Fetroja® – Use in Pediatric Patients

This medical response contains information in addition to that provided in the Fetroja® (cefiderocol) for injection, for intravenous use Full Prescribing Information approved by the US Food and Drug Administration (FDA). Shionogi does not recommend the use of Fetroja in any manner other than as described in the Full Prescribing Information. **Please read the attached Fetroja Full Prescribing Information.**

Summary

Clinical Studies

Bradley et al (2025) reported the results of the **PEDI-CEFI study** (NCT04335539), a Phase 2, single-arm, open-label study evaluating the safety, tolerability and PK of single or multiple cefiderocol doses in 53 pediatric patients aged 3 months to <18 years with Gram-negative infections requiring hospitalization and IV antibiotic treatment. Patients with CNS infection, osteomyelitis, or CF were excluded from the study.[1–3]

- Patients were subdivided into 4 age-based cohorts: 12 to <18 years, 6 to <12 years, 2 to <6 years, and 3 months to <2 years
- Cefiderocol was added to SOC at different times during treatment based on single- or multiple-dose phases. Dosing in both phases was based on renal function and body weight
- Cefiderocol was well-tolerated, and total plasma concentrations were similar across patients in all cohorts after both single and multiple doses

Roilides et al (2026) reported data from the **APEKS-PEDI study** (NCT04215991), a Phase 1b–2, multicenter, open-label trial that assessed the PK, safety, and tolerability of cefiderocol in 84 hospitalized pediatric patients (3 months to <18 years of age) who had suspected or confirmed Gram-negative bacterial infections and were concurrently receiving SOC antibiotics for a treatment duration of 5–14 days.[4]

- Patients were subdivided into 4 age-based cohorts (12 to <18 years, 6 to <12 years, 2 to <6 years, and 3 months to <2 years), and a total of 84 patients were enrolled across single- and multiple-dose phases with dosing based on renal function and body weight
- Total plasma trough cefiderocol concentrations remained >4 µg/mL (ie, above the CLSI susceptibility breakpoint for Enterobacterales, *Pseudomonas aeruginosa*, and *Acinetobacter* spp.) for the entire dosing period across all age cohorts
- Overall, cefiderocol treatment was well tolerated, with a safety profile similar to that of other β-lactam antibiotic regimens

The **NEO-CEFI study** (NCT06086626) was a Phase 2, multicenter, single-arm, open-label study that assessed the PK, safety, and tolerability of cefiderocol in 30 hospitalized neonates and infants (from birth to <3 months of age, including premature infants with GA ≥26 weeks) who had suspected or confirmed Gram-negative bacterial infections and were concurrently receiving SOC antibiotic treatment for an expected 5–14 days.[5]

- Patients were stratified into 6 subgroups based on GA and PNA, including term neonates (GA ≥26 weeks), with dosing determined by body weight, GA, and PNA
- In both the single-dose (n=12) and multiple-dose (n=18) phases, geometric mean plasma cefiderocol concentrations remained ≥8 µg/mL across all age subgroups regardless of infusion duration (1 h or 3 h). The safety profile of cefiderocol was consistent with that expected of a β-lactam when administered alongside SOC antibiotics

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Summary (Cont.)

Real-World Data: Case Series

Mantsiou et al (2026) published the combination of a case series, plus a systematic review of all previously available instances of cefiderocol use in pediatric patients for the treatment of Gram-negative bacterial infections.[6]

Case Series:

- Between February 2023 and August 2025, 21 courses of IV cefiderocol were administered to a total of 15 pediatric patients
- Clinical response was achieved in 10 (76.2%) patients (16 of 21 courses) with a median time to clinical response of 72 h (range: 24–240), and laboratory response (defined as ≥50% CRP reduction) was achieved within a median of 72 h (range: 24–240)

Systematic Literature Review:

- Out of the 243 reports identified, 17 were included describing 32 pediatric patients (receiving a total of 37 courses of cefiderocol)
- Dosing of cefiderocol ranged from 30–100 mg/kg (usually 60 mg/kg), with dosing intervals of 6 or 8 h, often administered as extended infusions over 3 h, and duration of treatment varied widely (range: 1–98 days; median: 12 days)
- Clinical effectiveness was reported in most of the 37 cefiderocol courses

Schmid et al (2024) described a retrospective case series review, involving the treatment of pediatric patients with cefiderocol as a result of infection or colonization with MDR Gram-negative bacteria at the Great Ormond Street Hospital in the UK.[7]

- In total, 18 courses of cefiderocol were administered to 14 patients
- Median treatment duration for cefiderocol was 11 days (IQR: 7–14), with a favorable clinical response observed in 6 of 10 cases involving serious or invasive infections
- Overall, 30-day mortality was 12%, and cefiderocol was generally well tolerated throughout the study period

Real-World Data: Case Reports

Use of cefiderocol in pediatric patients has also been described in individual case reports. Cases included neonates to patients aged 17 years.[8–18]

- Multiple pathogens were identified across cases, including those that were XDR/DTR or MBL producers
- Cefiderocol doses ranged from 30 mg/kg to 2 g; treatment duration ranged from 7 to 56 days
- Overall, treatment with cefiderocol was associated with clinical improvement and microbiological response. An AE, reduced WBC count, was reported in 1 case

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Summary (Cont.)

Surveillance Studies

Nguyen et al (2024) evaluated the *in vitro* activity of cefiderocol and comparator agents against bacterial isolates from pediatric patients (hospitalized with pneumonia between 2020 and 2022) as part of the SENTRY Antimicrobial Surveillance Program.[19]

- A total of 1389 isolates were collected (from 30 European and 31 US medical centers)
- Most isolates were shown to be susceptible to cefiderocol (including Carb-NS isolates), with 99.5% and 99.6% of isolates having MIC values of ≤2 and ≤4 µg/mL, respectively

Nguyen et al (2023) also assessed the *in vitro* activity of cefiderocol and comparator agents against the entire library of bacterial isolates collected from pediatric patients as part of the SENTRY Antimicrobial Surveillance Program between 2020 and 2022.[20]

- Isolates included Enterobacterales (N=2249), *P. aeruginosa* (N=707), ABC (N=194), and *Stenotrophomonas maltophilia* (N=220)
- Compared to other agents, cefiderocol was highly active against all isolate types, including MDR and Carb-NS Enterobacterales and *P. aeruginosa*

PK/PD Studies

Katsube et al (2019) reported a PK model extrapolating data from adult patients in order to identify appropriate cefiderocol dosage regimens for pediatric patients.[21,22]

- Resulting dosage regimens included 60 mg/kg q8h over a 3-h infusion for patients aged 3 months to <18 y and 30 to 60 mg/kg q8h over a 1-h infusion for patients aged <3 months
- Cefiderocol 2 g q8h was used for patients with body weight of ≥34 kg

