Insulin degludec plus liraglutide: No hint of added benefit in type 2 diabetes

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The fixed-ratio combination of the two drugs insulin degludec and liraglutide (trade name: Xultophy) has been approved since September 2014 for adults with type 2 diabetes mellitus. It is given as an injection in addition to other blood-glucose lowering drugs when these alone or in combination with basal insulin are insufficient to lower blood glucose levels. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this fixed-ratio combination offers an added benefit over the appropriate comparator therapy.

Such an added benefit cannot be derived from the dossier, however, because the drug manufacturer presented no studies suitable for the assessment. One of the reasons was that the design of two important studies led to an unfair comparison.

G-BA distinguished between two research questions

The Federal Joint Committee (G-BA) distinguished between two treatment situations in its commission: Patients can use this new drug combination in addition to other oral antidiabetics (OADs) when either oral antidiabetic combination therapy with several OADs or OADs in combination with basal insulin do not provide adequate glycaemic control.

Majority of patients had received only one OAD

before

The manufacturer conducted a randomized controlled trial for the first research question (DUAL I). However, the vast majority of the patients included in this study had only received one OAD (metformin) in monotherapy before and therefore did not comply with the population for which the G-BA had envisaged the assessment.

Furthermore, the patients in the control arm were not treated according to the appropriate comparator therapy specified by the G-BA. They did not receive human insulin, but an analogue (insulin degludec). Since the manufacturer has not shown that the treatment results of insulin degludec are transferable to human insulin, they cannot be used for the assessment.

Therapeutic strategy continued unchanged only in the comparator arm

For the second research question, the manufacturer used two randomized controlled trials (DUAL II and DUAL V). These were also not relevant for the assessment of the added benefit. As in DUAL I, the appropriate comparator therapy was not implemented in DUAL II either.

In addition, in DUAL II and DUAL V treatment was intensified by adding liraglutide only in the intervention arm, but not in the comparator arm. Here the therapeutic strategy with basal insulin was continued, and only dose adjustments were possible. This approach is not meaningful, however. The guidelines also recommend changing the strategy after three to six months if the target blood glucose levels are not met.

Above all, continuing the therapeutic strategy unchanged in only one arm, which in this study was the comparator arm, leads to an unfair

comparison. Both studies are therefore unsuitable to derive conclusions on the added benefit of insulin degludec plus liraglutide.

G-BA decides on the extent of added benefit

This dossier assessment is part of the early benefit assessment according to AMNOG supervised by the Federal Joint Committee (G-BA). After publication of the dossier assessment, the G-BA conducts a commenting procedure and makes a final decision on the extent of the added benefit.

An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the Website gesundheitsinformation.de, published by IQWiG, provides easily understandable German-language Information.

More English-language information will be available soon (Sections 2.1 to 2.6 of the dossier assessment as well as subsequently published health information on informedhealthonline.org). If you would like to be informed when these documents are available, please send an e-mail to " info@iqwig.de.

More information: www.iqwig.de/download/A15-15_I … ertung-35a-SGB-V.pdf

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