Supplementary Table I. Comparative summary of *In vitro* activity of cefepime–enmetazobactam (CPM–EMT) against gram-negative infections (GNIs) (selected studies)

Study (yr)	Isolates and region	Resistance mechanisms	CPM–EMT MIC_{90} (µg/mL)	% Susceptible	Incremental benefit of EMT over cefepime alone	Key notes
Morrissey *et al*[17], 2019	1,993 *Enterobacteriaceae* + *P. aeruginosa* (US/EU, 2014–15)	*ESBLs* (*CTX-M*, *TEM*, *SHV*); non-*ESBLP. aeruginosa*	*E. coli*: 0.12; *K. pneumoniae*: 0.5; *E. cloacae*: 1; *E. aerogenes*: 0.25; *P. aeruginosa*: 16	*E. coli*: 99.9%; *K. pneumoniae*: 96.4%; *E. cloacae*: 97.0%; *E. aerogenes*: 100%; all Enterobacteriaceae: 98.1%; *P. aeruginosa*: 82.8%	128-fold for *E. coli* (16→0.12); ≥128-fold for *K. pneumoniae* (>64→0.5); 16-fold for *E. cloacae* (16→1); none for *P. aeruginosa*	Definitive large-scale surveillance baseline
Jean *et al*[37], 2022	Bloodstream *Enterobacterales* (n = 651), *P. aeruginosa* (n = 271), *A. baumannii* (n = 187) (Taiwan, SMART 2020)	*ESBL*, *AmpC*, carbapenem-nonsusceptible isolates	*Enterobacterales*: ≤0.5; *P. aeruginosa*: ~16; *A. baumannii*: >16	*Enterobacterales*: ≥97%; *P. aeruginosa*: ~80%-85%; *A. baumannii*: minimal	Large MIC reductions for Enterobacterales; negligible for non-fermenters	Regional SMART programme confirms global trends
Bonnin *et al*[c], 2025	Carbapenem-resistant *Enterobacterales* (CRE; 2,212 isolates: *OXA-48*-like, *KPC*, *NDM*, VIM, others) + 50 *P. aeruginosa* + 30 *A. baumannii* (France, 2023)	CRE (*OXA-48*, *KPC*, *MBL*: *NDM*/*VIM*)	*OXA-48*: ~1; *KPC*: variable (≤0.25 for resistant variants); MBL: >16; non-fermenters: >16	*OXA-48*: 96.7%; *KPC*: 63.3%; MBL: <5%; *P. aeruginosa* Minimal activity (largely cefepime-driven); *A. baumannii*: no benefit	≥16× reduction for *OXA-48*; none for *MBLs* or non-fermenters	Validates limited CPM–EMT utility beyond *OXA-48* CRE
Bhowmick *et al*[33], 2025	Multinational clinical *Enterobacterales* (3GC-R, *ESBL+OXA-48* producers)	*ESBL*, *AmpC*, *OXA-48* CRE	MIC_{90} generally ≤1 for *ESBL*/*OXA-48* producers	>95% susceptibility	High fold-reduction relative to cefepime	Narrative review summarizes global *in vitro* findings
Bakthavatchalam *et al*[d], 2025	566 Indian 3GC-R *Enterobacterales*+ *P. aeruginosa*	CTX-M, *AmpC* (*CMY*, *DHA*), *OXA-1*; MDR *P. aeruginosa*	*ESBL*: ≤2 *AmpC*: ≤4 *K. pneumoniae*: ≤ 1	100% *P. aeruginosa*; high *Enterobacterales*	Clear reduction in MIC across all	Strong bactericidal effect against Indian MDR isolates
Jasmine A[e], 2025	*ESBL*/*AmpC Enterobacterales* (India – institutional isolates)	*ESBL*, *AmpC*	Not specified	~91% clinical response	Not quantified	Supports *in vitro* trends qualitatively

CPM–EMT, cefepime–enmetazobactam (fixed 8 µg/mL enmetazobactam); MIC_{90}, minimum inhibitory concentration inhibiting 90% of isolates. SMART, study for monitoring antimicrobial resistance trends; CMY, cephamycin hydrolysing; DHA, Dhahran hospital; 3GC-R, third-generation cephalosporin-resistant; CRE, carbapenem-resistant Enterobacterales; Fold-reduction, Decrease in MIC when comparing cefepime alone to CPM–EMT; Cells marked 'Not specified' indicate the original study did not report numerical MIC_{90} values. *For P. aeruginosa,* EMT component offers little inhibition of prevalent resistance mechanisms; observed activity largely reflects cefepime susceptibility. The combination is not a targeted option for difficult-to-treat *P. aeruginosa;* agents such as ceftolozane–tazobactam or imipenem–relebactam may be preferred depending on susceptibility and local guidance (IDSA 2024)