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Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2755

eplontersen solution for injection in pre-filled pen (Wainzua®)

AstraZeneca UK Ltd

07 March 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

eplontersen (Wainzua®) is accepted for use within NHSScotland.

Indication under review: for the treatment of hereditary transthyretin-mediated amyloidosis (ATTRv amyloidosis) in adult patients with Stage 1 and 2 polyneuropathy.

Eplontersen offers an additional treatment choice of transthyretin (TTR) gene silencer for this indication.

Another TTR gene silencer was accepted for use under the ultra-orphan process.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Eplontersen is an antisense oligonucleotide silencer (ASO) licensed for the treatment of hereditary transthyretin-mediated amyloidosis (ATTRv amyloidosis) in adult patients with stage 1 and 2 polyneuropathy. The recommended dose is 45 mg via subcutaneous injection once each month. Treatment with eplontersen should be prescribed and supervised by a treating physician knowledgeable in the management of patients with amyloidosis. The first injection administered by the patient or caregiver should be performed under the guidance of an appropriately qualified health care professional. Subsequent doses may be administered by the patient / caregiver. Vitamin A supplementation at approximately, but not exceeding, 2,500 IU (female) to 3,000 IU (male) of vitamin A daily is advised. For further details please refer to the Summary of Product Characteristics (SPC).[1]

1.2. Relevant comparator

Vutrisiran (Amvuttra®) is a double-stranded small interfering ribonucleic acid (siRNA) within the same therapeutic class as eplontersen, the TTR gene silencers. Vutrisiran is accepted for use within NHSScotland for the treatment of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adult patients with stage 1 or stage 2 polyneuropathy (SMC2596).

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

The clinical effectiveness of eplontersen versus external placebo is supported by evidence from the phase III NEURO-TTRansform study.[2] This was a randomised, open-label, multi-centre, study conducted in adults with stage 1 or stage 2 ATTRv polyneuropathy (n=168). Patients treated with placebo in NEURO-TTR (a double-blind, placebo-controlled phase III study of inotersen in adults with stage 1 or stage 2 hATTR polyneuropathy) served as an external placebo group (n= 60 [3]). A small inotersen reference group was also included for cross-trial comparison of disease progression and treatment responses. Patients (n=144) aged 18 to 82 years were randomised in 6:1 ratio to open label treatment with eplontersen (n= 144) or inotersen (n=24).

The treatment groups (eplontersen and external placebo) were well balanced with respect to baseline demographics and disease characteristics. Primary outcomes included: percentage change from baseline in serum transthyretin concentration at week 65, change from baseline in modified Neuropathy Impairment Score +7 (mNIS+7) composite score and Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (QoL-DN) total score at week 66.

Patients treated with eplontersen demonstrated a significant reduction in serum transthyretin concentration (difference -70.4% [95% CI, -75.2% to -65.7%], p<0.001), less neuropathy impairment (mNIS+7 score difference -24.8% [95% CI, -31.0 to -18.6], p<0.001) and better

quality of life (QoL-DN score difference -19.7 [95% CI, -25.6 to -13.8], p<0.001) compared with an external placebo group.

There is no direct evidence of the clinical efficacy of eplontersen compared with vutrisiran, therefore, the company conducted an unanchored matching-adjusted indirect treatment comparison (MAIC).[4,2] In the MAIC, individual patient (IPD) data for eplontersen were from the NEURO-TTRansform study [2] described above. Data for vutrisiran were from HELIOS-A study [4], an international, multicentre, randomised, open-label phase III study which compared vutrisiran to an external placebo group from APOLLO study (a phase III, placebo-controlled study of patisiran).[5]

The results of the MAIC suggest no significant difference between eplontersen and vutrisiran in most outcomes, however, a statistically significant difference was found in Norfolk QoL-DN total scores in favour of eplontersen. The confidence intervals were wide for all assessed outcomes introducing uncertainties in the treatment effect of eplontersen. The safety profile of eplontersen was consistent with safety profile of vutrisiran.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

SMC is unable to publish the estimated patient numbers as the company considered that these were commercial in confidence.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

*Other data were also assessed but remain confidential.**

References

1. AstraZeneca UK Ltd. Eplontersen (Wainzua®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated [11 December 2024].
2. Coelho T, Marques W, Dasgupta NR, Chao C-C, Parman Y, França MC*, et al.* Eplontersen for hereditary transthyretin amyloidosis with polyneuropathy. JAMA. 2023.
3. Benson MD, Waddington-Cruz M, Berk JL, Polydefkis M, M.H.S. PJD, Wang AK*, et al.* Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis. NEJM. 2018;379.
4. Adams D, Tournev IL, Taylor MS, Coelho T, Planté-Bordeneuve V, Berk JL*, et al.* Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. Amyloid. 2023;30(1):18-26.
5. Maurer MS, Kale P, Fontana M, Berk JL, Grogan M, Gustafsson F*, et al.* Patisiran Treatment in Patients with Transthyretin Cardiac Amyloidosis. NEJM. 2023;389(17).

This assessment is based on data submitted by the applicant company up to and including 21 October 2024.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.