Resolution

Gemeinsamer Bundesausschuss

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 Dapagliflozin/Metformin (Reassessment Because of New Scientific Knowledge (Type 2 Diabetes Mellitus))

of 19 December 2019

At its session on 19 December 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 will be amended as follows:

1. The data concerning the active ingredient combination dapagliflozin/metformin as set out in the resolution of 7 August 2014 (BAnz AT 3 September 2014 B1) and the resolution of 21 June 2018 (BAnz AT 13 July 2018 B3) are hereby repealed.

2. Annex XII shall be amended in alphabetical order to include the active ingredient combination dapagliflozin/metformin as follows:

Dapagliflozin/Metformin

Resolution of: 19 December 2019
Entry into force on: 19 December 2019
Federal Gazette, BAnz AT DD MM YYYY Bx

Therapeutic indication (according to the product information of July 2019):

Xigduo is indicated in adults for the treatment of type 2 diabetes mellitus as an adjunct to diet and exercise:

- in patients insufficiently controlled on their maximally tolerated dose of metformin alone
- in combination with other medicinal products for the treatment of diabetes in patients insufficiently controlled with metformin and these medicinal products
- in patients already being treated with the combination of dapagliflozin and metformin as separate tablets

For study results with respect to combination of therapies, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1.

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

a) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with one other hypoglycaemic agent (apart from insulin, here metformin) do not sufficiently control the blood sugar

a1) in patients without high cardiovascular risk[1]

Appropriate comparator therapy:

- Metformin + sulphonylurea (glibenclamide or glimepiride) or
- Metformin + empagliflozin

Extent and probability of the additional benefit of dapagliflozin/metformin compared with the appropriate comparator therapy:

An additional benefit is not proven.

a2) in patients at high cardiovascular risk receiving further medication for the treatment of cardiovascular risk factors[2]

Appropriate comparator therapy:

- Metformin + sulphonylurea (glibenclamide or glimepiride) or
- Metformin + empagliflozin or

[1] In the present case, high cardiovascular risk is defined according to the DECLARE-TIMI 58 Study (see study protocol, Wiviott et. al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2019; 380(4):347–357. DOI: 10.1056/NEJMoa1812389) and summarised here approximately as ≥ 40 years with at least one cardiovascular disease (ischaemic heart disease, cerebrovascular disease, or peripheral arterial occlusive disease) or women ≥ 60 years and men ≥ 55 years with at least one risk factor for cardiovascular disease (dyslipidemia, hypertension, current smoking with ≥ 5 cigarettes/day for at least one year at the time of randomisation)

[2] In particular anti-hypertensive agents, anticoagulants, and/or lipid-lowering agents

- Metformin + liraglutide[3]

Extent and probability of the additional benefit of dapagliflozin/metformin compared with the appropriate comparator therapy:

Hint for a minor additional benefit

b) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with at least two hypoglycaemic agents (including metformin, apart from insulin) do not sufficiently control the blood sugar

b1) in patients without high cardiovascular risk[1]

Appropriate comparator therapy:

- Human insulin + metformin

Extent and probability of the additional benefit of dapagliflozin/metformin compared with the appropriate comparator therapy:

An additional benefit is not proven.

b2) in patients at high cardiovascular risk[1] receiving further medication for the treatment of cardiovascular risk factors[2]

Appropriate comparator therapy:

- Human insulin + metformin or
- Human insulin + empagliflozin[3] or
- Human insulin + liraglutide[3] 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 dapagliflozin/metformin compared with the appropriate comparator therapy:

Hint for a minor additional benefit

c) b) Adult patients with type 2 diabetes mellitus in whom diet and movement and treatment with insulin (with one other hypoglycaemic agent, here metformin) do not sufficiently control the blood sugar

c1) in patients without high cardiovascular risk[1]

Appropriate comparator therapy:

- The optimisation of the human insulin regime (possibly + metformin)

Extent and probability of the additional benefit of dapagliflozin/metformin compared with the appropriate comparator therapy:

[3] 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 agents, anticoagulants, and/or lipid-lowering agents (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).

