NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Vutrisiran for treating transthyretin-related amyloidosis cardiomyopathy [ID6470]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of vutrisiran within its marketing authorisation for treating transthyretin amyloidosis with cardiomyopathy.

Background

Transthyretin amyloidosis (ATTR) is caused by abnormal transthyretin (TTR) proteins being produced by the liver, which accumulate as deposits in the tissues of the body. These amyloid deposits can disrupt the structure and damage the function of the affected tissues.[1] Transthyretin amyloidosis cardiomyopathy (ATTR-CM) is a type of transthyretin amyloidosis in which most deposits accumulate in the heart, causing the heart tissue to thicken and stiffen.[2] There are two forms of ATTR-CM:

- Wild-type ATTR-CM is the more common of the two types. It mostly affects older individuals and is more common in men than women.[3]
- Hereditary ATTR-CM (also known as familial amyloid cardiomyopathy) affects people born with inherited mutations in the TTR gene. The most prevalent TTR variants in the UK are Val112Ile and Thr60Ala. People with African or Caribbean and Hispanic family backgrounds are more likely to have hereditary ATTR-CM because of the increased prevalence of variants (such as the Val112Ile variant) in these groups.[3,4] People in these groups are also more likely to develop cardiomyopathy, without neuropathy.

Symptoms of ATTR-CM can include shortness of breath, palpitations and abnormal heart rhythms, most frequently atrial fibrillation or atrial flutter, ankle swelling, fatigue, fainting and chest pain.

ATTR-CM is a progressive disease with symptoms usually starting after the age of 70 years in people with wildtype ATTR-CM, or after the age of 60 years in people with the Val112Ile and Thr60Ala variants of hereditary ATTR-CM.[5] Death in most people with ATTR-CM is from sudden death and progressive heart failure.[2] In England, around 1,500 people have been diagnosed with ATTR-CM.[6]

NICE technology appraisal guidance 984 recommends tafamidis for treating transthyretin amyloid cardiomyopathy in adults. Other current treatment options for ATTR-CM, such as diuretics, focus on symptom management and supportive care.

The technology

Vutrisiran (Amvuttra, Alnylam Pharmaceuticals) does not currently have a marketing authorisation in the UK for treating transthyretin amyloidosis with cardiomyopathy. It

has been studied in a clinical trial compared with placebo in people with transthyretin amyloidosis with cardiomyopathy.

Vutrisiran does have a marketing authorisation in the UK for treatment of hereditary transthyretin-mediated amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy.

Intervention(s)	Vutrisiran
Population(s)	People with transthyretin amyloidosis cardiomyopathy (ATTR-CM)
Subgroups	• Severity of heart failure (such as by New York Heart classification class) • Wild type or hereditary ATTR-CM
Comparators	• Tafamidis • Established clinical management without vutrisiran
Outcomes	The outcome measures to be considered include: • overall survival • cardiovascular-related mortality • cardiac function (such as global longitudinal strain or brain natriuretic peptide [BNP] level) • cardiovascular-related hospitalisation • functional exercise capacity • signs and symptoms of heart failure (such as breathlessness) • adverse effects of treatment • health-related quality of life (of patients and carers).
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.

	The availability and cost of biosimilar and generic products should 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:** Tafamidis for treating transthyretin amyloidosis with cardiomyopathy (2023) NICE technology appraisal guidance 984. Vutrisiran for treating hereditary transthyretin-related amyloidosis (2023) NICE technology appraisal guidance 868. **Related highly specialised technology appraisals:** Patisiran for treating hereditary transthyretin-related amyloidosis (2019) NICE highly specialised technology guidance 10. Inotersen for treating hereditary transthyretin-related amyloidosis (2019) NICE highly specialised technology guidance 9. **Related technology appraisals in development:** Eplontersen for treating hereditary transthyretin-related amyloidosis. NICE technology appraisal guidance [ID6337] Publication date to be confirmed.

References

1. Amyloidosis UK (2024) ATTR amyloidosis. Accessed November 2024.
2. Tsang C, Huda A, Norman M et al (2023) Detecting transthyretin amyloid cardiomyopathy (ATTR-CM) using machine learning: an evaluation of the performance of an algorithm in a UK setting. BMJ Open 1;13(10):e070028.
3. Gillmore JD, Damy T, Fontana M et al (2018) A new staging system for cardiac transthyretin amyloidosis. European Heart Journal 7;39(30):2799-806.
4. Porcari A, Razvi Y, Masi A et al (2023) Prevalence, characteristics and outcomes of older patients with hereditary versus wild-type transthyretin amyloid cardiomyopathy. European Journal of Heart Failure 25(4):515-24.
5. Patel KS, Hawkins PN (2015) Cardiac amyloidosis: where are we today? Journal of Internal Medicine. 278(2):126-44.

6. NHS England (2024) First ever life-saving treatment for rare heart condition available on the NHS. Accessed November 2024.