IQWiG Reports – Commission No. A22-59

Cabozantinib (thyroid carcinoma) –

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

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Cabozantinib (Schilddrüsenkarzinom) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 18 August 2022). 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
Cabozantinib (thyroid carcinoma) – Benefit assessment according to §35a Social Code Book V

Commissioning agency
Federal Joint Committee

Commission awarded on
27 May 2022

Internal Commission No.
A22-59

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

- Jochen Potenberg, Germany

IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by one person.

IQWiG employees involved in the dossier assessment

- Claudia Selbach
- Nadia Abu Rajab
- Christiane Balg
- Ulrich Grouven
- Simone Heß
- Prateek Mishra
- Ulrike Seay

Keywords: Cabozantinib, Thyroid Neoplasms, 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
BSC	best supportive care
DTC	differentiated thyroid carcinoma
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RAI	radioiodine
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 cabozantinib. 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 27 May 2022.

Research question

The aim of the present report was to assess the added benefit of cabozantinib in comparison with individualized treatment choosing from sorafenib, lenvatinib and best supportive care (BSC) and taking into account the prior therapy and the general condition, as appropriate comparator therapy (ACT) in adults with locally advanced or metastatic differentiated thyroid carcinoma (DTC), who are refractory or not eligible to radioiodine (RAI) and who have experienced progression during or after prior systemic therapy.

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

Table 2: Research question of the benefit assessment of cabozantinib

Therapeutic indication	**ACT**[a]
Adults with locally advanced or metastatic DTC, who are refractory or not eligible to radioiodine and who have progressed during or after prior systemic therapy	Individualized treatment selected from ▪ sorafenib, ▪ lenvatinib and ▪ BSC, taking into account the prior therapy and the general condition
a. Presented is the respective ACT specified by the G-BA. BSC: best supportive care; DTC: differentiated thyroid carcinoma; G-BA: Federal Joint Committee; RAI: radioiodine	

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

The company presented no data to assess the added benefit of cabozantinib compared with the ACT in adults with locally advanced or metastatic DTC who are refractory to or ineligible for RAI and who have experienced progression during or after prior systemic therapy. This resulted in no hint of an added benefit of cabozantinib 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 presents a summary of the probability and extent of the added benefit of cabozantinib.

Table 3: Cabozantinib – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adults with locally advanced or metastatic DTC, who are refractory or not eligible to radioiodine and who have progressed during or after prior systemic therapy	Individualized treatment selected from ▪ sorafenib, ▪ lenvatinib and ▪ BSC, taking into account the prior therapy and the general condition	Added benefit not proven
a. Presented is the respective ACT specified by the G-BA. BSC: best supportive care; DTC: differentiated thyroid carcinoma; G-BA: Federal Joint Committee; RAI: radioiodine		

The G-BA decides on the added benefit.

2.2 Research question

The aim of the present report was to assess the added benefit of cabozantinib as monotherapy in comparison with the ACT in adults with locally advanced or metastatic DTC, who are refractory or not eligible to RAI and who have experienced progression during or after prior systemic therapy.

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

[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].

Table 4: Research question of the benefit assessment of cabozantinib

Therapeutic indication	**ACT[a]**
Adults with locally advanced or metastatic DTC, who are refractory or not eligible to radioiodine and who have progressed during or after prior systemic therapy	Individualized treatment selected from ▪ sorafenib, ▪ lenvatinib and ▪ BSC, taking into account the prior therapy and the general condition
a. Presented is the respective ACT specified by the GBA. BSC: best supportive care; DTC: differentiated thyroid carcinoma; G-BA: Federal Joint Committee; RAI: radioiodine	

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 cabozantinib (status: 1 April 2022)
- bibliographical literature search on cabozantinib (last search on 1 April 2022)
- search in trial registries/trial results databases for studies on cabozantinib (last search on 1 April 2022)
- search on the G-BA website for cabozantinib (last search on 5 April 2022)
- bibliographical literature search on the ACT (last search on 1 April 2022)
- search in trial registries/trial results databases for studies on the ACT (last search on 1 April 2022)
- search on the G-BA website for the ACT (last search on 5 April 2022)

To check the completeness of the study pool:

- search in trial registries for studies on cabozantinib (last search on 7 June 2022); for search strategies, see Appendix A of the full dossier assessment.

No relevant randomized controlled trial (RCT) on the comparison of cabozantinib with the ACT was identified from the check. This concurs with the company's assessment.

As the company did not identify a relevant RCT, it aims for an indirect comparison. For the intervention, it identified the RCT COSMIC-311 [3], which compares cabozantinib + BSC with placebo + BSC. The study included patients with RAI-refractory DTC, who had progressed

after treatment with at least one tyrosine-kinase inhibitor (TKI) directed against the vascular endothelial growth factor receptor (VEGFR). No additional RCT on cabozantinib was identified from the check of the completeness of the study pool. For a comparison with the ACT, it searched for RCTs on the common comparator BSC, but could not identify any study. The completeness of the study pool on the ACT was not checked.

2.4 Results on added benefit

In its dossier, the company did not provide any data to assess the added benefit of cabozantinib compared with the ACT in adults with locally advanced or metastatic DTC who are refractory to or ineligible for RAI and who have experienced progression during or after prior systemic therapy. This resulted in no hint of an added benefit of cabozantinib in comparison with the ACT; an added benefit is therefore not proven.

2.5 Probability and extent of added benefit

As the company presented no data for the assessment of the added benefit of cabozantinib compared to the ACT in adults with locally advanced or metastatic DTC who are refractory to or ineligible for RAI and who have experienced progression during or after previous systemic therapy, an added benefit of cabozantinib for these patients is not proven.

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

Table 5: Cabozantinib – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adults with locally advanced or metastatic DTC, who are refractory or not eligible to radioiodine and who have progressed during or after prior systemic therapy	Individualized treatment selected from ▪ sorafenib, ▪ lenvatinib and ▪ BSC, taking into account the prior therapy and the general condition	Added benefit not proven
a. Presented is the respective ACT specified by the G-BA. BSC: best supportive care; DTC: differentiated thyroid carcinoma; G-BA: Federal Joint Committee; RAI: radioiodine		

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 (German version) [online]. 2022 [Accessed: 27.01.2022]. URL: https://www.iqwig.de/methoden/allgemeine-methoden-v6-1.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. Brose MS, Robinson B, Sherman SI et al. Cabozantinib for radioiodine-refractory differentiated thyroid cancer (COSMIC-311): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 2021; 22(8): 1126-1138. https://dx.doi.org/10.1016/S1470-2045(21)00332-6.

The full report (German version) is published under https://www.iqwig.de/en/projects/a22-59.html.