IQWiG Reports – Commission No. A18-31

Ertugliflozin/sitagliptin (type 2 diabetes mellitus) –

Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of the executive summary of the dossier assessment *Ertugliflozin/Sitagliptin (Diabetes mellitus Typ 2) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.1; Status: 6 September 2018). Please note: This document was translated by an external translator and is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SBG) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug ertugliflozin/sitagliptin. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 9 May 2018.

Research question

The aim of this report is to assess the added benefit of the fixed-dose combination of ertugliflozin and sitagliptin (ertugliflozin/sitagliptin) in the treatment of adults with type 2 diabetes mellitus in comparison with the appropriate comparator therapy (ACT) as an adjunct to diet and exercise for improved blood glucose control.

- In patients whose blood glucose levels are inadequately controlled with metformin and/or a sulfonylurea and one of the stand-alone substances in ertugliflozin/sitagliptin.

Furthermore, ertugliflozin/sitagliptin is approved for patients who are already being treated with the combination of ertugliflozin and sitagliptin in the form of separate tablets. However, this therapeutic indication is not relevant for the benefit assessment, since ertugliflozin is currently not available as a stand-alone product in Germany.

The assessment is performed in comparison with the ACT specified by the G-BA. The latter is presented in Table 2.

Table 2[2]: Research questions of the benefit assessment of ertugliflozin/sitagliptin

Indication	**ACT[a]**
Treatment as an adjunct to diet and exercise in adult patients with type 2 diabetes mellitus who are inadequately controlled under treatment with at least 2 blood glucose lowering drugs (except insulin; here metformin and/or sulfonylurea and ertugliflozin or sitagliptin)[b].	▪ **Human insulin + metformin** or ▪ Human insulin + empagliflozin[c] or ▪ Human insulin + liraglutide[c] or ▪ **Human insulin** if the Summaries of Product Characteristics mention any selected combination partner as contraindicated, not tolerated or insufficiently effective due to advanced type 2 diabetes mellitus.
a: Presentation of the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice by the company is printed in **bold**. b: Ertugliflozin is currently not available as a stand-alone product in Germany. Prior ertugliflozin monotherapy is therefore not a relevant treatment scenario for the German healthcare system. c: Empagliflozin or liraglutide were listed as part of the ACT only for patients with manifest cardiovascular disease. For this purpose, manifest cardiovascular disease was operationalized in accordance with the inclusion criteria of the relevant studies for empagliflozin (EMPAREG outcome study) or liraglutide (LEADER study). ACT: appropriate comparator therapy; G-BA: Federal Joint Committee	

[2] Table numbers start with "2" as numbering follows that of the full dossier assessment.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used for deriving the added benefit. This corresponds to the company's inclusion criteria.

Results

The company did not present any RCTs which permit a direct comparison with the ACT.

Based on its literature search for studies permitting an indirect comparison, the company identified the study VERTIS SITA 2. This study examined a subpopulation of the therapeutic indication to be assessed (adults with type 2 diabetes mellitus inadequately controlled with metformin and sitagliptin). Proceeding from this study, the company looked for suitable RCTs on the ACT through the common comparator sitagliptin plus metformin, but it failed to find a relevant study.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 presents a summary of the probability and extent of added benefit of ertugliflozin/ sitagliptin in comparison with the ACT.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Ertugliflozin/sitagliptin – probability and extent of added benefit

Indication	**ACT[a]**	**Probability and extent of added benefit**
Treatment as an adjunct to diet and exercise of adult patients with type 2 diabetes mellitus who are inadequately controlled under treatment with at least 2 blood glucose lowering drugs (except insulin; here metformin and/or sulfonylurea and ertugliflozin or sitagliptin)[b]	▪ **Human insulin + metformin** or ▪ Human insulin + empagliflozin[c] or ▪ Human insulin + liraglutide[c] or ▪ **Human insulin** if the Summaries of Product Characteristics mention any selected combination partner as contraindicated, not tolerated or insufficiently effective due to advanced type 2 diabetes mellitus.	Added benefit not proven

a: Presentation of the ACT specified by the G-BA. In cases where the ACT specified by the G-BA allows the company to choose a comparator therapy from several options, the respective choice by the company is printed in **bold**.
b: Ertugliflozin is currently not available as a stand-alone product in Germany. Prior ertugliflozin monotherapy is therefore not a relevant treatment scenario for the German healthcare system.
c: Empagliflozin or liraglutide were listed as part of the ACT only for patients with manifest cardiovascular disease. For this purpose, manifest cardiovascular disease was operationalized in accordance with the inclusion criteria of the relevant studies for empagliflozin (EMPAREG outcome study) or liraglutide (LEADER study).
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

References for English extract

Please see full dossier assessment for full reference list.

1. Institute for Quality and Efficiency in Health Care. General methods: version 5.0 [online]. 10 July 2017 [Accessed: 04 June 2018]. URL: https://www.iqwig.de/download/General-Methods_Version-5-0.pdf.

2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2015; 58(1): 43-58

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a18-31-ertugliflozin-sitagliptin-type-2-diabetes-mellitus-benefit-assessment-according-to-35a-social-code-book-v.9648.html.