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
Meropenem/ vaborbactam (bacterial infections, multiple therapeutic indications)

of 17 April 2025

At their session on 17 April 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. Annex XII shall be amended in alphabetical order to include the combination of active ingredients Meropenem/ vaborbactam as follows:

Meropenem/ vaborbactam

Resolution of: 17 April 2025
Entry into force on: 17 April 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 20 November 2018):

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

- Complicated urinary tract infection (cUTI), including pyelonephritis
- Complicated intra-abdominal infection (cIAI)
- 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.

Vaborem is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adults 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 17 April 2025):

See therapeutic indication according to marketing authorisation.

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

For the medicinal product Vaborem with the combination of active ingredients meropenem/ vaborbactam, 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 7 March 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 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 complicated urinary tract infection (cUTI), including pyelonephritis</u>

Additional benefit of meropenem/ vaborbactam:

The additional benefit is considered proven.

b) <u>Adults with complicated intra-abdominal infection (cIAI)</u>

Additional benefit of meropenem/ vaborbactam:

The additional benefit is considered proven.

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

Additional benefit of meropenem/ vaborbactam:

The additional benefit is considered proven.

d) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infection, including pyelonephritis, with complicated intra-abdominal infection, or with hospital-acquired pneumonia, including ventilator-associated pneumonia

Additional benefit of meropenem/ vaborbactam:

The additional benefit is considered proven.

e) Adults with infections caused by aerobic Gram-negative organisms with limited treatment options

Additional benefit of meropenem/ vaborbactam:

The additional benefit is considered proven.

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

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

and

b) Adults with complicated intra-abdominal infection (cIAI)

and

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

and

d) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infection, including pyelonephritis, with complicated intra-abdominal infection, or with hospital-acquired pneumonia, including ventilator-associated pneumonia

and

e) Adults with infections caused by 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 Vaborem (combination of active ingredients: meropenem/ vaborbactam) at the following publicly accessible link (last access: 12 March 2025):

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

The requirements for a quality-assured application of meropenem/ vaborbactam apply to the approved therapeutic indications as of November 2024.

Meropenem/ vaborbactam may be used in adults for the treatment of

- complicated urinary tract infections, including pyelonephritis,
- complicated intra-abdominal infections,
- hospital-acquired pneumonia, including ventilator-associated pneumonia,
- bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above,
- 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, efficacy of meropenem/ vaborbactam can be expected and only limited treatment options are available (see also information on pathogen detection).

Before using meropenem/ vaborbactam, 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.

Severe and occasionally fatal hypersensitivity reactions have been reported with meropenem and/or meropenem/ vaborbactam. Patients with a history of hypersensitivity to carbapenems, penicillins or other beta-lactam antibiotics may also react hypersensitively to meropenem/ vaborbactam. Prior to therapy with Vaborem, a careful check should be made for previous hypersensitivity reactions to 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 meropenem/ vaborbactam 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 meropenem/ vaborbactam 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.

Meropenem/ vaborbactam 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 meropenem/ vaborbactam 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 meropenem/ vaborbactam 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 meropenem/ vaborbactam 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 surveillance 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: 8 November 2024):

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

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Meropenem/ vaborbactam	€ 2,826.25 – € 5,652.50

b) Adults with complicated intra-abdominal infections (cIAI)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Meropenem/ vaborbactam	€ 2,826.25 – € 5,652.50

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Meropenem/ vaborbactam	€ 3,956.75 – € 7,913.50

d) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infection, including pyelonephritis, with complicated intra-abdominal infection, or with hospital-acquired pneumonia, including ventilator-associated pneumonia

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Meropenem/ vaborbactam	€ 2,826.25 – € 7,913.50

e) Adults with infections caused by aerobic Gram-negative organisms with limited treatment options

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Meropenem/ vaborbactam	€ 2,826.25 – € 7,913.50

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 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) Adults with complicated urinary tract infection (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 complicated intra-abdominal infection (cIAI)

- 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 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.

d) Adults with bacteraemia that occurs in association with, or is suspected to be associated with complicated urinary tract infection, including pyelonephritis, with complicated intra-abdominal infection, or with hospital-acquired pneumonia, including ventilator-associated pneumonia

- 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.

e) Adults with infections caused by 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 exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical

companies. 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 17 April 2025.

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

Berlin, 17 April 2025

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

Prof. Hecken