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Clinical Studies

The PEDI-CEFI Study

The PEDI-CEFI study (NCT04335539) was an international, multicenter, single-arm, open-label, Phase 2 study designed to evaluate the safety, tolerability, and PK of cefiderocol in 53 pediatric patients (aged 3 months to <18 years). The study induded both single- and multiple-dose phases of cefiderocol added to SOC.[1–3]

Study Design[2]

- Eligible patients had confirmed or suspected Gram-negative infections requiring hospitalization and IV antibiotic treatment, including but not limited to:
  - cUTI
  - cIAI
  - HABP/VABP
  - Sepsis or BSI
- Patients with CNS infection, osteomyelitis, or CF were ineligible for study participation
- In the single-dose phase, cefiderocol was added as adjunctive treatment at any time during SOC therapy
- In the multiple-dose phase, cefiderocol was added within 72 h of SOC treatment initiation and administered q8h for 5 to 14 days
- Patients were further grouped into age-based cohorts:
  - Cohort 1: aged 12 to <18 years (single-dose phase only)
  - Cohort 2: aged 6 to <12 years
  - Cohort 3: aged 2 to <6 years
  - Cohort 4: aged 3 months to <2 years

Dosing[2]

- Study doses of cefiderocol were determined by weight and renal function and were administered over a 3-h infusion – see Table 1

Table 1. Dosing for Single- and Multiple-Dose Phases by Renal Impairment and Weight[2]

	Dose		Infusion Time[c]
	Body Weight ≥34 kg[b]	Body Weight <34 kg[b]	
Single- and multiple-dose phase			
Normal to mild renal impairment	2000 mg	60 mg/kg	3 h
Multiple-dose phase only			
Moderate renal impairment	1500 mg	45 mg/kg	3 h
Severe renal impairment	1000 mg	30 mg/kg	3 h

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Clinical Studies

Table 1. Dosing for Single- and Multiple-Dose Phases by Renal Impairment[a] and Weight[2]

	Dose		Infusion Time[c]
	Body Weight ≥34 kg	Body Weight <34 kg[b]	
Single- and multiple-dose phase			
Normal to mild renal impairment	2000 mg	60 mg/kg	3 h
Multiple-dose phase only			
Moderate renal impairment	1500 mg	45 mg/kg	3 h
Severe renal impairment	1000 mg	30 mg/kg	3 h

Abbreviations: eGFR, estimated glomerular filtration rate; h, hours.
[a]Renal function categorized as: normal (eGFR of ≥90 mL/min/1.73m^2), mild renal impairment (eGFR of 60 to <90 mL/min/1.73m^2), moderate renal impairment (eGFR of 30 to <60 mL/min/1.73m^2), severe renal impairment (eGFR of 15 to <30 mL/min/1.73m^2).
[b]No more than 2000 mg of cefiderocol could be administered.
[c]Shorter infusion time was allowed in the multiple-dose phase if agreed by the sponsor and if in the best interest of the patient.
Table adapted from Bradley et al. *Pediatr Infect Dis J*. 2025.

– Cohort 4: aged 3 months to <2 years

Dosing[2]

- Study doses of cefiderocol were determined by weight and renal function and were administered over a 3-h infusion (see Table 1)

Table 1. Dosing for Single- and Multiple-Dose Phases by Renal Impairment and Weight[2]

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Clinical Studies

The PEDI-CEFI Study (Cont.)

Results[2,3]

Patient Baseline Characteristics[2,3]

- A total of 53 patients were enrolled
  - The single- and multiple-dose phases included 24 and 29 patients, respectively
  - Additional patient demographic and baseline information is presented in **Table 2**

Plasma Concentrations of Cefiderocol[2]

- Geometric mean values (µg/mL) of cefiderocol plasma concentrations were determined at various timepoints after initiation of cefiderocol treatment – see **Table 3**
  - At the end of infusion (3 h), the peak concentrations ranged between 72.7 and 97.1 µg/mL for single-dose and between 88.8 and 106 µg/mL for multiple-dose cohorts
  - After 8 h, the corresponding trough concentrations ranged between 7.86 to 10.8 µg/mL for single-dose and between 9.64 and 18.1 µg/mL for multiple-dose cohorts
- Across all patients, weight-adjusted doses attained steady-state plasma concentrations exceeding the necessary susceptibility breakpoints for Gram-negative pathogens throughout the treatment period

Table 2. Patient Baseline Characteristics[2,3]

C1: Adolescents C2: School Aged C3: Pre-School C4: Infants	Single-Dose Phase					Multiple-Dose Phase			
	C1 (n=6)	C2 (n=6)	C3 (n=6)	C4 (n=6)	Overall (N=24)	C2 (n=12)	C3 (n=11)	C4 (n=6)	Overall (N=29)
Age, years									
Mean±SD	14.27±1.34	9.1±1.68	2.87±1.3	1.05±0.53	6.82±5.48	8.72±1.88	4.35±1.2	0.73±0.42	5.41±3.43
Sex, n (%)									
Male	2 (33.3)	2 (33.3)	3 (50)	[illegible]	10 (41.7)	3 (25)	2 (18.2)	4 (66.7)	9 (31)
Female	4 (66.7)	4 (66.7)	3 [illegible]		[illegible]	9 (75)	9 (81.8)	2 (33.3)	20 (69)
Body weight, kg									
Mean±SD	60.17±10.19	30.32±8.43	[illegible]		[illegible]	27.37±3.85	16.95±3.97	6.82±0.84	19.16±8.66
eGFR grading group, n (%)									
≥120 mL/min/1.73 m²	2 (33.3)	1 (16.7)	[illegible]		[illegible]	3 (25)	1 (9.1)	4 (66.7)	8 (27.6)
90 to <120 mL/min/1.73 m²	4 (66.7)	4 (66.7)	[illegible]		[illegible]	(58.3)	5 (45.5)	2 (33.3)	14 (48.3)
60 to <90 mL/min/1.73 m²	0	1 (16.7)	[illegible]		[illegible]	2 (16.7)	5 (45.5)	0	7 (24.1)
Infection type, n (%)									
cUTI	0	2 (33.3)	[illegible]		[illegible]	3 (25)	4 (36.4)	3 (50)	10 (34.5)
cIAI	6 (100)	3 (50)	1 (16.7)	[illegible]	[illegible]	9 (75)	4 (36.4)	1 (16.7)	14 (48.3)
HAP/VAP	0	0	1 (16.7)	0	1 (4.2)	0	2 (18.2)	0	2 (6.9)
BSI	0	0	0	3 (50)	3 (12.5)	0	0	1 (16.7)	1 (3.4)
Sepsis	0	0	1 (16.7)	0	1 (4.2)	0	0	1 (16.7)	1 (3.4)
Other[a]	0	1 (16.7)	1 (16.7)	2 (33.3)	4 (16.7)	0	1 (9.1)	0	1 (3.4)