An additional benefit is not proven.

c2) in patients at high cardiovascular risk[1] receiving further medication for the treatment of cardiovascular risk factors[2]

Appropriate comparator therapy:

- The optimisation of the human insulin regimen (possibly + metformin *or* empagliflozin[3] *or* liraglutide[3])

Extent and probability of the additional benefit of dapagliflozin/metformin compared with the appropriate comparator therapy:

Hint for a minor additional benefit

Study results by endpoints[4] of the DECLARE-TIMI 58 Study for patient groups a), b), and c) in adult patients with inadequately controlled diabetes mellitus and increased cardiovascular risk (sub-population at least 1700 mg of metformin at start of study):

Endpoint category Endpoint	Intervention Dapagliflozin + metformin		Control Placebo + metformin		Intervention vs control
	N	Median time to event Patients with event n (%)	N	Median time to event Patients with event n (%)	HR [95% CI]; p value[a]
Mortality					
Overall mortality	4627	no data available 244 (5.3)	4691	no data available 267 (5.7)	0.93 [0.78; 1.11]; 0.410
Morbidity					
MACE					
Myocardial infarction[b, c, d]	4627	no data available 208 (4.5)	4691	no data available 253 (5.4)	0.83 [0.69; 1.00]; 0.051
fatal	4627	no data available 12 (0.3)	4691	no data available 23 (0.5)	0.53 [0.26; 1.06]; 0.073
non-fatal	4627	no data available 197 (4.3)	4691	no data available 233 (5.0)	0.86 [0.71; 1.04]; 0.112
ischaemic stroke[b, c, d]	4627	no data available 130 (2.8)	4691	no data available 110 (2.3)	1.20 [0.93; 1.54]; 0.163
fatal	4627	no data available 15 (0.3)	4691	no data available 8 (0.2)	1.90 [0.81; 4.49]; 0.142
non-fatal	4627	no data available 117 (2.5)	4691	no data available 102 (2.2)	1.16 [0.89; 1.52]; 0.265
stroke (fatal or non-fatal)[b, c, e]	4627	no data available 138 (3.0)	4691	no data available 129 (2.7)	no data available[f]
haemorrhagic		no data available		no data available	no data available

[4] Data from the dossier evaluation of the IQWiG (A19-52) of 27 September 2019 unless otherwise indicated.

of unknown aetiology		no data available		no data available	no data available
TIA[b]		no data available		no data available	no data available
Cardiac failure					
Hospitalisation because of cardiac failure[b]	4627	no data available 84 (1.8)	4691	no data available 146 (3.1)	0.58 [0.44; 0.76]; < 0.001 *AD 1.3%*
severe cardiac failure (SMQ cardiac failure)	4627	no data available 179 (3.9)	4691	no data available 264 (5.6)	0.68 [0.56; 0.82]; < 0.001 *AD 1.7%*
Kidney disease[g]	4627	no data available 69 (1.5)	4691	no data available 145 (3.1)	0.48 [0.36; 0.63]; < 0.001 *AD 1.6%*
Confirmed sustained reduction in eGFR[h, i]	4627	no data available 68 (1.5)	4691	no data available 140 (3.0)	0.49 [0.36; 0.65]; < 0.001 *AD 1.5%*
End-stage kidney disease[h]	4627	no data available 1 (< 0.1)	4691	no data available 6 (0.1)	0.17 [0.02; 1.42]; 0.101
Dialysis ≥ 90 days[h]		no data available		no data available	no data available
Kidney transplant[h]		no data available		no data available	no data available
confirmed sustained eGFR < 15 ml/min/1.73 m^2 [h]		no data available		no data available	no data available
Death because of kidney disease[h]	4627	no data available 1 (< 0.1)	4691	no data available 4 (< 0.1)	0.25 [0.03; 2.24]; 0.216
Treatment of retinopathy[j, k]	4627	no data available 67 (1.4)	4691	no data available 49 (1.0)	no data available[l]
surgical or spontaneous non-surgical amputations	4627	no data available 59 (1.3)	4691	no data available 63 (1.3)	no data available[m]
Health-related quality of life					
	Endpoint not recorded				

