

# Odronextamab (follicular lymphoma)

Benefit assessment according to §35a SGB V<sup>1</sup>



EXTRACT

Project: A25-101

Version: 1.0

Status: 28 Oct 2025

DOI: 10.60584/A25-101\_en

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<sup>1</sup> Translation of Sections I 1 to I 6 of the dossier assessment *Odronextamab (follikuläres Lymphom)* – *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**

Odronextamab (follicular lymphoma) – Benefit assessment according to §35a SGB V

**Commissioning agency**

Federal Joint Committee

**Commission awarded on**

31 July 2025

**Internal Project No.**

A25-101

**DOI-URL**

[https://doi.org/10.60584/A25-101\\_en](https://doi.org/10.60584/A25-101_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](mailto:berichte@iqwig.de)

Internet: [www.iqwig.de](http://www.iqwig.de)

### **Recommended citation**

Institute for Quality and Efficiency in Health Care. Odronextamab (follicular lymphoma); Benefit assessment according to §35a SGB V; Extract [online]. 2025 [Accessed: DD.MM.YYYY]. URL: [https://doi.org/10.60584/A25-101\\_en](https://doi.org/10.60584/A25-101_en).

### **Keywords**

Odronextamab, Lymphoma – Follicular, Benefit Assessment

### **Medical and scientific advice**

- Ingo Schmidt-Wolf, University Hospital Bonn, 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**

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

### **IQWiG employees involved in the dossier assessment**

- Can Ünal
- Kirsten Janke
- Claudia Kapp
- Stefan Kobza
- Philip Kranz
- Prateek Mishra
- Mattea Patt
- Felix Schwarz
- Pamela Wronski

## **Part I: Benefit assessment**

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<sup>2</sup> Table numbers start with “2” as numbering follows that of the full dossier assessment.

# I List of abbreviations

<b>Abbreviation</b>	<b>Meaning</b>
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)
SmPC	summary of product characteristics

## **I 1 Executive summary of the benefit assessment**

### **Background**

The Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug odronextamab in accordance with §35a Social Code Book V. 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 July 2025.

### **Research question**

The aim of this report is to assess the added benefit of odronextamab as monotherapy in comparison with the appropriate comparator therapy (ACT) in adult patients with relapsed or refractory follicular lymphoma, after at least 2 lines of systemic therapy.

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 odronextamab

Therapeutic indication	ACT <sup>a</sup>
Adults with relapsed or refractory follicular lymphoma <sup>b</sup> , after at least 2 lines of systemic therapy <sup>c</sup>	Individualized treatment <sup>d, e, f</sup> selecting from <ul style="list-style-type: none"> <li>▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per the marketing authorization</li> <li>▪ lenalidomide + rituximab</li> <li>▪ rituximab monotherapy</li> <li>▪ mosunetuzumab</li> <li>▪ tisagenlecleucel and</li> <li>▪ zanubrutinib + obinutuzumab</li> </ul>
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. Irrespective of the fact that grade 3b follicular lymphoma is formally covered by the therapeutic indication, when determining the ACT, the G-BA assumes that odronextamab is not an option for the treatment of diagnosed grade 3b follicular lymphoma in this therapeutic indication. This subentity is not assigned to the indolent non-Hodgkin lymphomas. Accordingly, the new WHO classification 2022 of lymphoid tumours uses the new term ‘follicular large cell lymphoma’ to distinguish the entity formerly known as ‘follicular lymphoma grade 3b’ from classic follicular lymphomas (grades 1 to 3a).</p> <p>c. In this therapeutic indication it is assumed, according to the G-BA, that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to the advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. It is also assumed that there is no indication for radiotherapy at the time of treatment with odronextamab. Furthermore, for this therapeutic indication, it is assumed that stem cell transplantation is not indicated at the time of treatment with odronextamab.</p> <p>d. The term ‘individualized treatment’ is used instead of previously used terms such as ‘patient-specific therapy’ or ‘treatment of physician’s choice’. This ensures consistency with the terms used in European health technology assessments (EU HTAs).</p> <p>e. The treatment decision is made in particular taking into account the prior therapy, the course of the disease and the patient’s general condition.</p> <p>f. For the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study).</p> <p>EU: European Union; G-BA: Federal Joint Committee; GELF: Groupe d’Etude des Lymphomes Folliculaires; HTA: health technology assessment WHO: World Health Organization</p>	

On 12 August 2025, after the dossier was submitted by the company, the G-BA modified the ACT to that shown in Table 2. In its dossier, the company referred to the ACT from its consultation with the G-BA on 10 April 2024. The company deviated both from the ACT specified in this consultation and from the current ACT as defined by the G-BA. The deviation concerned the treatment options that can be considered as part of individualized treatment, taking into account the prior therapy, the course of the disease and the patient’s general condition. The company cited mosunetuzumab, tisagenlecleucel and zanubrutinib + obinutuzumab as treatment options, which was in line with the specification of the G-BA, but also listed axicabtagene ciloleucel (for patients with at least 3 prior systemic treatment regimens) and epcoritamab as further treatment options. In contrast, the company did not name bendamustine + obinutuzumab, lenalidomide + rituximab or rituximab as monotherapy

as possible treatment options, deviating from the specification of the G-BA. The deviations described were of no consequence for this benefit assessment, as the company did not present any suitable data for the comparison of odronextamab with the treatment options specified by the G-BA or with the options additionally specified by the company.

This benefit assessment was conducted in comparison with the ACT specified by the G-BA on 12 August 2025 and by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

## **Results**

The review of the completeness of the study pool did not identify any studies that would allow a direct comparison of odronextamab versus the ACT.

As the company did not identify any studies for a direct comparison either, it conducted an information retrieval for further studies on odronextamab. In doing so, it identified the single-arm study ELM-2 on treatment with odronextamab and used this study for its assessment of the added benefit. In Module 4 B of the dossier, the company stated that it would not conduct any indirect comparisons of the treatment arm from ELM-2 with individual arms from studies with drugs of the ACT. Accordingly, the company did not conduct an information retrieval for studies with the ACT and only used data from the ELM-2 study on treatment with odronextamab for its assessment.

The use of data from the single-arm study ELM-2 on treatment with odronextamab was not suitable for the benefit assessment, as it did not allow a comparison of odronextamab versus the ACT. No suitable data were therefore available.

## **Results on added benefit**

Since no suitable data were available for the benefit assessment, there is no hint of an added benefit of odronextamab 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<sup>3</sup>

Table 3 presents a summary of the probability and extent of the added benefit of odronextamab.

Table 3: Odronextamab – probability and extent of added benefit

Therapeutic indication	ACT <sup>a</sup>	Probability and extent of added benefit
Adults with relapsed or refractory follicular lymphoma <sup>b</sup> , after at least 2 lines of systemic therapy <sup>c</sup>	Individualized treatment <sup>d, e, f</sup> selecting from <ul style="list-style-type: none"> <li>▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per the marketing authorization</li> <li>▪ lenalidomide + rituximab</li> <li>▪ rituximab monotherapy</li> <li>▪ mosunetuzumab</li> <li>▪ tisagenlecleucel and</li> <li>▪ zanubrutinib + obinutuzumab</li> </ul>	Added benefit not proven
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. Irrespective of the fact that grade 3b follicular lymphoma is formally covered by the therapeutic indication, when determining the ACT, the G-BA assumes that odronextamab is not an option for the treatment of diagnosed grade 3b follicular lymphoma in this therapeutic indication. This subentity is not assigned to the indolent non-Hodgkin lymphomas. Accordingly, the new WHO classification 2022 of lymphoid tumours uses the new term ‘follicular large cell lymphoma’ to distinguish the entity formerly known as ‘follicular lymphoma grade 3b’ from classic follicular lymphomas (grades 1 to 3a).</p> <p>c. In this therapeutic indication it is assumed, according to the G-BA, that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to the advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. It is also assumed that there is no indication for radiotherapy at the time of treatment with odronextamab. Furthermore, for this therapeutic indication, it is assumed that stem cell transplantation is not indicated at the time of treatment with odronextamab.</p> <p>d. The term ‘individualized treatment’ is used instead of previously used terms such as ‘patient-specific therapy’ or ‘treatment of physician’s choice’. This ensures consistency with the terms used in European health technology assessments (EU HTAs).</p> <p>e. The treatment decision is made in particular taking into account the prior therapy, the course of the disease and the patient’s general condition.</p> <p>f. For the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study).</p> <p>EU: European Union; G-BA: Federal Joint Committee; GELF: Groupe d’Etude des Lymphomes Folliculaires; HTA: health technology assessment WHO: World Health Organization</p>		

The G-BA decides on the added benefit.

<sup>3</sup> 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].

## 1.2 Research question

The aim of this report is to assess the added benefit of odronextamab as monotherapy in comparison with the appropriate comparator therapy (ACT) in adult patients with relapsed or refractory follicular lymphoma, after at least 2 lines of systemic therapy.