Table 3. Total Plasma Concentrations of Cefiderocol in the Single- and Multiple-Dose Cohorts[2]

	Single-Dose Phase (Levels Taken on Day 1)					Multiple-Dose Phase (Levels Taken on Day 3 or 4)			
	C1 (n=6)	C2 (n=6)	C3 (n=6)	C4 (n=6)	Overall (N=24)	C2 (n=12)	C3 (n=10)	C4 (n=6)	Overall (N=28)
1 h after start of infusion (n)	6	6	0	0	12	12	0	0	12
Geometric mean (µg/mL)	32.7	61.8	NA	NA	44.9	43	NA	NA	43
Geometric CV (%)	24.5	33.2	[illegible]		45	88.8			88.8
3 h after start of infusion (n)	5	6	[illegible]		[illegible]	10	5	4	19
Geometric mean (µg/mL)	72.7	97.1	[illegible]		[illegible]	88.8	103	106	96.2
Geometric CV (%)	40.5	26.8	[illegible]		[illegible]	50.6	36	20.8	41
3.5 h after start of infusion (n)	5	6	[illegible]		[illegible]	12	0	0	12
Geometric mean (µg/mL)	68.1	66.2	[illegible]		[illegible]	60.1	NA	NA	60.1
Geometric CV (%)	21.1	40.9	[illegible]		[illegible]	35.4			35.4
5 h after start of infusion (n)	6	6	[illegible]		[illegible]	12	10	6	28
Geometric mean (µg/mL)	26.3	30.8	[illegible]		[illegible]	24	45	46.8	34.7
Geometric CV (%)	22	95.6	104	[illegible]	67.3	46	72.8	27.3	63.4
8 h after start of infusion (n)	6	6	6	6	24	11	10	5	26
Geometric mean (µg/mL)	9.89	10	7.86	10.8	9.59	9.64	17.9	18.1	13.8
Geometric CV (%)	53.1	92.2	64.6	29.6	58.8	56.9	165	33.3	101

Clinical Studies

Table 2. Patient Baseline Characteristics[2,3]

C1: Adolescents C2: School Aged C3: Pre-School C4: Infants	Single-Dose Phase					Multiple-Dose Phase			
	C1 (n=6)	C2 (n=6)	C3 (n=6)	C4 (n=6)	Overall (N=24)	C2 (n=12)	C3 (n=11)	C4 (n=6)	Overall (N=29)
Age, years									
Mean±SD	14.27±1.34	9.1±1.68	2.87±1.3	1.05±0.53	6.82±5.48	8.72±1.88	4.35±1.2	0.73±0.42	5.41±3.43
Sex, n (%)									
Male	2 (33.3)	2 (33.3)	3 (50)	3 (50)	10 (41.7)	3 (25)	2 (18.2)	4 (66.7)	9 (31)
Female	4 (66.7)	4 (66.7)	3 (50)	3 (50)	14 (58.3)	9 (75)	9 (81.8)	2 (33.3)	20 (69)
Body weight, kg									
Mean±SD	60.17±10.19	30.32±8.43	14.25±4.03	8.62±2.13	28.34±21.47	27.37±3.85	16.95±3.97	6.82±0.84	19.16±8.66
eGFR grading group, n (%)									
≥120 mL/min/1.73 m^2	2 (33.3)	1 (16.7)	2 (33.3)	4 (66.7)	9 (37.5)	3 (25)	1 (9.1)	4 (66.7)	8 (27.6)
90 to <120 mL/min/1.73 m^2	4 (66.7)	4 (66.7)	4 (66.7)	0	12 (50)	7 (58.3)	5 (45.5)	2 (33.3)	14 (48.3)
60 to <90 mL/min/1.73 m^2	0	1 (16.7)	0	2 (33.3)	3 (12.5)	2 (16.7)	5 (45.5)	0	7 (24.1)
Infection type, n (%)									
cUTI	0	2 (33.3)	2 (33.3)	1 (16.7)	5 (20.8)	3 (25)	4 (36.4)	3 (50)	10 (34.5)
cIAI	6 (100)	3 (50)	1 (16.7)	0	10 (41.7)	9 (75)	4 (36.4)	1 (16.7)	14 (48.3)
HAP/VAP	0	0	1 (16.7)	0	1 (4.2)	0	2 (18.2)	0	2 (6.9)
BSI	0	0	0	3 (50)	3 (12.5)	0	0	1 (16.7)	1 (3.4)
Sepsis	0	0	1 (16.7)	0	1 (4.2)	0	0	1 (16.7)	1 (3.4)
Other[b]	0	1 (16.7)	1 (16.7)	2 (33.3)	4 (16.7)	0	1 (9.1)	0	1 (3.4)

Cohort ages as follows: C1, 12 to <18 years (single-dose phase only); C2, 6 to <12 years; C3, 2 to <6 years; C4, 3 months to <2 years.
Abbreviations: BSI, bloodstream infection; C, cohort; cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; eGFR, estimated glomerular filtration rate; HAP, hospital-acquired pneumonia; SCr, standardized serum creatinine; SD, standard deviation; VAP, ventilator-associated pneumonia.
[a]For ages ≥3 months to <1 year, eGFR = 0.45 × (height/SCr); for ages ≥1 to <18 years, eGFR = 0.413 × (height/SCr), where height is expressed in centimeters and SCr is expressed in mg/dL.
[b]2 participants with community-associated pneumonia, 1 participant with cutaneous infection, and 1 participant with lingering bronchitis in the single-dose phase, and 1 participant with community-associated pneumonia in the multiple-dose phase.
Table adapted from Bradley et al. *Pediatr Infect Dis J*. 2025.

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Clinical Studies

Table 3. Total Plasma Concentrations of Cefiderocol in the Single- and Multiple-Dose Cohorts[2]

	Single-Dose Phase (Levels Taken on Day 1)					Multiple-Dose Phase (Levels Taken on Day 3 or 4)			
	C1 (n=6)	C2 (n=6)	C3 (n=6)	C4 (n=6)	Overall (N=24)	C2 (n=12)	C3 (n=10)	C4 (n=6)	Overall (N=28)
1 h after start of infusion (n)	6	6	0	0	12	12	0	0	12
Geometric mean (µg/mL)	32.7	61.8	NA	NA	44.9	43	NA	NA	43
Geometric CV (%)	24.5	33.2			45	88.8			88.8
3 h after start of infusion (n)	5	6	6	4	21	10	5	4	19
Geometric mean (µg/mL)	72.7	97.1	86.6	96.5	87.6	88.8	103	106	96.2
Geometric CV (%)	40.5	26.8	26.4	15	29.2	50.6	36	20.8	41
3.5 h after start of infusion (n)	5	6	0	0	11	12	0	0	12
Geometric mean (µg/mL)	68.1	66.2	NA	NA	67.1	60.1	NA	NA	60.1
Geometric CV (%)	21.1	40.9			31.5	35.4			35.4
5 h after start of infusion (n)	6	6	6	6	24	12	10	6	28
Geometric mean (µg/mL)	26.3	30.8	19.9	36	27.6	24	45	46.8	34.7
Geometric CV (%)	22	95.6	104	24.1	67.3	46	72.8	27.3	63.4
8 h after start of infusion (n)	6	6	6	6	24	11	10	5	26
Geometric mean (µg/mL)	9.89	10	7.86	10.8	9.59	9.64	17.9	18.1	13.8
Geometric CV (%)	53.1	92.2	64.6	29.6	58.8	56.9	165	33.3	101

Cohort ages as follows: C1, 12 to <18 years (single-dose phase only); C2, 6 to <12 years; C3, 2 to <6 years; C4, 3 months to <2 years.
Geometric mean = exp(mean(log(x))); geometric CV (%) = 100*sqrt(exp(sd(ln(x))^2)-1), where geometric SD = standard deviation of natural log (ln)-transformed data.
Plasma concentrations below lower limit of quantification were treated as missing for calculations of geometric mean and geometric CV (%).
Abbreviations: C, cohort; CV, coefficient of variation; NA, not applicable; SD, standard deviation.
Table adapted from Bradley et al. *Pediatr Infect Dis J*. 2025.

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Clinical Studies

The PEDI-CEFI Study (Cont.)

Clinical and Microbiological Outcomes[3]

In the mITT population from the multiple-dose phase, outcomes were assessed at EOT, PT, and EOS. The mITT population included a total of 18 patients: 7 in Cohort 2, 8 in Cohort 3, and 3 in Cohort 4.

Clinical Outcomes[3]

- At EOT and EOS, 100% of patients in all cohorts achieved clinical cure
- Clinical outcome at PT was achieved by 89.9% of the overall population
  - 100% of patients in Cohort 2
  - 75% of patients in Cohort 3
  - 100% of patients in Cohort 4

Microbiological Outcomes[3]

- Bacterial eradication at EOT was observed in 66.7% of the total mITT population (33.3% indeterminate)
  - 71.4% of Cohort 2 patients
  - 75% of Cohort 3 patient
  - 33.3% of Cohort 4 patients
- Eradication at PT was observed in 72.2% of the total mITT population (27.8% indeterminate)
  - 71.4% of Cohort 2 patients
  - 62.5% of Cohort 3 patients
  - 100% of Cohort 4 patients
- Eradication at EOS was observed in 77.8% of the total mITT population (22.2% indeterminate)
  - 71.4% of Cohort 2 patients
  - 75% of Cohort 3 patients
  - 100% of Cohort 4 patients

Safety[2]

- Overall, in the single-dose phase, 5 (20.8%) patients experienced a total of 12 TEAEs
  - 1 (16.7%) patient in Cohort 2, 3 (50%) patients in Cohort 3, and 1 (16.7%) patient in Cohort 4
- Overall, in the multiple-dose phase, there were a total of 10 TEAEs occurring in 7 (24.1%) patients
  - 2 (16.7%) patients in Cohort 2, 1 (9.1%) patient in Cohort 3, and 4 (66.7%) patients in Cohort 4
  - Additionally, 1 (16.7%) patient in Cohort 4 experienced 2 treatment-emergent SAEs (a UTI that resolved on Day 37, and staphylococcal bacteremia that resolved on Day 44), both classed as moderate in severity and considered unrelated to cefiderocol by the investigator
- There was no evidence of liver toxicity, and there were no abnormal findings regarding vital signs and changes in laboratory results from baseline in either the single-dose or multiple-dose phases of the study

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Clinical Studies

The APEKS-PEDI Study

APEKS-PEDI (NCT04215991) was a multicenter, open-label, Phase 1b–2 trial conducted in hospitalized pediatric patients (aged 3 months to <18 years) with suspected or confirmed Gram-negative bacterial infections. The study aimed to characterize the PK profile, safety, and tolerability of cefiderocol when administered alongside SOC antibiotics over a 5- to 14-day treatment course.[4]

Study Design[4]

- Patients were grouped into age-based cohorts:
  - Cohort 1: aged 12 to <18 years (multiple-dose phase only)
  - Cohort 2: aged 6 to <12 years
  - Cohort 3: aged 2 to <6 years
  - Cohort 4: aged 3 months to <2 years
- The non-randomized single-dose phase enrolled patients in Cohorts 2–4 who had suspected or documented Gram-negative infections. Each patient received a single 3-h infusion of cefiderocol while also receiving SOC antibiotic therapy
  - Patients with suspected/documented Gram-negative infections were enrolled
- In the randomized multiple-dose phase (4:1 ratio; Cohorts 1–4), patients received cefiderocol as a 3-h infusion q8h for 5–14 days, administered alongside SOC antibiotics, with a comparator arm of SOC alone
  - Enrollment was restricted to patients with cUTI, HABP, or VABP
  - Cefiderocol monotherapy was permitted if SOC antibiotics had not been initiated by the time infection was confirmed as Gram-negative only
- Total plasma cefiderocol concentrations were measured from blood samples obtained at baseline and at pre-specified timepoints
- Safety was evaluated by clinical and laboratory assessment; TEAEs were reported from the day informed consent was obtained up to EOS (ie, 28 [+7] days after EOT)

Dosing[4]

- Study doses of cefiderocol were determined by weight and renal function and were administered over a 3-h infusion – see Table 4

Table 4. Dosing for Single- and Multiple-Dose Phases by Renal Impairment and Weight[4]

	Dose		Infusion Time
	Body W	Body Weight <34 kg	
Single- or multiple-dose phase			
Normal or mild renal impairment		60 mg/kg	3 h
Multiple-dose phase			
Moderate renal impairment	1	45 mg/kg	3 h
Severe renal impairment	1000 mg	30 mg/kg	3 h

This medical response contains information in addition to that provided in the Fetroja® (cefiderocol) for injection, for intravenous use Full Prescribing Information approved by the US Food and Drug Administration (FDA). Shionogi does not recommend the use of Fetroja in any manner other than as described in the Full Prescribing Information. **Please read the attached Fetroja Full Prescribing Information.**

Clinical Studies

Table 4. Dosing for Single- and Multiple-Dose Phases by Renal Impairment[a] and Weight[4]

	Dose		Infusion Time
	Body Weight ≥34 kg	Body Weight <34 kg	
Single- or multiple-dose phase			
Normal or mild renal impairment	2000 mg	60 mg/kg	3 h
Multiple-dose phase			
Moderate renal impairment	1500 mg	45 mg/kg	3 h
Severe renal impairment	1000 mg	30 mg/kg	3 h

Abbreviations: eGFR, estimated glomerular filtration rate; h, hours.
[a]Renal function categorized as: normal (eGFR of ≥90 mL/min/1.73m^2), mild renal impairment (eGFR of 60 to <90 mL/min/1.73m^2), moderate renal impairment (eGFR of 30 to <60 mL/min/1.73m^2), severe renal impairment (eGFR of 15 to <30 mL/min/1.73m^2).
Table adapted from Roilides et al. ESCMID. 2026

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Clinical Studies

The APEKS-PEDI Study (Cont.)

