Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Ceftazidime/ avibactam (new therapeutic indication: Bacterial infections, multiple therapeutic indications, from birth to < 3 months)

of 15 May 2025

At their session on 15 May 2025, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Ceftazidime/ avibactam in accordance with the resolution of 3 November 2022:

Ceftazidime/ avibactam

Resolution of: 15 May 2025
Entry into force on: 15 May 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 21 October 2024):

"Zavicefta is indicated in adults and paediatric patients from birth for the treatment of the following infections:

− Complicated intra-abdominal infection (cIAI)

− Complicated urinary tract infection (cUTI), including pyelonephritis

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

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

Zavicefta is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adults and paediatric patients from birth with limited treatment options.

Consideration should be given to official guidance on the appropriate use of antibacterial agents."

Therapeutic indication of the resolution (resolution of 15 May 2025):

"Zavicefta is indicated in paediatric patients from birth to < 3 months for the treatment of the following infections:

− Complicated intra-abdominal infection (cIAI)

− Complicated urinary tract infection (cUTI), including pyelonephritis

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

Zavicefta is also indicated for the treatment of infections due to aerobic Gram-negative organisms in paediatric patients from birth to < 3 months with limited treatment options."

1. Extent of the additional benefit and significance of the evidence

For the medicinal product Zavicefta with the combination of active ingredients ceftazidime/ avibactam, 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 20 January 2022, 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 shall specify requirements for a quality-assured application of the reserve antibiotic, taking into account the effects on the resistance situation.

a) Children from birth to < 3 months with complicated intra-abdominal infection (cIAI)

Additional benefit of ceftazidime/ avibactam:

The additional benefit is considered proven.

b) Children from birth to < 3 months with complicated urinary tract infection (cUTI), including pyelonephritis

Additional benefit of ceftazidime/ avibactam:

The additional benefit is considered proven.

c) Children from birth to < 3 months with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

Additional benefit of ceftazidime/ avibactam:

The additional benefit is considered proven.

d) Children from birth to < 3 months with infections due to aerobic Gram-negative organisms with limited treatment options

Additional benefit of ceftazidime/ avibactam:

The additional benefit is considered proven.

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

a) Children from birth to < 3 months with complicated intra-abdominal infection (cIAI)

and

b) Children from birth to < 3 months with complicated urinary tract infection (cUTI), including pyelonephritis

and

c) Children from birth to < 3 months with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

and

d) Children from birth to < 3 months with infections due to aerobic Gram-negative organisms with limited treatment options

Approx. 10 – 27 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Zavicefta (active ingredient: ceftazidime/ avibactam) at the following publicly accessible link (last access: 5 March 2025):

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

The following requirements for a quality-assured application of ceftazidime/ avibactam apply to the new therapeutic indications approved since October 2024.

Ceftazidime/ avibactam may only be used in patients from birth to < 3 months

- for the treatment of complicated intra-abdominal infections;
- for the treatment of complicated urinary tract infections, including pyelonephritis;
- for the treatment of hospital-acquired pneumonia, including ventilator-associated pneumonia;
- for the treatment of infections due to aerobic Gram-negative organisms

if there is evidence or, in exceptional cases, an urgent suspicion that the infection is caused by multi-drug resistant aerobic Gram-negative organisms, efficacy of ceftazidime/ avibactam can be expected and only limited treatment options are available (see also information on pathogen detection).

Before using ceftazidime/ avibactam, consult a specialist with an additional qualification in infectiology, a specialist in internal medicine and infectiology, or a specialist in microbiology, virology and epidemiology of infectious diseases. In case of unavailability of the above-mentioned groups of specialists at the time of use, a specialist with appropriate experience in the treatment of infectious diseases with multi-drug resistant pathogens must be consulted.

Additional antibiotics must be used if it is known or suspected that Gram-positive or anaerobic pathogens are also involved in the infection.

Severe and occasionally fatal hypersensitivity reactions are possible. In the event of an occurrence of hypersensitivity reactions, treatment with Zavicefta must be stopped immediately. Appropriate emergency measures must be taken. Before starting treatment, it should be determined whether the patient has a history of hypersensitivity reactions to ceftazidime, other cephalosporins or any other type of beta-lactam antibiotics. Ceftazidime/ avibactam is contraindicated in patients with severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibiotics (e.g. penicillins, monobactams or carbapenems). Ceftazidime/ avibactam should be used with caution in patients with a history of non-severe hypersensitivity to penicillins, monobactams or carbapenems.

<u>Notes on pathogen detection</u>

The reserve antibiotic may only be used as part of a targeted therapy. Before use, the causative pathogen and sensitivity to pathogen must always be proven by microbiological diagnostics of appropriate clinical material.

A calculated (empirical) use of ceftazidime/ avibactam without pathogen detection should only be carried out in exceptional cases. These include a known resistance problem in the treatment facility or in the case of a transfer from a facility with a known resistance problem, as well as in the case of a lack of therapeutic response to standard antibiotic therapy in the case of a serious infection and urgent suspicion that the infection is caused by multi-drug resistant aerobic Gram-negative organisms and efficacy of ceftazidime/ avibactam can be expected. Samples for pathogen detection must be taken before the start of treatment. The calculated therapy must usually be adjusted after a maximum of 72 hours, if necessary, when an antibiogram is available.

Ceftazidime/ avibactam may not be used if the pathogen shows sensitivity to other antibiotics (without reserve status), unless other antibiotics cannot be used, for example because of contraindications or expected severe complications.

Notes on implementation

The current guidelines of the AWMF and medical and, if applicable, also international scientific-medical societies for the appropriate use of antibiotics must be taken into account. Furthermore, reference should be made to the listed requirements for a quality-assured application of ceftazidime/ avibactam in the locally available treatment guidelines and regulations of the measures for restrictive antibiotic use.

The aforementioned specifications are to be implemented within the framework of regulations of the hospital's Drug Commission. Implementation should take place in particular within the framework of the in-house Antibiotic Stewardship Programme (ABS).

The treatment facility or clinic must have a local clearance policy for the use of ceftazidime/ avibactam in the respective treatment facility.

The restriction measures shall be drafted and explained in writing.

Consumption and resistance surveillance in accordance with Section 23 paragraph 4 Infection Protection Act must be implemented. This is to be done through participation in the AVS (Antibiotic Consumption Surveillance) and ARS (Antibiotic Resistance Surveillance) or ARVIA (ARS and AVS – Integrated Analysis) systems.

The reporting of consumption and resistance data on ceftazidime/ avibactam 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.

The principles of antibiotic therapy of the Commission on Anti-infectives, Resistance and Therapy (ART) at the Robert Koch Institute must be observed (last access: 22 November 2024):

https://www.rki.de/DE/Content/Kommissionen/ART/Links/Grundsaetze-der-Therapie.html

4. Treatment costs

Annual treatment costs:

a) Children from birth to < 3 months with complicated intra-abdominal infection (cIAI)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ceftazidime/ avibactam	€ 2,737.00 – € 6,842.50

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 April 2025)

b) Children from birth to < 3 months with complicated urinary tract infection (cUTI), including pyelonephritis

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ceftazidime/ avibactam	€ 2,737.00 – € 6,842.50

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 April 2025)

c) Children from birth to < 3 months with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ceftazidime/ avibactam	€ 4,105.50 – € 6,842.50

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 April 2025)

d) Children from birth to < 3 months with infections due to aerobic Gram-negative organisms with limited treatment options

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Ceftazidime/ avibactam	Different from patient to patient

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 April 2025)

Costs for additionally required SHI services: not applicable

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

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

a) Children from birth to < 3 months with complicated intra-abdominal infection (cIAI)

and

b) Children from birth to < 3 months with complicated urinary tract infection (cUTI), including pyelonephritis

and

c) Children from birth to < 3 months with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

and

d) Children from birth to < 3 months with infections due to aerobic Gram-negative organisms with limited treatment options

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.

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 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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 May 2025.

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

Berlin, 15 May 2025

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

Prof. Hecken