Burosumab
(X-linked hypophosphataemia, 1 month to 1 year)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Siegburger Str. 237
50679 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
Email: info@iqwig.de
Internet: www.iqwig.de

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Medical and scientific advice

- Wolfgang Rascher, Erlangen

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Patient and family involvement

The questionnaire on the disease and its treatment was answered by Monika Helfert und Martha Kirchhoff.

IQWiG thanks the respondents and the patient organisation Phosphatdiabetes e. V. for participating in the written exchange and for their support. The respondents and Phosphatdiabetes e. V. were not involved in the actual preparation of the dossier assessment.

IQWiG employees involved in the dossier assessment

- Christof Dücker
- Annalena Dunkel
- Tobias Effertz
- Katharina Frangen
- Ulrich Grouven
- Deborah Ingenhag-Reister
- Michaela Florina Kerekes
- Stefan Kobza
- Moritz Platen
- Daniela Preukschat

Part I: Benefit assessment

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

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
GBA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomised controlled trial
SGB	Sozialgesetzbuch (Social Code Book)
XLH	X-linked hypophosphataemia

I 1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book V, the Federal Joint Committee (GBA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug burosumab. 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 23 June 2026.

Research question

The aim of this report is to assess the added benefit of burosumab compared with phosphate substitution in combination with active vitamin D (calcitriol or alfacalcidol) as an appropriate comparator therapy (ACT) for the treatment of X-linked hypophosphataemia (XLH) in infants from 1 month to 1 year of age with hypophosphataemia.

The research question shown in Table 2 was defined in accordance with the ACT specified by the GBA.

Table 2: Research question of the benefit assessment of burosumab

Therapeutic indication	**ACT**[a]
Treatment of X-linked hypophosphataemia (XLH) in infants from 1 month to 1 year of age with hypophosphataemia	Phosphate substitution and active vitamin D (calcitriol or alfacalcidol) in combination
a. Presented is the ACT specified by the GBA. GBA: Federal Joint Committee; XLH: X-linked hypophosphataemia	

The company followed the ACT specified by the GBA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Studies with a minimum duration of 24 weeks were used for the derivation of the added benefit.

Results

There are no RCTs available for this research question on infants aged between 1 month and 1 year. However, regardless of this, the company states that it had identified the UX023-CL301 study on the GBA website as part of its information retrieval, which had already been used to derive the added benefit for patients with XLH aged between 1 and 17 years. The UX023-CL301 study is an open-label, randomised controlled trial (RCT) comparing burosumab with oral phosphate substitution and active vitamin D in paediatric patients aged 1 to 12 years in this therapeutic indication; it is already known from a previous benefit assessment procedure. The company additionally conducted an information retrieval for further studies with

burosumab for infants aged between 1 month and 1 year within this therapeutic indication, and in doing so identified the BUR-CL207 study, which it presents in Module 4 A for supporting information. The BUR-CL207 study is a single-arm study for the assessment of the safety, tolerability, pharmacokinetics and efficacy of burosumab in infants < 1 year of age with XLH. The company did not conduct any information retrieval for further studies for the ACT.

Transfer of results of patients from the RCT UX023-CL301 to the target population not possible

Approach and reasoning of the company on the transfer of the study results

The company argues that it was possible to transfer evidence based on the RCT UX023-CL301 in combination with the evidence from the single-arm study BUR-CL207. However, when assessing the transferability of efficacy and safety between the two age groups, the company merely compares, in narrative form, the results from the RCT UX023-CL301 with those from the BUR-CL207 study. Thereafter, the company concluded that the mechanism of action was identical in both age groups, that the pathophysiology was independent of age, and that both studies (BUR-CL207 and UX023-CL301) showed statistically significant and clinically relevant improvements in the symptoms of rickets and the increase in serum phosphate levels, which together constituted the two main objectives of treatment in children with XLH. Taken as a whole, and taking into account the comparable pathophysiology, the identical mechanism of action, the consistent efficacy and safety, the identical ACT as well as regulatory precedents, a transfer of evidence could take place. Given the associated uncertainties and the limitations of the available evidence, the extent of the added benefit cannot be quantified; consequently, for patients aged between 1 month and 1 year with XLH, there is a hint of non-quantifiable added benefit.

Assessment of the data presented by the company

The data presented by the company were unsuitable to derive conclusions on the added benefit of burosumab versus the ACT. The company did not conduct a complete information retrieval; in particular, it did not search for further studies on the ACT that would support a transfer of the results. Consequently, there is no analysis of the information on the basis of which the company could assess the course of the disease for the relevant age group (1 month to 1 year) under the ACT. In addition, the company presented the UX023-CL301 study for the adjacent age group of 1- to 17-year-olds, but did not carry out any information retrieval for RCTs for this age group.

