IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A12-05

# Belimumab –

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

## Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment ("Belimumab – Nutzenbewertung gemäß § 35a SGB V" (Version 1.0; Status: 26.04.2012). 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.

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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. Individual sections and conclusions in the dossier assessment therefore do not necessarily reflect his opinion.

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[2] Due to legal data protection regulations, employees have the right not to be named.

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**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) |
| NSAID | non-steroidal anti-inflammatory drug |
| SGB | Sozialgesetzbuch (Social Code Book) |
| SLE | systemic lupus erythematosus |
| SPC | Summary of Product Characteristics |

# 2. Benefit assessment

## 2.1 Executive summary of the benefit assessment

### Background

On 01.02.2012 in accordance with § 35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) wrote to the Institute for Quality and Efficiency in Health Care (IQWiG) to commission the benefit assessment of the drug belimumab. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter "the company"). The dossier was sent to IQWiG on 01.02.2012.

### Research question

The benefit assessment of belimumab was carried out for the following approved therapeutic indication: add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity despite standard therapy.

The benefit assessment was undertaken in comparison with an optimized standard therapy (chloroquine/hydroxychloroquine, non-steroidal anti-inflammatory drugs (NSAID), glucocorticoids, azathioprine) bearing in mind the approved dosages and the approval status of each drug, with respect to patient-relevant outcomes.

### Results

In the Institute's view, the studies (BLISS52 and BLISS76) included in the study pool by the company are not relevant for this benefit assessment for the following reasons:

According to the specification of the G-BA, the appropriate comparator therapy (ACT) must be used in an optimized manner. "Optimization" of the standard therapy means that the therapy is individually defined for each individual patient and, if necessary, tailored (optimized) depending on tolerability, effect and disease activity during the course of treatment. The possible uses specified in the respective approval are to be observed. Dose adjustments should not be restricted beyond the guidelines in the Summary of Product Characteristics (SPC). Contrary to the specification regarding the ACT by the G-BA, the standard therapy used in the BLISS52 and BLISS76 studies was not used in an optimized manner because its adjustment – particularly with regard to the administration of glucocorticoids – was restricted during the course of treatment. It is clear from the company's remarks that this protocol requirement was made with the aim of minimizing the masking of the effects of belimumab by treatment effects of the standard therapy. Hence, the design of these studies was drawn up for the approval (demonstration of therapeutic efficacy and safety) and is also suitable for this, but not for the assessment of added benefit. The reason for this is not the administration of placebo, but that adjusting the standard therapy was only possible to a restricted extent.

In contrast, the LBSL02 study explicitly excluded by the company is a relevant study for the assessment of added benefit, because use of the standard therapy could be adjusted during the course of the study according to the actual need. The study is accordingly suitable to answer the question of whether belimumab as add-on therapy to standard therapy has added benefit over merely optimizing the standard therapy. In the Institute's view, the company's justification for excluding the LBSL02 study is inadequate.

Overall, the company submitted no studies relevant for the benefit assessment.

The assessment presented by the company in its dossier therefore gives no proof of added benefit of belimumab compared to the ACT.

**Extent and probability of the added benefit, patient groups with therapeutically important added benefits**

Based on the results presented, the extent and probability of the added benefits of the drug belimumab is assessed as follows:

- There is no proof of added benefit.

In respect of patient groups with therapeutically important added benefits, the result is as follows:

- There are no groups of patients for whom a therapeutically important added benefit is proven.

The decision regarding added benefit is made by the G-BA.

## 2.2 Research question

The benefit assessment of belimumab was carried out according to its approval status for the following indication: "…add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity … despite standard therapy" [1].

In accord with the specification of the G-BA, the company designated an optimized standard therapy (chloroquine/hydroxychloroquine, NSAID, glucocorticoids, azathioprine, and cyclophosphamide if necessary) as ACT for the treatment with belimumab, bearing in mind the approved dosages and the approval status of each drug.

Because belimumab is, however, not approved for patients with severe active lupus nephritis [1] and cyclophosphamide is approved only for patients with a severe progressive form of lupus nephritis [2], cyclophosphamide as a constituent of the ACT was not considered any further by the Institute in the benefit assessment.

The assessment was carried out in relation to patient-relevant outcomes.

*Further information about the research question can be found in Module 3, Section 3.1 and Module 4, Section 4.2.1 of the dossier and in Sections 2.7.1 and 2.7.2.1 of the full dossier assessment.*

## 2.3 Information retrieval and study pool

The study pool of the assessment was compiled from the following data:

- Studies on belimumab completed by the company up to 15.06.2011 (study list of the company).
- Results of a search in trial registries for studies on belimumab (last search 14.06.2011, searches by the company).
- The Institute's own searches for studies on belimumab in trial registries to check the search results of the company up to 16.02.2012. This produced no additional relevant studies.
- A check of the company's information retrieval using the inclusion criteria specified by the Institute, which deviated markedly from those of the company particularly in relation to optimization of the standard therapy. This identified one study (LBLS02) relevant for the research question.

The company explicitly excluded Study LBSL02 from the assessment. In the Institute's view, the studies (BLISS52 and BLISS76) included in the study pool by the company are not relevant for this benefit assessment for the following reasons:

Contrary to the specification regarding the ACT by the G-BA, the standard therapy used in the BLISS52 and BLISS76 studies was not used in an optimized manner because its adjustment – particularly with regard to the administration of glucocorticoids – was restricted during the course of treatment. It is clear from the company's remarks that this protocol requirement was made with the aim of minimizing the masking of the effects of belimumab by treatment effects of the standard therapy. Hence, the design of these studies was drawn up for the approval (demonstration of therapeutic efficacy and safety) and is also suitable for this but not for the assessment of added benefit. The reason for this is not the administration of placebo, but that adjusting the standard therapy was only possible to a restricted extent.

In contrast, the LBSL02 study is a relevant study for the assessment of the added benefit, because the use of the standard therapy could be adjusted during the course of the study according to the actual need. The study is accordingly suitable to answer the question of whether belimumab as add-on therapy to standard therapy has added benefit over merely optimizing the standard therapy. In the Institute's view, the company's justification for excluding the LBSL02 study is inadequate. In its dossier, the company did not present any analyses for this study according to the requirements described in the dossier templates.

A detailed explanation about the company's study pool can be found in Section 2.7.2.2.2 of the full dossier assessment.

Overall, the company submitted no studies relevant for the benefit assessment.

*Further information about the inclusion criteria for studies in the benefit assessment and the methods and results of information retrieval and the study pool derived from it, can be found in Module 4, Sections 4.2.2, 4.2.3, 4.3.1.1 and of the dossier and in Sections 2.7.2.1, 2.7.2.2 as well as 2.7.2.2.1 and 2.7.2.2.2 of the full dossier assessment.*

## 2.4 Results concerning added benefit

Since the company submitted no relevant studies for the benefit assessment, there is no proof of added benefit from belimumab compared to the ACT specified by the G-BA.

This differs from the company's procedure, which carried out an assessment based on the results of its chosen studies (BLISS52 and BLISS76) and from which in total it derived an added benefit for belimumab.

*Further information about the results on added benefit can be found in Module 4, Section 4.3.1.3 and Appendix 4-I of the dossier and in Section 2.7.2.4 of the full dossier assessment.*

## 2.5 Extent and probability of the added benefit

On the basis of the submitted data, there is no proof of an added benefit of belimumab in comparison with the ACT specified by the G-BA. Hence, there are also no patient groups for whom a therapeutically important added benefit can be derived.

This overall assessment differs substantially from that of the company, which claims a major added benefit for belimumab on the basis of the results of its chosen studies (BLISS52 and BLISS76).

The decision regarding added benefit is made by the G-BA.

*Further information about the extent and probability of the added benefit can be found in Module 4, Section 4.4 of the dossier and in Section 2.7.2.8 of the full dossier assessment.*

## 2.6 List of included studies

No information is provided in this section, as the company did not present any relevant studies in its dossier from which an added benefit of belimumab over the ACT specified by the G-BA could be determined.

**References**

(for English extract; please see full dossier assessment for full reference list)

1) Product Information. 25.05.2012, Benlysta -EMEA/H/C/002015 -II/0005. Annex 1 – Summary of Product Characteristics. URL: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002015/human_med_001466.jsp&mid=WC0b01ac058001d124

2) Baxter Oncology. Endoxan: Fachinformation [Summary of Product Characteristics] [online]. 11.2008 [accessed: 03.02.2012]. URL: http://www.fachinfo.de.