

Product Data Sheet

Product Name: Doripenem Hydrate

Cat. No.: GC16675

Chemical Properties

Cas. No. 364622-82-2

Chemical Name (4R,5S,6S)-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-3-[(3S,5S)-5-[(sulfamoylamino)methyl]pyrrolidin-3-yl]sulfanyl-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid;hydrate

SMILES CC1C2C(C(=O)N2C(=C1SC3CC(NC3)CNS(=O)(=O)N)C(=O)O)C(C)O.O

Formula $C_{15}H_{24}N_4O_6S_2 \cdot H_2O$

M.Wt 438.52

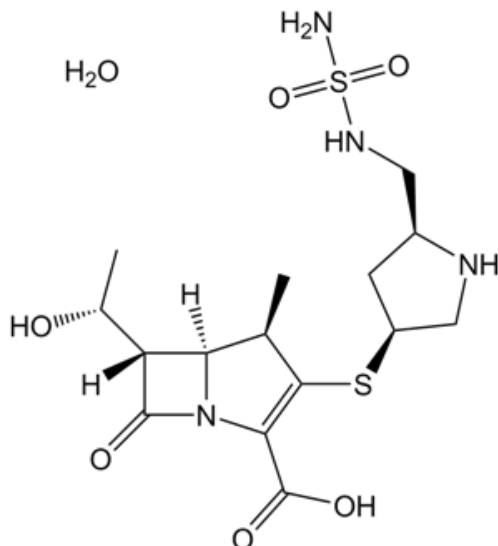
Solubility $\geq 10.96\text{mg/mL}$ in DMSO

Storage Store at -20°C

General 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

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines bacteria

Preparation method The solubility of this compound in DMSO is >11mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Applications S-4661 was potent against methicillin-susceptible *Staphylococcus aureus* and methicillin-susceptible *Staphylococcus epidermidis* with the MIC₉₀ of 0.063 µg/ml. S-4661 was potent against penicillin-resistant *S. pneumoniae*. S-4661 showed activities against *S. pyogenes* and penicillin-resistant *S. pneumoniae*. S-4661 was active against *Enterococcus faecalis*. S-4661 was particularly active against *Enterobacteriaceae* and *H. influenzae*. The MIC₉₀s for *Escherichia*, *Klebsiella*, *Proteus*, *Providencia*, *Morganella*, *Citrobacter*, *Enterobacter*, and *Serratia* spp. ranged from 0.063 to 0.5 µg/ml.

Animal experiment [1]:

Animal models Male SLC/ICR mouse model of bacteremia, mouse model of respiratory tract infection induced by *S. pneumonia*, male CBA/JNCrj mouse model of pulmonary infection induced by penicillin-resistant *S. Pneumonia* TUH741

Dosage form Subcutaneously administration, twice daily for 2 days

Application The ED₅₀ of S-4661 against *S. aureus* Smith was 0.066 mg/kg. The ED₅₀ of S-4661 was 0.23 mg/kg against *S. pneumonia* TUH39, the same as that of imipenem-cilastatin. S-4661 (10 mg/kg) showed significant antibacterial activity.

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Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Tsuji M, Ishii Y, Ohno A, et al. In vitro and in vivo antibacterial activities of S-4661, a new carbapenem[J]. Antimicrobial agents and chemotherapy, 1998, 42(1): 94-99.

Background

Doripenem hydrate is a parenteral, potent, and well-balanced antibiotic against a wide range of both Gram+ and Gram- bacteria including *Pseudomonas aeruginosa* [1] with MIC90 values of $\leq 0.5 \mu\text{g/ml}$ against methicillin-susceptible streptococci and staphylococci, $0.032\text{-}0.5 \mu\text{g/ml}$ against members of the family Enterobacteriaceae, *Moraxella catarrhalis*, and *Haemophilus influenza*, and $8 \mu\text{g/ml}$ against *Pseudomonas aeruginosa* [2].

Patients with cystic fibrosis can be infected with several pathogens such as *Haemophilus influenzae*, *Staphylococcus aureus* and *P. aeruginosa*, chronically. By 18 years of age, 80% of cystic fibrosis patients are infected with *P. aeruginosa* [3].

Doripenem hydrate was potent against *Staphylococcus aureus* and *Staphylococcus epidermidis* with the same MIC90 value of $0.063 \mu\text{g/ml}$. Doripenem hydrate was 2-4 times more active than other tested carbapenems against *S. aureus*. The activity of doripenem hydrate against *S. pneumoniae* was similar to that of imipenem but higher than that of other tested agents. Doripenem hydrate was potent against *S. pneumoniae* with an activity similar to that of other tested carbapenems (MIC90, $0.5 \mu\text{g/ml}$). Doripenem hydrate had an activity similar to that of cefpirome against *S. pneumoniae* and *S. pyogenes*. Doripenem hydrate was more active against *Enterococcus faecalis* than other tested agents except for imipenem [2].

In mice experimentally induced with acute bacteremia, the ED50 of doripenem hydrate against *S. aureus* Smith was 0.066 mg/kg . Doripenem hydrate was more effective than other tested carbapenems against *S. aureus* TUH1. Doripenem hydrate was more effective than other tested

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agents except for meropenem-cilastatin against E. coli C-11. Doripenem hydrate almost shared the same effectiveness with other tested carbapenems against P. aeruginosa E7. Against P. aeruginosa TUH302, doripenem hydrate was the most effective among tested drugs [2].

References:

- [1]. Yutaka Nishino, Makoto Kobayashi, Taneyoshi Shinno, et al. Practical Large-Scale Synthesis of Doripenem: A Novel 1 β -Methylcarbapenem Antibiotic. Organic Process Research & Development, 2003, 7:846-850.
- [2]. Masakatsu Tsuji, Yoshikazu Ishii, Akira Ohno, et al. In Vitro and In Vivo Antibacterial Activities of S-4661, a New Carbapenem. Antimicrobial Agents and Chemotherapy, 1998, 42(1): 94-99.
- [3]. Yunhua Chen, Elizabeth Garber, Qiuqu Zhao, et al. In Vitro Activity of Doripenem (S-4661) against Multidrug-Resistant Gram-Negative Bacilli Isolated from Patients with Cystic Fibrosis. Antimicrobial Agents and Chemotherapy, 2005, 49(6):2510-2511.

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