a: HR and CI from Cox proportional hazards model, stratified by cardiovascular risk and hematuria status at baseline with treatment group as model term; p value from Wald test
b: Adjudicated by an endpoint committee
c: Patients who have had multiple events are counted only once
d: The combined endpoint MACE also shows no statistically significant results.
e: Information refers to ischaemic and haemorrhagic strokes as well as strokes with unclear aetiology
f: RR: 1.08 [0.86; 1.37]; p = 0.533. Effect, CI, and p value: unconditional exact test (CSZ method according to Andrés)
g: Combined endpoint consisting of the components: confirmed sustained ≥ 40% reduction of eGFR to eGFR < 60 ml/min/1.73 m^2 (using the CKD-EPI equation); end-stage kidney disease (consisting of the components: Dialysis ≥ 90 days, kidney transplant and/or confirmed sustained eGFR < 15 ml/min/1.73 m^2) and/or kidney death
h: All events in the entire course of the study and not the events included in the combined endpoint are presented
i: Comparable results to the endpoint doubling of serum creatinine levels accompanied by eGFR ≤ 45 ml/min/1.73 m^2 occur.
j: Combined endpoint consisting of the components: at least one laser treatment and/or intra-ocular treatment because of the progression and/or deterioration of diabetic retinopathy
k: There is no visual acuity assessment within the study.
l: RR: 1.39 [0.96; 2.00]; p = 0.080; calculation of the pharmaceutical company, p value from Wald test
m: RR: 0.95 [0.67; 1.35]; p = 0.773; calculation of the pharmaceutical company, p value from Wald test

Abbreviations:
CKD-EPI: Chronic-Kidney-Disease-Epidemiology-Collaboration; eGFR: estimated glomerular filtration rate; HR: hazard ratio; CI: Confidence interval; MACE: major adverse cardiovascular event (cardiovascular death, myocardial infarction; stroke); MedDRA: Medical Dictionary for Regulatory Activities; n: number of patients with event; N: number of patients evaluated; SMQ: standardised MedDRA queries; TIA: transitory ischaemic attack

Endpoint category **Endpoint**	**Intervention** **Dapagliflozin + metformin**		**Control** **Placebo + metformin**		**Intervention vs control**
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[a]
Side effects[j]					
Total rates					
AEs (additionally shown)	No usable data[b]				
SAE (non-fatal, excluding subsequent complications)[f]	4622	1263 (27.3)	4689	1455 (31.0)	0.88 [0.83; 0.94]; < 0.001 *AD 3.7%*
Discontinuation because of AE	4622	310 (6.7)	4689	301 (6.3)	1.04 [0.90; 1.22]; 0.575
Specific AE					

Hypoglycaemia (PT, SAE)	4622	32 (0.7)	4689	48 (1.0)	0.68 [0.43; 1.06] 0.084[g]
Bladder cancer[c, d]	4622	12 (0.3)	4689	25 (0.5)	0.49 [0.24; 0.97]; 0.040 *AD 0.2%*
Breast cancer[c, d]	4622	17 (0.4)	4689	23 (0.5)	0.75 [0.40; 1.40]; 0.367
Prostate carcinoma[c, d, e]	3048	36 (1.2)	2994	31 (1.0)	1.14 [0.71; 1.84]; 0.589
DKAs[c, d] (all, AE)	no evaluations available				
definitive DKAs	4622	12 (0.3[i])	4689	6 (0.1[i])	2.03 [0.76; 5.40]; 0.153[g]
probable DKAs	4622	3 (0.1[i])	4689	3 (0.1[i])	1.01 [0.20; 5.02]; > 0.999[g]
possible DKAs	no evaluations available				
Symptoms of a lack of volume[c] (AE)	4622	125 (2.7)	4689	107 (2.3)	1.19 [0.92; 1.53]; 0.192
Respiratory, thoracic, and mediastinal disorders (SOC, SAE)	4622	97 (2.1)	4689	134 (2.9)	0.73 [0.57; 0.95]; 0.019[g] *AD 0.8%*
Hepatobiliary disorders (SOC, SAE)	4622	52 (1.1)	4689	77 (1.6)	0.69 [0.48; 0.97]; 0.033[g] *AD 0.5%*

