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)
Empagliflozin (new therapeutic indication: chronic kidney disease)

of 1 February 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 24 July 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 28 July 2023, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, No.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 in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication):

"Jardiance is indicated in adults for the treatment of chronic kidney disease"

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The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 1 November 2023 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of empagliflozin compared to the appropriate comparator therapy could be determined on the basis of 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. 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 the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of empagliflozin.

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 for the treatment of chronic kidney disease.

Therapeutic indication of the resolution (resolution of 1 February 2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with chronic kidney disease

Appropriate comparator therapy for empagliflozin:

> An optimised standard therapy for the treatment of chronic kidney disease, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure).

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

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 para. 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.

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

on 1. In addition to the active ingredient to be assessed, dapagliflozin is specifically approved for the treatment of kidney disease.

Finerenone is approved for the treatment of chronic kidney disease (with albuminuria) in conjunction with type 2 diabetes.

The medicinal products approved in the respective indications are eligible for the treatment of the underlying diseases of kidney disease and common comorbidities such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia and heart failure.

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

on 3. In the therapeutic indication under consideration here, the following resolutions of the G-BA are available:

- Dapagliflozin (resolution according to Section 35a SGB V of 17.02.2022)
- Finerenone (resolution according to Section 35a SGB V of 17.08.2023)

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.

The present indication is understood as a complex of chronic kidney disease and diseases involved in its development or contributing to its progression (diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure). In accordance with national and international guidelines, the G-BA considers patient-individual treatment to be appropriate, taking into account the type and manifestations of the comorbidities present. ACE inhibitors and AT-1 antagonists play an important role in this therapeutic complex in the context of patient-individual therapy, since a positive influence on the progression of kidney disease has been demonstrated for these product classes.

In addition, the significance of SGLT2 inhibitors for the treatment of chronic kidney disease is now particularly emphasised, also taking into account the experts in the written statement procedure. For dapagliflozin, a hint for a considerable additional benefit was identified for adults with chronic kidney disease without symptomatic chronic heart failure as a comorbidity, and a hint for a minor additional benefit was identified for adults with chronic kidney disease with additional symptomatic chronic heart failure as a comorbidity.

Therefore, the treatment of chronic kidney disease should particularly include the use of SGLT2 inhibitors (dapagliflozin in the present benefit assessment procedure).

In addition, according to the current state of medical knowledge, it is assumed that treatment of chronic kidney disease includes the use of ACE inhibitors or AT-1 antagonists, if they are indicated for concomitant diseases in compliance with the marketing authorisation.

Within the framework of the appropriate comparator therapy, it is assumed that a patient-individual treatment of the underlying disease and any comorbidities that may be present is carried out in accordance with the current state of medical knowledge, while avoiding the use of nephrotoxic agents in both treatment arms.

Overall, it is assumed that a slowing of disease progression in patients is continued to be sought in the therapeutic indication, so that renal replacement therapy in the form of dialysis or transplantation is not yet indicated.

Taking into account the treatment options as well as the recommendations, the G-BA determines an optimised standard therapy for the treatment of chronic kidney disease as an appropriate comparator therapy, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, dyslipoproteinaemia, hypertension, anaemia, heart failure).

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:

Adults with chronic kidney disease

An additional benefit is not proven.

Justification:

For the assessment of the additional benefit of empagliflozin, the pharmaceutical company submits the EMPA-KIDNEY study as well as the sub-populations of the EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved studies.

EMPA-KIDNEY study

The EMPA-KIDNEY study is a placebo-controlled, double-blind RCT of empagliflozin in patients with CKD at risk of disease progression and an estimated glomerular filtration rate (eGFR) of ≥ 20 to < 45 ml/min/1.73m^2 or an eGFR of ≥ 45 to < 90 ml/min/1.73m^2 with a urinary albumin-to-creatinine ratio (UACR) of ≥ 200 mg/g. Patients should receive an appropriate dose of renin-angiotensin-aldosterone system (RAAS) inhibitor (either ACE inhibitor or AT-1 antagonist) unless they could not tolerate such treatment or it was not indicated. In addition, patients in both study arms should receive individualised standard therapy from their treating physician, taking into account cardiovascular risk factors and existing comorbidities (e.g. high blood pressure, diabetes) in accordance with local, national or international guidelines.

A total of 6,609 patients were enrolled and randomly assigned in a 1:1 ratio to treatment with empagliflozin (N = 3,304) or to the placebo group (N = 3,305).

The primary endpoint of the study was the composite endpoint of kidney disease progression and cardiovascular death. Patient-relevant endpoints were assessed in the categories of mortality, morbidity and side effects.

EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved studies

The three studies EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved are placebo-controlled RCTs on empagliflozin that have already been presented in the therapeutic indications of type 2 diabetes mellitus (EMPA-REG OUTCOME), symptomatic chronic heart failure with reduced ejection fraction (EMPEROR-Reduced) and symptomatic chronic heart failure with preserved ejection fraction (EMPEROR-Preserved).

The pharmaceutical company shows sub-populations based on the diagnostic criteria of the Kidney Disease Improving Global Outcomes (KDIGO) guideline with the criterion eGFR < 60 ml/min/1.73 m^2 and/or a UACR ≥ 30 mg/g and additionally presents the results.

This classification results in a sub-population of 2,359 patients (1,171 in the intervention arm and 1,188 in the comparator arm) from the EMPA-REG OUTCOME study and a sub-population of 6,610 patients (3,331 in the intervention arm and 3,279 in the comparator arm) from the EMPEROR-Reduced and EMPEROR-Preserved studies.

