NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Nitisinone for treating alkaptonuria (ID2691)

Draft scope (pre-referral)

Draft remit/appraisal objective

To evaluate the clinical and cost effectiveness of nitisinone within its marketing authorisation for treating alkaptonuria.

Background

Alkaptonuria, also known as AKU or Black Bone Disease, is a rare genetic metabolic disorder. Mutations in the gene for homogentisate oxidase reduce the function of this enzyme. People with alkaptonuria cannot break down homogentisic acid, a substance produced by the body during digestion of food. Build-up of this toxic acid leads to black urine which is an early sign of the condition noticeable from childhood. Over time it leads to black and brittle bones and cartilage, and early onset osteoarthritis. People with alkaptonuria often experience pain, and loss of movements which negatively affects quality of life.

Alkaptonuria is rare affecting 1 in 250,000 to 1,000,000 births in most ethnic groups.[1] In 2017/2018 there were 53 people with alkaptonuria registered at the National Alkaptonuria Centre in the UK.[2]

Alkaptonuria is a lifelong condition. There are currently no licenced treatments for it. People with alkaptonuria are treated at the National Alkaptonuria Centre where they are given nitisinone off label as part of clinical trials. Surgery might be needed to replace damaged joints or treat hardened and blocked heart valves or vessels.

The technology

Nitisinone (Orfadin, Swedish Orphan Biovitrum AB) prevents the production and accumulation of homogentisic acid by blocking para-hydroxyphenylpyruvic acid oxygenase. It is given orally.

Nitisinone does not currently have a marketing authorisation in the UK for alkaptonuria. It has a marketing authorisation for treating hereditary tyrosinemia type 1 (HT-1) another rare metabolic disease and is used off label for alkaptonuria in the specialised centre in the UK. Nitisinone has been studied alone in open-label clinical trials in adults with alkaptonuria.

Intervention(s)	Nitisinone
Population(s)	Adults with alkaptonuria
Comparators	Established clinical management without nitisinone

Outcomes	The outcome measures to be considered include: • reduction in level of urine homogentisic acid • reduction in orthopaedic surgery • mobility • mortality • adverse effects of treatment • health-related 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. Guidance will take into account any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	None
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS Manual For Prescribed Specialist Services (2018/2019) Chapters 19 and 62 NHS England (2018) Highly Specialised Services 2018 - see page 11 NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2013) 2013/14 NHS Standard Contract For Alkaptonuria Service (Adults). Ref: E06/S(HSS)/a NHS England (2013) 2013/14 NHS Standard Contract For Metabolic Disorders (Adult). Ref: E06/S/A Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2, 4. https://www.gov.uk/government/publications/nhs-outcomes-

	framework-2016-to-2017

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for alkaptonuria?

Are the outcomes listed appropriate? Should any others be included?

Are there any subgroups of people in whom nitisinone is expected to be more clinically effective and cost effective or other groups that should 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 nitisinone 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 Committee to identify and consider such impacts.

Do you consider nitisinone 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 appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Phornphutkul C, Introne WJ, Perry MB et al. (2002) Natural history of alkaptonuria. N Engl J Med. 347: 2111–21

2. NHS England (2018) Highly Specialised Services 2018 - see page 11