Gemeinsamer Bundesausschuss

**Ceftazidime/ Avibactam** (repeal of the exemption; bacterial infections, several therapeutic indications)

Resolution of: 3 November 2022 Valid until: unlimited
Entry into force on: 3 November 2022
Federal Gazette, BAnz AT 23 01 2023 B2

**Therapeutic indication (according to the marketing authorisation of 22 October 2020):**

Zavicefta is indicated in adults and paediatric patients aged 3 months and older for the treatment of the following infections:

- Complicated intra-abdominal infections (cIAI)
- Complicated urinary tract infections (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 aged 3 months and older with limited treatment options.

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

**Therapeutic indication of the resolution (resolution of 3 November 2022):**

See therapeutic indication according to marketing authorisation.

## 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) Adults and paediatric patients aged 3 months and older with complicated intra-abdominal infections (cIAI)

**Additional benefit of ceftazidime/ avibactam:**

The additional benefit is considered proven.

b) Adults and paediatric patients aged 3 months and older with complicated urinary tract infections (cUTI), including pyelonephritis

**Additional benefit of ceftazidime/ avibactam:**

The additional benefit is considered proven.

c) Adults and paediatric patients aged 3 months and older with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

**Additional benefit of ceftazidime/ avibactam:**

The additional benefit is considered proven.

d) Adult patients with bacteraemia that occurs in association with, or is suspected to be associated with complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), including pyelonephritis, or nosocomial or hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

**Additional benefit of ceftazidime/ avibactam:**

The additional benefit is considered proven.

e) Adults and paediatric patients aged 3 months and older 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) Adults and paediatric patients aged 3 months and older with complicated intra-abdominal infections (cIAI)

and

b) Adults and paediatric patients aged 3 months and older with complicated urinary tract infections (cUTI), including pyelonephritis

and

c) Adults and paediatric patients aged 3 months and older with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

and

d) Adult patients with bacteraemia that occurs in association with, or is suspected to be associated with complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), including pyelonephritis, or nosocomial or hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

and

e) Adults and paediatric patients aged 3 months and older with infections due to aerobic Gram-negative organisms with limited treatment options

approx. 2,600 – 6,600 patients

## 3. Requirements for a quality-assured application

Notes on 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: 21 October 2022):

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

The requirements for a quality-assured application of ceftazidime/ avibactam apply to the approved therapeutic indications as of May 2022.

Ceftazidime/ avibactam is indicated in adults and paediatric patients aged 3 months and older

- 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 caused by aerobic Gram-negative organisms

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

Ceftazidime/ avibactam is also indicated in adults for the treatment of bacteraemia that occurs in association with, or is suspected to be associated with complicated intra-abdominal infections, complicated urinary tract infection, including pyelonephritis, or hospital-acquired pneumonia, including ventilator-associated pneumonia; but only if there is evidence or, in exceptional cases, an urgent suspicion that the infection is caused by multi-drug resistant aerobic Gram-negative organisms and only limited treatment options are available (see also notes 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 organisms 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.

Notes on pathogen detection

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. 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)[1].

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 systems shall be ensured by 1 January 2024 at the latest.

[1] See S3 guideline: strategies to ensure rational antibiotic use in hospitals, 2018 update: https://www.awmf.org/uploads/tx_szleitlinien/092-001l_S3_Strategien-zur-Sicherung-rationaler-Antibiotika-Anwendung-im-Krankenhaus_2020-02.pdf

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: 05.05.2022):

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

## 4. Treatment costs

**Annual treatment costs:**

a) Adults and paediatric patients aged 3 months and older with complicated intra-abdominal infections (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 October 2022)

b) Adults and paediatric patients aged 3 months and older with complicated urinary tract infections (cUTI), including pyelonephritis

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Ceftazidime/ avibactam | |
| Adults | € 2,737.00 - € 4,105.50 |
| Paediatric patients aged 3 months and older | € 2,737.00 - € 6,842.50 |

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 October 2022)

c) Adults and paediatric patients aged 3 months and older 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 October 2022)

d) Adult patients with bacteraemia that occurs in association with, or is suspected to be associated with complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), including pyelonephritis, or nosocomial or hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)

| 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 October 2022)

e) Adults and paediatric patients aged 3 months and older 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 October 2022)

Costs for additionally required SHI services: not applicable

Other SHI services:

| Designation of the therapy | Type of service | Costs/ unit | Number/ treatment day | Number/ patient/ year | Costs/ patient/ year |
|---|---|---|---|---|---|
| Ceftazidime/ avibactam | Surcharge for the preparation of an infusion solution containing antibiotics and virustatics | € 39 | 3 | 15 – 42 | € 585 – € 1,638 |