Added benefit of linagliptin is not proven

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Linagliptin (trade name: Trajenta) has been approved since August 2011 to improve blood glucose control ("glycaemic control") in adults with type 2 diabetes mellitus whose elevated blood glucose levels are inadequately controlled by diet and exercise. It is an option for patients who do not tolerate or should not take the usual treatment with the drug metformin. Moreover, linagliptin can be added if treatment with metformin alone is not sufficient.

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 linagliptin offers an added benefit versus the appropriate comparator therapy specified by the Federal Joint Committee (G-BA). No such added benefit can be inferred from the dossier, as the drug manufacturer deviated from the G-BA's specifications and chose a different comparator therapy.

Approval status distinguishes between three treatment situations

The appropriate comparator therapy specified by the G-BA distinguishes between three treatment situations:

* Administration of linagliptin alone (monotherapy) as a substitute for metformin if this drug is not tolerated by patients or should not be taken because of impaired kidney function. To assess the added benefit, linagliptin monotherapy should be compared with a drug from the

sulfonylurea class (glibenclamide or glimepiride).

* Dual therapy combines linagliptin and metformin and is indicated if treatment with metformin alone is insufficient to control blood glucose levels. To assess the added benefit, dual therapy with linagliptin should be compared with a combination of metformin and a sulfonylurea (glibenclamide or glimepiride).

* Triple therapy combines linagliptin, metformin and a sulfonylurea and is used if dual therapy with metformin and a sulfonylurea is no longer a sufficient treatment option. To assess the added benefit, triple therapy should be compared with a combination of insulin and metformin.

Drug manufacturer chose a gliptin as comparator therapy

In its dossier, the manufacturer compared linagliptin with a different drug from the gliptin class (sitagliptin) in all three treatment situations and thereby deviated from the specifications of the G-BA. However, in IQWiG's opinion, the manufacturer insufficiently justified this deviation. For the dossier assessment IQWiG therefore uses the appropriate comparator therapy specified by the G-BA.

In the dossier, the manufacturer makes no statements on the extent and probability of an added benefit of linagliptin versus the appropriate comparator therapy specified by the G-BA. Studies that would have been relevant for this purpose were explicitly excluded from the assessment. The manufacturer's dossier therefore provides no proof of an added benefit of linagliptin versus the G-BA's appropriate comparator therapy. This applies to all three treatment situations mentioned above, that is, monotherapy, dual and triple combination therapy.

In the dossier the manufacturer did not determine an added benefit of linagliptin versus the comparator therapy they had chosen themselves (sitagliptin).

G-BA decides on the extent of added benefit

The procedure for inferring the overall conclusion on the extent of added benefit is a proposal from IQWiG. The G-BA, which has opened a formal commenting procedure, will decide on the extent of added benefit.

Provided by Institute for Quality and Efficiency in Health Care