NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Arimoclomol for treating Niemann-Pick disease Type C

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of arimoclomol within its marketing authorisation for treating Niemann-Pick disease type C for national commissioning by NHS England.

Background

Niemann-Pick type C (also known as NPC) is a progressive neurodegenerative disorder. It as an autosomal recessive lysosomal storage disorder that affects infants, children and adults. It is characterised by the inability to properly metabolise lipids (fats). Mutations in the NPC genes cause the accumulation of fats – such as sphingomyelin, cholesterol, glycosphingolipids and sphingosine – in the liver, brain and spleen. There are two subtypes (NPC1 and NPC2) caused by mutations in either the NPC1 or NPC2 gene. NPC1 is the most prevalent: approximately 95% of cases are caused by genetic mutations in the NPC1 gene.[1] The incidence of NPC is currently estimated at 1 in 100,000 live births.[1]

Accumulation of lipids lead to a variety of symptoms, including liver and spleen enlargement, liver dysfunction and neurological abnormalities. Children frequently have vertical supranuclear gaze palsy, progressive ataxia, cognitive impairment and cataplexy. Young people and adults have psychiatric illness, dementia and progressive neurological deterioration.[2] Most people also have difficulties with swallowing. The age of onset and severity of symptoms varies substantially from person to person. Patients with neurological onset early in life deteriorate faster and have a shorter life expectancy than those with adult onset.[3] Most people with NPC die between the ages of 10 and 25 years.

Treatment options for NPC include substrate reduction therapy and management of symptoms and complications. Miglustat is a substrate reduction therapy with a marketing authorisation for treating progressive neurological deterioration in children and adults with NPC. Supportive care is directed toward the specific symptoms apparent in each individual. This may include palliative treatment and occupational therapy to help with posture, speech and movement.

The technology

Arimoclomol (MIPLYFFA, Orphazyme) aims to increase the production and activation of molecular chaperone proteins which could increase breakdown of lipids accumulating as result of mutations in the NPC genes. Arimoclomol is administered orally.

Arimoclomol does not currently have marketing authorisation in the UK. It has been compared with placebo in a clinical trial in people with NPC aged between 2 and 18 years and in a single-arm paediatric sub-study in people aged 6 to 24 months.

Intervention(s)	Arimoclomol, alone or in combination with miglustat
Population(s)	People with Niemann-Pick disease Type C
Comparators	• Established clinical management without arimoclomol
Outcomes	The outcome measures to be considered include: • disease severity • cognitive function (including speech and hearing) • neurological function (including cataplexy, seizures, gaze palsy) • motor and muscle function (including swallowing, balance and coordination, mobility) • psychiatric symptoms • liver function • 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	• 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 • If the evidence allows, the following subgroups may be considered: ○ Subgroups defined by severity of disease at onset • Guidance will take into account any commericial or managed access arrangements
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England (2019) The NHS long term plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2019) Highly specialised services 2018 Lysosomal storage disorders service (children & adults) p.50 NHS England. (2018) Manual for prescribed specialised services 2018/19 Chapter 71. Lysosomal storage disorder service (adults and children) NHS England. (2013/14) NHS Standard Contract for Lysosomal Storage Disorders Service (Children). E06/S(HSS)/c. NHS England. (2013/14) NHS Standard Contract for Metabolic Disorders (Adult). E06/S/a. NHS England. (2013/14) NHS Standard Contract for Metabolic Disorders (Children). E06/S/b. **National Service Frameworks** Long Term Conditions (including neurological) - archived

References

1. Geberhiwot T. et al. (2018) Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet Journal of Rare Diseases 13: 50

2. Patient.co.uk (professional). https://patient.info/doctor/niemann-pick-disease-pro [Accessed June 2020]