Belimumab for lupus erythematosus: Added benefit not proven

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Belimumab (trade name Benlysta) has been approved since July 2011 as an add-on therapy for adult patients with the autoimmune disease systemic lupus erythematosus (SLE). This monoclonal antibody is only considered as treatment when the disease is still active in spite of standard therapy. The German Institute for Quality and Efficiency in Health Care (IQWiG) has now examined the added benefit of this drug pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG).

According to the findings, there is no proof that belimumab provides added benefit as the manufacturer's dossier does not contain any relevant studies for the assessment of added benefit.

Belimumab in comparison to optimized standard therapy

The Federal Joint Committee (G-BA) specified that the appropriate comparator therapy should be an optimized standard therapy with various drugs that have been approved in Germany. A (standard) therapy is said to be "optimized" when the treatment has been adapted to the individual patient with respect to tolerability, effect and clinical course. The dossier - or its assessment by IQWiG - was supposed to answer the question as to whether the additional administration of belimumab offers advantages in comparison with the optimization of standard therapy alone.

Adaptation of standard therapy was only possible in the studies to a limited extent

The manufacturer uses two approval studies in the dossier (BLISS52 and BLISS76). However, these are not suited to prove added benefit, as the study protocols inappropriately restricted the possibilities for adapting the standard therapy. In particular, the administration of glucocorticoids was explicitly restricted.

This restriction is a consequence of the intended purpose of these studies. In drug approval the main focus is on proving efficacy. If the adaptation of the standard therapy had not been restricted, the differences in the effects between the belimumab and comparator groups might have been smaller, or indeed totally absent.

A study design of this type is suitable for approval purposes, but not for a benefit assessment in accordance with § 35a Social Code Book (SGB) V, as the purpose of the latter is to determine added benefit in comparison to an alternative treatment option. According to the specifications of the G-BA for the specific case of belimumab, this is solely the optimization of standard therapy.

Relevant study excluded

On the one hand, the manufacturer argues on the basis of these two unsuitable studies in the dossier. On the other hand, another study (LBSL02) is explicitly excluded, even though optimization of the standard therapy was possible here. This study would have been relevant for the assessment. IQWiG cannot support the justification for excluding the study. Thus the pharmaceutical company has not presented any relevant studies or analyses of study data in its dossier.

G-BA decides on the extent of added benefit.

The dossier assessment is part of the overall procedure for early benefit assessment conducted by the G-BA. After publication of the manufacturer's dossier and its assessment by IQWiG, the G-BA initiates a formal commenting procedure which can provide further information and result in a change to the benefit assessment. The G-BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

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