Appropriate comparator therapy not implemented

In the EMPA-KIDNEY study, the use of SGLT2 inhibitors was permitted in principle, but the patients then had to stop taking the study medication. During the course of the EMPA-KIDNEY study, 3.0% of patients in the comparator arm and 1.7% of patients in the intervention arm started treatment with dapagliflozin.

In the additionally presented studies EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved, the use of SGLT2 inhibitors was not permitted, with the exception of the study medication in the intervention arm.

The lack or minimal use of dapagliflozin in the comparator arm of the studies did not allow treatment of CKD in any of the four studies, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure) in the sense of an optimised standard therapy in line with the appropriate comparator therapy. The EMPA-KIDNEY study and the additionally presented data on sub-populations of the three studies EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved are therefore unsuitable for the assessment of additional benefit for the present research question, as the appropriate comparator therapy has not been implemented.

As the EMPA-KIDNEY study and the sub-populations of the EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved studies do not provide any data compared with the currently determined appropriate comparator therapy, the studies cannot be used to derive the additional benefit of empagliflozin. This is a consequence of the rapid therapeutic paradigm shift in the sense of the establishment of SGLT2 inhibitors in this therapeutic indication and justifies the result "additional benefit is not proven" in this procedure.
Taking into account the experts in the written statement procedure, it is assumed that both SGLT2 inhibitors, empagliflozin and dapagliflozin, have a similar therapeutic significance for the treatment of chronic kidney disease in the German healthcare context.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient empagliflozin. The therapeutic indication assessed here is as follows: Jardiance is indicated in adults for the treatment of chronic kidney disease.

The G-BA determined "an optimised standard therapy for the treatment of chronic kidney disease, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure)" as the appropriate comparator therapy.

The pharmaceutical company submits the EMPA-KIDNEY study and, in addition, the sub-populations of the EMPA-REG OUTCOME, EMPEROR-Reduced and EMPEROR-Preserved studies. The lack or minimal use of dapagliflozin in the comparator arm of the studies did not allow treatment of CKD in any of the four studies, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure) in the sense of an optimised standard therapy in line with the appropriate comparator therapy. Since the studies do not provide data compared to the currently determined appropriate comparator therapy, they cannot be used to derive the additional benefit of empagliflozin. An additional benefit is not proven. This is a consequence of the rapid therapeutic paradigm shift in the sense of the establishment of SGLT2 inhibitors in this therapeutic indication and justifies the result "additional benefit is not proven" in this procedure.

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 data is based on the patient numbers from the dossier of the pharmaceutical company. The information is uncertain overall. Uncertainties exist in particular in the methodological approach of the pharmaceutical company in the proportional consideration of CKD stages 1 and 2 (no data available on a literature source for the traceability of the proportional value) and in the approach to the unknown CKD stage (assumption of an equal distribution of stages among patients with known and unknown stages).

Despite uncertainties, these patient numbers are considered to be a better approximation than the patient numbers in the dapagliflozin resolution on chronic kidney disease of 17 February 2022, where an overestimation of the size of the SHI target population was to be assumed, particularly due to the enrolment of all patients in stages 1, 2 and 5.

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: 19 September 2023):

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 requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 15 January 2024).

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

The appropriate comparator therapy "An optimised standard therapy for the treatment of chronic kidney disease, taking into account the underlying disease and common comorbidities (such as diabetes mellitus, hypertension, dyslipoproteinaemia, anaemia, heart failure)" includes many treatment options that are very different in nature. Chronic kidney disease is

treated in particular with angiotensin-converting enzyme (ACE) inhibitors, angiotensin-1 (AT-1) antagonists and sodium/glucose cotransporter 2 (SGLT2) inhibitors.

Since the optimised standard therapy of chronic kidney disease is patient-individual, no specific costs for the appropriate comparator therapy can be mentioned here. In addition, optimised standard therapy for the treatment of symptomatic chronic kidney disease and the underlying diseases is provided both in the context of the medicinal product to be assessed, empagliflozin, and in the context of the appropriate comparator therapy.

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	1	365
+ optimised standard therapy	Different from patient to patient			
Appropriate comparator therapy				
Optimised standard therapy	Different from patient to patient			

Consumption:

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	10 mg	1 x 10 mg	365	365 x 10 mg
+ optimised standard therapy	Different from patient to patient				
Appropriate comparator therapy					
Optimised standard therapy	Different from patient to patient				

Costs:

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	€ 244.39	€ 2.00	€ 12.90	€ 229.49
+ optimised standard therapy	Different from patient to patient				
Appropriate comparator therapy					
Optimised standard therapy	Different from patient to patient				
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 15 January 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.

Because there are no 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, no costs for additionally required SHI services need to be taken into account.

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.

<u>Concomitant active ingredient:</u>

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:

Adults with chronic kidney disease

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

References:
Product information for empagliflozin (Jardiance); Jardiance 10 mg film-coated tablets / Jardiance 25 mg film-coated tablets; last revised: August 2023

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 7 February 2023, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 July 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 31 July 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 30 October 2023, and the written statement procedure was initiated with publication on the G-BA website on 1 November 2023. The deadline for submitting statements was 22 November 2023.

The oral hearing was held on 11 December 2023.

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 23 January 2024, and the proposed resolution was approved.

At its session on 1 February 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	7 February 2023	Determination of the appropriate comparator therapy
Working group Section 35a	5 December 2023	Information on written statements received, preparation of the oral hearing
Subcommittee Medicinal products	11 December 2023	Conduct of the oral hearing,
Working group Section 35a	19 December 2023 3 January 2024 16 January 2024	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal products	23 January 2024	Concluding discussion of the draft resolution
Plenum	1 February 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 1 February 2024

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

Prof. Hecken