Added benefit of saxagliptin/metformin combination is not proven

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The fixed combination of the drugs saxagliptin and metformin (Komboglyze) has been approved in Germany since November 2011 for the treatment of type 2 diabetes mellitus. 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 this fixed combination product offers an added benefit versus the current standard treatment. Such an added benefit cannot be derived from the dossier, however, as the manufacturer did not submit any relevant data.

The combination is an option for adult patients who do not benefit sufficiently from the commonly used drug metformin or who are already taking saxagliptin and metformin as individual tablets. It can also be used together with insulin if insulin and metformin are insufficient.

The Federal Joint Committee (G-BA) has specified metformin in combination with a sulfonylurea (glibenclamide or glimepiride) as the appropriate comparator therapy for saxagliptin/metformin. The triple combination therapy, i.e. saxagliptin/metformin and insulin, was to be compared with metformin and human insulin.

Regarding the dual combination therapy, the manufacturer deviated from the G-BA's specifications and submitted data from an approval study in which the patients in the control group did not receive glibenclamide or glimepiride, but another sulfonylurea, namely glipizide. However, this drug has no longer been approved in Germany since 2007.

In addition, the manufacturer did not provide sufficient explanation in its dossier that glipizide is equivalent to the other two sulfonylureas.

Regarding the combination with insulin, the manufacturer submitted a study that directly compared saxagliptin/metformin and insulin with metformin und human insulin. But the results of this study cannot be used for the assessment of the added benefit.

The main reason for this is that the insulin therapy could not be tailored sufficiently to the individual patient in the first treatment phase: even though their current insulin therapy was insufficient, patients were neither supposed to change the insulin nor to adapt the dose. But to be able to draw conclusions about the added benefit, the combination of saxagliptin/metformin and insulin would have to be compared with other strategies for optimizing treatment, for example optimizing insulin use.

Not tailoring treatment to the individual patient does not meet the current standard of diabetological practice anyway. Instead, insulin therapy is optimized for the individual patient so that hyperglycaemia and hypoglycaemia do not occur in the first place. So in the study, insulin was not used in a way that would be necessary and appropriate in this indication.

Therefore, there are no study results for either of the two therapeutic indications of the fixed combination saxagliptin/metformin from which an added benefit could be derived.

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.

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