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: Cefepime/ enmetazobactam (bacterial infections, multiple therapeutic indications)

of 5 December 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.

Pursuant to Section 35a, paragraph 1c, sentence 1 SGB V, the Federal Joint Committee shall exempt the pharmaceutical company from the obligation to submit the evidence pursuant to Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V (medical benefit and additional medical benefit in relation to the appropriate comparator therapy) upon request, if it is an antibiotic that is effective against infections caused by multi-resistant bacterial pathogens with limited treatment options and the use of this antibiotic is subject to a strict indication (reserve antibiotic).

The additional benefit is deemed to be proven if the Federal Joint Committee 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 Federal Joint Committee.

By resolution pursuant to Section 35a, paragraph 3, sentence 1 SGB V, the Federal Joint Committee shall specify the requirements for a quality-assured application of the reserve antibiotic pursuant to Section 35a, paragraph 1c, sentence 8 SGB V, taking into account the effects on the resistance situation. Pursuant to Chapter 5, Section 20, paragraph 6, sentence 3 of the Rules of Procedure (VerfO), the Federal Joint Committee may lay down restrictive requirements for the use of the antibiotic in order to ensure a strict indication, if this is necessary to maintain the reserve status of the medicinal product. With regard to these requirements for a quality-assured application of the reserve antibiotic, it shall obtain a statement from the Robert Koch Institute, which shall be prepared in agreement with the Federal Institute for Drugs and Medical Devices.

Pursuant to Section 35a, paragraph 3 SGB V, the G-BA decides on the benefit assessment, taking into account the requirements for a quality-assured application according to Section 35a, paragraph 1c, sentence 8 SGB V, 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

By resolution of 2 May 2024, the Federal Joint Committee decided that the pharmaceutical company is exempted from the obligation to submit evidence in the benefit assessment procedure for the medicinal product Exblifep with the combination of active ingredients cefepime/ enmetazobactam according to Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V, since the medicinal product Exblifep with the combination of active ingredients cefepime/ enmetazobactam for the treatment of bacterial infections is a reserve antibiotic within the meaning of Section 35a, paragraph 1c, sentence 1 SGB V.

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the combination of active ingredients cefepime/ enmetazobactam on 15 June 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA.

The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number

1 VerfO on 13 June 2024. In this, the pharmaceutical company submitted evidence pursuant to Section 35a, paragraph 1, sentence 3, numbers 1, 4 and 5 SGB V and evidence on the requirements for a quality-assured application of the reserve antibiotic, taking into account the effects on the resistance situation (Chapter 5 VerfO Annex II. 1 Section 1.4). The assessment procedure started on 15 June 2024.

The additional benefit is deemed to be proven if the Federal Joint Committee 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 Federal Joint Committee. By resolution pursuant to Section 35a, paragraph 3, sentence 1 SGB V, the Federal Joint Committee shall specify requirements for a quality-assured application of the reserve antibiotic, taking into account the effects on the resistance situation.

A draft of the requirements for a quality-assured application of the reserve antibiotic was made available to the Robert Koch Institute for drafting a statement in agreement with the BfArM in accordance with Section 35a, paragraph 1c SGB V.

The G-BA commissioned the IQWiG to assess the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers.

The draft of the requirements for a quality-assured application as well as the RKI statement drafted in agreement with the BfArM were published on the G-BA's website (www.g-ba.de) together with IQWiG's assessment of treatment costs and patient numbers, thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA made its resolution on the basis of the pharmaceutical company's dossier, the draft requirements for a quality-assured application prepared by the G-BA taking into account the statement of the RKI/BfArM, the IQWiG assessment of treatment costs and patient numbers (IQWiG G24-15) and the statements made in the written statement and oral hearing procedure, as well of the addendum drawn up by the IQWiG on the benefit assessment.

Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Cefepime/ enmetazobactam (Exblifep) in accordance with the product information

Exblifep is indicated for the treatment of the following infections in adults:

- Complicated urinary tract infections (cUTI), including pyelonephritis

- Hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Consideration should be given to official guidelines on the appropriate use of antibiotics.

Therapeutic indication of the resolution (resolution of 5 December 2024):

see the approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

The additional benefit of cefepime/ enmetazobactam is assessed as follows:

a) Adults with complicated urinary tract infections (cUTI), including pyelonephritis

The additional benefit is considered proven.

b) Adults with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

The additional benefit is considered proven.

c) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infections (cUTI), including pyelonephritis, or with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

The additional benefit is considered proven.

Justification:

For the medicinal product Exblifep with the combination of active ingredients cefepime/ enmetazobactam, an exemption from the obligation to submit the evidence according to Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V was granted by resolution of 2 May 2024, as it is a reserve antibiotic within the meaning of Section 35a, paragraph 1c, sentence 1 SGB V.

The additional benefit is deemed to be proven if the Federal Joint Committee 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 Federal Joint Committee.

