Added benefit of vedolizumab is not proven

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Vedolizumab (trade name Entyvio) has been approved since May 2014 for patients with moderately to severely active Crohn disease or ulcerative colitis. In an early benefit assessment pursuant to the Act on the Reform of the Market for Medicinal Products (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined whether the drug offers an added benefit over the appropriate comparator therapy in these patient groups. According to the findings, such an added benefit is not proven because the dossier contained no suitable data for any of the two therapeutic indications.

G-BA specified adalimumab or infliximab as comparator therapy

Crohn disease and ulcerative colitis are chronic inflammatory bowel diseases. Vedolizumab is an option when conventional therapy is not tolerated or does not provide sufficient release of symptoms. This conventional treatment can also be a tumour necrosis factor alpha (TNF?) antagonist.

The Federal Joint Committee (G-BA) specified a TNF? antagonist (adalimumab or infliximab) as appropriate comparator therapy for both therapeutic indications. It is to be noted that it is possible to switch to a different TNF? antagonist or to adjust the dose in case of treatment failure with a TNF? Antagonist.

Drug manufacturer presented no studies for Crohn disease

In its dossier, the manufacturer identified no randomized controlled trial (RCT) that directly compared vedolizumab with adalimumab for patients with moderately to severely active Crohn disease. Since it also conducted no indirect comparisons on the basis of RCTs, an added benefit of vedolizumab for the therapeutic indication Crohn disease is not proven.

Ulcerative colitis: indirect comparison with placebo as common comparator

The dossier also contained no direct comparative RCTs on the therapeutic indication of moderately to severely active ulcerative colitis. However, the manufacturer conducted an adjusted indirect comparison. On the one hand, it used an RCT that compared vedolizumab with placebo (study C13006). On the other, it used three RCTs in which adalimumab was tested against placebo (ULTRA 1, ULTRA 2, M10-447). The placebo was used as common comparator.

Compared populations were not sufficiently similar

In principle, this approach is suitable to prove an added benefit. One important prerequisite was not fulfilled however: The compared populations of the vedolizumab and adalimumab studies were not sufficiently similar. The main reason for this was that the studies had different designs.

Both the vedolizumab study and two of the three adalimumab studies (ULTRA 2 and M10 447) had a two-phase design: an induction phase and a subsequent maintenance phase. In the vedolizumab study, however, only those patients were randomized and treated who had responded to vedolizumab in the induction phase. In the two adalimumab studies, in contrast, both responders and non-responders received continued treatment in the maintenance Phase.

Side effects were not analysed adequately

The indirect comparison was also unsuitable for a second reason: The adverse events in the vedolizumab study were not analysed adequately.

An added benefit of vedolizumab in comparison with adalimumab is therefore also not proven for patients with moderately to severely active ulcerative colitis.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall

procedure for early benefit assessments supervised by the G-BA. After publication of the manufacturer's dossier and IQWiG's assessment, the G-BA conducts a commenting procedure, which may 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.

More information: An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the website www.gesundheitsinformation.de, published by IQWiG, provides easily understandable and brief German-language information on vedolizumab.

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