Vutrisiran (transthyretin amyloidosis with cardiomyopathy)

Addendum to Project A25-93 (dossier assessment)[1]

ADDENDUM (DOSSIER ASSESSMENT)

Project: A25-149 Version: 1.0 Status: 5 Jan 2026 DOI: 10.60584/A25-149_en

[1] Translation of the addendum *Vutrisiran (Transthyretin-Amyloidose mit Kardiomyopathie) – Addendum zum Projekt A25-93 (Dossierbewertung)*. Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Vutrisiran (transthyretin amyloidosis with cardiomyopathy) – Addendum to Project A25-93

Commissioning agency

Federal Joint Committee

Commission awarded on

28 November 2025

Internal Project No.

A25-149

https://doi.org/10.60584/A25-149_en

Address of publisher

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Siegburger Str. 237
50679 Köln
Germany

Phone:+49 221 35685-0
Fax: +49 221 35685-1
E-mail: info@iqwig.de
Internet: www.iqwig.de

Recommended citation

Institute for Quality and Efficiency in Health Care. Vutrisiran (transthyretin amyloidosis with cardiomyopathy); Addendum to Project A25-93 (dossier assessment) [online]. 2026 [Accessed: DD.MM.YYYY]. URL: https://doi.org/10.60584/A25-149_en.

Keywords

Vutrisiran, Amyloidosis, Cardiomyopathies, Benefit Assessment, NCT04153149

IQWiG employees involved in the addendum

- Claudia Selbach
- Philip Kranz

Table of contents

List of tables

Page

List of abbreviations

Abbreviation	Meaning
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

On 28 November 2025, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Project A25-93 (Vutrisiran – Benefit assessment according to §35a Social Code Book V) [1].

Dossier assessment A25-93 described that the randomized controlled trial (RCT) HELIOS-B [2-6] contained potentially suitable data of a subpopulation for the benefit assessment of vutrisiran in combination with tafamidis (hereinafter referred to as 'vutrisiran + tafamidis') in comparison with tafamidis. As the pharmaceutical company (hereinafter referred to as 'the company') had not submitted this data even in its comments [7], the G-BA again requested that it provide this data following the oral hearing on 25 November 2025. This addendum assesses the company's documents subsequently submitted on 28 November 2025 [7] following the request for submission of the data by the G-BA.

The responsibility for this assessment and the assessment result lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment

In its supplementary submission of 28 November 2025, the pharmaceutical company (hereinafter referred to as 'the company') did not present the data on the HELIOS-B subpopulation with tafamidis as background therapy, which were requested by the Federal Joint Committee (G-BA), in accordance with the requirements of the module templates. In these documents, it essentially repeated its arguments from Module 4 B, its comments and the oral hearing (selection bias, HELIOS-B not designed for a direct comparison with tafamidis) [7] and referred to publicly available subgroup analyses on the population with tafamidis background therapy [4,6,8-10]. It stated that overall, the subpopulation of the HELIOS-B study did not provide any robust evidence for the early benefit assessment.

The company's approach was not appropriate. In HELIOS-B, 130 patients in the vutrisiran arm and 129 patients in the placebo arm (40 % of the total population) were receiving tafamidis as background therapy at baseline. The data of this subpopulation were relevant for the assessment of the research question regarding the added benefit of vutrisiran + tafamidis in comparison with tafamidis (for details see dossier assessment A25-93) and therefore should have been presented in accordance with the module templates. Despite corresponding remarks in dossier assessment A25-93, the oral hearing and the written request to submit analyses on this subpopulation by the G-BA after the commenting procedure, the company did not submit the data for this subpopulation. The analyses presented by the company for the research question of vutrisiran + tafamidis in comparison with tafamidis were therefore incomplete in terms of content. No relevant study was available for the research question of vutrisiran monotherapy compared with tafamidis monotherapy.

2.1 Summary

The argumentation subsequently presented by the company in the commenting procedure does not change the conclusion on the added benefit of vutrisiran from dossier assessment A25-93.

The following Table 1 shows the result of the benefit assessment of vutrisiran taking into account both dossier assessment A25-93 and the present addendum.

Table 1: Vutrisiran – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM)	tafamidis[b, c]	▪ vutrisiran as an add-on to existing tafamidis therapy: added benefit not proven (data from the HELIOS-B study were not presented) ▪ vutrisiran monotherapy: added benefit not proven (no relevant study)

a. Presented is the ACT specified by the G-BA.
b. It is assumed that in both study arms individualized appropriate treatment of the respective organ manifestation (such as heart failure and/or polyneuropathy) corresponding to the generally accepted current state of medical knowledge is provided, taking into account the special characteristics of the disease ATTR amyloidosis, and that this is documented as concomitant treatment.
c. It is assumed that liver transplantation or heart transplantation is not an option at the time of therapy with vutrisiran.

ACT: appropriate comparator therapy; ATTR-CM: transthyretin amyloidosis with cardiomyopathy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

3 References

The reference list contains citations provided by the company in which bibliographical information may be missing.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Vutrisiran (Transthyretin-Amyloidose mit Kardiomyopathie); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2025 [Accessed: 15.10.2025]. URL: https://doi.org/10.60584/A25-93.

2. Alnylam Pharmaceuticals. HELIOS-B: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy (ATTR Amyloidosis with Cardiomyopathy); Clinical Study Report ALN-TTRSC02-003 CSR 1 [unpublished]. 2024.

3. Alnylam Pharmaceuticals. HELIOS-B: A Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy (ATTR Amyloidosis with Cardiomyopathy); Statistical Analysis Plan, Study ALN-TTRSC02-003, Amendment 2 [unpublished]. 2024.

4. Fontana M, Berk JL, Gillmore JD et al. Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy. N Engl J Med 2024; 392: 33-44. https://doi.org/10.1056/NEJMoa2409134.

5. Sheikh FH, Habib G, Tang WHW et al. Impact of Vutrisiran on Functional Capacity and Quality of Life in Transthyretin Amyloidosis With Cardiomyopathy. JACC 2025; 85(20): 1943-1955. https://doi.org/10.1016/j.jacc.2025.03.454.

6. Witteles RM, Garcia-Pavia P, Damy T et al. Vutrisiran Improves Survival and Reduces Cardiovascular Events in ATTR Amyloid Cardiomyopathy. JACC 2025; 85(20): 1959-1970. https://doi.org/10.1016/j.jacc.2025.04.008.

7. Gemeinsamer Bundesausschuss. Nutzenbewertungsverfahren zum Wirkstoff Vutrisiran (Neues Anwendungsgebiet: Wildtyp- oder hereditäre Transthyretin-Amyloidose mit Kardiomyopathie); zusammenfassende Dokumentation. [Soon available at: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1241/#beschluesse].

8. Alnylam Pharmaceuticals. Amvuttra 25 mg Injektionslösung in einer Fertigspritze [online]. 06.2025 [Accessed: 10.07.2025]. URL: https://www.fachinfo.de.

9. European Medicines Agency. Amvuttra; assessment report [online]. 2025 [Accessed: 01.08.2025]. URL: https://www.ema.europa.eu/en/documents/variation-report/amvuttra-h-c-005852-ii-0015-epar-assessment-report-variation_en.pdf.

10. Fontana M, Berk JL, Gillmore JD et al. Primary Results from HELIOS-B, a Phase 3 Study of Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy (European Society of Cardiology Congress 2024, London, UK) [online]. 2024 [Accessed: 16.12.2025]. URL: https://capella.alnylam.com/wp-content/uploads/2024/08/Primary-Results-from-HELIOS-B-a-Phase-3-Study-of-Vutrisiran-in-Patients-with-Transthyretin-Amyloidosis-with-Cardiomyopathy.pdf.