Resolution

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Empagliflozin/Linagliptin

of 22 November 2019

At its session on 22 November 2019, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (Pharmaceuticals Directive, AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended on DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient empagliflozin/linagliptin as follows:

Empagliflozin/Linagliptin

Resolution of: 22 November 2019
Entry into force on: 22 November 2019
Federal Gazette, BAnz AT DD MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 11 November 2016):

Glyxambi, fixed dose combination of empagliflozin and linagliptin, is indicated in adults aged 18 years and older with type 2 diabetes mellitus:

- to improve glycaemic control when metformin and/or sulphonylurea (SU) and one of the monocomponents of Glyxambi do not provide adequate glycaemic control
- when already being treated with the free combination of empagliflozin and linagliptin[1].

(See Sections 4.2, 4.4, 4.5, and 5.1 for available data on combinations studied)

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adult patients with type 2 diabetes mellitus, whose blood sugar cannot be adequately controlled by diet and movement and the treatment with at least two hypoglycaemic agents (apart from insulin, here metformin and/or sulfonylurea and empagliflozin or linagliptin[1])

Appropriate comparator therapy:

- Human insulin + metformin or
- Human insulin + empagliflozin[2] or
- Human insulin + liraglutide[2] or
- Human insulin if the particular combination partners in accordance with the product information are incompatible or contraindicated or not sufficiently effective because of an advanced type 2 diabetes mellitus

Extent and probability of the additional benefit of empagliflozin/linagliptin compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

There are no relevant data in comparison to the appropriate comparator therapy.

[1] Linagliptin as a monopreparation is currently not on the market in Germany.
[2] Empagliflozin or liraglutide only for patients with manifest cardiovascular disease who receive further medication for the treatment of cardiovascular risk factors, in particular anti-hypertensive drugs, anticoagulants, and/or lipid-reducers (for the operationalisation, see study protocols: Zinman et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015; 373: 2117–28. DOI 10.1056/NEJMoa1504720 or Marso et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes, N Engl J Med 2016; 375: 311–322. DOI: 10.1056/NEJMoa1603827).

2. Number of patients or demarcation of patient groups eligible for treatment

Adult patients with type 2 diabetes mellitus, whose blood sugar cannot be adequately controlled by diet and movement and the treatment with at least two hypoglycaemic agents (apart from insulin, here metformin and/or sulfonylurea and empagliflozin or linagliptin[1])

approx. 326,100 – 341,100 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Glyxambi® (active ingredient: empagliflozin/linagliptin) at the following publicly accessible link (last access: 15 October 2019): https://www.ema.europa.eu/documents/product-information/glyxambi-epar-product-information_de.pdf

The use of DPP4 inhibitors (e.g. linagliptin) was associated with a risk of developing acute pancreatitis. Patients should be informed about characteristic symptoms of acute pancreatitis, and the therapy should be changed if necessary.

Overall, the current data basis with regard to pancreatic carcinomas is not clear[3,4]. In view of the lack of a conclusive assessment of the risk of pancreatic carcinoma or pancreatic damage in this substance class, increased monitoring of patients for pancreatic diseases is recommended. In suspected cases, DPP4 inhibitor-based therapy should be dispensed with.

4. Treatment costs

Annual treatment costs:

Adult patients with type 2 diabetes mellitus, whose blood sugar cannot be adequately controlled by diet and movement and the treatment with at least two hypoglycaemic agents (apart from insulin, here metformin and/or sulfonylurea and empagliflozin or linagliptin[1])

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be assessed	
Empagliflozin/linagliptin (10 mg/5 mg; 25 mg/5 mg)	€ 1,167.05
Appropriate comparator therapy	
Metformin	€ 33.24 – 99.71

[3] https://cordis.europa.eu/result/rcn/183717_de.html [Accessed: 7 October 2019]
[4] https://www.akdae.de/Arzneimitteltherapie/AVP/Artikel/201703/112.pdf [Accessed: 7 October 2019]

Designation of the therapy	Annual treatment costs per patient
Empagliflozin[2]	€ 658.93
Liraglutide[2]	€ 1,308.84 – € 1,963.26
Human insulin (NPH insulin)	€ 382.46 – € 764.92
	Total:
Human insulin (NPH-insulin) + metformin	€ 415.70 – € 864.63
Human insulin (NPH insulin) + empagliflozin[2]	€ 1,041.40 – € 1,423.86
Human insulin (NPH insulin) + liraglutide[2]	€ 1,691.30 – € 2,728.19
Possibly therapy only with human insulin if metformin and empagliflozin[2] and liraglutide[2] in accordance with the product information are incompatible or contraindicated or are not sufficiently effective because of an advanced type 2 diabetes mellitus	
Conventional insulin therapy (premixed insulin)	€ 382.46 – € 764.92

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 2019

Costs for additionally required SHI services:

Designation of the therapy	Designation	Costs/year
Appropriate comparator therapy		
Human insulin (NPH insulin) as well as conventional insulin therapy (premixed insulin)	Blood glucose test strips Lancets Disposable needles	€ 135.05 – € 405.15 € 7.48 – € 22.45 € 61.69 – € 123.37
Liraglutide[2]	Disposable needles	€ 61.69

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 2019

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 22 November 2019.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de
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Berlin, 22 November 2019

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The chair

Prof Hecken