NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

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 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 2 types of HAE where the deficiency of the protein C1-esterase inhibitor occurs. These 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.

It is estimated that HAE affects between 1 per 50,000 to 1 per 100,000 of the population.[1] 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 (which is not due to the deficiency of protein C1-inhibitor but to the elevated levels of bradykinin) 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 at least 1 angioedema attack every 4 weeks
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, attenuated androgens and anti-fibrinolytics)

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

References

1 NHS Clinical commissioning: plasma derived C1-esterase inhibitor for prophylactic treatment of HAE (2013). Accessed May 2018 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2013/05/16045_FINAL.pdf