NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Patisiran for treating hereditary transthyretin-related amyloidosis

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of patisiran within its marketing authorisation for treating hereditary transthyretin-related amyloidosis for national commissioning by NHS England.

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 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 aspect of the disease can be classified into 4 stages. Stage 0 denotes asymptomatic disease: patients with stage I disease have mild symptoms and can walk, patients with stage II disease have moderate symptoms and require assistance to walk, and patients 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 are limited and mainly focus on symptom relief and supportive care including pain management, nutritional and mobility support and mitigation of the effects of the disease on other organs. Tafamidis has a marketing authorisation for treating transthyretin amyloidosis in adults with stage 1 (early) symptomatic polyneuropathy, but it is not used in clinical practice in England. 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

Patisiran (brand name unknown, Alnylam Pharmaceuticals) is a ribonucleic acid interference agent that suppresses the production of transthyretin by the liver (including abnormal transthyretin). It is administered by intravenous infusion.

Patisiran does not currently have a marketing authorisation in the UK for treating hATTR amyloidosis. It has been studied in a phase II trial and a phase III placebo-controlled trial for people with polyneuropathy caused by hereditary transthyretin amyloidosis.

Intervention(s)	Patisiran
Population(s)	People with hereditary transthyretin-related amyloidosis.
Comparators	Established clinical management without patisiran.
Outcomes	The outcome measures to be considered include: • 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 • mortality • adverse effects of treatment • health-related quality of life (for patients and

	carers).
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• cost effectiveness using incremental cost per quality-adjusted life year • patient access schemes and other commercial agreements • the nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	• guidance will only be issued in accordance with the marketing authorisation. • guidance will take into account any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	None

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

References

1. Orpha.net. Prevalence of rare diseases. Bibliographic data (June 2018) http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf.