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
Ceftolozane/ tazobactam (new therapeutic indication: bacterial infections, multiple therapeutic indications, < 18 years)

of 2 February 2023

At its session on 2 February 2023, 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 Ceftolozane/ tazobactam in accordance with the resolution of 3 November 2022**

**Ceftolozane/ tazobactam**

Resolution of: 2 February 2023
Entry into force on: 2 February 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

**Therapeutic indication (according to the marketing authorisation of 25 July 2022):**

Zerbaxa is indicated for the treatment of the following infections in adult and paediatric patients:

- Complicated intra-abdominal infections;
- Acute pyelonephritis;
- Complicated urinary tract infections.

Zerbaxa is also indicated for the treatment of the following infection in adult patients (18 years or older):

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

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

**Therapeutic indication of the resolution (resolution of 2 February 2023):**

Zerbaxa is indicated for the treatment of the following infections in paediatric patients:

- Complicated intra-abdominal infections;
- Acute pyelonephritis;
- Complicated urinary tract infections.

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

For the medicinal product Zerbaxa with the combination of active ingredients ceftolozane/ tazobactam, an exemption from the obligation to submit the evidence according to Section 35a paragraph 1 sentence 3 number 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) <u>Paediatric patients with complicated intra-abdominal infections</u>

**Additional benefit of active ingredient:**

The additional benefit is considered proven.

b) Paediatric patients with acute pyelonephritis

**Additional benefit of active ingredient:**

The additional benefit is considered proven.

c) Paediatric patients with complicated urinary tract infection

**Additional benefit of active ingredient:**

The additional benefit is considered proven.

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

a) Paediatric patients with complicated intra-abdominal infections

and

b) Paediatric patients with acute pyelonephritis

and

c) Paediatric patients with complicated urinary tract infection

approx. 40 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 Zerbaxa (active ingredient: ceftolozane/ tazobactam) at the following publicly accessible link (last access: 25.08.2022):

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

The following requirements for a quality-assured application of ceftolozane/ tazobactam apply to all approved new therapeutic indications as of July 2022.

Ceftolozane/ tazobactam may be used in paediatric patients

- for the treatment of complicated intra-abdominal infections;
- for the treatment of acute pyelonephritis;
- for the treatment of complicated urinary tract infections;

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).

Before using ceftolozane/ tazobactam, 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.

Serious and occasionally lethal hypersensitivity reactions (anaphylactic reactions) are possible. If a severe allergic reaction occurs during treatment with ceftolozane/ tazobactam, discontinue the medicinal product and take appropriate measures. Patients with a history of hypersensitivity to cephalosporins, penicillins or other beta-lactam antibiotics may also be hypersensitive to ceftolozane/ tazobactam. Ceftolozane/ tazobactam is also contraindicated in patients with severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to other beta-lactam antibiotics (e.g. penicillins or carbapenems). Ceftolozane/ tazobactam should be used with caution in patients with any other known hypersensitivity reactions to penicillins or to other beta-lactam antibiotics.

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 ceftolozane/ tazobactam 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.

Ceftolozane/ tazobactam 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 ceftolozane/ tazobactam 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 ceftolozane/ tazobactam in the respective treatment facility.

The restriction measures shall be drafted and explained in writing.

[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

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 ceftolozane/ tazobactam to the above systems shall be ensured by 01.01.2024 at the latest.

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) Paediatric patients with complicated intra-abdominal infections

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Ceftolozane/ tazobactam | € 2,177.70 - € 5,444.25 |

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 January 2023)

b) Paediatric patients with acute pyelonephritis

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Ceftolozane/ tazobactam | € 3,266.55 -€ 5,444.25 |

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 January 2023)

c) Paediatric patients with complicated urinary tract infection

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Ceftolozane/ tazobactam | € 3,266.55 -€ 5,444.25 |

Cost of the clinic pack plus value added tax of 19% (LAUER-TAXE® last revised: 15 January 2023)

**5. 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 ceftolozane/ tazobactam**

Medicinal products with the following new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that can be used in a combination therapy with ceftolozane/ tazobactam for the treatment of bacterial infections on the basis of the marketing authorisation granted under Medicinal Products Act:

a) Paediatric patients with complicated intra-abdominal infections

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Paediatric patients with acute pyelonephritis

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

c) Paediatric patients with complicated urinary tract infection

- No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

**II. The resolution will enter into force on the day of its publication on the website of the G-BA on 2 February 2023.**

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

Berlin, 2 February 2023

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

Prof. Hecken