NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Sebetralstat for treating acute attacks of hereditary angioedema in people 12 years and over

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of sebetralstat within its marketing authorisation for treating acute attacks of hereditary angioedema.

Background

Hereditary angioedema (HAE) is a rare genetic disorder, associated with the deficiency of the protein C1-esterase inhibitor, which is a regulator of inflammatory pathways. Normally, C1-esterase inhibitor controls the enzyme cascade reactions so that uncontrolled swelling of the subcutaneous and submucosal tissues do not occur. In patients with HAE, at times of physiological or psychological stress, the function of the C1-esterase inhibitor is insufficient, resulting in the accumulation of excessive fluid (oedema) and localised oedematous swellings. The swellings usually occur in the mouth, the gut (affecting the submucosal tissues) and the airway, causing difficulty with breathing (with potential asphyxia) and severe pain in the stomach. The swellings can also occur in the deep tissues of the skin (affecting the dermis and subcutaneous tissues) causing significant impact, for example if the hands, feet or genitals are affected.

Most angioedema attacks are associated with trauma, medical procedures, emotional stress, menstruation, oral contraceptive use, infections, or the use of medications such as ACE inhibitors. Attacks are unpredictable; severity and frequency of previous attacks do not predict severity and frequency of future attacks. Attacks usually last approximately 2 to 5 days before resolving spontaneously.

There are 3 types of HAE. Types I (85%) and II (15%) are a result of a known genetic mutation and account for almost all cases of HAE[1]:

- type I is defined by low levels of a normal protein C1-esterase inhibitor in the plasma.
- type II is defined by normal level of a dysfunctional protein C1-esterase inhibitor in the plasma.
- type III is not a result of the deficiency of protein C1-esterase inhibitor. However, it is known that oestrogen has a role not yet fully understood.[2]

It is estimated that HAE affects between 1 per 50,000 to 1 per 100,000 of the population and can affect people of any ethnic group or gender.[1] HAE usually presents in childhood, with the mean age of onset being between 8 and 12 years.[1]

There are 3 approaches to managing HAE: avoidance of factors that trigger HAE (e.g. minor trauma, hormone replacement therapy), acute treatments and preventive (prophylactic) treatments of acute attacks. Short-term preventive treatments aim to prevent an attack before known triggers for example, dental work or surgery. Long-

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term preventative treatments are used routinely to reduce the need for treatment of acute attacks. Icatibant and C1-esterase inhibitors (C1-INH) such as Cinryze, Berinert and Ruconest are used for treating acute attacks.

The technology

Sebetralstat (brand name unknown, KalVista Pharmaceuticals) does not currently have a marketing authorisation in the UK for treating acute attacks of HAE in people 12 years and over. It has been studied in phase 3 clinical trials for on-demand treatment of HAE attacks in people 12 years and over with a clinical diagnosis of C1-inhibitor (type I or type II) HAE.

Intervention(s)	Sebetralstat
Population(s)	People 12 years and over with hereditary angioedema
Comparators	Established clinical management for the treatment of acute attacks of hereditary angioedema which may include: • C1-esterase inhibitors (this includes Cinryze, Berinert and Ruconest) • Icatibant
Outcomes	The outcome measures to be considered include: • severity of angioedema attacks • duration of angioedema attacks • time to beginning of symptom relief • reduction in symptoms of angioedema attacks • mortality • use of rescue medication • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

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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	**Related technology appraisals:** Berotralstat for preventing recurrent attacks of hereditary angioedema (2021) NICE technology appraisal guidance 738. Lanadelumab for preventing recurrent attacks of hereditary angioedema (2019) NICE technology appraisal guidance 606.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) chapter 59, 115 and 115A NHS Commissioning Board (2013) Clinical Commissioning Policy: Treatment of Acute Attacks in Hereditary Angioedema

Questions for consultation

Where do you consider sebetralstat will fit into the existing care pathway for the treatment of acute attacks of hereditary angioedema?

Please select from the following, will sebetralstat be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

Apart from C1-esterase inhibitors and icatibant, are any other treatments used for the treatment of acute attacks of HAE in NHS clinical practice?

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Are there any subgroups of people in whom sebetralstat is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would sebetralstat be a candidate for managed access?

Do you consider that the use of sebetralstat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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

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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 sebetralstat 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS Clinical commissioning: plasma derived C1-esterase inhibitor for prophylactic treatment of HAE (2016). Accessed May 2024 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/05/16045_FINAL.pdf

2. Amanda Rodrigues Miranda APFdU, Dominique Vilarinho Sabbag, Wellington de Jesus Furlani, Patrícia Karla de Souza, Osmar Rotta. Hereditary angioedema type III (estrogen-dependent) report of three cases and literature review. An Bras Dermatol. 2013;88(4):578–84.

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