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 odronextamab

Therapeutic indication	ACT <sup>a</sup>
Adults with relapsed or refractory follicular lymphoma <sup>b</sup> , after at least 2 lines of systemic therapy <sup>c</sup>	Individualized treatment <sup>d, e, f</sup> selecting from <ul style="list-style-type: none"> <li>▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per the marketing authorization</li> <li>▪ lenalidomide + rituximab</li> <li>▪ rituximab monotherapy</li> <li>▪ mosunetuzumab</li> <li>▪ tisagenlecleucel and</li> <li>▪ zanubrutinib + obinutuzumab</li> </ul>
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. Irrespective of the fact that grade 3b follicular lymphoma is formally covered by the therapeutic indication, when determining the ACT, the G-BA assumes that odronextamab is not an option for the treatment of diagnosed grade 3b follicular lymphoma in this therapeutic indication. This subentity is not assigned to the indolent non-Hodgkin lymphomas. Accordingly, the new WHO classification 2022 of lymphoid tumours [3] uses the new term ‘follicular large cell lymphoma’ to distinguish the entity formerly known as ‘follicular lymphoma grade 3b’ from classic follicular lymphomas (grades 1 to 3a).</p> <p>c. In this therapeutic indication it is assumed, according to the G-BA, that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to the advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. It is also assumed that there is no indication for radiotherapy at the time of treatment with odronextamab. Furthermore, for this therapeutic indication, it is assumed that stem cell transplantation is not indicated at the time of treatment with odronextamab.</p> <p>d. The term ‘individualized treatment’ is used instead of previously used terms such as ‘patient-specific therapy’ or ‘treatment of physician’s choice’. This ensures consistency with the terms used in European health technology assessments (EU HTAs).</p> <p>e. The treatment decision is made in particular taking into account the prior therapy, the course of the disease and the patient’s general condition.</p> <p>f. For the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study).</p> <p>EU: European Union; G-BA: Federal Joint Committee; GELF: Groupe d’Etude des Lymphomes Folliculaires; HTA: health technology assessment WHO: World Health Organization</p>	

On 12 August 2025, after the dossier was submitted by the company, the G-BA modified the ACT to that shown in Table 4. In its dossier, the company referred to the ACT from its consultation with the G-BA on 10 April 2024. The company deviated both from the ACT

specified in this consultation and from the current ACT as defined by the G-BA. The deviation concerned the treatment options that can be considered as part of individualized treatment, taking into account the prior therapy, the course of the disease and the patient's general condition. The company cited mosunetuzumab, tisagenlecleucel and zanubrutinib + obinutuzumab as treatment options, which was in line with the specification of the G-BA, but also listed axicabtagene ciloleucel (for patients with at least 3 prior systemic treatment regimens) and epcoritamab as further treatment options. In contrast, the company did not name bendamustine + obinutuzumab, lenalidomide + rituximab or rituximab as monotherapy as possible treatment options, deviating from the specification of the G-BA. The deviations described were of no consequence for this benefit assessment, as the company did not present any suitable data for the comparison of odronextamab with the treatment options specified by the G-BA or with the options additionally specified by the company (see Chapter I 3 for details).

This benefit assessment was conducted in comparison with the ACT specified by the G-BA on 12 August 2025 and by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

### **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 list on odronextamab (status: 10 June 2025)
- Bibliographical literature search on odronextamab (last search on 10 June 2025)
- Search of trial registries / trial results databases for studies on odronextamab (last search on 11 June 2025)
- Search on the G-BA website for odronextamab (last search on 12 June 2025)

To check the completeness of the study pool:

- Search of trial registries for studies on odronextamab (last search on 12 August 2025); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the review of the completeness of the study pool did not identify any studies that would allow a direct comparison of odronextamab versus the ACT.

As the company did not identify any studies for a direct comparison, it conducted an information retrieval for further studies on odronextamab. In doing so, it identified the single-arm study ELM-2 [4] on treatment with odronextamab and used this study for its assessment of the added benefit. In Module 4 B of the dossier, the company stated that it would not conduct any indirect comparisons of the treatment arm from ELM-2 with individual arms from studies with drugs of the ACT. It justified this, among other things, with the challenges of a comprehensive confounder adjustment and the high heterogeneity of study populations that have undergone extensive prior treatment. Correspondingly, the company did not conduct an information retrieval for the ACT. The completeness of the study pool presented by the company for further investigations was not checked.

The data presented by the company were unsuitable for drawing conclusions on the added benefit of odronextamab in comparison with the ACT. The following section describes the ELM-2 study and explains why it is unsuitable.

#### **Evidence provided by the company**

##### ***ELM-2***

The ELM-2 study is an ongoing, single-arm study of treatment with odronextamab in adult patients with relapsed or refractory B-cell non-Hodgkin lymphoma, which was pivotal for the marketing authorization of odronextamab.

