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

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Our reference
2025028453

Date 8 December 2025
Re: expansion of additional conditions vutrisiran (Amvuttra®) for transthyretin amyloidosis with cardiomyopathy

Dear Mr Bruijn,

The National Health Care Institute advises you on the expansion of the additional conditions in List 2 of the Medicine Reimbursement System (GVS) for vutrisiran (Amvuttra®) with the indication: treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy. This advice was prompted by your request in the letter of 12 August 2025 (CIBG-25-08558).

The National Health Care Institute advises you to expand the additional conditions in List 2 for vutrisiran (Amvuttra®) for the treatment of wild-type or transthyretin amyloidosis variant in adult patients with cardiomyopathy (ATTR-CM) with NYHA classes I and II. In this respect, the net price of vutrisiran on the basis of the equivalent value cannot exceed the net price of tafamidis 61 mg.

Transthyretin amyloidosis cardiomyopathy (ATTR-CM) is a progressive and potentially fatal heart disease. The protein transthyretin, which normally circulates in the bloodstream, accumulates mainly in the heart, causing thickening and increased stiffness of the cardiac wall. This is called cardiomyopathy and can lead to heart failure. Examples of symptoms of the disease are shortness of breath at rest or with minimal exertion, fatigue, swelling and numbness in extremities, reduced ability to make physical efforts. The severity of heart failure is indicated by the New York Heart Association (NYHA) classification and ranges from I to IV, with IV being the most severe. In the Netherlands, an estimated 3,700 people suffer from this disease. The average life expectancy after diagnosis and without treatment is 3 to 5 years. A higher NYHA classification leads to a poorer life expectancy, but the exact prognosis depends on several factors, such as age, gender, other medical conditions and response to treatment. In Dutch expertise centres, patients with reasonable life expectancy and NYHA classes I and II are now treated with tafamidis. Recently, the National Health Care Institute has advised that acoramidis should also be included in the GVS for this indication. Although vutrisiran has a different mechanism of action and dosage form from tafamidis and acoramidis, it is intended for the same patient group.

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Registered indications
Vutrisiran (Amvuttra®) is indicated for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM) and is available in a pre-filled syringe containing 25 mg in a 0.5 ml solution.

In addition, vutrisiran is registered and reimbursed for the treatment of hereditary transthyretin amyloidosis in adult patients with stage 1 or 2 polyneuropathy (hATTR-PN).

At present, vutrisiran is already listed in the GVS on List 1B and being reimbursed with the following List 2 conditions. Tafamidis is also already listed in the GVS on List 1B, also with List 2 conditions.

Current condition vutrisiran:
Only for an insured person aged 18 years and older with genetically confirmed hereditary transthyretin amyloidosis and stage 1 or 2 polyneuropathy who is being treated at or under the supervision of a centre of expertise.

Claim by the marketing authorisation holder
Vutrisiran (Amvuttra®) for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy and NYHA classes I and II is equivalent to tafamidis 61 mg.

The marketing authorisation holder therefore requests the expansion of additional conditions in List 2 of the Health Insurance Regulation with this indication.

Advisory report
The National Health Care Institute has concluded that vutrisiran for this indication has a similar value to tafamidis 61 mg in NYHA Class I and II. The National Health Care Institute therefore advises you to expand the additional conditions in List 2 of the GVS for vutrisiran (Amvuttra®) with the following List 2 conditions. The net price of vutrisiran must not exceed that of tafamidis 61 mg.
As the main indication for vutrisiran changes from hATTR-PN (hereditary transthyretin amyloidosis with polyneuropathy) to wild-type and hereditary ATTR-CM as a result of this assessment, and eplontersen is registered only for hATTR-PN, the advice given in August of this year, (which as far as known has not yet been implemented)[2] to cluster vutrisiran with eplontersen, no longer applies. The advice is to maintain vutrisiran on List 1B. The recommended price negotiations to avoid additional costs of including eplontersen remain in force.

New condition vutrisiran (Amvuttra®)
Only for an insured person aged 18 years or older with

- genetically confirmed hereditary transthyretin amyloidosis and stage 1 or 2 polyneuropathy, who is being treated at or under the supervision of a centre of expertise; or
- *wild-type or hereditary transthyretin amyloidosis in cardiomyopathy and NYHA class I-II, who is being treated at or under the supervision of a centre of expertise.*

We have explained below how we reached this advisory report.

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Substantive assessment

Assessment of interchangeability

Based on the criteria for interchangeability, the National Health Care Institute concludes that vutrisiran is not interchangeable with tafamidis 61 mg or the recently assessed acoramidis due to a difference in dosage form.[1]
In the absence of a DDD for vutrisiran by the WHO, we have set the standard dose at 0.27 mg per day. The WHO-defined DDD for tafamidis is 20 mg daily based on the treatment of polyneuropathy as a result of transthyretin amyloidosis. The dose of tafamidis for ATTR-CM is 61 mg (equivalent to 80 mg tafamidis meglumine).

Therapeutic value

The National Health Care Institute has concluded that vutrisiran has an equivalent value to tafamidis 61 mg for NYHA class I and II in the previously mentioned indication and thus complies with the established medical science and medical practice. Due to the lack of a direct comparative study between the medicinal products, an indirect comparison of the HELIOS-B study (vutrisiran) and the ATTR-ACT study (tafamidis) has been assumed. For key endpoints such as survival and hospitalisation, they show a similar effect. The same applies to the adverse effects and the number of discontinuations due to adverse effects. Recently, the National Health Care Institute concluded that acoramidis for this indication also has an equivalent value to tafamidis 61 mg.[1]

In the assessment of tafamidis, the National Health Care Institute previously concluded that tafamidis appears to increase the risk of cardiovascular hospitalisation in NYHA class III. Therefore, there is no reimbursement of tafamidis for this patient subgroup. Because standard treatment is not available for these patients now, and there is a high unmet need, the effects of vutrisiran in NYHA class III were also considered by the National Health Care Institute in this assessment. However, the number of patients in this subgroup is too small to draw conclusions about its effects in this subgroup. This means that vutrisiran in this NYHA class does not comply with the established medical science and medical practice. The advice is therefore not to reimburse vutrisiran for NYHA class III.

Budget impact

On the basis of the equal value conclusion, the net price of vutrisiran should not exceed the net price of tafamidis 61 mg and acoramidis. In these calculations, the negotiated price of tafamidis is leading. See the package advice for tafamidis[3].
Based on the current use of tafamidis 61 mg, the expected number of starters and discontinuations and the estimated market penetration, the National Health Care Institute estimates 188 patients for vutrisiran for the mentioned indication in year 3 after inclusion in the health insurance package.

Cost-effectiveness

Based on the conclusion that vutrisiran and tafamidis 61 mg have equal value, an assessment of the cost-effectiveness of vutrisiran is not required.

Appropriate care

Appropriate use agreements have been made with the Dutch Working Group on Cardiac Amyloidosis to standardise diagnostics and treatment and to streamline joint scientific research. This has led to the formation of the Amyloidosis Expertise Network. The purpose of the appropriate use arrangement is to stimulate and

ensure appropriate use of tafamidis (and acoramidis), by formulating clear start and stop criteria and by agreeing on data collection and reporting. The National Health Care Institute advises that these appropriate use arrangements should also apply to vutrisiran and is already discussing this with the professional association.

Should you need any further information, please do not hesitate to contact us. The assessment reports have been added as annexes (pharmacotherapeutic report, interchangeability test, estimation of number of future users of vutrisiran).

Yours sincerely,

M.J. Janssen
Chair of the Executive Board

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