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2024039708

Our reference
2025019191

Date 20 August 2025
Re: GVS advice eplontersen (Wainzua®) for hereditary form of amyloidosis

Dear Ms Jansen,

The National Health Care Institute advises you on the inclusion of eplontersen (Wainzua®) in the Medicine Reimbursement System (GVS) for the treatment of a hereditary form of amyloidosis and polyneuropathy. This advice was prompted by your request in the letter of 16 June 2025 (CIBG-25-08361). The National Health Care Institute advises you to place eplontersen (Wainzua®) for the indication hereditary transthyretin amyloidosis and polyneuropathy stage 1 or 2 on List 1A in a new cluster to be formed together with vutrisiran (Amvuttra®).

Amyloidosis is a rare disease of improperly folded proteins that accumulate in organs and tissues. The functioning of vital organs such as the heart and nerves will gradually deteriorate. This ultimately leads to death. Symptoms usually start after the age of 25. A patient often first suffers from sensory changes in the feet ('neuropathy'), and as a result, walking becomes increasingly difficult. Gradually, the functions of the heart, gastrointestinal tract and urinary tract are also affected. In the final stage of the disease, a patient will no longer be able to walk, becoming bound to a wheelchair or bed due to general weakness, and will usually die due to severe heart failure. Currently, approximately 65 patients with this disease are treated with patisiran in the Netherlands. Vutrisiran is also reimbursed for this indication as of 1 July 2025.

Registered indication
Eplontersen (Wainzua®) is indicated for the treatment of hereditary transthyretin-mediated amyloidosis (ATTRv) in adult patients with stage 1 and stage 2 polyneuropathy, and is available in a 45 mg solution for injection in a pre-filled pen.

Claim by the marketing authorisation holder
In the treatment of hereditary transthyretin-mediated amyloidosis (ATTRv) in adult patients with stage 1 or stage 2 polyneuropathy, eplontersen has an equal therapeutic value compared to vutrisiran.

The marketing authorisation holder (MAH) is requesting inclusion in List 1A of the Health Insurance Regulation for hereditary transthyretin amyloidosis and polyneuropathy stage 1 or 2 in a new cluster to be formed with vutrisiran.

National Health Care Institute
Research, Development and Medicinal Products
Medicinal Products Team

Date
20 August 2025

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Advice
The National Health Care Institute advises you to place eplontersen (Wainzua®) for the indication hereditary transthyretin amyloidosis and polyneuropathy stage 1 or 2 on List 1A in a new cluster to be formed together with vutrisiran (Amvuttra®).

In addition, we advise you to place eplontersen as well as vutrisiran on List 2 of the GVS. The following further conditions may apply to both medicinal products:

Only for an insured person with genetically confirmed hereditary transthyretin amyloidosis and polyneuropathy stage 1 or 2 who is being treated at or under the supervision of a centre of expertise.

We explain the preparation of this advice below.

Substantive assessment
Assessment of interchangeability
On the basis of the criteria for interchangeability, it can be concluded that eplontersen is interchangeable with vutrisiran. The standard dose of eplontersen is set at 45 mg per month. That is equivalent to 1.48 mg a day. The standard dose of vutrisiran is 25 mg per quarter. That is equivalent to 0.27 mg a day.

Therapeutic value
Based on the available data, the National Health Care Institute concludes that eplontersen has an equal value to vutrisiran. Eplontersen complies with the established medical science and medical practice for the treatment of adults with hereditary transthyretin amyloidosis and polyneuropathy stage 1 or 2 (ATTRv-PN).

After vutrisiran, eplontersen is the second medicinal product that is assessed by the National Health Care Institute for this indication. Patisiran was included in the health insurance package in 2018 as an intramural medicine. It is not included in the GVS but it is available through intramural funding via an add-on. In accordance with the orphan drug arrangement that has been agreed, patisiran can only be administered under the supervision of the UMCG centre of expertise. A confidential price agreement with the health insurers is in force for this arrangement. The National Health Care Institute therefore recommended price negotiations for vutrisiran in 2024 to ensure that its inclusion in the health insurance package would not lead to additional costs. Vutrisiran has been included in the health insurance package since 1 July 2025. The National Health Care Institute also advises price negotiations for eplontersen prior to inclusion in the GVS to ensure that it does not lead to additional costs.

Appropriate use
Finally, given the high cost of eplontersen per patient per year, as for patisiran and vutrisiran, appropriate use remains very important. The National Health Care Institute therefore also advises List 2 conditions for eplontersen. In addition, the existing orphan drug arrangement for treatment with patisiran and vutrisiran

should be extended to include eplontersen, with the same start and stop criteria also in force for eplontersen.

Should you need any further information, please do not hesitate to contact us. The assessment reports (interchangeability test and Pharmacotherapeutic report) are added as annexes.

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board

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