a: p value from Wald test
b: Not all AEs were fully documented in the study (only SAE, discontinuations because of AE, and AE of special interest as per predefined PT collection).
c: Collected via pre-defined PT collection of the pharmaceutical company
d: Adjudicated by an endpoint committee
e: Data related to male patients
f: To the exclusion of subsequent complications: Death (including cardiovascular death), myocardial infarction, ischaemic stroke, hospitalisation because of cardiac failure, unstable angina pectoris, adjudicated revascularisation, renal events, and retinopathies
g: Calculation by the IQWiG, exact unconditional test (CSZ method according to Andrés
i: Calculation of the IQWiG
j: Follow-up until the last round

Abbreviations:

DKA: diabetic ketoacidosis; CI: confidence interval; n: number of patients with (at least one) event; N: number of patients evaluated; PT: preferred term; RR: relative risk; SOC: system organ class; SAE: serious adverse event; AE: adverse event

Additionally presented endpoints of the DECLARE-TIMI 58 Study (sub-population, at least 1700 mg of metformin at the start of study)

	Intervention Dapagliflozin + metformin			Control Placebo + metformin			Intervention vs control
	N[a]	Values at start of study MV (SD)	Change at month 48 MV[b] (SE)	N[a]	Values at start of study MV (SD)	Change at month 48 MV[b] (SE)	MD [95% CI]; p value
Body weight [kg]	no data available	93.0 (19.6)	−3.7 (0.1)	no data available	92.1 (20.0)	−1.6 (0.1)	−2.04 [−2.25; −1.83]; < 0.001
HbA1c [%]	no data available	8.3 (1.2)	−0.4 (0.0)	no data available	8.3 (1.2)	−0.2 (0.0)	−0.25 [−0.31; −0.20]; < 0.001

a: The pharmaceutical company does not indicate how many patients were included in the analysis. At month 48, data for the endpoint body weight was collected from 75% of the patients; for the endpoint HbA1c, data was collected from 73% of the patients.
b: Calculation using a repeated measures model with treatment group, baseline, cardiovascular risk category, baseline hematuria status, rounds, and the interaction of rounds and treatment group as model terms. The pharmaceutical company does not specify the method of p value calculation.
Abbreviations:
HbA1c: Glycohaemoglobin; CI: confidence interval; MD: mean difference; MV: Mean Value; N: number of patients evaluated; RCT: randomised controlled study; SD: Standard deviation

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

a) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with one other hypoglycaemic agent (apart from insulin, here metformin) do not sufficiently control the blood sugar

approx. 607,000 patients

b) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with at least two hypoglycaemic agents (including metformin, apart from insulin) do not sufficiently control the blood sugar
approx. 261,000 patients

c) b) Adult patients with type 2 diabetes mellitus in whom diet and movement and treatment with insulin (with one other hypoglycaemic agent, here metformin) do not sufficiently control the blood sugar

approx. 271,000 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 Forxiga® (active ingredient: dapagliflozin/metformin) at the following publicly accessible link (last access: 13 November 2019):

https://www.ema.europa.eu/documents/product-information/xigduo-epar-product-information_de.pdf

4. Treatment costs

Annual treatment costs:

a) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with one hypoglycaemic agent (apart from insulin, here metformin) do not sufficiently control the blood sugar

a1) patients without high cardiovascular risk[1]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be assessed (dapagliflozin/metformin)	
Dapagliflozin/metformin[5]	€ 359.45
Appropriate comparator therapy	
Metformin	€ 33.24 – € 99.71
Sulphonylurea Glibenclamide or Glimepiride	 € 13.03 – € 78.17 € 29.67 – € 152.29
Empagliflozin	€ 658.93
 Metformin + glibenclamide *or* metformin + glimepiride Metformin + empagliflozin	Total: € 46.26–177.88 € 62.90–251.99 € 692.17 – € 758.64

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2019

a2) in patients at high cardiovascular risk[1] receiving further medication for the treatment of cardiovascular risk factors[2]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be assessed (dapagliflozin/metformin)	
Dapagliflozin/metformin[5]	€ 359.45
Appropriate comparator therapy	

[5] Potencies available (dapagliflozin/metformin) 5/850 mg; 5/1000 mg.

