NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Lanadelumab for the long-term prevention of angioedema attacks in hereditary angioedema types I and II

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lanadelumab within its marketing authorisation for the long-term prevention of angioedema attacks in hereditary angioedema types I and II.

Background

Hereditary angioedema (HAE) is an 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 airway, the mouth and the gut (affecting the submucosal tissues) causing difficulty with breathing 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 disability 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 usually last approximately 2 to 5 days before resolving spontaneously.

There are 3 types of HAE. Types I (85%) and II (15%) are due to 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 of a dysfunctional protein C1-esterase inhibitor in the plasma.

It is estimated that HAE affects between 1 per 10,000 to 1 per 50,000 of the population.[1] Half of the children born to people with this condition will inherit the condition. Most cases develop in childhood and some cases develop in early adulthood. HAE usually occurs during the first 10 to 20 years of life.

There are broadly 3 approaches to managing HAE: avoidance of precipitating factors (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 which include, for example, dental work or surgery, whereas long-term preventative treatments are used routinely to reduce the need for treatment of acute attacks. As a long-term strategy, attenuated androgens (such as danazol) or C1-esterase inhibitor (such as Cinryze) can be used. Danazol does not have a marketing authorisation in the UK for HEA. Anti-fibrinolytics, such as tranexamic acid, can also be used.

This appraisal only considers the long-term prevention of angioedema attacks in hereditary angioedema types I and II. The treatment of acute attacks or pre-procedure prevention (that is short-term prevention) for hereditary angioedema types I to III and the long-term prevention of angioedema attacks in hereditary angioedema type III are outside are outside the scope of this appraisal.

The technology

Lanadelumab (DX-2930, Shire Pharmaceuticals) is a fully human monoclonal antibody that targets the protein kallikrein and prevent the production of bradykinin which is an inflammatory mediator. Lanadelumab is administered subcutaneously.

Lanadelumab does not currently have a marketing authorisation in the UK for preventing angioedema attacks in hereditary angioedema types I and II. It has been studied in a clinical trial, compared with placebo, in people aged 12 years and older with hereditary angioedema types I or II who have at least 1 attack every 4 weeks.

Intervention(s)	Lanadelumab
Population(s)	People aged 12 years and older with hereditary angioedema types I or II who have frequent recurrent angioedema attacks
Comparators	Established clinical management for preventing long-term angioedema attacks in hereditary angioedema types I and II without lanadelumab (including but not limited to C1-esterase inhibitors and attenuated androgens)
Outcomes	The outcome measures to be considered include: • frequency of angioedema attacks • severity of angioedema attacks • need for acute treatment • 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	If the evidence allows, the following subgroups will be considered: • severity of angioedema attacks • frequency of angioedema attacks 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 and NICE Pathways	None
Related National Policy	NHS England (2017) Specialist immunology services for adults with deficient immune systems https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf NHS England (2016) Clinical Commissioning Policy: Plasma derived C1-esterase inhibitor for prophylactic treatment of hereditary angioedema (HAE) types I and II https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/05/16045_FINAL.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is the population in the scope defined appropriately? In particular, should it

be narrowed to specify the number and frequency of angioedema attacks? The clinical trial recruited people with hereditary angioedema types I or II who have at least 1 attack every 4 weeks. Would people with less frequent attacks be given the treatment? If yes, what is the minimum number of attacks that would allow a person to receive lanadelumab?

Which treatments are considered to be established clinical practice in the NHS for long-term prevention of the acute attacks in people with types I and II HAE? In particular is Cinryze considered established clinical practice in the NHS for the long-term prevention of angioedema attacks in people with types I and II HAE?

Are the outcomes listed appropriate?

How many people with types I and II HAE would be expected to have treatment with lanadelumab in England each year?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom lanadelumab 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 lanadelumab 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 lanadelumab 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)?

Do you consider that the use of lanadelumab can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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 Hereditary Angioedema UK (2017). Accessed January 2018 http://www.haeuk.org/what-is-hae/types-of-hae/