Acoramidis (transthyretin amyloidosis with cardiomyopathy)

Benefit assessment according to §35a SGB V[1]

EXTRACT

Project: A25-46 Version: 1.0 Status: 27 Jun 2025 DOI: 10.60584/A25-46_en

[1] Translation of Sections I 1 to I 4 of the dossier assessment *Acoramidis (Transthyretin-Amyloidose mit Kardiomyopathie) – Nutzenbewertung gemäß § 35a SGB V*. 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

Acoramidis (transthyretin amyloidosis with cardiomyopathy) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

1 April 2025

Internal Project No.

A25-46

DOI-URL

https://doi.org/10.60584/A25-46_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: berichte@iqwig.de
Internet: www.iqwig.de

Recommended citation

Institute for Quality and Efficiency in Health Care. Acoramidis (transthyretin amyloidosis with cardiomyopathy); Benefit assessment according to §35a SGB V; Extract [online]. 2025 [Accessed: DD.MM.YYYY]. URL: https://doi.org/10.60584/A25-46_en.

Keywords

Acoramidis, Amyloidosis, Cardiomyopathies, Benefit Assessment

Medical and scientific advice

No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

No patients or families were involved in the present dossier assessment.

IQWiG employees involved in the dossier assessment

- Ulrike Mikulić
- Merlin Bittlinger
- Claudia Kapp
- Maximilian Kind
- Stefan Kobza
- Ulrike Lampert
- Max Oberste-Frielinghaus
- Daniela Preukschat
- Katharina Wölke

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ATTR-CM	transthyretin amyloid cardiomyopathy
ACT	appropriate comparator therapy
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

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug acoramidis. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 01 April 2025.

Research question

The aim of this report is to assess the added benefit of acoramidis in comparison with tafamidis as the appropriate comparator therapy (ACT) for the treatment of wild-type or variant transthyretin amyloid cardiomyopathy (ATTR-CM) in adult patients.

The research question shown in Table 2 was defined in accordance with the ACT specified by the G-BA.

Table 2: Research question for the benefit assessment of acoramidis

Therapeutic indication	**ACT**[a]
Wild-type or variant ATTR-CM in adult patients	Tafamidis[b, c]

a. Presented is the ACT specified by the G-BA.
b. It is assumed that a patient-specific adequate treatment of the respective organ manifestation (such as cardiac failure and/or polyneuropathy) corresponding to the state of medical knowledge is carried out in both study arms, taking into account the special features of the disease hATTR amyloidosis, and 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 acoramidis.

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

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used for deriving the added benefit.

Results

The check of the information retrieval did not identify any relevant study for assessing the added benefit of acoramidis in comparison with the ACT.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of acoramidis in comparison with the ACT; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 shows a summary of probability and extent of the added benefit of acoramidis.

Table 3: Acoramidis – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Wild-type or variant ATTR-CM in adult patients	Tafamidis[b, c]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. It is assumed that a patient-specific adequate treatment of the respective organ manifestation (such as cardiac failure and/or polyneuropathy) corresponding to the state of medical knowledge is carried out in both study arms, taking into account the special features of the disease hATTR amyloidosis, and 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 acoramidis.

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

The G-BA decides on the added benefit.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) “proof”, (2) “indication”, (3) “hint”, or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

I 2 Research question

The aim of this report is to assess the added benefit of acoramidis in comparison with tafamidis as the appropriate comparator therapy (ACT) for the treatment of wild-type or variant transthyretin amyloidosis (ATTR-CM) in adult patients.

The research question shown in Table 4 was defined in accordance with the ACT specified by the G-BA.

Table 4: Research question for the benefit assessment of acoramidis

Therapeutic indication	**ACT**[a]
Wild-type or variant ATTR-CM in adult patients	Tafamidis[b, c]

a. Presented is the ACT specified by the G-BA.
b. It is assumed that a patient-specific adequate treatment of the respective organ manifestation (such as cardiac failure and/or polyneuropathy) corresponding to the state of medical knowledge is carried out in both study arms, taking into account the special features of the disease hATTR amyloidosis, and 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 acoramidis.

