NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Arimoclomol for treating Niemann-Pick disease Type C

Draft scope

Draft 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 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 different gene mutations. NPC1 is the most prevalent: approximately 95% of cases are caused by genetic mutations in the NPC1 gene.[1]

Accumulation of lipids lead to a variety of symptoms, including hepatosplenomegaly (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] 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.

The incidence of NPC is estimated at 1 in 100,000 live births.[1] However, it is thought that this may be an underestimate.[1]

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 (brand name unknown, Orphazyme) aims to increase the production of molecular chaperone proteins in cells. Molecular chaperone proteins assist in the folding of other proteins; in NPC, this would help to produce functional enzymes which allow the cells to process the accumulated lipids. 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)	Children and adults with Niemann-Pick disease Type C
Comparators	• Miglustat • 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, narcolepsy, seizures, gaze palsy) • motor and muscle function (including balance and coordination) • 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	• Whether there are significant benefits other than

technology beyond direct health benefits	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 genotypes of NPC • Guidance will take into account any 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

Questions for consultation

How many people have NPC in England, and how many would be offered arimoclomol therapy?

How is arimoclomol expected to be used in clinical practice?

- Is arimoclomol expected to be used as a monotherapy or an add on therapy in combination with miglustat?

- At what point in the treatment pathway would arimoclomol be considered?

Have all relevant comparators for arimoclomol been included in the scope?

- Which treatments are considered established clinical practice in the NHS for NPC1 and NCP2? Are there any a differences?

- Is miglustat used in clinical practice? And in which patients?

- What supportive care options are considered for people with NPC?

Are the outcomes listed appropriate? Are there any other outcomes that should be included in the scope?

- Would arimoclomol be expected to affect non-neurological aspects of NPC, such as liver function?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money?

- Is it relevant to explore subgroups for types of NPC?

- Should any or other groups be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which arimoclomol will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

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]

3. Imrie, J., Heptinstall, L., Knight, S., & Strong, K. (2015). Observational cohort study of the natural history of Niemann-Pick disease type C in the UK: a 5-year update from the UK clinical database. BMC neurology 15: 257