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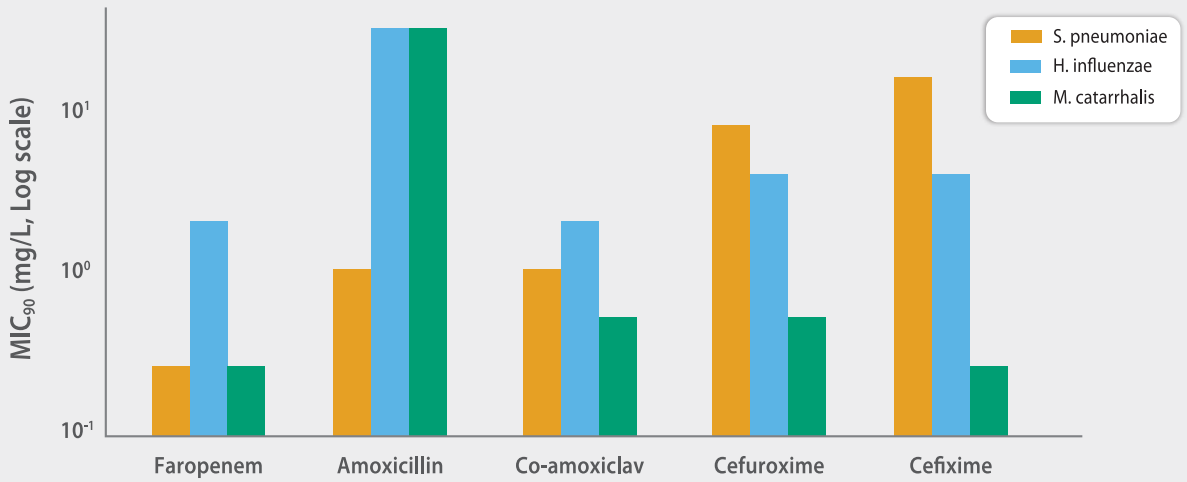
Antimicrobial activity of faropenem, a new oral penem, against lower respiratory tract pathogens

- Faropenem, a novel oral penem antibiotic, demonstrates a broad spectrum of antimicrobial activity, particularly against major respiratory pathogens such as Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis.
- With rising resistance to conventional agents, including penicillin and macrolides, this study evaluated faropenem's potency in vitro, including against β-lactamase–producing strains, and assessed its bactericidal performance using time-kill experiments.

Study Design	In vitro microbiological study; time-kill experiments		
Duration	**Comparators**	**Organisms**	**Outcomes**
4 years	Faropenem vs. multiple oral antibiotics (amoxicillin, co-amoxiclav, cefuroxime, cefixime, cefpodoxime, macrolides, fluoroquinolones)	876 isolates: 503 S. pneumoniae (incl. penicillin-resistant), 310 H. influenzae (14 β-lactamase+), 63 M. catarrhalis (48 β-lactamase+)	Faropenem had comparatively lower MIC than comparators

MIC_{90} comparison of Faropenem vs other oral antibiotics



Faropenem demonstrated 100% activity against all tested isolates, including resistant S. pneumoniae and β-lactamase–producing H. influenzae and M. catarrhalis. With rapid bactericidal action and consistently lower MIC values than comparators, faropenem is a highly effective oral option for respiratory infections. It is also well-suited for sequential therapy after hospital discharge, including in conditions such as aspiration pneumonia and osteomyelitis.

Ref.: Clin Microbiol Infect 1999; 5: 282-287

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Faropenem-the novel oral penem

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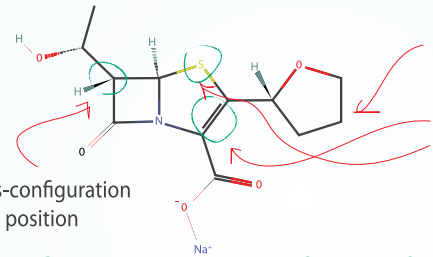
Drug Review

Antimicrobial resistance

- Antimicrobial resistance (AMR) has been prioritized by the World Health Organization (WHO) as one of the top 10 global public health threats facing humanity.[2]
- Resistance to beta-lactams is an alarming and growing phenomenon and, in turn, a public health challenge. Following are the mechanisms of resistance[3] :
  - Inactivation by the production of beta-lactamases.
  - Decreased penetration to the target site (e.g., the resistance of *Pseudomonas aeruginosa*).
  - Alteration of target site Penicillin Binding Proteins (PBPs) (e.g., penicillin resistance in *pneumococci*).
  - Efflux from the periplasmic space through specific pumping mechanisms.

The key distinguishing features of faropenem[4-7]

Faropenem- a penem with unique chemical structure



Trans-configuration at C6 position

Its chiral tetrahydrofuran substituent at position C2 **(Orally effective)**

The sulfur at position 1 reduces intra ring stress and the double bond between C2 and C3 increases the activity of β-Lactam ring

Broad- spectrum, penem antibiotic with stability against all types of β-lactamases in classes A, C and D including ESBLs* and AmpC

Time, concentration and oxygen dependent **bactericidal effect** against **Aerobic, Anaerobic, Gram-positive & Gram-negative** bacteria.

Faropenem has shown lower MICs (Minimum Inhibitory Concentrations) than other beta-lactam antibiotics against certain bacteria.

	Bacteria	Faropenem			Amox - clav		Cefuroxime		Imipenem	
		MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
Gram (+)ve	*Staphylococcus aureus* (MS)	0.12	0.12	0.03–0.5	1	2	1	2	≤ 0.5	≤ 0.5
	S. aureus (MR)	>32	>32	0.12– >32	8	16	>32	>32	32	32
	Staphylococcus epidermidis (All)	0.12	0.5	0.06 – >128	1	8	0.5	16	0.016	16
	S. epidermidis (MS)	0.12	0.5	0.06 – 4	1	2	0.5	1	0.016	0.016
	Streptococcus pyogenes	0.03	0.03	≤ 0.015 – 0.06	0.03	0.03	≤ 0.015	≤ 0.015	≤ 0.008	≤ 0.008
	Streptococcus pneumoniae	0.008	0.25	≤ 0.004 – 2	0.03	0.5	≤ 0.12	4	≤ 0.5	≤ 0.5
Gram (-)ve	*Escherichia coli*	0.5	1	0.12 – 32	4	16	4	8	≤ 0.5	≤ 0.5
	Haemophilus influenzae	0.25	1	≤ 0.004 – 4	0.5	1	0.5	2	1	4
	H.influenzae (BLN)	0.25	1	≤ 0.004 – 4	0.5	1	0.5	2	1	2
	Klebsiella pneumoniae	0.5	2	0.25 – >32	2	8	4	>32	0.25	1

Ref: 1.Chimura T, Kaneko N, Hayashi Y, Funayama T, Numazaki M, Oda T, Murayama K, Morisaki N, Hirayama T, Sato F, Akatsuka K. [Clinical studies of faropenem in the field of obstetrics and gynecology]. Jpn J Antibiot. 1999 Jul;52(7):504-10. Japanese. PMID: 10516930.| 2. 10 global health issues to track in 2021, World Health Organization Newsroom (24 Dec 2020) | 3. Phenotypic Characterization and Antibiotic Resistance Patterns of Extended-Spectrum β- Lactamase- and AmpC β -Lactamase-Producing Gram-Negative Bacteria in a Referral Hospital, Saudi Arabia,Ibrahim ME, Abbas M, Al-Shahrai AM, Elamin BK,. Can J Infect Dis Med Microbiol | 4. Dalhoff A, Janjic N, Echols R. Redefining penems. Biochem. Pharmacol. 71(7), 1085–1095 (2006) | 5. Dalhoff A, Nasu T, Okamoto K, β-lactamase stability of Faropenem,Chemotherapy 49(5), 229–236 (2003) | 6. Faropenem: review of a new oral penem, Kristen N Schurek, Ryan Wiebe, James A Karlowsky, Ethan Rubinstein, Daryl J Hoban and George G Zhanel, Expert Rev. Anti Infect. Ther. 5(2), (2007) | 7. Boswell FJ, Andrews JM, Wise R. Pharmacodynamic properties of faropenem demonstrated by studies of time–kill kinetics and post-antibiotic effect. J. Antimicrob. Chemother. 39(3), 415–418 (1997) |

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