Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive: Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V and Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V Empagliflozin (new therapeutic indication: type 2 diabetes mellitus, ≥ 10 to ≤ 17 years)

of 20 June 2024

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient empagliflozin (Jardiance) was listed for the first time on 15 August 2014 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 7 December 2023, empagliflozin received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334 from 12.12.2008, sentence 7).

On 19 December 2023, the pharmaceutical company has submitted a dossier in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the

approval for a new therapeutic indication) in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient empagliflozin with the new therapeutic indication "Jardiance is indicated in adults and children aged 10 years and above for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance
- in addition to other medicinal products for the treatment of diabetes mellitus".

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 2 April 2024 on the G-BA website (www.g-ba.de), therefore initiating the written statement procedure. In addition, an oral hearing was held.

Based on the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure, the G-BA decided on the question on whether an additional benefit of empagliflozin compared with the appropriate comparator therapy could be determined – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by IQWiG[1] according to the General Methods was not used in the benefit assessment of empagliflozin – Annex XII - Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

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

2.1.1 Approved therapeutic indication of Empagliflozin (Jardiance) in accordance with the product information

Jardiance is indicated in adults and children aged 10 years and above for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance
- in addition to other medicinal products for the treatment of diabetes

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Therapeutic indication of the resolution (resolution of 20.06.2024):

Jardiance is indicated in adolescents and children aged 10 to 17 years for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance
- in addition to other medicinal products for the treatment of diabetes

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Children and adolescents aged 10 to 17 years with type 2 diabetes mellitus, who have not achieved sufficient glycaemic control with their previous medicinal therapy consisting of at least one hypoglycaemic agent in addition to diet and exercise

Appropriate comparator therapy:

A patient-individual therapy, taking into account the HbA1c value, previous therapies and complications with selection of

- metformin + human insulin
- metformin + liraglutide or dulaglutide
- metformin + dapagliflozin
- Escalation of insulin therapy: conventional therapy (CT) or intensified insulin therapy (ICT), in each case in combination with metformin and dapagliflozin or liraglutide or dulaglutide

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

<u>Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:</u>

on 1. Apart from empagliflozin, the active ingredient metformin, the GLP-1 receptor agonists liraglutide, dulaglutide and exenatide, the SGLT-2 inhibitor dapagliflozin and insulin (human insulin, insulin analogues) are approved for the treatment of type 2 diabetes mellitus in children and adolescents aged 10 years and above.

on 2. A non-medicinal treatment cannot be considered as a comparator therapy in this therapeutic indication.

on 3. The following resolutions of the G-BA on the early benefit assessment of medicinal products with new active ingredients are available for this therapeutic indication in children and adolescents with type 2 diabetes mellitus (Annex XII to the Pharmaceuticals Directive):
- insulin degludec from 20 August 2015,
- dapagliflozin from 16 June 2022,
- dulaglutide from 21 September 2023.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

There is a current S3 guideline[2] on the diagnosis, treatment and follow-up of diabetes mellitus in children and adolescents. According to the recommendations, metformin is the first choice for the medicinal treatment of type 2 diabetes mellitus. If the HbA1c-value is ≥ 8.5% without acidosis, the combination of metformin with basal insulin is recommended as initial therapy. Patients with acidosis or diabetic ketoacidosis should initially receive insulin therapy. However, once the acidosis has normalised, metformin therapy should also be started in these children and adolescents (while maintaining basal insulin therapy).

It is assumed that metformin contraindications, which exist according to the product information of metformin, for example in severe renal failure, metabolic acidoses, diabetic precoma or liver failure, occur less frequently in children and adolescents.
Metformin intolerances, for example gastrointestinal intolerances can also occur in children and adolescents with type 2 diabetes mellitus, especially at the start of treatment. Clinical experience shows that metformin intolerance occurs with a comparable frequency in children and adolescents with type 2 diabetes mellitus as in adult patients. According to the product information of metformin for use in children and adolescents, a gradual increase in the dosage has a positive effect on the gastrointestinal tolerability of metformin.
Overall, it is therefore assumed that only a smaller percentage of children and adolescents have a metformin contraindication or permanent intolerance compared to the total population.

