NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Highly Specialised Technologies Evaluation

Patisiran for treating hereditary transthyretin-related amyloidosis

Draft scope (pre-referral)

Draft remit/evaluation objective

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

Background

Hereditary transthyretin-related amyloidosis (hATTR), also known as familial amyloid polyneuropathy, 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. Over time, these deposits can cause symptoms of polyneuropathy such as pain, loss of sensation and weakness in the hands, arms, legs or feet. 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. Amyloid deposits can also form in the tissues of the heart. This can lead to heart failure and associated symptoms such as chest pain, shortness of breath and fluid overload.

The condition is progressive and 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 5-15 years of symptoms developing.

The prevalence of polyneuropathy caused by hATTR 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 70 people with the disease.

Current treatment options for people with polyneuropathy caused by hATTR 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 is a disease-modifying therapy with a marketing authorisation for the treatment of transthyretin amyloidosis in adult patients with stage 1 (early) symptomatic polyneuropathy to delay peripheral neurologic impairment. 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 polyneuropathy caused by hATTR. Doxycycline, an antibiotic that disrupts transthyretin amyloid formation, has been studied in combination with tauroursodeoxycholic acid, which can reduce transthyretin deposits, in a phase II trial in people with hATTR.

Liver transplantation is an option for some people. Transplantation prevents the formation of additional amyloid deposits by removing the main source of abnormal transthyretin production, slowing or halting the progression of the disease. It is only an option for people early in the course of the disease, before tissues become too damaged.

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 polyneuropathy caused by hATTR. 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 polyneuropathy caused by hereditary transthyretin-related amyloidosis.
Comparators	Established clinical management without patisiran, including: • disease modifying therapies such as diflunisal • liver transplantation.
Outcomes	The outcome measures to be considered include: • neurological impairment • disability • symptoms of polyneuropathy • autonomic function • 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), May 2016. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.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 2017) http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf.

Questions for consultation

Have all relevant comparators for patisiran been included in the scope? Which treatments are considered to be established clinical practice in the NHS for hereditary transthyretin-related amyloidosis:

- Are tafamidis and diflunisal comparators?
- Are other experimental treatments such as doxycycline plus tauroursodeoxycholic acid comparators?
- Is liver transplantation a comparator?
- Are there any other treatments that should be included as comparators?

Are the outcomes listed appropriate?

- Is serum transthyretin a relevant outcome?
- Which elements of autonomic function are affected by the condition and might be improved by patisiran?
- Would patisiran have an effect on cardiomyopathy outcomes?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

Would patisiran be used at a particular stage of the disease?

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 eteplirsen 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 Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

Do you consider the technology 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)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.