

Imipenem: Rationale for EUCAST Clinical Breakpoints

Current version	3.0	January 2024
Previous versions	2.0	January 2021

Introduction

Imipenem is a carbapenem, available only for parenteral use. It is combined with cilastatin, which has no antimicrobial activity but is necessary to avoid degradation of imipenem.

Imipenem 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. Imipenem can be used in the treatment of both Gram-positive and Gram-negative infections.

Imipenem is not considered active against *Stenotrophomonas maltophilia* and *Enterococcus faecium*.

Resistance to imipenem is conferred by PBP changes also 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*. Imipenem is not affected by classical ESBL and AmpC beta-lactamases in *Enterobacterales*. In *Enterobacterales*, combinations of an ESBL or AmpC enzyme and impermeability confer reduced susceptibility to imipenem, often without causing clinical resistance. In *Pseudomonas aeruginosa*, porin loss and alteration in efflux pumps may also reduce imipenem 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: 0.5 g x 4 iv over 30 minutes
High dosage: 1 g x 4 iv over 30 minutes

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>

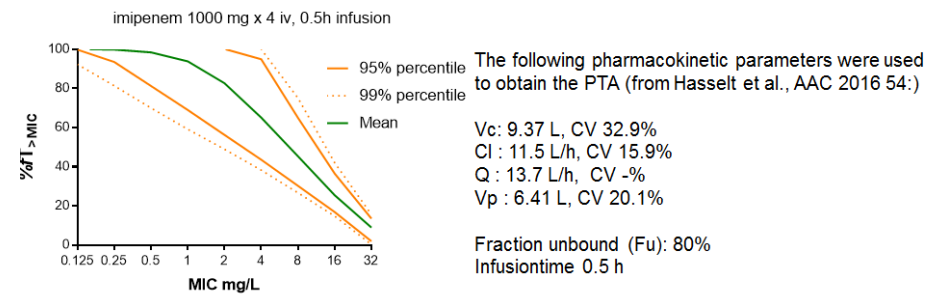
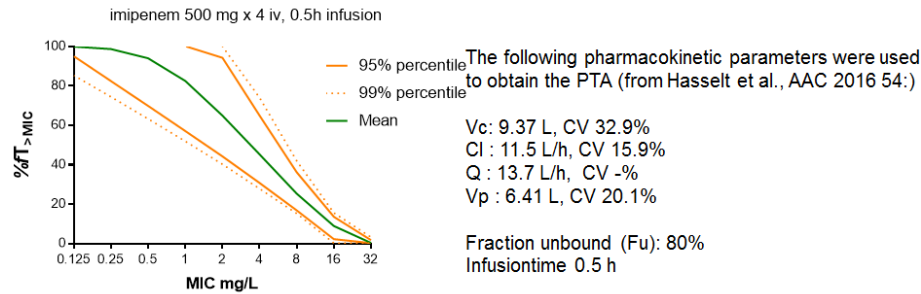
Pharmacokinetics

PK parameter	Pharmacological studies		Efficacy studies	
Dosage	0.5 g x 4	1 g x 4		
C _{max} (mg/L)	30-40 mg/L	60-70 mg/L		
C _{min} (mg/L)	0.25-0.5	0.5-1		
Total body clearance (L/h)	11-15	11-15		
T _{1/2} (h), mean (range)	1	1		
AUC ₀₋₁₂ (mg.h/L)				
AUC ₀₋₂₄ (mg.h/L)	100-150	200-300		
AUC _{0-∞} (mg.h/L)				
Fraction unbound (%)	80	80		
Volume of distribution _{ss} (L)	14-16	14-16		

Pharmacodynamics

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

Monte Carlo simulations



Clinical studies

Clinical trials have shown the efficacy of imipenem in treatment of patients with septicaemia, post-operative sepsis, nosocomial pneumonia, community acquired pneumonia, and complicated skin and soft tissue infections caused by micro-organisms categorized as wild type

Clinical breakpoints

The clinical breakpoints for imipenem can be found in the most recent version of the Breakpoint tables: https://www.eucast.org/clinical_breakpoints

References

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