Results[4]

Patient Baseline Characteristics[4]

- A total of 84 patients were enrolled
  - The single- and multiple-dose phases included 12 and 72 patients, respectively
  - Additional patient demographic and baseline information is presented in **Table 5**

Table 5. Patient Baseline Characteristics (Safety/ITT Population)[4]

	Single-Dose Phase				Multiple-Dose Phase									
	Cefiderocol+SOC				Cefiderocol±SOC					SOC Only				
	C2 (n=5)	C3 (n=2)	C4 (n=5)	Overall (N=12)	C1 (n=14)	C2 (n=14)	C3 (n=17)	C4 (n=14)	Overall (N=59)	C1 (n=3)	C2 (n=3)	C3 (n=4)	C4 (n=3)	Overall (N=13)
Age, median (min; max), years	9.7 (6.7; 11.6)	4.9 (4.9; 4.9)	0.4 (0.3; 0.9)	4.9 (0.3; 11.6)	15 (12.8; 17.7)	9.25 (6.5; 11.3)	3.8 (2.2; 5.8)	0.45 (0.3; 1.7)	5.8 (0.3; 17.7)	15 (14.7; 15.4)	6.8 (6.7; 11.3)	4.2 (3.3; 4.6)	0.6 (0.3; 0.7)	4.6 (0.3; 15.4)
Sex, male, n (%)	3 (60)	0	2 (40)	5 (41.7)	7 (50)	6 (42.9)	3 (17.6)	8 (57.1)	24 (40.7)	1 (33.3)	2 (66.7)	1 (25)	2 (66.7)	6 (46.2)
Body weight, n[a]	5	2	5	12	14	14	17	14	59	2	3	3	0	8
Body weight, median (min; max), kg	34.7 (18.9; 37.5)	26.9 (18.6; 35.1)	7 (6.8; 7.4)	18.8 (6.8; 37.5)	52.3 (16; 83.4)	25.8 (17.2; 48.3)	14.6 (9.4; 27)	7.1 (4.9; 12.7)	17.2 (4.9; 83.4)	57 (57; 57)	25.4 (19.9; 72.5)	15 (11.9; 15)	NA	22.7 (11.9; 72.5)
eGFR grading group, n (%), mL/min/1.73 m²														
≥120	1 (20)	0	1 (20)	2 (16.7)	4 (28.6)				18 (30.5)	0	1 (33.3)	1 (25)	0	2 (15.4)
90 to <120	2 (40)	0	2 (40)	4 (33.3)	5 (35				21 (35.6)	0	1 (33.3)	2 (50)	1 (33.3)	4 (30.8)
60 to <90	2 (40)	2 (100)	2 (40)	6 (50)	3 (2				14 (23.7)	2 (66.7)	1 (33.3)	0	1 (33.3)	4 (30.8)
30 to <60	0	0	0	0	2 (				5 (8.5)	0	0	0	0	0
15 to <30	0	0	0	0	0				1 (1.7)	0	0	0	0	0
Missing	0	0	0	0	0				0	1 (33.3)	0	1 (25)	1 (33.3)	3 (23.1)
eGFR, n[b]	5	2	5	12	14				59	2	3	3	2	10
eGFR, median (min; max), mL/min/1.73 m²	101.3 (71.6; 171.7)	72.4 (67.5; 77.3)	94.6 (76.2; 146.3)	89.8 (67.5; 171.7)	96.55 (40.4; 469.3)	103.5 (27.3; 308.3)	[illegible] (73.5; 165.2)	89 (40.2; 262.8)	97.8 (27.3; 469.3)	68.35 (64.2; 72.5)	108.8 (68; 135.1)	119.3 (97.3; 271.4)	84.2 (63.4; 105)	101.15 (63.4; 271.4)
Infection, n (%)														
cUTI	2 (40)	2 (100)	4 (80)	8 (66.7)	10 (71.4)	14 (100)	16 (94.1)	14 (100)	54 (91.5)	3 (100)	3 (100)	4 (100)	3 (100)	13 (100)
HABP/VABP	0	0	0	0	4 (28.6)	0	1 (5.9)	0	5 (8.5)	0	0	0	0	0
cIAI	1 (20)	0	0	1 (8.3)	0	0	0	0	0	0	0	0	0	0
BSI	1 (20)	0	1 (20)	2 (16.7)	0	0	0	0	0	0	0	0	0	0
Sepsis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other[c]	1 (20)	0	0	1 (8.3)	0	0	0	0	0	0	0	0	0	0

- In the multiple-dose phase, 54 patients receiving cefiderocol±SOC and 13 patients receiving SOC only had cUTIs, and 38 and 8 patients had confirmed Gram-negative infection, respectively
  - Among patients with confirmed cUTI in the multiple-dose phase, *Escherichia* was the predominant pathogen, identified in 24 (63.2%) patients in the cefiderocol±SOC group and 5 (62.5%) patients in the SOC-only group
  - *K. pneumoniae* and *P. aeruginosa* were the next most commonly isolated organisms in the cefiderocol±SOC arm, occurring in 4 (10.5%) and 3 (7.9%) patients, respectively. *P. aeruginosa* was also isolated in 3 (37.5%) patients in the SOC-only group
- Of the 5 patients with HABP/VABP, ABC complex was isolated in 2 patients (both in the cefiderocol±SOC arm). All isolated species demonstrated cefiderocol MICs ≤2 µg/mL

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Clinical Studies

Table 5. Patient Baseline Characteristics (Safety/ITT Population)[4]

