NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Vutrisiran for treating hereditary transthyretin-related amyloidosis [ID5074]

Final scope

Remit/evaluation objective

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

Background

Hereditary transthyretin-related amyloidosis (hATTR) affects people born with inherited mutations in the transthyretin gene. This causes the liver to produce abnormal transthyretin protein which accumulates as deposits in the tissues of the body (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 or in the tissues of the heart. 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.

The condition is progressive and the neuropathy can be classified into 4 stages. Stage 0 denotes asymptomatic disease, people with stage I disease have mild symptoms and can walk, people with stage II disease have moderate symptoms and require assistance to walk, and people with stage III 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 hATTR amyloidosis is estimated to be less than 1 in 100,000 people in the general European population.[1] In the UK there are thought to be around 150 people with the disease.

Current treatment options for people with hATTR 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. Patisirian is recommended for treating hATTR amyloidosis in adults with stage 1 and stage 2 polyneuropathy (HST10). Inotersen is recommended for treating stage 1 and stage 2 polyneuropathy in adults with hATTR amyloidosis (HST 9). Diflunisal is a non-steroidal anti-inflammatory drug which makes transthyretin less likely to form amyloid accumulations. It is sometimes used outside of its marketing authorisation to treat hATTR 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

Vutrisiran (Amvuttra, Alnylam Pharmaceuticals) is an RNA interference (RNAi) therapeutic that inhibits the production of disease-causing transthyretin (TTR) protein by the liver, leading to a reduction in the level of TTR in the blood. It is administered by subcutaneous injection.

Vutrisiran does not currently have a marketing authorisation in the UK for polyneuropathy caused by hATTR. It has been studied in a phase III clinical trial compared with patisiran for people with polyneuropathy caused by hereditary transthyretin amyloidosis.

Intervention(s)	Vutrisiran
Population(s)	Adults with hereditary transthyretin-related amyloidosis and stage 1 or stage 2 polyneuropathy
Comparators	Established clinical management without vutrisiran including: • Inotersen • Patisiran
Outcomes	The outcome measures to be considered include: • 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

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. The availability of any managed access arrangement for the intervention will be taken into account.
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:** Inotersen for treating hereditary transthyretin amyloidosis (2019). NICE Highly specialised technologies guidance 9 (HST 9). Patisiran for treating hereditary transthyretin amyloidosis (2019). NICE Highly specialised technologies guidance 10 (HST 10).
Related National Policy	NHS England Manual for prescribed specialised services, service 46: Diagnostic service for amyloidosis (adults), 2017/18. https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf NHS England standard contract for diagnostic service for amyloidosis (all ages), 2013/14. https://www.england.nhs.uk/wp-content/uploads/2013/06/e13-diag-serv-amyloidosis.pdf The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

References

1. Orpha.net. Prevalence of rare diseases. Bibliographic data (June 2022). https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf