

## Meropenem: Rationale for EUCAST Clinical Breakpoints

|                        |            |                     |
|------------------------|------------|---------------------|
| <b>Current version</b> | <b>3.0</b> | <b>January 2024</b> |
| Previous version       | 2.0        | January 2021        |

### Introduction

Meropenem is a carbapenem, available only for parenteral use.

Meropenem is relevant for therapy of septicaemia, post-operative sepsis, nosocomial pneumonia, community acquired pneumonia and complicated skin and soft tissue infections caused by *Staphylococcus* spp., *Streptococcus* spp. (including *Streptococcus pneumoniae*), *Haemophilus influenzae*, *Enterobacterales* and *Pseudomonas* spp. It also has a restricted role in the treatment of meningitis caused by common bacterial pathogens and *Enterobacterales*.

Meropenem is not considered active against *Stenotrophomonas maltophilia* and *Enterococcus* spp.

Resistance to meropenem is conferred by PBP changes mediating high-level penicillin resistance in *S. pneumoniae*, by PBP changes mediating beta-lactam resistance in *H. influenzae*, and by production of carbapenemases in *Pseudomonas* spp. and *Enterobacterales*. Meropenem is not affected by classical ESBL and AmpC beta-lactamases in *Enterobacterales*. In *Pseudomonas aeruginosa*, porin loss and alteration in efflux pumps may also reduce meropenem susceptibility.

This version is extracted from version 2.0, and will be the format for future updates. Previous versions are available on request.

### Dosages related to clinical breakpoints

**Standard dosage:** 1 g x 3 iv over 30 minutes  
**High dosage:** 2 g x 3 iv over 3 hours  
**Meningitis dosage:** 2 g x 3 iv over 30 minutes (or 3 hours)

### MIC distributions and epidemiological cut-off (ECOFF) values

MIC distributions and ECOFFs can be found at <https://mic.eucast.org/Eucast2/SearchController/search.jsp?action=init>

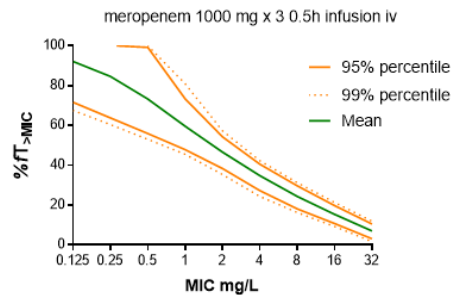
## Pharmacokinetics

| PK parameter                             | Pharmacological studies |            | Efficacy studies |  |
|--|-------------------------|------------|------------------|--|
|  | 500 mg x 3 iv           | 1 g x 3 iv |                  |  |
| Dosage                                   | 500 mg x 3 iv           | 1 g x 3 iv |                  |  |
| C <sub>max</sub> (mg/L)                  | 15-20                   | 40-50      |                  |  |
| C <sub>min</sub> (mg/L)                  | 0.1                     | 0.2        |                  |  |
| Total body clearance (L/h)               | 14-18                   | 14-18      |                  |  |
| T <sub>½</sub> (h), mean (range)         | 1                       | 1          |                  |  |
| AUC <sub>0-12</sub> (mg.h/L)             |                         |            |                  |  |
| AUC <sub>0-24</sub> (mg.h/L)             | 75-100                  | 150-200    |                  |  |
| AUC <sub>0-∞</sub> (mg.h/L)              |                         |            |                  |  |
| Fraction unbound (%)                     | 91-98                   | 91-98      |                  |  |
| Volume of distribution <sub>ss</sub> (L) | 18-25                   | 18-25      |                  |  |

## Pharmacodynamics

| Index  | Various models          | Various models       | Various models       | Various models   |  |  |
|--|-------------------------|----------------------|----------------------|------------------|--|--|
|  | <i>Enterobacterales</i> | <i>P. aeruginosa</i> | <i>S. pneumoniae</i> | <i>S. aureus</i> |  |  |
|  | Range                   | Range                | Range                | Range            |  |  |
| f <sub>T</sub> >MIC for bacteriostasis           | 25-40                   | 25-40                | 15-20                | 10-30            |  |  |
| f <sub>T</sub> >MIC for 1-log <sub>10</sub> kill | 35-55                   | 35-55                | 25-40                | 15-40            |  |  |

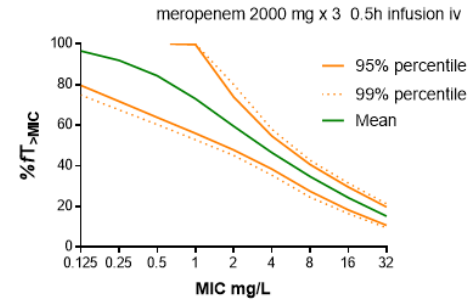
## Monte Carlo simulations



The following pharmacokinetic parameters were used to obtain the PTA (Wijma, 2018, based on data from Krueger, 2005)

Vc: 10.5 L, CV 17.7%  
Cl: 15.6 L/h, CV 15.3%  
Q: 7.17 L/h, CV 66.8%  
Vp: 5.09 L, CV 44.9%

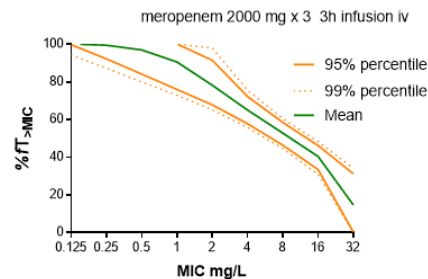
Fraction unbound (Fu): 90%  
Infusiontime 0.5 h  
Note : Covariance matrix used in simulations



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Vp: 5.09 L, CV 44.9%

Fraction unbound (Fu): 90%  
Infusiontime 3 h  
Note : Covariance matrix used in simulations

## Clinical studies

Clinical trials have shown the efficacy of meropenem in treatment of patients with septicaemia, post-operative sepsis, nosocomial pneumonia, community acquired pneumonia, complicated skin and soft tissue infections, complicated intra-abdominal infections and neutropenic sepsis. Acute meningitis caused by *S. pneumoniae*, *H. influenzae* and *N. meningitidis* categorized as wild type can be treated with high-dose therapy.

## Clinical breakpoints

The clinical breakpoints for meropenem can be found in the most recent version of the Breakpoint tables: [https://www.eucast.org/clinical\\_breakpoints](https://www.eucast.org/clinical_breakpoints)

## References

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- Baldwin CM, Lyseng-Williamson KA, Keam SJ. Meropenem: a review of its use in the treatment of serious bacterial infections. Drugs. 2008;68(6):803-38.