

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Eplontersen for treating hereditary transthyretin amyloidosis [ID6337]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of eplontersen within its marketing authorisation for treating hereditary transthyretin amyloidosis.

Background

Hereditary transthyretin amyloidosis affects people born with inherited mutations in the transthyretin (TTR) gene. This causes the liver to produce abnormal transthyretin protein (ATTR) which accumulates as deposits in the tissues of the body (ATTR amyloid deposits) and causes amyloidosis. These accumulated deposits can disrupt the structure and damage the function of the affected tissues. Most commonly deposits accumulate in the peripheral nervous system (polyneuropathy) or in the tissues of the heart (cardiomyopathy). Over time, these deposits can cause symptoms of polyneuropathy (such as pain, loss of sensation and weakness in the hands, arms, legs or feet) and symptoms of cardiomyopathy (such as chest pain, shortness of breath and fluid overload). In some cases, the autonomic nervous system which controls involuntary body functions such as blood pressure, heart rate, and digestion, may also be affected by amyloidosis.

Hereditary ATTR amyloidosis is a progressive, debilitating, and ultimately fatal condition. It can be classified into 4 stages (Coutinho et al. 1980).¹ Stage 0 denotes asymptomatic disease, people with stage 1 disease have mild symptoms and can walk, people with stage 2 disease have moderate symptoms and require assistance to walk, and people with stage 3 disease have severe symptoms and need to use a wheelchair or are bedbound. The effects and complications of the disease can lead to death within 5 to 15 years of symptoms developing.

The prevalence of hereditary ATTR amyloidosis is estimated to be less than 1 in 100,000 people in the general European population.² In the UK there are thought to be around 230 people with the disease.³

Current treatment options for people with polyneuropathy caused by hereditary ATTR amyloidosis include symptom relief and supportive care including pain management, nutritional and mobility support and mitigation of the effects of the disease on other organs.

- Vutrisiran is recommended for treating hereditary ATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy ([NICE technology appraisal 868](#)).
- Patisiran is recommended for treating hereditary ATTR amyloidosis in adults with stage 1 and stage 2 polyneuropathy ([NICE highly specialised technologies guidance 10](#)).
- Inotersen is recommended for treating stage 1 and stage 2 polyneuropathy in adults with hereditary ATTR amyloidosis ([NICE highly specialised technologies guidance 9](#)).

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Page 1 of 4

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Other pharmacological treatments may be used, including diflunisal, which is sometimes used outside of its marketing authorisation to treat hereditary ATTR amyloidosis. It is contraindicated in people with cardiac impairment and those taking anticoagulants.

Liver transplantation, which prevents the formation of additional amyloid deposits by removing the main source of abnormal transthyretin production, is an option for some people with a specific genetic mutation. However, this mutation is uncommon in England, and transplantation can only take place early in the course of the disease, so it is very rarely used in England.

The technology

Eplontersen (brand name unknown, AstraZeneca) does not currently have a marketing authorisation in the UK for hereditary ATTR amyloidosis.

It has been studied in a clinical trial and compared with an external placebo group in adults with hereditary ATTR amyloidosis who have stage 1 or stage 2 polyneuropathy.

Intervention(s)	Eplontersen
Population(s)	Adults with hereditary ATTR amyloidosis who have stage 1 or stage 2 polyneuropathy .
Comparators	<ul style="list-style-type: none"> • Vutrisiran • Patisiran • Inotersen
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • neurological impairment • symptoms of polyneuropathy • cardiac function • autonomic function (including the effects on the gastrointestinal system and postural hypotension) • weight loss • effects of amyloid deposits in other organs and tissues (including the eye) • serum transthyretin • motor function • adverse effects of treatment • health-related quality of life

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<p>Other considerations</p>	<p>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.</p>
<p>Related NICE recommendations</p>	<p>Related technology appraisals:</p> <p>Vutrisiran for treating hereditary transthyretin-related amyloidosis (2023) NICE Technology Appraisal 868.</p> <p>Tafamidis for treating transthyretin amyloidosis with cardiomyopathy (2021) NICE Technology Appraisal 696.</p> <p>Patisiran for treating hereditary transthyretin-related amyloidosis (2019) NICE Highly Specialised Technology 10.</p> <p>Inotersen for treating hereditary transthyretin-related amyloidosis (2019) NICE Highly Specialised Technology 9</p> <p>Ongoing technology appraisals:</p> <p>Tafamidis for treating transthyretin amyloidosis with cardiomyopathy ID6327</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England Manual for prescribed specialised services, service 46: Diagnostic service for amyloidosis (adults), March 2023.</p> <p>NHS England Highly specialised services 2019/20: diagnostic service for amyloidosis. 2022</p> <p>NHS England standard contract for diagnostic service for amyloidosis (all ages). 2013/14.</p>

References

1. Coutinho PD, Lima JL, Barbosa AR. 1980. Forty years of experience with type I amyloid neuropathy: review of 436 cases In: Glenner GG, de Freitas AF, editors. Amyloid and amyloidosis. Amsterdam: Excerpta Medica; p. 88-98.
2. Orpha.net. 2022 [Prevalence of rare diseases: Bibliographic data](#).
3. National Institute for Health and Care Excellence (NICE). 2023. [Resource impact report: Vutrisiran for treating hereditary transthyretin related amyloidosis \(TA868\)](#).