2.1.3 Summary of the assessment

Cefepime/ enmetazobactam is indicated for the treatment of the following infections in adults:

- Complicated urinary tract infections (cUTI), including pyelonephritis,
- Hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP),
- Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Three patient groups were formed according to the individual therapeutic indications.

The additional benefit of cefepime/ enmetazobactam is assessed for each of the patient groups as follows:

The additional benefit is considered proven.

For the medicinal product Exblifep with the combination of active ingredients cefepime/ enmetazobactam, an exemption from the obligation to submit the evidence according to Section 35a, paragraph 1, sentence 3, numbers 2 and 3 SGB V was granted by resolution of 2 May 2024, as it is a reserve antibiotic within the meaning of Section 35a, paragraph 1c, sentence 1 SGB V.

The additional benefit is deemed to be proven if the Federal Joint Committee 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 Federal Joint Committee.

By resolution pursuant to Section 35a, paragraph 3, sentence 1 SGB V, the Federal Joint Committee specified the requirements for a quality-assured application of the reserve antibiotic pursuant to Section 35a, paragraph 1c, sentence 8 SGB V, taking into account the effects on the resistance situation.

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 derivation of the patient numbers in the pharmaceutical company's dossier is subject to greater uncertainties. Owing to the restrictive use for all therapeutic indications in line with the requirements for a quality-assured application of cefepime/ enmetazobactam on the one hand and the predominant use for infections with Gram-negative organisms in line with the spectrum of efficacy stated in the product information on the other, the calculation of patient numbers is approximately analogous to that in the resolution on cefiderocol (resolution of the G-BA of 5 May 2022) in the therapeutic indication "Infections caused by aerobic Gram-negative organisms for which only limited treatment options are available". Therefore, the data from the resolution on cefiderocol are used as a basis for the presentation of patient numbers for the entire therapeutic indication (all patient groups) of cefepime/ enmetazobactam.

The calculation was made using two different approaches based on data from the RKI and the HISS (Hospital Infection Surveillance System) pathogen surveillance, respectively, for 2019. These patient numbers are also to be assessed as uncertain overall.

However, a lower number of patients in the SHI target population may result particularly against the background of the restrictive use of cefepime/ enmetazobactam within the framework of the quality-assured application. In addition, the therapeutic indication of cefepime/ enmetazobactam is restricted to individual infections (cUTI, HAP/VAP, bacteraemia) compared to that of cefiderocol.

The information on the patient numbers is therefore based on the statements from the written statement procedure, in which data from the National Reference Centre for Surveillance of Nosocomial Infections was used. The information on the relevant infections in this case corresponds to approx. 40 per cent of the total number; this percentage value was added to the patient numbers as stated in the procedure for cefiderocol. This procedure is subject to uncertainty as the percentage value relates to a partly different pathogen spectrum. In addition, uncomplicated urinary tract infections are also included – in contrast to the present therapeutic indication.

Overall, the patient numbers are therefore subject to uncertainty.

2.3 Requirements for a quality-assured application

By resolution pursuant to Section 35a, paragraph 3, sentence 1 SGB V, the Federal Joint Committee shall specify requirements for a quality-assured application of the reserve antibiotic, taking into account the effects on the resistance situation. The requirements for a quality-assured application are based on the draft prepared by the Federal Joint Committee and the statement of the Robert Koch Institute, which was prepared in agreement with the BfArM. The statements made in the written statement and oral hearing procedure were taken into account.

About the notes on application

Reference is made to the specifications of the marketing authorisation. The requirement that cefepime/ enmetazobactam may only be used for the treatment of infections mentioned in the therapeutic indication if only limited treatment options are available is specified in the present resolution within the framework of the requirements for a quality-assured application in order to ensure the strict indication pursuant to Section 35a, paragraph 1c SGB V.

According to the field of expertise, qualified consultation takes place with a specialist in the field of infectiology (internal medicine and infectiology[1], microbiology, virology and epidemiology of infectious diseases or additional qualification in infectiology) or, if not available, with a specialist from other disciplines who must have appropriate experience in the treatment of infectious diseases with multi-drug resistant pathogens. In this context, the wording "in case of unavailability" illustrates the special importance of the field of infectiology.

About the notes on pathogen detection

In principle, cefepime/ enmetazobactam should not be used as part of a calculated (empirical) therapy. The strict indication as a reserve antibiotic requires knowledge of the pathogen. Even in the exceptional cases mentioned, infection with a multi-drug resistant aerobic Gram-negative pathogen is at least probable. As a rule, pathogen detection can be expected after 72 hours at the latest. If the pathogen detection reveals that the pathogen is sensitive to other antibiotics (without reserve status), the therapy must be de-escalated accordingly to avoid unnecessary use of the reserve antibiotic. An empirical therapy with cefepime/ enmetazobactam should be as short as possible.

About the instructions for implementation

In order to implement the requirements for a quality-assured application, it is necessary that they are taken into account in the hospital's internal regulations/ processes.

The respective Drug Commission is responsible for integration into the processes. Evidence-based antibiotic stewardship teams are particularly suitable for implementation.