According to the current recommendations, the therapy of type 2 diabetes mellitus in children and adolescents does not represent a static therapy concept. Rather, the medication should be reviewed regularly and adjusted patient-individually. The treatment decision is made, in particular, taking into account the HbA1c-value, previous therapies and any complications (e.g. ketosis or diabetic ketoacidosis).

With the GLP-1 receptor agonists liraglutide, dulaglutide and exenatide and the SGLT-2 inhibitor dapagliflozin, additional therapy options are available for the treatment of children and adolescents aged 10 years and above with type 2 diabetes mellitus.

According to the current recommendations of the S3 guideline, if the patient-individual therapeutic goals with metformin alone are not achieved in children and adolescents, additional therapy with a GLP-1 receptor agonist or an SGLT-2 inhibitor should be given. If insulin therapy is already in place (in combination with metformin), this should - if possible - be replaced by either a GLP-1-receptor agonist or an SGLT-2 inhibitor, taking into account patient-individual criteria (HbA1c value, previous therapies and

[2] S3 guideline Diagnosis, therapy and follow-up of diabetes mellitus in childhood and adolescence. Version 4 (awmf.org)

complications). In the German healthcare context, the active ingredients liraglutide and dulaglutide assume the maximum significance among the GLP-1-receptor agonists.

Escalation of insulin therapy is recommended if adequate glycaemic control is not achieved under combination regimen with metformin and a GLP-1-receptor agonist or an SGLT-2-inhibitor, and if metabolic crises occur (e.g. ketoacidosis). This can take the form of either conventional (insulin) therapy (CT) or intensified conventional (insulin) therapy (ICT). In children and adolescents, insulin therapy can take the form of pump therapy. New recommendations also consider the continuation of the previous combination therapy with metformin and a GLP-1-receptor agonist or an SGLT-2-inhibitor to be indicated even in the case of escalation of insulin therapy.

Overall, especially for children and adolescents, one therapeutic goal is to keep the period of insulin intake as short as possible. The administration of insulin in children and adolescents is usually not a long-term therapy and should be replaced by other therapy options, if possible.

Taking into account the available evidence, a patient-individual therapy therefore represents the appropriate comparator therapy, taking into account the HbA1c-value, previous therapies and complications (e.g. the occurrence of ketoacidosis). As part of the patient-individual therapy, the following escalation therapies are considered appropriate for children and adolescents aged 10 to 17 years with type 2 diabetes mellitus, who have not achieved sufficient glycaemic control with their previous medicinal therapy consisting of at least one hypoglycaemic agent in addition to diet and exercise: a combination therapy of metformin with human insulin, with a GLP-1-receptor agonist (liraglutide or dulaglutide) or an SGLT-2-inhibitor (dapagliflozin) or an escalation of insulin therapy in the form of conventional (insulin) therapy (CT) or intensified conventional (insulin) therapy (ICT), in each case in combination with metformin and dapagliflozin or liraglutide or dulaglutide.

The continuation of an inadequate therapy (regimen) for the treatment of type 2 diabetes mellitus, if there are still possibilities of therapy escalation, does not correspond to the appropriate comparator therapy.

It is assumed that possible comorbidities or risk factors of type 2 diabetes mellitus (e.g. hypertension, dyslipidaemia, microvascular complications – nephropathy, neuropathy, retinopathy) are treated patient-individually according to the current state of medical knowledge, in particular by administering antihypertensive drugs and/or lipid-lowering agents.

According to the current generally recognised state of medical knowledge, there are neither advantages nor disadvantages for insulin analogues compared to human insulin, but there are no long-term data with advantages regarding hard endpoints for insulin analogues. The benefit assessment also considers evidence from studies in which insulin analogues were used, provided that the results from studies with insulin analogues are transferable to human insulin. The authorisation status of the insulin analogues must be taken into account. Study results should be examined for possible effect modification by the type of insulin used if the studies were conducted with both human insulin and insulin analogues. However, when comparing costs, the treatment

costs for human insulin must be taken into account, as this was determined to be the appropriate comparator therapy.

Change of the appropriate comparator therapy

To date, for children and adolescents aged 10 to 17 years with type 2 diabetes mellitus, the following escalation therapies have been considered appropriate as part of patient-individual therapy: Metformin either in combination with liraglutide or human insulin, or an escalation of insulin therapy in the form of conventional (insulin) therapy (CT, mixed insulin if necessary + metformin) or intensified conventional (insulin) therapy (ICT).