Designation of the therapy	Annual treatment costs per patient
Metformin	€ 33.24 – € 99.71
Sulphonylurea Glibenclamide or Glimepiride	 € 13.03 – € 78.17 € 29.67 – € 152.29
Empagliflozin	€ 658.93
Liraglutide[3]	€ 1,308.84 – € 1,963.26
 Metformin + glibenclamide *or* metformin + glimepiride Metformin + empagliflozin Metformin + liraglutide[1]	Total: € 46.26–177.88 € 62.90–251.99 € 692.17 – € 758.64 € 1,342.08 – € 2,062.97

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2019

Costs for additionally required SHI services:

Appropriate comparator therapy		
Liraglutide[3]	Disposable needles	€ 61.69

b) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with at least two hypoglycaemic agents (including metformin, apart from insulin) do not sufficiently control the blood sugar

b1) in patients without high cardiovascular risk[1]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be evaluated (dapagliflozin/metformin in combination with other hypoglycaemic agents[6] (except insulin))	
Dapagliflozin/metformin[5]	€ 359.45
Glibenclamide *or* Glimepiride	€ 13.03 – € 78.17 € 29.67 – € 152.29

[6] An example of combination therapy with other hypoglycaemic agents is the combination with a sulphonylurea (glibenclamide or glimepiride)

Designation of the therapy	Annual treatment costs per patient
Dapagliflozin/metformin + glibenclamide *or* Dapagliflozin/metformin + glimepiride	Total: € 372.48 – € 437.62 € 389.12 – € 511.74
Appropriate comparator therapy	
Metformin	€ 33.24 – € 99.71
Human insulin (NPH insulin)	€ 382.46 – € 764.92
Human insulin (NPH-insulin) + metformin	Total: € 415.70 – € 864.63
Possibly therapy only with human insulin if, in accordance with the product information, metformin and empagliflozin[1] and liraglutide[1] 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: 1 December 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

b2) in patients at high cardiovascular risk[1] ~~in combination with~~ receiving further medication for the treatment of cardiovascular risk factors[2]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be evaluated (dapagliflozin/metformin in combination with other hypoglycaemic agents[7] (except insulin))	
Dapagliflozin/metformin[5]	€ 359.45
Glibenclamide *or* Glimepiride	€ 13.03 – € 78.17 € 29.67 – € 152.29

[7] An example of combination therapy with other hypoglycaemic agents is the combination with a sulphonylurea (glibenclamide or glimepiride)

Designation of the therapy	Annual treatment costs per patient
Dapagliflozin/metformin + glibenclamide *or* Dapagliflozin/metformin + glimepiride	Total: € 372.48 – € 437.62 € 389.12 – € 511.74
Appropriate comparator therapy	
Metformin	€ 33.24 – € 99.71
Empagliflozin[3]	€ 658.93
Liraglutide[3]	€ 1,308.84 – € 1,963.26
Human insulin (NPH insulin)	€ 382.46 – € 764.92
Human insulin (NPH-insulin) + metformin	Total: € 415.70 – € 864.63
Human insulin (NPH insulin) + empagliflozin[3]	€ 1,041.40 – € 1,423.86
Human insulin (NPH insulin) + liraglutide[3]	€ 1,691.30 – € 2,728.19
Possibly therapy only with human insulin if, in accordance with the product information, metformin and empagliflozin[1] and liraglutide[1] 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: 1 December 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[3]	Disposable needles	€ 61.69

c) Adult patients with type 2 diabetes mellitus in whom diet and movement and the treatment with insulin (with or without another hypoglycaemic agent) do not sufficiently control the blood sugar

