IQWiG Reports – Commission No. A22-09

Calcifediol (secondary hyperparathyroidism) –

Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Calcifediol (sekundärer Hyperparathyreoidismus) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 25 April 2022). Please note: This document was translated by an external translator and 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
Calcifediol (secondary hyperparathyroidism) – Benefit assessment according to §35a Social Code Book V

Commissioning agency
Federal Joint Committee

Commission awarded on
31 January 2022

Internal Commission No.
A22-09

Address of publisher
Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

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

Medical and scientific advice

No advisor on medical and scientific questions was available for the present dossier assessment.

Patient and family involvement

No feedback was received in the framework of the present dossier assessment.

IQWiG employees involved in the dossier assessment

- Can Ünal
- Ulrich Grouven
- Tatjana Hermanns
- Annette Pusch-Klein
- Min Ripoll
- Ulrike Seay
- Carolin Weigel

Keywords: Calcifediol, Hyperparathyroidism – Secondary, Benefit Assessment

Table of contents

List of tables[2]

Page

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

List of abbreviations

Abbreviation	Meaning
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
SGB	Sozialgesetzbuch (Social Code Book)

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug calcifediol. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 31 January 2022.

Research question

The aim of the present report was to assess the added benefit of calcifediol in comparison with paricalcitol as the appropriate comparator therapy (ACT) for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency.

The research question presented in Table 2 was derived from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of calcifediol

Therapeutic indication	**ACT**[a]
Treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency[b]	Paricalcitol[c]
a. Presented is the respective ACT specified by the G-BA. b. For the present therapeutic indication, patients are presumed not to be indicated for parathyroidectomy at the time of study enrolment. c. Patients are assumed to receive additional phosphate binders where necessary. ACT: appropriate comparator therapy; 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.

Results

In line with the company's assessment, the check of completeness of the study pool did not identify any relevant randomized controlled trial (RCT) for assessing the added benefit of calcifediol in comparison with the ACT.

Hence, no suitable data are available for assessing the added benefit of calcifediol in comparison with the ACT for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency. This results in

no hint of an added benefit of calcifediol 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 the probability and extent of added benefit of calcifediol.

Table 3: Calcifediol – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency[b]	Paricalcitol[c]	Added benefit not proven
a. Presented is the respective ACT specified by the G-BA. b. For the present therapeutic indication, patients are presumed not to be indicated for parathyroidectomy at the time of study enrolment. c. Patients are assumed to receive additional phosphate binders where necessary. ACT: appropriate comparator therapy; 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].

2.2 Research question

The aim of the present report was to assess the added benefit of calcifediol in comparison with paricalcitol as the ACT for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency.

The research question presented in Table 4 was derived from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of calcifediol

Therapeutic indication	**ACT[a]**
Treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency[b]	Paricalcitol[c]
a. Presented is the respective ACT specified by the G-BA. b. For the present therapeutic indication, patients are presumed not to be indicated for parathyroidectomy at the time of study enrolment. c. Patients are assumed to receive additional phosphate binders where necessary. ACT: appropriate comparator therapy; 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.

2.3 Information retrieval and study pool

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

Sources of the company in the dossier:

- study list on calcifediol (status: 18 November 2021)
- bibliographical literature search on calcifediol (last search on 18 November 2021)
- search in trial registries / trial results databases for studies on calcifediol (last search on 17 November 2021)
- search on the G-BA website for calcifediol (last search on 16 November 2021)

To check the completeness of the study pool:

search in trial registries for studies on calcifediol (last search on 4 February 2022); for search strategies, see Appendix A of the full dossier assessment

In its information retrieval, the company identified no RCTs with a direct comparison of calcifediol versus the ACT. The check of completeness also produced no directly comparative RCTs.

In its information retrieval, the company found the placebo-controlled RCTs CTAP-CL-3001 [3] and CTAP-CL-3002 [3] and presented the results of these 2 studies in Module 4; however, it did not use them to derive added benefit. The studies included adult patients with secondary hyperparathyroidism, grade 3 or 4 chronic kidney disease, and vitamin D insufficiency/ deficiency (25-hydroxy vitamin D serum levels [25(OH)D levels] ≥ 10 to < 30 ng/mL). In both studies, calcifediol treatment was administered for 26 weeks. Primary outcomes were the percentage of patients exhibiting a ≥ 30% decrease in intact parathyroid hormone level from baseline as well as adverse events.

As acknowledged by the company, the CTAP-CL-3001 and CTAP-CL-3002 studies are unsuitable for assessing the added benefit of calcifediol in comparison with the ACT since they did not implement the ACT.

2.4 Results on added benefit

No suitable data are available to assess the added benefit of calcifediol in comparison with the ACT for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency. This results in no hint of an added benefit of calcifediol in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

Table 5 summarizes the result of the assessment of the added benefit of calcifediol in comparison with the ACT.

Table 5: Calcifediol – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease and vitamin D insufficiency/deficiency[b]	Paricalcitol[c]	Added benefit not proven
a. Presented is the respective ACT specified by the G-BA. b. For the present therapeutic indication, patients are presumed not to be indicated for parathyroidectomy at the time of study enrolment. c. Patients are assumed to receive additional phosphate binders where necessary. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The assessment described above concurs with that of the company.

The G-BA decides on the added benefit.

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. Institute for Quality and Efficiency in Health Care. General Methods; Version 6.1 [online]. 2022 [Accessed: 17.08.2022]. URL: https://www.iqwig.de/methoden/general-methods_version-6-1.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://dx.doi.org/10.1002/bimj.201300274.

3. Sprague SM, Crawford PW, Melnick JZ et al. Use of Extended-Release Calcifediol to Treat Secondary Hyperparathyroidism in Stages 3 and 4 Chronic Kidney Disease. Am J Nephrol 2016; 44(4): 316-325. https://dx.doi.org/10.1159/000450766.

The full report (German version) is published under https://www.iqwig.de/en/projects/a22-09.html.