On the basis of the newly published S3-guideline on the diagnosis, therapy and follow-up of diabetes mellitus in childhood and adolescence, SGLT-2 inhibitors also assume a relevant significance in the treatment of type 2 diabetes mellitus alongside GLP-1 receptor agonists. For the present assessment, only the SGLT-2-inhibitor dapagliflozin can be considered as an appropriate comparator therapy.

In March 2023, the GLP-1 receptor agonist dulaglutide was also approved for the treatment of children and adolescents aged 10 years and above with type 2 diabetes mellitus. Overall, the active ingredients liraglutide and dulaglutide assume the maximum significance among the GLP 1 receptor agonists in the German healthcare context. In addition to liraglutide, dulaglutide is therefore added as part of the appropriate comparator therapy.

Moreover, the current recommendations of the S3 guideline state that the combination therapy of metformin and a GLP-1 receptor agonist (liraglutide, dulaglutide) or an SGLT-2 inhibitor (dapagliflozin) should also be continued during an escalation of insulin therapy.

Based on the updated guideline recommendations, the G-BA therefore considers it appropriate to adjust the appropriate comparator therapy and to add the following escalation therapies as part of a patient-individual therapy: a combination therapy of metformin with dulaglutide and a combination therapy of metformin with dapagliflozin. In addition, the continuation of treatment with metformin in combination with dapagliflozin or liraglutide or dulaglutide is considered appropriate in the case of escalation of insulin therapy.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of empagliflozin is assessed as follows:

Children and adolescents aged 10 to 17 years with type 2 diabetes mellitus, who have not achieved sufficient glycaemic control with their previous medicinal therapy consisting of at least one hypoglycaemic agent in addition to diet and exercise

An additional benefit is not proven.

Justification:

As part of the benefit assessment, the pharmaceutical company presented the results of the double-blind, multicentre DINAMO study, in which empagliflozin was compared with linagliptin and placebo in patients with type 2 diabetes mellitus aged 10 up to and including 17 years, in each case in addition to diet, exercise and a stable dose of metformin, insulin or metformin + insulin. Patients with a glycated haemoglobin (HbA1c) value ≥ 6.5% and ≤ 10.5% who had been diagnosed with type 2 diabetes mellitus for ≥ 8 weeks at the time of screening were enrolled. According to the inclusion criteria, anti-diabetic treatment with metformin, insulin or metformin + insulin had to have been ongoing at a stable dose for ≥ 8 weeks prior to the start of study, whereby the daily metformin dose had to be ≥ 1,000 mg.

A total of 158 patients were enrolled in the DINAMO study. After screening, all patients were treated in a 2-week run-in phase with placebo in addition to diet, exercise and the existing stable dose of metformin, insulin or metformin + insulin. Subsequently, 52 patients were randomised to the empagliflozin arm, 53 patients to the linagliptin arm and 53 patients to the placebo arm. Randomisation was stratified by age and sex. As linagliptin is not part of the appropriate comparator therapy, the pharmaceutical company did not present the results of the linagliptin arm.

In the study, all patients received their background therapy of metformin, insulin or metformin + insulin in addition to the study medication. However, the dosages should remain unchanged as far as medically appropriate. The use of anti-diabetics other than metformin and insulin was not permitted in the study.

The primary endpoint of the study was the change in HbA1c value from the start of study till week 26. Other endpoints were collected in the categories of morbidity and side effects.

Overall, the DINAMO study is unsuitable for deriving an additional benefit, as the treatment carried out in the comparator arms of the study does not correspond to the determined appropriate comparator therapy for the majority of the patients enrolled.

In the placebo arm, 53% of the patients received monotherapy with metformin as anti-diabetic therapy. However, metformin alone is not part of the patient-individual therapy determined as the appropriate comparator therapy.

