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
Imipenem/ Cilastatin/ Relebactam (bacterial infections, several therapeutic indications)

of 3 November 2022

At its session on 3 November 2022, 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. **Annex XII shall be amended in alphabetical order to include the active ingredient Imipenem/ Cilastatin/ Relebactam as follows:**

Imipenem/ Cilastatin/ Relebactam

Resolution of: 3 November 2022
Entry into force on: 3 November 2022
Federal Gazette, BAnz AT DD MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 13.02.2020)

Recarbrio is indicated for:

- Treatment of hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) in adults.
- Treatment of bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP, in adults.
- Treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options.

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

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 Recarbrio with the combination of active ingredients imipenem/ cilastatin/ relebactam, 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) <u>Adults with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)</u>

Additional benefit of imipenem/ cilastatin/ relebactam:

The additional benefit is considered proven.

b) Adults with bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP

Additional benefit of imipenem/ cilastatin/ relebactam:

The additional benefit is considered proven.

c) Adults with infections due to aerobic Gram-negative organisms with limited treatment options

Additional benefit of imipenem/ cilastatin/ relebactam:

The additional benefit is considered proven.

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

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

and

b) Adults with bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP

and

c) Adults 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

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 Recarbrio (active ingredient: imipenem/ cilastatin/ relebactam) at the following publicly accessible link (last access: 21 October 2022):

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

The requirements for a quality-assured application of imipenem/ cilastatin/ relebactam apply to all approved therapeutic indications as of May 2022.

Imipenem/ cilastatin/ relebactam is indicated in adults

- for the treatment of hospital-acquired pneumonia, including ventilator-associated pneumonia,
- for the treatment of bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP,

- 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).

Before using imipenem/ cilastatin/ relebactam, 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.

Serious and sometimes lethal (anaphylactic) hypersensitivity reactions have been described in patients receiving beta-lactam antibiotics. These reactions are more likely to occur in subjects with a known history of hypersensitivity to multiple allergens. Before starting treatment with imipenem/ cilastatin/ relebactam, previous hypersensitivity reactions to carbapenems, penicillins, cephalosporins, other beta-lactam antibiotics and other allergens should be carefully queried. If an allergic reaction to imipenem/ cilastatin/ relebactam occurs, treatment with imipenem/ cilastatin/ relebactam must be discontinued immediately. In case of severe anaphylactic reactions, appropriate emergency measures must be taken immediately.

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 imipenem/ cilastatin/ relebactam 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.

Imipenem/ cilastatin/ relebactam 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 imipenem/ cilastatin/ relebactam 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 imipenem/ cilastatin/ relebactam 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 consumption and resistance data on imipenem/ cilastatin/ relebactam must be reported to the above systems by 1 January 2024 at the latest.

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 with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)
b) Adults with bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Imipenem/ cilastatin/ relebactam	€ 14,131.25 - € 21,196.88

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 2022)

[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

c) Adults 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:	
Imipenem/ cilastatin/ relebactam	€ 7,065.63 - € 21,196.88

Costs after deduction of statutory rebates (LAUER-TAXE®) as 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
Imipenem/ cilastatin/ relebactam	Surcharge for the preparation of an infusion solution containing antibiotics and virustatics	€ 39	4	20 – 56	€ 780 – € 2,184

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 3 November 2022.

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

Berlin, 3 November 2022

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

Prof. Hecken