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

The company followed the G-BA's specification of the ACT.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 24 weeks are used for deriving the added benefit. This concurred with the company’s inclusion criteria.

I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- study lists on acoramidis (status: 3 March 2025)
- bibliographical literature search on acoramidis (last search on 03 March 2025)
- search in trial registries/trial results databases for studies on acoramidis (last search on 03 March 2025)
- search on the G-BA website for acoramidis (last search on 03 March 2025)
- bibliographical literature search on the ACT (last search on 03 March 2025)
- search in trial registries/trial results databases for studies on the ACT (last search on 03 March 2025)
- search on the G-BA website for the ACT (last search on 3 March 2025)

To check the completeness of the study pool:

- search in trial registries for studies on acoramidis (last search on 15 April 2025); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check did not identify any relevant study for assessing the added benefit of acoramidis in comparison with the G-BA's ACT.

The company presents the randomized, double-blind pivotal study ATTRibute-CM [3] as the best available evidence only for the description of the medical benefit. The ATTRibute-CM study compared acoramidis with placebo in adult patients with wild-type or variant ATTR-CM. The administration of tafamidis was not randomized although - if locally available - this was permitted as part of the background therapy in the study in patients who had been treated with the study medication for at least 12 months. According to the data provided in Module 4 A, 11.2% of the patients in the intervention arm and 19.4% of the patients in the comparator arm received background therapy with tafamidis from Month 12. Further information on the treatment with tafamidis is not available. Treatment in the comparator arm does therefore not correspond to the ACT. This means that there are no data for the comparison of acoramidis with the G-BA’s comparator therapy. Concurring with the company, the ATTRibute-CM study is assessed as unsuitable for the assessment of the added benefit of acoramidis due to the lack of comparison with the ACT.

As the company did not identify a suitable study for the direct comparison, it conducted a search for studies that might be considered for indirect comparisons of acoramidis versus the

ACT via the common comparator placebo. In its information retrieval, the company identified the randomized, double-blind study ATTR-ACT [4], in which tafamidis was compared with placebo. However, the company did not consider this study to be suitable for conducting an indirect comparison with the ATTRibute-CM study in the given research question. It cites a lack of similarity of the study populations, differing study periods and differences in the potential common comparators.

Thus, neither results from studies of direct comparisons nor from indirect comparisons were available for the present assessment.

I 4 Results on added benefit

No suitable data are available for the assessment of the added benefit of acoramidis for the treatment of wild-type or variant ATTR-CM in adult patients. There is no hint of an added benefit of acoramidis in comparison with the ACT. An added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of acoramidis in comparison with the ACT is summarized in Table 5.

Table 5: Acoramidis – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Wild-type or variant ATTR-CM in adult patients	Tafamidis[b, c]	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. It is assumed that a patient-specific adequate treatment of the respective organ manifestation (such as cardiac failure and/or polyneuropathy) corresponding to the state of medical knowledge is carried out in both study arms, taking into account the special features of the disease hATTR amyloidosis, and 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 acoramidis.

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

The assessment described above concurs with that by the company.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

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

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 02.09.2024]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://doi.org/10.1002/bimj.201300274.

3. Gillmore JD, Judge DP, Cappelli F et al. Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy. N Engl J Med 2024; 390(2): 132 - 142. https://doi.org/10.1056/NEJMoa2305434.

4. Damy T, Garcia-Pavia P, Hanna M et al. Efficacy and safety of tafamidis doses in the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) and long-term extension study. Eur J Heart Fail 2021; 23(2): 277 - 285. https://doi.org/10.1002/ejhf.2027.

The full report (German version) is published under
https://www.iqwig.de/en/projects/a25-46.html