c1) in patients without high cardiovascular risk[1]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be evaluated (dapagliflozin/metformin in combination with insulin)	
Dapagliflozin/metformin[5]	€ 359.45
Human insulin (NPH insulin)	€ 382.46 – € 764.92
Dapagliflozin/metformin + human insulin (NPH insulin)	Total: € 741.91 – € 1,124.37
Appropriate comparator therapy	
Metformin	€ 33.24 – € 99.71
Conventional insulin therapy (premixed insulin) Conventional insulin therapy (premixed insulin) possibly + metformin Conventional insulin therapy (premixed insulin) + metformin	€ 382.46 – € 764.92 Total: € 415.70 – € 864.63
Intensified conventional insulin therapy Human insulin (NPH insulin) Human insulin (bolus insulin)	 € 152.98 – € 458.95 € 152.98 – €458.95 Total: € 382.46 – € 764.92

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2019

Costs for additionally required SHI services:

Designation of the therapy	Designation	Costs/year
Medicinal product to be assessed (dapagliflozin/metformin in combination with insulin (with or without another hypoglycaemic agent))		
Human insulin (NPH insulin)	Blood glucose test strips Lancets Disposable needles	€ 135.05 – € 405.15 € 7.48 – € 22.45 € 61.69 – € 123.37
Appropriate comparator therapy		
Conventional insulin therapy (premixed insulin)	Blood glucose test strips	€ 135.05 – € 405.15

Designation of the therapy	Designation	Costs/year
	Lancets Disposable needles	€ 7.48 – € 22.45 € 61.69 – € 123.37
Intensified conventional insulin therapy	Blood glucose test strips Lancets Disposable needles	€ 540.20 – € 810.30 € 29.93 – € 44.90 € 246.74 – € 308.43

c2) in patients at high cardiovascular risk[1] receiving further medication for the treatment of cardiovascular risk factors[2]

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be evaluated (dapagliflozin/metformin in combination with insulin)	
Dapagliflozin/metformin[5]	€ 359.45
Human insulin (NPH insulin)	€ 382.46 – € 764.92
Dapagliflozin/metformin + human insulin (NPH insulin)	Total: € 741.91 – € 1,124.37
Appropriate comparator therapy	
Metformin	€ 33.24 – € 99.71
Empagliflozin[3]	€ 658.93
Liraglutide[3]	€ 1,308.84 – € 1,963.26
<u>Conventional insulin therapy (premixed insulin)</u> <u>Conventional insulin therapy (premixed insulin) possibly + metformin *or* empagliflozin *or* liraglutide</u> Conventional insulin therapy (premixed insulin) + metformin Conventional insulin therapy (premixed insulin) + empagliflozin[3] Conventional insulin therapy (premixed insulin) + liraglutide[3]	€ 382.46 – € 764.92 Total: € 415.70 – € 864.63 € 1.041.40 – € 1,423.86 € 1,691.30 – € 2,728.19
<u>Intensified conventional insulin therapy</u>	

Designation of the therapy	Annual treatment costs per patient
Human insulin (NPH insulin) Human insulin (bolus insulin)	€ 152.98 – € 458.95 € 152.98 – €458.95 Total: € 382.46 – € 764.92

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2019

Costs for additionally required SHI services:

Designation of the therapy	Designation	Costs/year
Medicinal product to be assessed (dapagliflozin/metformin in combination with insulin (with or without another hypoglycaemic agent))		
Human insulin (NPH insulin)	Blood glucose test strips Lancets Disposable needles	€ 135.05 – € 405.15 € 7.48 – € 22.45 € 61.69 – € 123.37
Appropriate comparator therapy		
Conventional insulin therapy (premixed insulin)	Blood glucose test strips Lancets Disposable needles	€ 135.05 – € 405.15 € 7.48 – € 22.45 € 61.69 – € 123.37
Intensified conventional insulin therapy	Blood glucose test strips Lancets Disposable needles	€ 540.20 – € 810.30 € 29.93 – € 44.90 € 246.74 – € 308.43
Liraglutide[3]	Disposable needles	€ 61.69

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 19 December 2019.

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

Berlin, 19 December 2019

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken