IQWiG Reports – Commission No. A21-127

Vandetanib (medullary thyroid cancer) –

Benefit assessment according to §35a Social Code Book V[1] (expiry of the decision)

Extract

[1] Translation of Sections 2.1 to 2.5 of the dossier assessment *Vandetanib (medulläres Schilddrüsenkarzinom) – Nutzenbewertung gemäß § 35a SGB V (Ablauf Befristung)* (Version 1.0; Status: 17 December 2021). 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
Vandetanib (medullary thyroid cancer) – Benefit assessment according to §35a Social Code Book V

Commissioning agency
Federal Joint Committee

Commission awarded on
1 October 2021

Internal Commission No.
A21-127

Address of publisher
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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

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

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Keywords: Vandetanib, 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
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MTC	medullary thyroid cancer
RCT	randomized controlled trial
RET	rearranged during transfection
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 vandetanib. 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 1 October 2021.

The company had already submitted a dossier for a previous benefit assessment of the drug to be assessed. In this procedure, a time limit was imposed on the G-BA's decision dated 5 September 2013 until 5 September 2016 and then extended until 1 October 2021.

A time limit was imposed because the approval was contingent upon the company submitting for review to the European Medicines Agency (EMA) additional comprehensive clinical data on the safety and efficacy of vandetanib, including data on efficacy and safety outcomes of studies such as a study on the rearranged during transfection (RET) mutation status in patients with sporadic medullary thyroid cancer. For this purpose, the company presented the data on the uncontrolled D4200C00104 study.

Research question

The aim of this report is to assess the added benefit of vandetanib in comparison with the appropriate comparator therapy (ACT) of cabozantinib in adult patients with aggressive and symptomatic unresectable locally advanced or metastatic medullary thyroid cancer (MTC).

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 vandetanib

Therapeutic indication	**ACT[a]**
Treatment of aggressive and symptomatic MTC in adult patients with unresectable locally advanced or metastatic disease	Cabozantinib
a. Presented is the ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; MTC: medullary thyroid cancer	

After approval for adults had been granted in 2012, vandetanib was most recently evaluated in an early benefit assessment in comparison with the ACT of best supportive care (BSC), and the validity period of the G-BA's decision was limited. For the assessment after expiry of the validity period, the G-BA specified, in departure from its 2013 decision, cabozantinib as the ACT.

The company designated cabozantinib as the comparator therapy, thus following the G-BA's specification.

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) were used for the derivation of added benefit. This concurs with the company's inclusion criteria.

Study pool and study design

Concurring with the company, the check of the completeness of the study pool produced no RCTs on the direct comparison of vandetanib versus the ACT (cabozantinib).

For the G-BA's re-evaluation after expiry of the time limit, the company submitted, as supplementary information, the uncontrolled D4200C00104 study with vandetanib. The study included patients with aggressive and symptomatic unresectable locally advanced or metastatic MTC with RET-positive or RET-negative mutation status. The company submitted results separately for patients with RET-positive versus RET-negative status. The D4200C00104 study is unsuitable for assessing the added benefit of vandetanib in comparison with cabozantinib. This concurs with the company's assessment.

Results

For adult patients with aggressive and symptomatic unresectable locally advanced or metastatic MTC, the company has not presented any data for assessing the added benefit of vandetanib in comparison with the ACT (cabozantinib). Consequently, there is no added benefit of vandetanib in comparison with the ACT of cabozantinib; 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 extent and probability of added benefit of vandetanib.

Table 3: Vandetanib – extent and probability of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Treatment of aggressive and symptomatic MTC in adult patients with unresectable locally advanced or metastatic disease	Cabozantinib	Added benefit not proven
a. Presented is the ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; MTC: medullary thyroid cancer		

[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].

The G-BA decides on the added benefit.

2.2 Research question

The aim of this report is to assess the added benefit of vandetanib in comparison with the ACT of cabozantinib in adult patients with aggressive and symptomatic unresectable locally advanced or metastatic MTC.

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

Table 4: Research question of the benefit assessment of vandetanib

Therapeutic indication	**ACT[a]**
Treatment of aggressive and symptomatic MTC in adult patients with unresectable locally advanced or metastatic disease	Cabozantinib
a. Presented is the ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; MTC: medullary thyroid cancer	

After having been approved for adults in 2012, vandetanib was most recently evaluated in an early benefit assessment versus the ACT of BSC in 2013 [3,4], and the validity period of the G-BA's decision was limited [5]. For the assessment after expiry of the validity period, the G-BA specified, in departure from its 2013 decision, cabozantinib as the ACT [5].

The company designated cabozantinib as the comparator therapy and thus followed the G-BA's specification.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs were used for the derivation of added benefit. This concurs with the company's inclusion criteria.

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 lists on vandetanib (status: 9 August 2021)
- bibliographical literature search on vandetanib (last search on 17 August 2021)
- search in trial registries/trial results databases for studies on vandetanib (last search on 17 August 2021)

To check the completeness of the study pool:

- search in trial registries for studies on vandetanib (last search on 21 October 2021); for search strategies, see Appendix A of the full dossier assessment

Concurring with the company, the check of the completeness of the study pool produced no RCTs on the direct comparison of vandetanib versus the ACT (cabozantinib).

The company has not pursued an indirect comparison, nor has it carried out information retrievals for other investigations. To meet the G-BA's conditions of the limitation, however, the company submitted, as supplementary information, the uncontrolled D4200C00104 study [6]. The study included patients with aggressive and symptomatic unresectable locally advanced or metastatic MTC. For mortality and side effects outcomes, the company submitted results separately for patients with RET-positive (N = 64) versus RET-negative mutation status (N = 27). The D4200C00104 study is unsuitable for assessing the added benefit of vandetanib in comparison with cabozantinib. This concurs with the company's assessment.

2.4 Results on added benefit

For adult patients with aggressive and symptomatic unresectable locally advanced or metastatic MTC, the company did not present any data for assessing the added benefit of vandetanib in comparison with the ACT (cabozantinib). Consequently, there is no added benefit of vandetanib in comparison with the ACT of cabozantinib; 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 vandetanib in comparison with the ACT.

Table 5: Vandetanib – extent and probability of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of aggressive and symptomatic MTC in adult patients with unresectable locally advanced or metastatic disease	Cabozantinib	Added benefit not proven
a. Presented is the ACT specified by the G-BA. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; MTC: medullary thyroid cancer		

The assessment described above concurs with the company's assessment.

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.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a21-127.html.