Furthermore, the company did not carry out a sufficient information synthesis, in the sense that it did not adequately process and compare the data from the studies. In Module 4A, the company merely provides data for the single-arm BUR-CL207 study regarding study details and results. However, with regard to the details and results of the UX023-CL301 study, the company refers to the respective Module 4 on the previous benefit assessment procedure.

The data from the UX023-CL301 study were not analysed as part of the dossier relevant to the present research question. In Section 4.4.2 of Module 4A, the company narratively compares extracts of the results of RCT UX023-CL301 with the results of the single-arm study. Based on this information analysis, it is not possible to assess the transferability of the results from older patients in the UX023-CL301 study to the age group of 1 month to < 1 year, which is relevant to this benefit assessment. Therefore, there are overall no suitable data to derive conclusions on the added benefit of burosumab versus the ACT in the present research question.

Results on added benefit

There are no suitable data available to assess the added benefit of burosumab compared with the ACT for the treatment of XLH in infants aged between 1 month and 1 year with hypophosphataemia. There is no hint of an added benefit of burosumab in comparison with the ACT; an added benefit is therefore not proven.

Table 3 summarises the probability and extent of added benefit of burosumab.

Table 3: Burosumab – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment of X-linked hypophosphataemia (XLH) in infants from 1 month to 1 year of age with hypophosphataemia	Phosphate substitution and active vitamin D (calcitriol or alfacalcidol) in combination	Added benefit not proven
a. Presented is the ACT specified by the GBA. GBA: Federal Joint Committee; XLH: X-linked hypophosphataemia		

The GBA decides on the added benefit.

I 2 Research question

The aim of this report is to assess the added benefit of burosumab compared with phosphate substitution in combination with active vitamin D (calcitriol or alfacalcidol) as an ACT for the treatment of XLH in infants from 1 month to 1 year of age with hypophosphataemia.

The research question shown in Table 4 was defined in accordance with the ACT specified by the GBA.

Table 4: Research question of the benefit assessment of burosumab

Therapeutic indication	**ACT**[a]
Treatment of X-linked hypophosphataemia (XLH) in infants from 1 month to 1 year of age with hypophosphataemia	Phosphate substitution and active vitamin D (calcitriol or alfacalcidol) in combination
a. Presented is the ACT specified by the GBA. GBA: Federal Joint Committee; XLH: X-linked hypophosphataemia	

The company followed the ACT specified by the GBA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Studies with a minimum duration of 24 weeks were used for the derivation of the added benefit. This deviated from the company's approach, which planned no limitation of the study duration.

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 lists on burosumab (status: 19 May 2026)
- Bibliographical literature search on burosumab (last search on 12 May 2026)
- Search of trial registries / trial results databases for studies on burosumab (last search on 4 May 2026)
- Search on the GBA website for burosumab (last search on 12 May 2026)

To check the completeness of the study pool:

- Search of trial registries for studies on burosumab (last search on 09 July 2026); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check of the completeness of the study pool produced no RCT for the present research question on infants aged between 1 month and 1 year.

However, regardless of this, the company states that its information retrieval on the GBA's website yielded the study UX023-CL301 [1], which had already been used to derive the added benefit in patients with XLH aged between 1 and 17 years. The UX023-CL301 study is an open-label RCT comparing burosumab with oral phosphate substitution and active vitamin D in paediatric patients aged 1 to 12 years in this therapeutic indication; it is already known from an earlier benefit assessment procedure [2]. The company used the study UX023-CL301 as part of an evidence transfer. The company did not conduct any information retrieval for studies with patients with XLH aged between 1 and 17 years for the purposes of such evidence transfer.

The company additionally conducted an information retrieval for further studies with burosumab in infants aged between 1 month and 1 year within this therapeutic indication, and identified the BUR-CL207 study [3], which it presents as supporting information in Module 4 A. The BUR-CL207 study is a single-arm study for the assessment of the safety, tolerability, pharmacokinetics and efficacy of burosumab in infants < 1 year of age with XLH. The company did not conduct any information retrieval for further studies for the ACT.

The data presented by the company were unsuitable to derive conclusions on the added benefit of burosumab for this research question. The evidence presented by the company is described below, and the reasons for its unsuitability for the benefit assessment are provided.

Transfer of results of patients from the RCT UX023-CL301 to the target population not possible

Approach and reasoning of the company on the transfer of the study results

In Section 4.4 of Module 4A, the company describes that conducting an RCT involving a larger study population and the allocation of patients to a control arm would have been neither ethically nor practically justifiable in the particularly vulnerable age group of infants aged between 1 month and 1 year. A single-arm study design was therefore chosen for the BUR-CL207 study. As there is the same loss-of-function mutation in this therapeutic indication as in the previously assessed therapeutic indication of patients aged between 1 and at most 17 years, it was plausible to transfer the results on the added benefit from this age group. The company therefore argues that it was possible to transfer evidence based on the RCT UX023-CL301 in combination with the evidence from the single-arm study BUR-CL207.

In the dossier, the company states that, in the context of the benefit assessment, evidence may be transferred between age groups, provided that the populations are sufficiently comparable. Thereby, the concept of comparability was based on three criteria. The mechanism of action had to be identical, the appearance of the disease was not allowed to differ, and the efficacy and safety had to be transferable. The company then explained why it believed to meet these criteria in the present situation.

In order to assess the transferability of efficacy and safety between the two age groups, the company narratively compares results from the RCT UX023-CL301 with those of the BUR-CL207 study. Thereafter, the company concluded that the mechanism of action was identical in both age groups, that the pathophysiology was independent of age, and that both studies (BUR-CL207 and UX023-CL301) showed statistically significant and clinically relevant improvements in the symptoms of rickets and the increase in serum phosphate levels, which together constituted the two main objectives of treatment in children with XLH. The company then stated that, based on the data from the UX023-CL301 study, an indication of a non-quantifiable added benefit had been derived for patients with XLH aged between 1 and at most 17 years, in accordance with the GBA decision. Taken as a whole, and taking into account the comparable pathophysiology, the identical mechanism of action, the consistent efficacy and safety, the identical ACT as well as regulatory precedents, a transfer of evidence could take place. Given the associated uncertainties and the limitations of the available evidence, the extent of the added benefit cannot be quantified; consequently, for patients aged between 1 month and 1 year with XLH, there is a hint of non-quantifiable added benefit.

For an assessment of the data submitted by the company, please refer to the following section. With regard to the company's statement that the GBA had identified an indication of a non-quantifiable added benefit for patients with XLH aged between 1 and 17 years, it should

be noted that this is incorrect and that only a hint of a non-quantifiable additional benefit was derived [4].

Assessment of the data presented by the company

The data presented by the company were unsuitable to derive conclusions on the added benefit of burosumab versus the ACT: The reasons for this are provided below.

The company did not conduct a complete information retrieval; in particular, it did not search for further studies on the ACT that would support a transfer of the results. Accordingly, there is no analysis of information on the basis of which the company assesses the course of the disease for the relevant age group (1 month to 1 year) under the ACT. In addition, the company presented the UX023-CL301 study for the adjacent age group of 1- to 17-year-olds, but did not carry out any information retrieval for RCTs for this age group.

Furthermore, the company did not carry out a sufficient information synthesis, in the sense that it did not adequately process and compare the data from the studies. In Module 4A, the company merely provides data for the single-arm BUR-CL207 study regarding study details and results. However, with regard to the details and results of the UX023-CL301 study, the company refers to the respective Module 4 on the previous benefit assessment procedure [2]. The data from the UX023-CL301 study were not analysed as part of the dossier relevant to the present research question. In Section 4.4.2 of Module 4A, the company narratively compares extracts of the results of RCT UX023-CL301 with the results of the single-arm study. Based on this information analysis, it is not possible to assess the transferability of the results from older patients in the UX023-CL301 study to the age group of 1 month to < 1 year, which is relevant to this benefit assessment.

Therefore, there are overall no suitable data to derive conclusions on the added benefit of burosumab versus the ACT in the present research question.

I 4 Results on added benefit

There are no suitable data available to assess the added benefit of burosumab compared with the ACT for the treatment of XLH in infants aged between 1 month and 1 year with hypophosphataemia. There is no hint of an added benefit of burosumab in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

Table 5 summarises the result of the assessment of the added benefit of burosumab in comparison with the ACT.

Table 5: Burosumab – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**
Treatment of X-linked hypophosphataemia (XLH) in infants from 1 month to 1 year of age with hypophosphataemia	Phosphate substitution and active vitamin D (calcitriol or alfacalcidol) in combination	Added benefit not proven
a. Presented is the ACT specified by the GBA. GBA: Federal Joint Committee; XLH: X-linked hypophosphataemia		

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

The GBA decides on the added benefit.

I 6 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. Imel EA, Glorieux FH, Whyte MP et al. Burosumab versus conventional therapy in children with X-linked hypophosphataemia: a randomised, active-controlled, open-label, phase 3 trial. Lancet 2019; 393(10189): 2416-2427. https://doi.org/10.1016/s0140-6736(19)30654-3.

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The full report (German version) is published at https://www.iqwig.de/en/projects/a26-74.html.