[1] Further training to become a specialist in internal medicine and infectiology was included in the sample further training regulations of the German Medical Association in 2021.

Pursuant to Section 23 paragraph 4 Infection Protection Act, the treatment facility is obliged to carry out consumption and resistance surveillance, whereby there is no specification of the systems to be used. The use of a uniform system is necessary for the future assessment of the resistance and consumption situation. The RKI's ARS, AVS and ARVIA systems aggregate Germany-wide data on antibiotic resistance and consumption. ARS also forms the basis for Germany's participation in international surveillance systems.[2] For this reason, the participation of clinics using cefepime/ enmetazobactam in these systems should be sought.

The reporting of consumption and resistance data on cefepime/ enmetazobactam to the above-mentioned systems should be ensured within six months of the entry into force of this resolution. Until participation in the mentioned systems, consumption and resistance situation must be ensured via the existing systems.

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 November 2024).

The calculation is based on the purchase price of the clinic pack plus 19 per cent value added tax, in deviation from the LAUER-TAXE® data usually taken into account.

However, it is assumed as part of the assessment that cefepime/ enmetazobactam is primarily used in inpatient settings due to the potential severity of the infections in the present therapeutic indications.

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

Treatment period:

a) Adults with complicated urinary tract infections (cUTI), including pyelonephritis

and

b) Adults with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Cefepime/ enmetazobactam	3 x daily, over 7 -10 days	1.0	7.0 - 10.0	7.0 - 10.0

[2] Information at https://ars.rki.de/

c) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infections (cUTI), including pyelonephritis, or with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Cefepime/ enmetazobactam	3 x daily, over 7 -14 days	1.0	7.0 - 14.0	7.0 - 14.0

Consumption:

a) Adults with complicated urinary tract infections (cUTI), including pyelonephritis

and

b) Adults with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

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					
Cefepime/ enmetazobactam	2 g/0.5 g	6 g/1.5 g	3 x 2 g/0.5 g	7.0 – 10.0	21 x 2 g/0.5 g - 30 x 2 g/0.5 g

c) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infections (cUTI), including pyelonephritis, or with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

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					
Cefepime/ enmetazobactam	2 g/0.5 g	6 g/1.5 g	3 x 2 g/0.5 g	7.0 – 14.0	21 x 2 g/0.5 g - 42 x 2 g/0.5 g

Costs:

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.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (clinic purchase registry)	Value added tax (19%)	Costs of the medicinal product
Cefepime/ enmetazobactam 2.0 g/0.5 g	10 PCI	€ 1,483.50	€ 281.87	€ 1,765.37
Abbreviations: PCI = powder for a concentrate for the preparation of an infusion solution				

LAUER-TAXE® last revised: 15 November 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.

No additionally required SHI services are taken into account for the cost representation.

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 requirements 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:

a) Adults with complicated urinary tract infections (cUTI), including pyelonephritis

No designation of medicinal products with new active ingredients that can be used in combination therapy in accordance with Section 35a, paragraph 3, sentence 4 SGB V, as the G-BA has decided to exempt the assessed medicinal product as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V.

b) Adults with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

No designation of medicinal products with new active ingredients that can be used in combination therapy in accordance with Section 35a, paragraph 3, sentence 4 SGB V, as the G-BA has decided to exempt the assessed medicinal product as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V.

c) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infections (cUTI), including pyelonephritis, or with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

No designation of medicinal products with new active ingredients that can be used in combination therapy in accordance with Section 35a, paragraph 3, sentence 4 SGB V, as the G-BA has decided to exempt the assessed medicinal product as a reserve antibiotic in

accordance with Section 35a, paragraph 1c, sentence 1 SGB V.

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

On 13 June 2024, the pharmaceutical company submitted a dossier for the benefit assessment of cefepime/ enmetazobactam to the G-BA in due time.

The draft of the G-BA's requirements for a quality-assured application was published on the G-BA's website (www.g-ba.de) on 16 September 2024 together with the IQWiG's assessment of treatment costs and patient numbers, thus initiating the written statement procedure. The deadline for submitting statements was 7 October 2024.

The oral hearing was held on 28 October 2024.

By letter dated 29 October 2024, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 13 November 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 26 November 2024, and the draft resolution was approved.

At its session on 5 December 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Working group Section 35a	17 July 2024 4 September 2024	Consultation on the draft requirements for a quality-assured application
Subcommittee Medicinal products	23 July 2024	Draft requirements for a quality-assured application; notification of the RKI and the BfArM
Subcommittee Medicinal products	10 September 2024	Draft requirements for a quality-assured application under consideration of the statement of the Robert Koch Institute

Working group Section 35a	16 October 2024	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	28 October 2024	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	6 November 2024 20 November 2024	Consultation on the draft requirements for a quality-assured application of the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal products	26 November 2024	Concluding discussion of the draft resolution
Plenum	5 December 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 5 December 2024

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

Prof. Hecken