Faropenem-The novel oral penem

Farobac®
Faropenem 150 mg & 200 mg Tablet

Power & Confidence* of penem with *oral convenience

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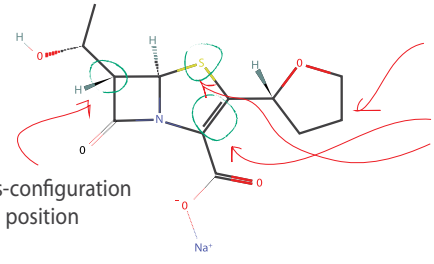
Drug Review

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.[1]
- Resistance to beta-lactams is an alarming and growing phenomenon and, in turn, a public health challenge. Following are the mechanisms of resistance[2] :
  - 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[3-6]

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.

Proven Results

- Faropenem has shown the similar activity to the carbapenems, imipenem and meropenem.[5]
- Faropenem is four- to eightfold more active against penicillin-resistant of *S. pneumoniae* than amoxicillin-clavulanate and cefuroxime.[5]
- Like the carbapenems, faropenem exerts a Post Antibiotic Effect (PAE) against aerobic, anaerobic, gram-positive & gram-negative bacteria.[6]

Faropenem have shown impressive clinical & mycological cure rate in clinical trials[7]

Indications	Clinical cure rate (%)	Mycological cure (%)
CAP	91.5	80.6
ABS	89	90.1
ABECB	87.6	68.6
USSTI	85.4	86.4
UTI	86.2	80.8

CAP- Community Acquired Pneumonia | ABS-Acute Bacterial Sinusitis | ABECB- Acute Bacterial Exacerbation of Chronic Bronchitis | USSTI-Uncomplicated Skin and Skin Structure Infections | *UTI- Urinary Tract Infection | *ESBLs: Extended-Spectrum Beta-Lactamases

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

In vitro activity of faropenem and comparators against Gram-positive aerobes[8]

Bacteria	Faropenem			Amox - clav		Cefuroxime		Imipenem	
	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
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
S. epidermidis(MR)	2	>128	0.06 – >128	8	16	2	32	32	32
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
S. pneumoniae (PS)	≤ 0.004	0.008	≤ 0.004 – 0.12	0.03	0.03	0.03	0.06	≤ 0.008	≤ 0.008
S. pneumoniae (PI)	0.12	0.25	≤ 0.004–1	0.25	1	2	4	0.06	0.12
S. pneumoniae (PR)	0.5	1	≤ 0.004–2	2	8	8	16	0.5	1

In vitro activity of faropenem and comparators against Gram-negative aerobes[8]

Bacteria	Faropenem			Amox – clav		Cefuroxime		Imipenem	
	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
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
H.influenzae (BLP)	0.25	0.5	≤ 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
Klebsiella spp.	0.5	2	0.06–8	2	8	2	32	0.12	0.12
Moraxella Catarrhalis	0.25	0.5	0.008–2	0.12	0.25	1	2	0.06	0.125
M.catarrhalis (BLN)	0.03	0.12	0.015–1	0.25	0.5	0.5	0.5	0.5	1
M.catarrhalis (BLP)	0.25	0.5	0.008–2	0.25	0.5	1	2	0.5	1

In vitro activity of faropenem and comparators against anerobes[9]

Bacteria	Faropenem		
	MIC_{50}	MIC_{90}	Range
Clostridium perfringens	0.5	1	0.12-32
Clostridium difficile	4	8	1- 8
Bacteroides fragilis	1	4	0.12 - 32
Pepto streptococcus spp.	0.06	0.5	0.008 - 1

Amox–clav: Amoxicillin–Clavulanic acid
MIC_{50} : Minimum Inhibitory Concentration (mg/l) of 50% of isolates
MIC_{90} : Minimum Inhibitory Concentration of 90% of isolates
MR : Methicillin Resistant
MS : Methicillin Sensitive
PI : Penicillin Intermediate (penicillin MIC 0.12–1 mg/l)
PR : Penicillin Resistant (penicillin MIC ≥ 2.0 mg/l)
PS : Penicillin Susceptible (penicillin MIC ≤ 0.06 mg/l) BLN: beta-lactamase negative
BLP : Beta Lactamase Positive

Ref.: 1. 10 global health issues to track in 2021, World Health Organization Newsroom (24 Dec 2020) | 2. Phenotypic Characterization and Antibiotic Resistance Patterns of Extended-Spectrum β-Lactamase- and AmpCβ -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 | 3. Dalhoff A, Janjic N, Echols R. Redefining penems. Biochem. Pharmacol. 71(7), 1085–1095 (2006) | 4. Dalhoff A, Nasu T, Okamoto K, β-lactamase stability of Faropenem,Chemotherapy 49(5), 229–236 (2003) | 5. 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) | 6. 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) |7. MacGowan A, Bowker K. In vitro studies on the impact of human serum on the antibacterial effect of faropenem. J. Chemother. 16(1), 23–29 (2004) | 8. 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) | 9. The in-vitro activity of faropenem, a novel oral penem, J. M. Woodcock, J. M. Andrews, N. P. Brenwald, J. P. Ashby and R. Wise, Journal of Antimicrobial Chemotherapy (1997) 39, 35–43.

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