The continuation of an inadequate therapy for the treatment of type 2 diabetes mellitus does not correspond to the implementation of the appropriate comparator therapy, provided that there are still options of therapy escalation. Since the patients had a mean HbA1c value of approx. 8.0% at the start of study, it can be assumed that a therapy escalation for reduction of the HbA1c value would have been indicated and also possible in principle (e.g. by insulin intake) for the majority of the patients in the comparator arm according to the guideline recommendations. In the DINAMO study, the anti-diabetic background therapy should however remain as unchanged as possible during the study. In addition, there is no

information in the study documents as to whether the anti-diabetic medication was adjusted at the start of study. The lack of escalation of anti-diabetic therapy is also reflected in the continuous increase in HbA1c values compared to the start of study in the placebo arm.

Empagliflozin was therefore not compared with the appropriate comparator therapy, as no patient-individual therapy was carried out in the study with exhaustion of all existing options for therapy escalation at the start of study. In the study, only the existing anti-diabetic therapy was continued for the most part without adjustment, although it can be assumed that there were still options for patient-individual therapy escalation.

The additional information submitted by the pharmaceutical company on the transfer of additional benefit from adult patients on the basis of the EMPA-REG OUTCOME and EMPA-KIDNEY studies is also unsuitable for the present benefit assessment, as, among other things, there is inadequate similarity between the patient populations.

In the overall assessment, there are therefore no suitable data for the assessment of the additional benefit of empagliflozin compared with the appropriate comparator therapy in children and adolescents aged 10 to 17 years with uncontrolled type 2 diabetes mellitus. An additional benefit of empagliflozin comparted to the appropriate comparator therapy is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient empagliflozin (Jardiance).

The therapeutic indication assessed here is as follows: "Jardiance is indicated in children adolescents aged 10 to 17 years for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- as monotherapy when metformin is considered inappropriate due to intolerance
- in addition to other medicinal products for the treatment of diabetes."

As appropriate comparator therapy, the G-BA determined a patient-individual therapy, taking into account the HbA1c value, previous therapies and complications by selecting metformin in combination with human insulin, a GLP-1-receptor agonist (liraglutide or dulaglutide) or an SGLT-2 inhibitor (dapagliflozin) as well as escalation of insulin therapy (conventional therapy or intensified conventional therapy) in combination with metformin and dapagliflozin or liraglutide or dulaglutide .

For the benefit assessment, the pharmaceutical company presented the double-blind, direct comparator DINAMO study for comparing empagliflozin with linagliptin and placebo in patients with type 2 diabetes mellitus aged 10 up to and including 17 years, in each case in addition to diet, exercise and a stable dose of metformin, insulin or metformin + insulin. Since no patient-individual therapy was carried out in the study with exhaustion of all existing options for therapy escalation, the determined appropriate comparator therapy was not implemented for the majority of the patients enrolled. Accordingly, the DINAMO study is unsuitable for deriving an additional benefit compared with the determined appropriate comparator therapy.

In the overall assessment, the additional benefit of empagliflozin over the appropriate comparator therapy for children and adolescents aged 10 to 17 years with type 2 diabetes mellitus, who have not achieved sufficient glycaemic control with their previous medicinal therapy consisting of at least one hypoglycaemic agent in addition to diet and exercise, is not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The G-BA takes into account the patient numbers stated in the pharmaceutical company's dossier, which are, however, subject to uncertainty due to various methodological aspects. However, compared to the resolution on the active ingredient dulaglutide[3] from 2023, more up-to-date sources on the prevalence of the disease and the criterion of inadequate glycaemic control were taken into account. Therefore, despite the existing uncertainty, the available patient numbers represent a better estimate overall than the patient numbers stated in the resolution on dulaglutide.

2.3 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 Jardiance (active ingredient: empagliflozin) at the following publicly accessible link (last access: 26 April 2024):

https://www.ema.europa.eu/en/documents/product-information/jardiance-epar-product-information_en.pdf

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 1 June 2024).

Treatment duration and consumption

With regard to consumption, the average annual consumption was determined by indicating the number of tablets or international units. The daily dosages recommended in the product information were used as a basis for calculation and, if necessary, appropriate ranges were formed. The costs of a possibly necessary titration phase have not been shown, since the anti-diabetic therapy is a continuous long-term therapy and the titration is patient-individual.

The information on treatment duration and dosage was taken from the corresponding product information.

[3] https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/939/

The daily starting dose of empagliflozin for children and adolescents aged 10 years and above is 10 mg and can be increased to 25 mg once daily, if needed.

The recommended dose of dapagliflozin is 10 mg once daily for all patients aged 10 years and above.

The weekly starting dose of dulaglutide for children and adolescents aged 10 years and above is 0.75 mg and can be increased to 1.5 mg once a week after at least 4 weeks, if needed.

The daily starting dose of liraglutide for all patients aged 10 years and above is 0.6 mg; after one week, this is increased to 1.2 mg. According to the product information, patients may benefit from a further increase in the dose from 1.2 mg to 1.8 mg. The appropriate dose of liraglutide is injected subcutaneously daily (pre-filled pen).

For metformin, starting doses of 500 mg once daily are recommended for children aged 10 years and above. Dose increases up to 2,000 mg metformin daily are possible according to the product information; the total daily dose is usually divided into 2 - 3 doses.

A variety of different insulin dosage regimens are available for insulin therapy. In addition, according to the insulin dosage regimen used, the amount of insulin and the frequency of application must be individually adjusted according to the patient's physical activity and lifestyle. To ensure comparability of costs, simplified assumptions have been made for the presentation of treatment duration and dosage. In the "Treatment duration" table, the treatment mode for human insulin (NPH insulin or mixed insulin) is shown as "1 - 2 x daily", although the frequency of application may differ for individual patients.

The insulin dosages (I.U.) per patient are calculated based on the dosage requirement in the age group (children and adolescents aged 10 years and above). The consumption is calculated based on a dosage requirement of 0.7 to 2 I.U./ kg BW/ day for children and adolescents in puberty[4,5].

The basal insulin daily requirement is usually 40 - 60% of the insulin daily requirement, the remaining requirement is covered accordingly by meal-dependent bolus insulin. Three main meals are assumed when calculating bolus insulin consumption. This information was used to calculate the dose of insulin per patient.

For the calculation of the consumption of medicinal products to be dosed according to weight, the G-BA generally uses non-indication-specific average weights as a basis. For body weight, a range between 37.6 kg for 10-year-olds and 67.2 kg for 17-year-olds is therefore assumed according to the official representative statistics "Microcensus 2017 and 2021"[6].

Consequently, weight differences between boys and girls as well as the fact that the bodyweight of patients with type 2 diabetes mellitus may be higher than the average values typical of the age are not taken into account for the cost calculation.

[4] According to the WHO definition, adolescents aged 10 to 19 are in puberty. World Health Organisation. Maternal, Newborn, Child and Adolescent Health and Ageing Data portal [online] URL: https://platform.who.int/data/maternal-newborn-child-adolescent-ageing/adolescent-data

[5] Danne T, Phillip M, Buckingham BA, Jarosz-Chobot P, Saboo B, Urakami T, Battelino T, Hanas R, Codner E. ISPAD Clinical Practice Consensus Guidelines 2018: Insulin treatment in children and adolescents with diabetes. Pediatr Diabetes. 2018 Oct;19 Suppl 27:115-135. doi: 10.1111/pedi.12718.

[6] Federal Health Reporting. Average body measurements of the population (2017 and 2021: both, aged 1 year and 15 years and over), www.gbe-bund.de.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Empagliflozin	Continuously, 1 x daily	365.0	1	365.0
Concomitant active ingredient of the medicinal product to be assessed[7]				
Metformin	Continuously, 1-3 x daily	365.0	1	365.0
Liraglutide	Continuously, 1 x daily	365.0	1	365.0
Dulaglutide	Continuously, 1 x every 7 days	52.1	1	52.1
Human insulin (NPH insulin)	Continuously, 1-2 x daily	365.0	1	365.0
Conventional insulin therapy (CT, mixed insulin)[8]	Continuously, 1-2 x daily	365.0	1	365.0
Intensified conventional (insulin) therapy (ICT)[9] Human insulin (NPH insulin) Human insulin (bolus insulin)	Continuously, 1-2 x daily Continuously, 3 x daily	365.0 365.0	1 1	365.0 365.0
Appropriate comparator therapy				
A patient-individual therapy, taking into account the HbA1c value, previous therapies and complications with selection of the following active ingredients:				

[7] For the combination of empagliflozin with a hypoglycaemic agent, metformin, liraglutide, dulaglutide and human insulin are presented as possible concomitant active ingredients.

[8] The combination with mixed insulin and with mixed insulin together with metformin is shown as an example of the combination of empagliflozin with an insulin in the context of escalation of insulin therapy, in this case with conventional insulin therapy.

[9] The combination with and without metformin is shown as an example of the combination of empagliflozin with an insulin in the context of escalation of insulin therapy, in this case with an intensified conventional insulin therapy.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Metformin	Continuously, 1-3 x daily	365.0	1	365.0
Dapagliflozin	Continuously, 1 x daily	365.0	1	365.0
Liraglutide	Continuously, 1 x daily	365.0	1	365.0
Dulaglutide	Continuously, 1 x every 7 days	52.1	1	52.1
Human insulin (NPH insulin)	Continuously, 1-2 x daily	365.0	1	365.0
Conventional insulin therapy (CT, mixed insulin)	Continuously, 1-2 x daily	365.0	1	365.0
<u>Intensified conventional (insulin) therapy (ICT)</u>				
Human insulin (NPH-insulin)	Continuously, 1-2 x daily	365.0	1	365.0
Human insulin (bolus insulin)	Continuously, 3 x daily	365.0	1	365.0

<u>Consumption:</u>

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Empagliflozin	10 mg – 25 mg	10 mg – 25 mg	1 x 10 mg – 1 x 25 mg	365.0	365.0 x 10 mg – 365.0 x 25 mg
Concomitant active ingredient of the medicinal product to be assessed[7]					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Metformin	500 mg – 1,000 mg	500 mg – 2,000 mg	1 x 500 mg – 2 x 1,000 mg	365.0	365.0 x 500 mg – 730.0 x 1,000 mg
Liraglutide	1.2 mg – 1.8 mg	1.2 mg – 1.8 mg	1 x 1.2 mg – 1 x 1.8 mg	365.0	365.0 x 1.2 mg - 365 x 1.8 mg
Dulaglutide	0.75 mg - 1.5 mg	0.75 mg - 1.5 mg	1 x 0.75 mg – 1 x 1.5 mg	52.1	52.1 x 0.75 mg – 52.1 x 1.5 mg
Human insulin (NPH insulin)	0.7 I.U. / kg BW – 2 I.U. / kg BW	26.32 I.U. – 134.4 I.U.	1 x 26.32 I.U. – 1 x 134.4 I.U.	365.0	9,606.8 I.U. – 49,056 I.U.
Conventional (insulin) therapy (CT, mixed insulin)[8]	0.7 I.U. / kg BW – 2 I.U. / kg BW	26.32 I.U. – 134.4 I.U.	1 x 26.32 I.U. – 1 x 134.4 I.U.	365.0	9,606.8 I.U. – 49,056 I.U.
Intensified conventional (insulin) therapy (ICT)					
Human insulin (NPH insulin)	0.28 I.U./ kg BW – 1.2 I.U./ kg BW	10.53 I.U. – 80.64 I.U.	1 x 10.53 I.U. – 1 x 80.64 I.U.	365.0	3,842.72 I.U. – 29,433.6 I.U.
Human insulin (bolus insulin)	0.28 I.U./ kg BW – 1.2 I.U./ kg BW	10.53 I.U. – 80.64 I.U.	1 x 10.53 I.U. – 1 x 80.64 I.U.	365.0	3,842.72 I.U. – 29,433.6 I.U.

Appropriate comparator therapy					
A patient-individual therapy, taking into account the HbA1c value, previous therapies and complications with selection of the following active ingredients:					
Metformin	500 mg – 1,000 mg	500 mg – 2000 mg	1 x 500 mg – 2 x 1,000 mg	365.0	365.0 x 500 mg – 730.0 x 1,000 mg
Dapagliflozin	10 mg	10 mg	1 x 10 mg	365.0	365.0 x 10 mg
Liraglutide[10]	1.2 mg – 1.8 mg	1.2 mg – 1.8 mg	1 x 1.2 mg – 1 x 1.8 mg	365.0	365.0 x 1.2 mg - 365 x 1.8 mg
Dulaglutide	0.75 mg - 1.5 mg	0.75 mg - 1.5 mg	1 x 0.75 mg – 1 x 1.5 mg	52.1	52.1 x 0.75 mg – 52.1 x 1.5 mg
Human insulin (NPH insulin)	0.7 I.U. / kg BW – 2 I.U. / kg BW	26.32 I.U. – 134.4 I.U.	1 x 26.32 I.U. – 1 x 134.4 I.U.	365.0	9,606.8 I.U. – 49,056 I.U.
Conventional (insulin) therapy (CT, mixed insulin)[8]	0.7 I.U. / kg BW – 2 I.U. / kg BW	26.32 I.U. – 134.4 I.U.	1 x 26.32 I.U. – 1 x 134.4 I.U.	365.0	9,606.8 I.U. – 49,056 I.U.
Intensified conventional (insulin) therapy (ICT)					
Human insulin (NPH insulin)	0.28 I.U./ kg BW – 1.2 I.U./ kg BW	10.53 I.U. – 80.64 I.U.	1 x 10.53 I.U. – 1 x 80.64 I.U.	365.0	3,842.72 I.U. – 29,433.6 I.U.
Human insulin (bolus insulin)	0.28 I.U./ kg BW – 1.2 I.U./ kg BW	10.53 I.U. – 80.64 I.U.	1 x 10.53 I.U. – 1 x 80.64 I.U.	365.0	3,842.72 I.U. – 29,433.6 I.U.

[10] According to the product information, each pre-filled pen contains 18 mg liraglutide in 3 ml solution, corresponding to 10 – 15 single doses. Packs of 2, 5 and 10 pre-filled pens are available.

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any fixed reimbursement rates shown in the cost representation may not represent the cheapest available alternative.

The fixed reimbursement rate was used as the basis for calculating the treatment costs for the active ingredients metformin, human insulin and mixed insulin.

In the case of conventional insulin therapy, the costs for mixed insulin (i.e. a human insulin preparation in a specific mixing ratio of 30% normal insulin to 70% basal insulin) were used as a basis.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Empagliflozin 10 mg	100 FCT	€ 244.39	€ 2.00	€ 12.90	€ 229.49
Empagliflozin 25 mg	100 FCT	€ 192.67	€ 2.00	€ 10.04	€ 180.63
+ metformin 500 mg[11]	180 FCT	€ 16.52	€ 2.00	€ 0.41	€ 14.11
+ metformin 1,000 mg[9]	180 FCT	€ 19.11	€ 2.00	€ 0.62	€ 16.49
+ liraglutide	100 – 150 SD	€ 660.82	€ 2.00	€ 35.96	€ 622.86
+ dulaglutide	12 SFI	€ 287.75	€ 2.00	€ 15.30	€ 270.45
+ human insulin (NPH insulin)[9]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
+ conventional (insulin) therapy (CT, mixed insulin)[11]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
+ human insulin (bolus insulin)[9]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
Appropriate comparator therapy					
A patient-individual therapy, taking into account the HbA1c value, previous therapies and complications with selection of the following active ingredients:					
Metformin 500 mg[9]	180 FCT	€ 16.52	€ 2.00	€ 0.41	€ 14.11
Metformin 1,000 mg[9]	180 FCT	€ 19.11	€ 2.00	€ 0.62	€ 16.49
Liraglutide	100 – 150 SD	€ 660.82	€ 2.00	€ 35.96	€ 622.86

[11] Fixed reimbursement rate

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Dapagliflozin	98 FCT	€ 239.30	€ 2.00	€ 0.00	€ 237.30
Dulaglutide	12 SFI	€ 287.75	€ 2.00	€ 15.30	€ 270.45
Human insulin (NPH insulin)[11]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
Conventional (insulin) therapy (CT, mixed insulin)[11]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
Human insulin (bolus insulin)[9]	3,000 I.U.	€ 89.98	€ 2.00	€ 6.22	€ 81.76
Abbreviations: SD = single doses; FCT = film-coated tablets, I.U. = International Units; SFI = solution for injection i.e. pre-filled pen					

