundoscopy; gait; motor skills; peripheral nervous system; reflexes; sensory nervous system; strength and mental status) • change in biomarkers (including high sensitivity c-reactive protein; ceramide; iron; cardiac troponin I; ferritin; CCL18 levels; lysophingomyelin, oxysterols, lipid profile,

	interleukin-6; interlukin-8 and calcitonin) • change in fatigue and exercise tolerance • mortality • adverse effects of treatment • health-related quality of life • carer quality of life.
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	None.
Related National Policy	NHS England (2019) The NHS long term plan NHS England (2013) 2013/14 NHS standard contract for metabolic disorders (adult). Service Specification No. E06/S/a NHS England (2013) 2013/14 NHS standard contract for metabolic disorders (laboratory services). Service Specification No. E06/S/c NHS England (2018/2019) Manual for prescribed specialised services 2018/19. Chapter 62, Highly specialist metabolic disorder services (adults and children) Department of Health & Social Care (2021) The UK Rare Diseases Framework Department of Health & Social Care (2019) The UK strategy for rare diseases: 2019 update to the

	Implementation Plan for England Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 and 4.

References

1 National Organization for Rare Disorders (2019) Acid Sphingomyelinase Deficiency. Accessed June 2022

2 Patient UK (2016) Niemann-Pick Disease. Accessed June 2022