Garadacimab (hereditary angioedema)

Addendum to Project A25-41 (dossier assessment)[1]

ADDENDUM (DOSSIER ASSESSMENT)

Project: A25-94 Version: 1.0 Status: 29 Jul 2025 DOI: 10.60584/A25-94_en

[1] Translation of the addendum *Garadacimab (hereditäres Angioödem) – Addendum zum Projekt A25-41 (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

Garadacimab (hereditary angioedema) – Addendum to Project A25-41

Commissioning agency

Federal Joint Committee

Commission awarded on

8 July 2025

Internal Project No.

A25-94

https://doi.org/10.60584/A25-94_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. Garadacimab (hereditary angioedema); Addendum to Project A25-41 (dossier assessment) [online]. 2025 [Accessed: DD.MM.YYYY]. URL: https://doi.org/10.60584/A25-94_en.

Keywords

Garadacimab, Angioedemas – Hereditary, Adolescent, Adult, Benefit Assessment, NCT04656418, NCT03485911, NCT03873116

IQWiG employees involved in the addendum

- Marina Goddon
- Philip Kranz
- Katherine Rascher
- Claudia Selbach

Table of contents

List of tables

Page

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE-QoL	Angioedema Quality of Life Questionnaire
ANCOVA	analysis of covariance
CI	confidence interval
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HAE	hereditary angioedema
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MMRM	mixed-effects model with repeated measures
SGB	Sozialgesetzbuch (Social Code Book)
SMD	standardized mean difference
VAS	visual analogue scale
WPAI:GH	Work Productivity and Activity Impairment: General Health

1 Background

On 8 July 2025, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Project A25-41 (Garadacimab – Benefit assessment according to §35a Social Code Book V) [1].

The commission comprised the assessment of the following analyses presented by the pharmaceutical company (hereinafter referred to as 'the company') in the commenting procedure [2,3], taking into account the information provided in the dossier [4]:

- Mixed-effects model with repeated measures (MMRM) analysis for the outcome activity impairment, measured using question 6 of the Work Productivity and Activity Impairment: General Health (WPAI:GH)
- Subgroup analyses on the rate of monthly hereditary angioedema (HAE) attacks (< 2 attacks/month vs. ≥ 2 attacks/month)
- Subgroup analyses on the outcome health-related quality of life, recorded using the Angioedema Quality of Life Questionnaire (AE-QoL) in accordance with the defined operationalization

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

An adjusted indirect comparison according to Bucher [5] between garadacimab and berotralstat via the common comparator placebo was used for the benefit assessment of garadacimab in comparison with the appropriate comparator therapy (ACT) for routine prevention of recurrent attacks of HAE in adult and adolescent patients aged 12 years and older. The VANGUARD study [6-9] was included on the intervention side, and the studies APeX-2 [10-14] and APeX-J [13-16] were included on the berotralstat side. A detailed description of the studies can be found in dossier assessment A25-41.

The company's dossier did not contain an adjusted indirect comparison of garadacimab versus berotralstat for the outcome activity impairment (WPAI:GH question 6). In addition, there were no subgroup analyses for the indirect comparison of garadacimab versus berotralstat for the characteristic of age and for the characteristic of monthly HAE attack rate at baseline. For the outcome of health-related quality of life (AE-QoL), subgroup analyses for the indirect comparison of garadacimab versus berotralstat were also lacking for the characteristic of sex for the relevant operationalization of the change at the end of treatment.

As part of the commenting procedure, the company subsequently submitted results for the outcome activity impairment (WPAI:GH question 6). In its comments, it additionally presented subgroup analyses on the characteristic of rate of monthly HAE attacks (< 2 attacks/month versus ≥ 2 attacks/month), on the outcome of health-related quality of life (AE-QoL) and provided an explanation for the missing subgroup analyses on the characteristic of age.

In accordance with the commission, the analyses and data subsequently submitted by the company in the commenting procedure are assessed below, taking into account the information in the dossier.

Furthermore, an error in the derivation of the extent of the added benefit for the outcome health status (recorded using the visual analogue scale [VAS] of the EQ-5D) from the dossier assessment A25-41 is corrected in this addendum A25-94. Dossier assessment A25-41 determined an added benefit with the extent 'minor' for health status (EQ-5D VAS), assigned to the outcome category of non-serious/non-severe symptoms/late complications. This assessment was based on a rounded standardized mean difference (SMD) [95% confidence interval, CI] of 0.85 [0.40; 1.29]. However, the lower limit of the CI reported by the company in Module 4 A of the dossier was 0.404. According to the threshold values for determining the extent of the SMD specified in the *General Methods* of the Institute [17], there is therefore an added benefit with the extent 'considerable' for the outcome health status (EQ-5D VAS) (see Section 2.3.1).

2.1 MMRM analysis of activity impairment (WPAI:GH question 6)

For the APeX-2 and APeX-J studies, the company presented analyses of the change at the end of treatment compared with baseline for the WPAI:GH question 6, using an MMRM, in Module 4 A for the berotralstat procedure. For the VANGUARD study, an analysis of covariance (ANCOVA) was only available in the clinical study report (see dossier assessment A25-41). An analysis using MMRM for the outcome of activity impairment (WPAI:GH question 6) for the VANGUARD study and an adjusted indirect comparison of garadacimab versus berotralstat were not available. As part of the commenting procedure, the company submitted MMRM analyses for the VANGUARD study and the adjusted indirect comparison of garadacimab versus berotralstat according to Bucher [5] for this outcome. These analyses for the outcome activity impairment (WPAI:GH question 6) were used for the benefit assessment.

Risk of bias

As already described in dossier assessment A25-41, both the risk of bias across outcomes and the outcome-specific risk of bias of the 3 studies VANGUARD, APeX-2 and APeX-J were rated as low. On the basis of the available data from the adjusted indirect comparison – as explained in Section I 4.3 of dossier assessment A25-41 – a maximum of hints, for example of an added benefit, can be determined.

Results

Table 1: Results (morbidity) – RCT, indirect comparison: garadacimab vs. berotralstat

Outcome category Outcome Comparison Study	Garadacimab or berotralstat N[a]	Values at baseline mean (SD)	Mean change at the end of treatment[b] Mean (SE)[c]	Placebo N[a]	Values at baseline mean (SD)	Mean change at the end of treatment[b] Mean (SE)[c]	Group difference MD [95% CI][c]; p-value
Morbidity							
Activity impairment (WPAI:GH question 6[d])							
Garadacimab vs. placebo							
VANGUARD	37	32.6 (31.9)	ND	23	24.5 (26.0)	ND	−2.93 [−4.30; −1.55]; < 0.001
Berotralstat vs. placebo							
APeX-2	38[e]	3.6 (2.8)	−1.6 (0.4)	36[e]	4.1 (2.8)	−1.2 (0.4)	−0.5 [−1.7; 0.7]; 0.406
APeX-J	7	3.3 (2.8)	1.0 (1.0)	6	1.3 (3.3)	−1.0 (1.1)	2.1 [−1.2; 5.4]; 0.200
Total[f]							−0.20 [−1.32; 0.93]; 0.733
Indirect comparison using common comparators[g]:							
Garadacimab vs. berotralstat							−2.73 [−4.51; −0.95]; 0.003
						SMD [95% CI]:	−0.66 [−1.11; −0.22]

a. Number of patients taken into account in the effect estimation; baseline values may be based on different patient numbers.
b. VANGUARD: Week 26; APeX-2 and APeX-J: Week 24
c. VANGUARD: MD [95% CI]: MMRM model adjusted for baseline value, visit and the interaction term visit and treatment. The effect represents the difference in changes (from baseline) between the treatment groups at Week 26.
APeX-2 and APeX-J: mean (SE) and MD [95% CI]: MMRM model adjusted for baseline value, baseline HAE attack rate, visit and the interaction term of visit and treatment, patient ID was included in the model as a random variable. The effect represents the difference in changes (from baseline) between the treatment groups at Week 24.
d. Lower (decreasing) values indicate improved symptoms; negative effects (intervention minus comparison) indicate an advantage of the intervention (scale range: 0 to 10 points; in the VANGUARD study the baseline values are given in percentages).
e. Number of patients with values at the end of treatment; unclear how many patients were included in the model.
f. Meta-analysis using a fixed-effect model (inverse variance method).
g. Indirect comparison according to Bucher [5].

CI: confidence interval; HAE: hereditary angioedema; MD: mean difference; MMRM: mixed-effects model with repeated measures; N: number of analysed patients; ND: no data; RCT: randomized controlled trial; SD: standard deviation; SE: standard error; SMD: standardized mean difference; WPAI:GH: Work Productivity and Activity Impairment: General Health

For activity impairment assessed with the WPAI:GH question 6, the adjusted indirect comparison showed a statistically significant difference in favour of garadacimab compared with berotralstat. The 95% CI of the SMD was fully outside the irrelevance range [−0.2; 0.2]. This was interpreted to be a relevant effect. There was a hint of an added benefit of garadacimab in comparison with berotralstat.

Determination of the outcome category

For the outcome activity impairment (WPAI:GH question 6), insufficient severity data were available for a classification as serious/severe. In the VANGUARD study, as well as in the APeX-2 and APeX-J studies, values at baseline were between 3.3 and 3.6 (scale range: 0 to 10, with lower values indicating better symptoms). The outcome activity impairment (WPAI:GH question 6) was therefore allocated to the outcome category of non-serious/non-severe symptoms/late complications.

2.2 Subgroups and other effect modifiers

The following subgroup characteristics were relevant for the present benefit assessment (see also dossier assessment A25-41):

- Age
- Sex
- Monthly HAE attack rate at baseline

The methods described in Section I 4.4 of dossier assessment A25-41 were used. According to the company, no subgroup analyses were conducted for the APeX-J study because of the small study population. Therefore, it conducted subgroup analyses based on the studies VANGUARD and APeX-2 for the adjusted indirect comparison. The approach of the company is comprehensible.

The company stated in Module 4 A of the dossier that an indirect comparison for the characteristic age could not be conducted due to the different definitions of the subgroups. As described in dossier assessment A25-41, in the indirect comparison presented by the company in its dossier, age groups could have been defined post hoc for the VANGUARD study concurring with the categories in the APeX-2 study. In its comments, the company explained that it was not possible to conduct an indirect comparison of the subgroup analysis by age category (< 18 years, 18 to 65 years and > 65 years) because no such analysis had been conducted in the dossier on berotralstat. This was justified in the dossier on berotralstat by the fact that 2 of the 3 age subgroups comprised fewer than 10 patients each. The company stated that 2 of the age categories (< 18 years and > 65 years) in the VANGUARD study on garadacimab also comprised fewer than 10 patients, making a subgroup analysis of the

corresponding age categories or an indirect comparison based on this not feasible. This approach was appropriate.

For the subgroup characteristic of the monthly HAE attack rate at baseline, the categories were defined according to the respective stratification factor in the studies as 1 to < 3 attacks/month versus ≥ 3 attacks/month (VANGUARD) or ≥ 2 attacks/month versus < 2 attacks/month (APeX-2). The company's dossier did not present any subgroup analyses for the indirect comparison of garadacimab versus berotralstat for the characteristic monthly HAE attack rate at baseline. As described in dossier assessment A25-41, in the indirect comparison presented by the company in its dossier, subgroups based on the monthly HAE attack rate at baseline could have been defined post hoc for the VANGUARD study concurring with the categories in the APeX-2 study. With its comments, the company submitted these subgroup analyses on the characteristic of monthly HAE attack rate at baseline (< 2 attacks/month versus ≥ 2 attacks/month) for the outcomes HAE attacks, activity impairment (WPAI:GH question 6) and health-related quality of life (AE-QoL).

As described in dossier assessment A25-41, for the outcome of health-related quality of life (AE-QoL), subgroup analyses for the indirect comparison of garadacimab versus berotralstat were lacking for the characteristic of sex for the relevant operationalization of the change at the end of treatment. For the outcome of health-related quality of life (AE-QoL), the company submitted subgroup analyses for the indirect comparison of garadacimab versus berotralstat for the characteristic of sex in its comments.

When applying the methods described in dossier assessment A25-41, there were no effect modifications for the subgroup analyses subsequently submitted by the company as part of the commenting procedure.

However, the subgroup analyses were still incomplete. For the outcomes health status (EQ-5D VAS) and activity impairment (WPAI:GH question 6), there were no subgroup analyses for the characteristic of sex for the indirect comparison of garadacimab versus berotralstat. For health status (EQ-5D VAS), there was also no subgroup analysis for the subgroup characteristic of monthly HAE attack rate at baseline.

2.3 Probability and extent of added benefit

2.3.1 Assessment of added benefit at outcome level

The extent of the respective added benefit at outcome level was assessed based on the results presented in dossier assessment A25-41 and the previous sections (see Table 2).

Table 2: Extent of added benefit at outcome level: garadacimab vs. berotralstat (multipage table)

Outcome category **Outcome**	**Garadacimab (VANGUARD) vs. berotralstat (APeX-2 or APeX-J)** **Mean monthly rate or proportion of events (%) or mean change (mean value)** **Effect estimation [95% CI];** **p-value** **Probability**[a]	**Derivation of extent**[b]
Mortality		
All-cause mortality	0% vs. 0% or 0% RR: –[c]	Lesser benefit/added benefit not proven
Morbidity		
HAE attacks Monthly rate	0.22 vs. 1.33 or 1.08 Rate ratio: 0.20 [0.09; 0.47]; p < 0.001 Probability: hint	Outcome category: non-serious/non-severe symptoms/late complications CI_u < 0.80 Added benefit, extent: considerable
Freedom from attack	61.5% vs. 5.0% or 0% Rate ratio: 20.42 [0.68; 616.19]; p = 0.083	Lesser benefit/added benefit not proven
Activity impairment (WPAI:GH question 6)	ND vs. −1.6 / 1.0 MD: −2.73 [-4.51; −0.95]; p = 0.003 SMD [95% CI]: −0.66 [−1.11; −0.22] SMD [95% CI]: 0.66 [0.22; 1.11][d, e] Probability: hint	Outcome category: non-serious/non-severe symptoms/late complications 0.20 < CI_L ≤ 0.40 Added benefit, extent: minor
Health status (EQ-5D VAS)	6.1 vs. 2.7 or 8.4 MD: 14.37 [7.24; 21.50]; p < 0.001 SMD [95% CI]: 0.85 [0.404; 1.29][d] Probability: hint	Outcome category: non-serious/non-severe symptoms/late complications CI_u > 0.4 Added benefit, extent: considerable
Health-related quality of life		
AE-QoL total score	−26.5 vs. −15.8 or −17.1 MD: −19.74 [−31.75; −7.73]; p < 0.001 SMD [95% CI]: −0.74 [−1.21; −0.27] SMD [95% CI]: 0.74 [0.27; 1.21][d, e] Probability: hint	Outcome category: health-related quality of life 0.20 < CI_L ≤ 0.30 Added benefit, extent: minor

Table 2: Extent of added benefit at outcome level: garadacimab vs. berotralstat (multipage table)

Outcome category **Outcome**	**Garadacimab (VANGUARD) vs. berotralstat (APeX-2 or APeX-J)** **Mean monthly rate or proportion of events (%) or mean change (mean value)** **Effect estimation [95% CI];** **p-value** **Probability**[a]	**Derivation of extent**[b]
Side effects		
SAEs	2.6% vs. 0% or 0% RR: 14.03 [0.19; 1065.76]; p = 0.232	Greater/lesser harm not proven
Severe AEs	No suitable data for the indirect comparison[f]	Greater/lesser harm not proven
Discontinuation due to AEs	0% vs. 2.5% or 0% RR: –[c]	Greater/lesser harm not proven

a. Probability provided if statistically significant differences are present.
b. Depending on the outcome category and the scale level of the outcome, effect size is estimated with different limits based on the upper or lower limit of the confidence interval (CI_u or CI_L).
c. No indirect comparison was submitted by the company.
d. If the CI for the SMD is fully outside the irrelevance range [−0.2; 0.2], this is interpreted to be a relevant effect. In other cases, the presence of a relevant effect cannot be derived.
e. Institute's calculation, to determine the extent of the added benefit, the mean difference is formed in such a way that the effect estimates and confidence intervals are above 0.
f. See Section I 4.1 of dossier assessment A25-41 for an explanation.

AE: adverse event; AE-QoL: Angioedema Quality of Life Questionnaire; CI: confidence interval; Ci_u: upper limit of the confidence interval; CI_L: lower limit of the confidence interval; HAE: hereditary angioedema; MD: mean difference; RR: relative risk; SAE: serious adverse event; SMD: standardized mean difference; VAS: visual analogue scale; WPAI:GH: Work Productivity and Activity Impairment: General Health

2.3.2 Overall conclusion on added benefit

Table 3 presents the results of dossier assessment A25-41 and this addendum A25-94 that were taken into account in the overall conclusion on the added benefit.

Table 3: Positive and negative effects from the assessment of garadacimab compared with berotralstat

Positive effects	**Negative effects**
Non-serious/non-severe symptoms/late complications ▪ HAE attacks (monthly rate): hint of an added benefit – extent: considerable ▪ Activity impairment (WPAI:GH question 6): hint of an added benefit – extent: minor ▪ Health status (EQ-5D VAS): hint of an added benefit – extent: considerable	–
Health-related quality of life ▪ AE-QoL total score: hint of an added benefit – extent: minor	–
AE-QoL: Angioedema Quality of Life Questionnaire; HAE: hereditary angioedema; VAS: visual analogue scale; WPAI:GH: Work Productivity and Activity Impairment: General Health	

2.4 Summary

The data subsequently submitted by the company in the commenting procedure do not change the conclusion on the added benefit of garadacimab from dossier assessment A25-41.

The following Table 4 shows the result of the benefit assessment of garadacimab under consideration of dossier assessment A25-41 and this addendum.

Table 4: Garadacimab – probability and extent of the added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
For routine prevention of recurrent attacks of HAE[b] in adults and adolescents aged 12 years and older	Routine prevention with a C1 esterase inhibitor or lanadelumab or **berotralstat**[c]	Hint of considerable added benefit
a. Presented is the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice of the company according to the inclusion criteria in Module 4 A Section 4.2.2 is printed in **bold**. b. According to the G-BA, the therapeutic indication of garadacimab is assumed to comprise only patients with type I or type II HAE. c. Both study arms should offer the possibility of acute treatment of HAE attacks. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; HAE: hereditary angioedema		

The approach for the derivation of an overall conclusion on added benefit is a proposal by IQWiG. The G-BA decides on the added benefit.

3 References

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Garadacimab (hereditäres Angioödem); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2025 [Accessed: 02.06.2025]. URL: https://doi.org/10.60584/A25-41.

2. CSL Behring. Stellungnahme zum IQWiG-Bericht Nr. 2019: Garadacimab (hereditäres Angioödem); Nutzenbewertung gemäß § 35a SGB V. [Soon available at: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1190/#beschluesse in the document "Zusammenfassende Dokumentation"].

3. CSL Behring. Anlage zur Stellungnahme zum IQWiG-Bericht Nr. 2019: Garadacimab (hereditäres Angioödem); Nutzenbewertung gemäß § 35a SGB V. [Soon available at: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1190/#beschluesse in the document "Zusammenfassende Dokumentation"].

4. CSL Behring. Garadacimab (Andembry); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2025 [Accessed: 10.06.2025]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1190/#dossier.

5. Bucher HC, Guyatt GH, Griffith LE et al. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. J Clin Epidemiol 1997; 50(6): 683-691. https://doi.org/10.1016/s0895-4356(97)00049-8.

6. CSL Behring. A Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Arm Study to Investigate the Efficacy and Safety of Subcutaneous Administration of CSL312 (garadacimab) in the Prophylactic Treatment of Hereditary Angioedema; study CSL312_3001; Final Clinical Study Report [unpublished]. 2022.

7. CSL Behring. CSL312 (Garadacimab) in the Prevention of Hereditary Angioedema Attacks [online]. 2023 [Accessed: 25.03.2025]. URL: https://clinicaltrials.gov/study/NCT04656418.

8. CSL Behring. A multicenter, double-blind, randomized, placebo-controlled, parallel-arm study to investigate the efficacy and safety of subcutaneous administration of CSL312 (garadacimab) in the prophylactic treatment of hereditary angioedema [online]. [Accessed: 25.03.2025]. URL: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2020-000570-25.

9. Craig TJ, Reshef A, Li HH et al. Efficacy and safety of garadacimab, a factor XIIa inhibitor for hereditary angioedema prevention (VANGUARD): a global, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2023; 401(10382): 1079-1090. https://doi.org/10.1016/s0140-6736(23)00350-1.

10. BioCryst Pharmaceuticals. Efficacy and Safety Study of BCX7353 as an Oral Treatment for the Prevention of Attacks in HAE (APeX-2) [online]. 2023 [Accessed: 25.03.2025]. URL: https://clinicaltrials.gov/study/NCT03485911.

11. BioCryst Pharmaceuticals. A Phase 3, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of two dose levels of BCX7353 as an oral treatment for the prevention of attacks in subjects with hereditary angioedema [online]. [Accessed: 25.03.2025]. URL: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2017-003966-29.

12. Zuraw B, Lumry WR, Johnston DT et al. Oral once-daily berotralstat for the prevention of hereditary angioedema attacks: A randomized, double-blind, placebo-controlled phase 3 trial. J Allergy Clin Immunol 2021; 148(1): 164-172.e9. https://doi.org/10.1016/j.jaci.2020.10.015.

13. BioCryst Ireland. Dossier zur Nutzenbewertung gemäß § 35a SGB V; Berotralstat (ORLADEYO); Modul 4 A [online]. 2021 [Accessed: 30.04.2025]. URL: https://www.g-ba.de/downloads/92-975-4855/2021_06_03_Modul4A_Berotralstat.pdf.

14. European Medicines Agency. Orladeyo; Assessment report [online]. 2021 [Accessed: 26.03.2025]. URL: https://www.ema.europa.eu/en/documents/assessment-report/orladeyo-epar-public-assessment-report_en.pdf.

15. BioCryst Pharmaceuticals. Study to Evaluate the Efficacy and Safety of BCX7353 as an Oral Treatment for the Prevention of HAE Attacks in Japan (APeX-J) [online]. 2024 [Accessed: 25.03.2025]. URL: https://clinicaltrials.gov/study/NCT03873116.

16. Ohsawa I, Honda D, Suzuki Y et al. Oral berotralstat for the prophylaxis of hereditary angioedema attacks in patients in Japan: A phase 3 randomized trial. Allergy 2021; 76(6): 1789-1799. https://doi.org/10.1111/all.14670.

17. 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.