Depending on the tumour entity and the dosing regimen administered, patients in the study were treated in different cohorts, including a cohort of patients with grade 1 to 3a follicular lymphoma after 2 or more lines of prior systemic therapy. The dosage of odronextamab was gradually increased; however, the escalation scheme was modified during the ongoing study and therefore only met the specifications of the summary of product characteristics (SmPC) [5] for some of the patients included. Regardless of the escalation scheme, all patients in the follicular lymphoma cohort received the on-label target dose of odronextamab.

The primary outcome of the ELM-2 study was the tumour response according to the Lugano Classification for malignant lymphoma and as assessed by independent central review.

### ***Analyses presented by the company***

In Module 4 B of the dossier, the company used the results of the patients from the follicular lymphoma cohort for the ELM-2 study. The company considered all patients from this cohort regardless of whether the escalation scheme complied with the specifications of the SmPC. In addition, the company considered 2 different data cuts of the ELM-2 study (data cut-offs of 31 January 2023 and 20 October 2023) for its assessment, depending on the outcome; according to the company, the later data cut-off was requested by the European Medicines Agency as part of the marketing authorization procedure.

### **Evidence presented by the company unsuitable for the benefit assessment**

The use of data from the single-arm study ELM-2 on treatment with odronextamab was not suitable for the benefit assessment, as it did not allow a comparison of odronextamab versus the ACT. No suitable data were therefore available.

#### **I 4 Results on added benefit**

No suitable data were available to assess the added benefit of odronextamab as monotherapy in comparison with the ACT in adult patients with relapsed or refractory follicular lymphoma, after at least 2 lines of systemic therapy. There is no hint of an added benefit of odronextamab 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 odronextamab in comparison with the ACT is summarized in Table 5.

Table 5: Odronextamab – probability and extent of added benefit

Therapeutic indication	ACT <sup>a</sup>	Probability and extent of added benefit
Adults with relapsed or refractory follicular lymphoma <sup>b</sup> , after at least 2 lines of systemic therapy <sup>c</sup>	Individualized treatment <sup>d, e, f</sup> selecting from <ul style="list-style-type: none"> <li>▪ bendamustine + obinutuzumab followed by obinutuzumab maintenance therapy as per the marketing authorization</li> <li>▪ lenalidomide + rituximab</li> <li>▪ rituximab monotherapy</li> <li>▪ mosunetuzumab</li> <li>▪ tisagenlecleucel and</li> <li>▪ zanubrutinib + obinutuzumab</li> </ul>	Added benefit not proven
<p>a. Presented is the ACT specified by the G-BA.</p> <p>b. Irrespective of the fact that grade 3b follicular lymphoma is formally covered by the therapeutic indication, when determining the ACT, the G-BA assumes that odronextamab is not an option for the treatment of diagnosed grade 3b follicular lymphoma in this therapeutic indication. This subentity is not assigned to the indolent non-Hodgkin lymphomas. Accordingly, the new WHO classification 2022 of lymphoid tumours [3] uses the new term ‘follicular large cell lymphoma’ to distinguish the entity formerly known as ‘follicular lymphoma grade 3b’ from classic follicular lymphomas (grades 1 to 3a).</p> <p>c. In this therapeutic indication it is assumed, according to the G-BA, that there is an indication for systemic antineoplastic therapy for patients with follicular lymphoma due to the advanced stage of disease, particularly with regard to a symptomatic course (e.g. as per GELF criteria), and that, among others, a watch-and-wait strategy is not an option. It is also assumed that there is no indication for radiotherapy at the time of treatment with odronextamab. Furthermore, for this therapeutic indication, it is assumed that stem cell transplantation is not indicated at the time of treatment with odronextamab.</p> <p>d. The term ‘individualized treatment’ is used instead of previously used terms such as ‘patient-specific therapy’ or ‘treatment of physician’s choice’. This ensures consistency with the terms used in European health technology assessments (EU HTAs).</p> <p>e. The treatment decision is made in particular taking into account the prior therapy, the course of the disease and the patient’s general condition.</p> <p>f. For the implementation of individualized treatment in a study of direct comparison, it is expected that investigators have a choice of several treatment options at their disposal, enabling them to make individualized treatment decisions (multi-comparator study).</p> <p>EU: European Union; G-BA: Federal Joint Committee; GELF: Groupe d’Etude des Lymphomes Folliculaires; HTA: health technology assessment WHO: World Health Organization</p>		

The assessment described above deviates from that of the company, which derived a hint of a non-quantifiable added benefit.

The G-BA decides on the added benefit.

## I 6 References for English extract

Please see full dossier assessment for full reference list.

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](https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf).
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