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**Product Data Sheet**


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Product Name: Imipenem

Cat. No.: GP11075

**Chemical Properties**

Cas. No. 64221-86-9

Chemical Name (5R,6S)-3-[2-(aminomethylideneamino)ethylsulfanyl]-6-[(1R)-1-hydroxyethyl]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid

SMILES C[C@](O)([H])[C@](C1=O)([H])[C@@](N21)([H])CC(SCCNC=N)=C2C(O)=OFormula  $C_{12}H_{17}N_3O_4S$  M.Wt 299.35Solubility Water: 63 mg/mL; DMSO: 1 mg/mL (3.15 mM; DMSO Store  
moisture absorption will reduce compound solubility, please Storage at -  
use newly opened DMSO); Ethanol: Insoluble 20°CGeneral tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it  
in the ultrasonic bath for a while. Stock solution can be stored below -20°C for  
several months.Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship  
with RT , or blue ice upon request.Structure **Protocol****MIC experiment [1]:**Preparation Method Susceptibilities of *Y. pestis* strains were determined by  
the broth microdilution method according to CLSI M45-  
A2

Reaction Conditions 0.04-2mg/L imipenem in 35°C

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Applications	The MICs for the <i>Y. pestis</i> strains with imipenem ranged from a low of 0.12 mg/liter to a high of 1.0 mg/liter—the higher is 0.5 mg/liter
<b>Cell experiment[2]:</b>	
Cell experiment	THP-1 cells
Preparation Method	THP-1 cells were seeded into 24-well plates, differentiated for 24 h and infected with <i>M. abscessus</i> CIP104536. Imipenem (8 and 32 mg/L) or amoxicillin alone or in combination with relebactam (16 mg/L) or avibactam (16 mg/L) were added to each well. Rifabutin was also studied in combination with imipenem (8 mg/L), imipenem/relebactam or imipenem/avibactam. Imipenem was added every 24 h.
Reaction Conditions	Imipenem (8 and 32 mg/L) was added every 24 h.
Applications	Combination of relebactam with $\beta$ -lactams led to >128- and 2-fold decreases in the MICs of amoxicillin and imipenem (from 8 to 4 mg/L). In vitro, <i>M. abscessus</i> was not killed by the imipenem/relebactam combination. In contrast, relebactam increased the intracellular activity of imipenem, leading to 88% killing.
<b>Animal experiment [3]:</b>	
Animal models	Female C57BL/6 mice (6-8 weeks old, 20-25 g body weight)

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Preparation Method	Mice were randomly divided into four groups: the sham-operated mice as the control group, CLP-induced sepsis mice, CLP-induced sepsis mice treated with the low dose of imipenem (25 mg/kg), CLP-induced sepsis mice treated with the high dose of imipenem (125 mg/kg). Imipenem was injected one hour after sepsis induction, repeating the injection every 24 h up to 72 h.
Dosage form	25-200 mg/kg imipenem, repeating the injection every 24 h up to 72 h.
Applications	Sepsis mice treated with a high dose (125 mg/kg) of imipenem showed a significant reduction in bacterial load, while increased liver enzymes, endotoxin level, and inflammatory cytokine production in plasma and liver. Significant reduction in the liver enzymes, bacterial load, endotoxin levels, and inflammatory cytokine levels was observed in the mice treated with a low dose (25 mg/kg) of imipenem. Liver tissue pathology of mice indicated little tissue destruction in the sepsis mice treated with 25 mg/kg of imipenem compared to other groups. Mice receiving 25 mg/kg of imipenem had better survival rate.
References:	
	[1]. Heine HS, Louie A, et.al. Evaluation of imipenem for prophylaxis and therapy of Yersinia pestis delivered by aerosol in a mouse model of

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pneumonic plague. Antimicrob Agents Chemother. 2014 Jun;58(6):3276-84. doi: 10.1128/AAC.02420-14. Epub 2014 Mar 31. PMID: 24687492; PMCID: PMC4068467.

[2]. Le Run E, Atze H, et,al. Impact of relebactam-mediated inhibition of Mycobacterium abscessus BlaMab  $\beta$ -lactamase on the in vitro and intracellular efficacy of imipenem. J Antimicrob Chemother. 2020 Feb 1;75(2):379-383. doi: 10.1093/jac/dkz433. PMID: 31637424.

[3]. Khosrojerdi A, Soudi S, et,al. Imipenem alters systemic and liver inflammatory responses in CLP- induced sepsis mice in a dose-dependent manner. Int Immunopharmacol. 2021 Apr;93:107421. doi: 10.1016/j.intimp.2021.107421. Epub 2021 Feb 4. PMID: 33548581.

### Background

Imipenem is a semisynthetic thienamycin. Imipenem is one of the broad-spectrum antibiotics that has a bactericidal action against multiple gram-negative, gram-positive,

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aerobic, and anaerobic bacteria by binding to penicillin-binding protein 2 (PBP2) and interacting with bacterial cell wall synthesis<sup>[2,5]</sup>. It exerts a bactericidal effect by disrupting cell wall synthesis.

The MICs for the *Y. pestis* strains with imipenem ranged from a low of 0.12 mg/liter to a high of 1.0 mg/liter, the highest is 0.5 mg/liter<sup>[7]</sup>. Combination of relebactam with  $\beta$ -lactams led to >128- and 2-fold decreases in the MICs of amoxicillin and imipenem (from 8 to 4 mg/L). In vitro, *M. abscessus* was not killed by the imipenem/relebactam combination. In contrast, relebactam increased the intracellular activity of imipenem, leading to 88% killing<sup>[6]</sup>. A high dose of imipenem enhanced the interleukin (IL)-1 $\beta$  level<sup>[9]</sup> and natural killer (NK) cell activity<sup>[3]</sup>.

Dose-dependent effect of subcutaneous administration of imipenem on the inflammatory responses in sepsis mice. A dose of 25 mg/kg imipenem resulted in better pathology, lower inflammatory mediators, and increased survival rate in sepsis mice<sup>[1]</sup>.

### References:

- [1]: Khosrojerdi A, Soudi S, et al. Imipenem alters systemic and liver inflammatory responses in CLP- induced sepsis mice in a dose-dependent manner. *Int Immunopharmacol*. 2021 Apr;93:107421. doi: 10.1016/j.intimp.2021.107421. Epub 2021 Feb 4. PMID: 33548581.
- [2]: Acar JF, Goldstein FW, et al. Activity of imipenem on aerobic bacteria. *J Antimicrob Chemother*. 1983 Dec;12 Suppl D:37-45. doi: 10.1093/jac/12.suppl\_d.37. PMID: 6421793.
- [3]: Ortega E, de Pablo MA, et al. Modification of natural immunity in mice by imipenem/cilastatin. *J Antibiot (Tokyo)*. 1997 Jun;50(6):502-8. doi: 10.7164/antibiotics.50.502. PMID: 9268007.
- [4]: Ortega E, de Pablo MA, et al. Modification of acquired immunity in mice by imipenem/cilastatin. *J Antimicrob Chemother*. 1999 Oct;44(4):561-4. doi: 10.1093/jac/44.4.561. PMID: 10588322.
- [5]: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Imipenem-Cilastatin. 2017 Jan 17. PMID: 31644018.
- [6]: Le Run E, Atze H, et al. Impact of relebactam-mediated inhibition of *Mycobacterium abscessus* BlaMab  $\beta$ -lactamase on the in vitro and intracellular efficacy of imipenem. *J Antimicrob Chemother*. 2020 Feb 1;75(2):379-383. doi: 10.1093/jac/dkz433. PMID:

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[7]: Heine HS, Louie A, et,al. Evaluation of imipenem for prophylaxis and therapy of Yersinia pestis delivered by aerosol in a mouse model of pneumonic plague. Antimicrob Agents Chemother. 2014 Jun;58(6):3276-84. doi: 10.1128/AAC.02420-14. Epub 2014 Mar 31. PMID: 24687492; PMCID: PMC4068467.

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