	Single-Dose Phase				Multiple-Dose Phase									
	Cefiderocol+SOC				Cefiderocol±SOC					SOC Only				
	C2 (n=5)	C3 (n=2)	C4 (n=5)	Overall (N=12)	C1 (n=14)	C2 (n=14)	C3 (n=17)	C4 (n=14)	Overall (N=59)	C1 (n=3)	C2 (n=3)	C3 (n=4)	C4 (n=3)	Overall (N=13)
Age, median (min; max), years	9.7 (6.7; 11.6)	4.9 (4.9; 4.9)	0.4 (0.3; 0.9)	4.9 (0.3; 11.6)	15 (12.8; 17.7)	9.25 (6.5; 11.3)	3.8 (2.2; 5.8)	0.45 (0.3; 1.7)	5.8 (0.3; 17.7)	15 (14.7; 15.4)	6.8 (6.7; 11.3)	4.2 (3.3; 4.6)	0.6 (0.3; 0.7)	4.6 (0.3; 15.4)
Sex, male, n (%)	3 (60)	0	2 (40)	5 (41.7)	7 (50)	6 (42.9)	3 (17.6)	8 (57.1)	24 (40.7)	1 (33.3)	2 (66.7)	1 (25)	2 (66.7)	6 (46.2)
Body weight, n[a]	5	2	5	12	14	14	17	14	59	2	3	3	0	8
Body weight, median (min; max), kg	34.7 (18.9; 37.5)	26.9 (18.6; 35.1)	7 (6.8; 7.4)	18.8 (6.8; 37.5)	52.3 (16; 83.4)	25.8 (17.2; 48.3)	14.6 (9.4; 27)	7.1 (4.9; 12.7)	17.2 (4.9; 83.4)	57 (57; 57)	25.4 (19.9; 72.5)	15 (11.9; 15)	NA	22.7 (11.9; 72.5)
eGFR grading group, n (%), mL/min/1.73 m²														
≥120	1 (20)	0	1 (20)	2 (16.7)	4 (28.6)	3 (21.4)	8 (47.1)	3 (21.4)	18 (30.5)	0	1 (33.3)	1 (25)	0	2 (15.4)
90 to <120	2 (40)	0	2 (40)	4 (33.3)	5 (35.7)	7 (50)	5 (29.4)	4 (28.6)	21 (35.6)	0	1 (33.3)	2 (50)	1 (33.3)	4 (30.8)
60 to <90	2 (40)	2 (100)	2 (40)	6 (50)	3 (21.4)	2 (14.3)	4 (23.5)	5 (35.7)	14 (23.7)	2 (66.7)	1 (33.3)	0	1 (33.3)	4 (30.8)
30 to <60	0	0	0	0	2 (14.3)	1 (7.1)	0	2 (14.3)	5 (8.5)	0	0	0	0	0
15 to <30	0	0	0	0	0	1 (71.)	0	0	1 (1.7)	0	0	0	0	0
Missing	0	0	0	0	0	0	0	0	0	1 (33.3)	0	1 (25)	1 (33.3)	3 (23.1)
eGFR, n[b]	5	2	5	12	14	14	17	14	59	2	3	3	2	10
eGFR, median (min; max), mL/min/1.73 m²	101.3 (71.6; 171.7)	72.4 (67.5; 77.3)	94.6 (76.2; 146.3)	89.8 (67.5; 171.7)	96.55 (40.4; 469.3)	103.5 (27.3; 308.3)	101.6 (73.5; 165.2)	89 (40.2; 262.8)	97.8 (27.3; 469.3)	68.35 (64.2; 72.5)	108.8 (68; 135.1)	119.3 (97.3; 271.4)	84.2 (63.4; 105)	101.15 (63.4; 271.4)
Infection, n (%)														
cUTI	2 (40)	2 (100)	4 (80)	8 (66.7)	10 (71.4)	14 (100)	16 (94.1)	14 (100)	54 (91.5)	3 (100)	3 (100)	4 (100)	3 (100)	13 (100)
HABP/VABP	0	0	0	0	4 (28.6)	0	1 (5.9)	0	5 (8.5)	0	0	0	0	0
cIAI	1 (20)	0	0	1 (8.3)	0	0	0	0	0	0	0	0	0	0
BSI	1 (20)	0	1 (20)	2 (16.7)	0	0	0	0	0	0	0	0	0	0
Sepsis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other[c]	1 (20)	0	0	1 (8.3)	0	0	0	0	0	0	0	0	0	0

[a]Number of patients with body weight data available.
[b]Number of patients with eGFR data available.
[c]Patient had *P. aeruginosa* scalp infection.
Abbreviations: BSI, bloodstream infection; C, cohort; cIAI, complicated intra-abdominal infection; cUTI, complicated urinary tract infection; eGFR, estimated glomerular filtration rate; HABP, hospital-acquired bacterial pneumonia; ITT, intent-to-treat; max, maximum; min, minimum; NA, not available; SOC, standard of care; VABP, ventilator-associated bacterial pneumonia.
Table adapted from Roilides et al. ESCMID. 2026.

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Clinical Studies

The APEKS-PEDI Study (Cont.)

Results[4]

Cefiderocol Treatment Exposure and PK Data[4]

- All patients (n=12) received 1 dose of cefiderocol in the single-dose phase, while most patients received cefiderocol±SOC for 5–14 days in the multiple-dose phase – see **Table 6**
- During the multiple-dose phase, 56 patients received cefiderocol+SOC antibiotics, while only 3 patients received cefiderocol as monotherapy
- In the single-dose phase, geometric mean peak cefiderocol concentrations (at end of the 3-h infusion) were 76, 341, and 87.1 µg/mL in Cohorts 2 (n=4), 3 (n=1), and 4 (n=4), respectively – see **Table 7**
  - At 8 h (ie, end of dosing period), trough cefiderocol concentrations ranged from 6.6–14 µg/mL across the 3 cohorts
- In the multiple-dose phase (n=58), peak geometric mean concentrations at the end of the 3-h infusion ranged from 84.4 to 108 µg/mL across cohorts, with corresponding trough levels at 8 h between 10.6 and 16.2 µg/mL – see **Table 7**
- As a result, total plasma trough cefiderocol concentrations remained >4 µg/mL (ie, above the CLSI susceptibility breakpoint for Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp.) and >2 µg/mL (ie, above the EUCAST susceptibility breakpoint for Enterobacterales and *P. aeruginosa*) for the entire dosing period across all age cohorts

Table 6. Exposure to and Compliance with Cefiderocol Treatment (Safety Population)[4]

	Single-Dose Phase Cefiderocol+SOC				Multiple-Dose Phase Cefiderocol+SOC				
	C2 (n=5) n (%)	C3 (n=2)[b] n (%)	C4 (n=5) n (%)	Overall (N=12)	C1 (n=14) n (%)	C2 (n=14) n (%)	C3 (n=17) n (%)	C4 (n=15) n (%)	Overall (N=59) n (%)
Extent of exposure, days[a]									
Median (range)	1 (1–1)	1 (1–1)				(5–14)	7 (1–13)	5.5 (2–13)	8 (1–19)
Extent of exposure, days, categorical, n (%)									
1	5 (100)	2 (100)				0	1 (5.9)	0	1 (1.7)
2–4	0	0				0	2 (11.8)	6 (42.9)	10 (16.9)
5–14	0	0	0			14 (100)	14 (82.4)	8 (57.1)	46 (78)
>14–21	0	0	0		2 (14.3)	0	0	0	2 (3.4)
>21	0	0	0	0	0	0	0	0	0
Total number of doses received									
Median (range)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	30 (10–57)	27 (15–40)	21 (1–38)	16.5 (6–37)	24 (1–57)