LAUER-TAXE® last revised: 1 June 2024

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Designation of the therapy	Designation	Cost/ pack[12]	Number	Consumption/ year
Concomitant active ingredient of the medicinal product to be assessed				
Human insulin (NPH-insulin)	Blood glucose test strips	€ 17.95	1 – 3 x daily	365.0 – 1,095.0
	Lancets	€ 4.20	1 – 3 x daily	365.0 – 1,095.0
	Disposable needles	€ 13.00	1 – 2 x daily	365.0 – 730.0
Conventional insulin therapy (CT, mixed insulin)	Blood glucose test strips	€ 17.95	1 – 3 x daily	365.0 – 1,095.0
	Lancets	€ 4.20	1 – 3 x daily	365.0 – 1,095.0
	Disposable needles	€ 13.00	1 – 2 x daily	365.0 – 730.0
Intensified conventional insulin therapy (ICT)	Blood glucose test strips	€ 17.95	4 – 6 x daily	1,460 – 2,190
	Lancets	€ 4.20	4 – 6 x daily	1,460 – 2,190

[12] Number of test strips/ pack = 50 pcs.; number of lancets/ pack = 200 pcs.; number of disposable needles/ pack = 100 pcs.; presentation of the lowest-priced pack according to LAUER-TAXE®, last revised: 1 June 2024.

Designation of the therapy	Designation	Cost/ pack[12]	Number	Consumption/ year
	Disposable needles	€ 13.00	4 – 5 x daily	1,460 – 1,825
Liraglutide	Disposable needles	€ 13.00	1 x daily	365.0
Appropriate comparator therapy				
Human insulin (NPH-insulin)	Blood glucose test strips	€ 17.95	1 – 3 x daily	365.0 – 1,095.0
	Lancets	€ 4.20	1 – 3 x daily	365.0 – 1,095.0
	Disposable needles	€ 13.00	1 – 2 x daily	365.0 – 730.0
Conventional insulin therapy (CT, mixed insulin)	Blood glucose test strips	€ 17.95	1 – 3 x daily	365.0 – 1,095.0
	Lancets	€ 4.20	1 – 3 x daily	365.0 – 1,095.0
	Disposable needles	€ 13.00	1 – 2 x daily	365.0 – 730.0
Intensified conventional insulin therapy (ICT)	Blood glucose test strips	€ 17.95	4 – 6 x daily	1,460 – 2,190
	Lancets	€ 4.20	4 – 6 x daily	1,460 – 2,190
	Disposable needles	€ 13.00	4 – 5 x daily	1,460 – 1,825
Liraglutide	Disposable needles	€ 13.00	1 x daily	365.0

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered

due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the

assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding information in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section

35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

The designated medicinal products concern in each case an active ingredient which may be used in combination therapy with the assessed medicinal product in the context of a therapeutic indication specified in the product information for the assessed medicinal product. This therapeutic indication concerns other medicinal products for the treatment for diabetes according to the requirements in the product information.

For the designated medicinal products, the prerequisites of Section 35a, paragraph 3, sentence 4 SGB V are fulfilled and, according to the requirements in the product information, there are no reasons for exclusion that prevent a combination therapy with the assessed medicinal product.

References:
Product information for empagliflozin (Jardiance); Jardiance® film-coated tablets; last revised: December 2023

Product information for dulaglutide (Trulicity); Trulicity®; last revised: March 2023

Supplement to Annex XIIa of the Pharmaceuticals Directive

Since the resolution under I.5 mentions medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V, which can be used in a combination therapy with the assessed active ingredient in the therapeutic indication of the resolution, the information on this designation is to be added to Annex XIIa of the Pharmaceuticals Directive and provided with patient-group-related information on the period of validity of the designation.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 12 December 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 19 December 2023, the pharmaceutical company submitted a dossier for the benefit assessment of empagliflozin to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 20 December 2023 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient empagliflozin.

The dossier assessment by the IQWiG was submitted to the G-BA on 26 March 2024, and the written statement procedure was initiated with publication on the G-BA website on 2 April 2024. The deadline for submitting statements was 23 April 2024.

The oral hearing was held on 6 May 2024.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 11 June 2024, and the proposed resolution was approved.

At its session on 20 June 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	12 December 2023	Implementation of the appropriate comparator therapy
Working group Section 35a	29 April 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	6 May 2024	Conduct of the oral hearing
Working group Section 35a	14 May 2024 4 June 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	11 June 2024	Concluding discussion of the draft resolution
Plenum	20 June 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 June 2024

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

Prof. Hecken