Table 7. Cefiderocol PK in the Single- and Multiple Dose Phases (PKCS Population)[4]

Day 1	Total Cefiderocol Concentration (µg/mL) Geometric Mean (Geometric CV %) Single-Dose Phase				
Time after start of infusion	C1	C2[a] (n=4)	C3[b] (n=2)	C4[b] (n=5)	Overall (N=11)
1 h	N/A	60.4 (38.5) [n=4]	N/A	N/A	60.4 (38.5) [n=4]
3 h (end of infusion)	N/A		[n=1][c]	87.1 (9.6) [n=4]	95.4 (52.7) [n=9]
3.5 h	N/A			N/A	53.4 (16) [n=4]
5 h	N/A			35.7 (19.4) [n=5]	35 (35.4) [n=10]
8 h (end of dosing period)	N/A			10.4 (23.3) [n=5]	9.3 (44.6) [n=11]
Day 3 or 4					
Time after start of infusion	C1[a] (N=14)			C4[b] (N=14)	Overall (N=58)
1 h	50.2 (74.4) [n=14]			N/A	52.3 (81.9) [n=28]
3 h (end of infusion)	85.2 (25) [n=13]	108 (45.9) [n=4]	84.4 (24.5) [n=14]	93.6 (27.5) [n=9]	92.2 (32.7) [n=49]
3.5 h	65.4 (35.4) [n=14]	77.2 (33.1) [n=14]	N/A	N/A	71 (34.8) [n=28]
5 h	31.8 (44.9) [n=14]	34.8 (56.5) [n=14]	36.8 (53.3) [n=16]	37.8 (50.1) [n=14]	35.3 (50.4) [n=58]
8 h (end of dosing period)	13.6 (73.1) [n=10]	15.6 (148) [n=12]	10.6 (84) [n=16]	16.2 (48.4) [n=13]	13.6 (88.2) [n=51]

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Clinical Studies

Table 6. Exposure to and Compliance with Cefiderocol Treatment (Safety Population)[4]

	Single-Dose Phase Cefiderocol+SOC				Multiple-Dose Phase Cefiderocol±SOC				
	C2 (n=5) n (%)	C3 (n=2)[b] n (%)	C4 (n=5) n (%)	Overall (N=12) n (%)	C1 (n=14) n (%)	C2 (n=14) n (%)	C3 (n=17) n (%)	C4 (n=15) n (%)	Overall (N=59) n (%)
Extent of exposure, days[a]									
Median (range)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	10 (4–19)	9 (5–14)	7 (1–13)	5.5 (2–13)	8 (1–19)
Extent of exposure, days, categorical, n (%)									
1	5 (100)	2 (100)	5 (100)	12 (100)	0	0	1 (5.9)	0	1 (1.7)
2–4	0	0	0	0	2 (14.3)	0	2 (11.8)	6 (42.9)	10 (16.9)
5–14	0	0	0	0	10 (71.4)	14 (100)	14 (82.4)	8 (57.1)	46 (78)
>14–21	0	0	0	0	2 (14.3)	0	0	0	2 (3.4)
>21	0	0	0	0	0	0	0	0	0
Total number of doses received									
Median (range)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	30 (10–57)	27 (15–40)	21 (1–38)	16.5 (6–37)	24 (1–57)

Abbreviations: C, cohort; SOC, standard of care.
[a]Extent of exposure to study drug (days) = round up to an integer of (the stop date and time (HH:MM) of the last dose – the start date and time (HH:MM) of the first dose / [60×60×24]).
[b]Both patients in the single-dose phase in C3 had dosing errors.
Table adapted from Roilides et al. ESCMID. 2026.

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Clinical Studies

Table 7. Cefiderocol PK in the Single- and Multiple Dose Phases (PKCS Population)[4]

Day 1	Total Cefiderocol Concentration (µg/mL) Geometric Mean (Geometric CV %) Single-Dose Phase				
Time after start of infusion	C1	C2[a] (n=4)	C3[b] (n=2)	C4[b] (n=5)	Overall (N=11)
1 h	N/A	60.4 (38.5) [n=4]	N/A	N/A	60.4 (38.5) [n=4]
3 h (end of infusion)	N/A	76 (14.9) [n=4]	341 (–) [n=1][c]	87.1 (9.6) [n=4]	95.4 (52.7) [n=9]
3.5 h	N/A	53.4 (16) [n=4]	N/A	N/A	53.4 (16) [n=4]
5 h	N/A	27.2 (32.6) [n=3]	48.5 (60.1) [n=2]	35.7 (19.4) [n=5]	35 (35.4) [n=10]
8 h (end of dosing period)	N/A	6.6 (25.7) [n=4]	14 (83.3) [n=2]	10.4 (23.3) [n=5]	9.3 (44.6) [n=11]
Day 3 or 4	**Multiple-Dose Phase**				
Time after start of infusion	C1[a] (N=14)	C2[a] (N=14)	C3[b] (N=16)	C4[b] (N=14)	Overall (N=58)
1 h	50.2 (74.4) [n=14]	54.5 (92.9) [n=14]	N/A	N/A	52.3 (81.9) [n=28]
3 h (end of infusion)	85.2 (25) [n=13]	108 (45.8) [n=13]	84.4 (24.5) [n=14]	93.6 (27.5) [n=9]	92.2 (32.7) [n=49]
3.5 h	65.4 (35.4) [n=14]	77.2 (33.1) [n=14]	N/A	N/A	71 (34.8) [n=28]
5 h	31.8 (44.9) [n=14]	34.8 (56.5) [n=14]	36.8 (53.3) [n=16]	37.8 (50.1) [n=14]	35.3 (50.4) [n=58]
8 h (end of dosing period)	13.6 (73.1) [n=10]	15.6 (148) [n=12]	10.6 (84) [n=16]	16.2 (48.4) [n=13]	13.6 (88.2) [n=51]

Abbreviations: C, cohort; CV, coefficient of variance of the geometric mean; N/A, not applicable; N, number of patients in the PKCS population; n, number of non-missing concentrations for analysis of geometric mean and geometric CV %; PKCS, pharmacokinetic concentration summary.
[a]Blood samples were collected at 5 timepoints in Cohort 2 in the single-dose phase, and in Cohorts 1 and 2 in the multiple-dose phase.
[b]Blood samples were collected at 3 timepoints in both Cohorts 3 and 4 in the single-dose phase and the multiple-dose phase.
[c]The patient had an overdose of 2106 g cefiderocol (major protocol deviation).
Table adapted from Roilides et al. ESCMID. 2026.

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Clinical Studies

The APEKS-PEDI Study (Cont.)

Safety[4]

- In the single-dose phase, 5 (41.7%) patients experienced 20 TEAEs
  - Minor treatment-related TEAEs occurred in 3 patients
  - No deaths, SAEs, or discontinuations due to TEAEs were observed
- In the multiple-dose phase, 44 (74.6%) of 59 patients who received cefiderocol±SOC antibiotics experienced a total of 221 TEAEs, while 8 (61.5%) of 13 patients who received SOC alone experienced a total of 38 TEAEs
  - 1 (1.7%) patient treated with cefiderocol±SOC experienced 2 treatment-related TEAEs (thrombocytosis and transaminases increased)
  - No treatment-related SAEs were reported
  - 2 (3.4%) patients who received cefiderocol±SOC experienced 3 TEAEs leading to withdrawal of cefiderocol
    - 1 (1.7%) patient had 2 events considered treatment-related (thrombocytosis and transaminases increased), and 1 (1.7%) patient experienced unrelated electrolyte imbalance leading to withdrawal of cefiderocol±SOC
- No patients in the SOC-only group discontinued treatment as a result of TEAEs

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Clinical Studies

The NEO-CEFI Study

The NEO-CEFI study (NCT06086626) was a multicenter, single-arm, open-label, Phase 2 study conducted at 7 sites across South Africa (n=3 sites), the US (n=1 site), Israel (n=1 site), Vietnam (n=1 site), and Taiwan (n=1 site). The study assessed the PK, safety, and tolerability of cefiderocol in hospitalized neonates and infants from birth to <3 months of age who had suspected or confirmed aerobic Gram-negative bacterial infections requiring systemic IV antibiotic treatment for an expected 5–14 days.[5]

Study Design[5]

- Eligible patients included hospitalized infants from birth to <3 months of age (including premature infants with GA ≥26 weeks and body weight ≥1 kg) who required systemic IV antibiotic treatment for suspected or confirmed Gram-negative infections, including but not limited to cUTI, cIAI, HABP/VABP, and BSI/sepsis
- Patients were stratified into 6 subgroups based on GA and PNA (chronological age):
  - Subgroup 1: GA ≥37 weeks and PNA 28 days to <3 months
  - Subgroup 2: GA ≥37 weeks and PNA 0 to <28 days
  - Subgroup 3: GA ≥32 to 36 weeks and PNA ≥14 days
  - Subgroup 4: GA ≥32 to 36 weeks and PNA <14 days
  - Subgroup 5: GA ≥26 to <32 weeks and PNA ≥14 days
  - Subgroup 6: GA ≥26 to <32 weeks and PNA <14 days
- In the single-dose phase, patients received a single dose of cefiderocol administered as a 3 h IV infusion while concurrently receiving SOC antibiotics
- In the multiple-dose phase, cefiderocol was administered q8h (as a 1 h or 3 h IV infusion) for an expected 5–14 days, initiated within 72 h of the start of SOC antibiotic therapy
- Blood samples for plasma cefiderocol concentrations were collected at prespecified time points (3 h and 8 h after the start of infusion)
- Safety was evaluated with TEAEs captured from the time of informed consent through the EOS (follow-up) visit (28 [±7] days after the last dose of cefiderocol)

Dosing[5]

- Cefiderocol doses were determined by body weight, GA, and PNA – see Table 8

Table 8. Dosing Recommendations by PNA (Chronological) and GA[5]

PNA (Chronological)		GA <32 weeks
Birth to <2 months		30 mg/kg
2 to <3 months		40 mg/kg

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Clinical Studies

Table 8. Dosing Recommendations by PNA (Chronological) and GA[5]

PNA (Chronological)	GA ≥32 weeks	GA <32 weeks
Birth to <2 months	40 mg/kg	30 mg/kg
2 to <3 months	60 mg/kg	40 mg/kg

Note: In the single-dose phase, cefiderocol was infused IV over 3 h. In the multiple-dose phase, cefiderocol was infused IV over 1 or 3 h q8h for an expected 5–14 days. Shorter infusion times were permitted in the multiple-dose phase if agreed upon by the sponsor and deemed in the best interest of the patient.
Abbreviations: GA, gestational age; h, hours; IV, intravenously; PNA, postnatal age; q8h, every 8 hours.

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Clinical Studies

The NEO-CEFI Study (Cont.)

Results[5]

Patient Baseline Characteristics[5]

- A total of 30 patients were enrolled: 12 in the single-dose phase and 18 in the multiple-dose phase
- In the single-dose phase, the median GA was 31.5 weeks (range: 26–41 weeks) and the median PNA was 16.5 days (range: 4–60 days), with 58.3% of participants being male
- In the multiple-dose phase, the median GA was 33 weeks (range: 28–41 weeks) and the median PNA was 5.5 days (range: 2–25 days), with 50% of participants being male
- Infection types at baseline in the single-dose phase included cIAI (33.3%), sepsis (16.7%), HABP/VABP (16.7%), and other infections (33.3%; including UTI and hospital-acquired IAI)
- In the multiple-dose phase, baseline infection types were HABP/VABP (22.2%), BSI (16.7%), sepsis (11.1%), and other infections (50%; including congenital pneumonia, gastrointestinal infection, neonatal early onset sepsis, and hospital-acquired IAI)

Cefiderocol Treatment Exposure and PK Data[5]

- All 12 patients in the single-dose phase received and completed treatment with cefiderocol
- In the multiple-dose phase, the median duration of cefiderocol exposure was 6 days (range: 2–13 days). Approximately 28% of patients received 5 to <15 infusions, while ~72% received ≥15 infusions
  - Of 18 patients, 12 (66.7%) completed treatment
  - Reasons for discontinuation included recovery from infection (16.7%), investigator decision (11.1%), and AEs (5.6%)
- In the single-dose phase (n=11), geometric mean cefiderocol concentrations at the end of the 3 h infusion ranged from 35.5 to 66.9 µg/mL across 5 subgroups. At 8 h after the start of infusion, corresponding trough concentrations ranged from 12.6 to 28.2 µg/mL – see **Table 9**
- In the multiple-dose phase (n=18), geometric mean concentrations at the end of infusion and at 8 h were 59 to 128 µg/mL and 7.95 to 27.7 µg/mL, respectively, with a 1 h infusion (4 subgroups), and 70.3 to 129 µg/mL and 34.1 to 47 µg/mL, respectively, with a 3 h infusion (3 subgroups) – see **Table 9**
- Across all age subgroups, geometric mean plasma concentrations were ≥8 µg/mL regardless of infusion duration

Table 9. Summary of Plasma Cefiderocol Concentration by Timepoint and Infusion Duration (Single-Dose and Multiple-Dose Phases – PKCS Population)[5]

	Total Cefiderocol Concentration (µg/mL) / Geometric Mean (Geometric CV %)						
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4	Subgroup 5	Subgroup 6	Overall
Single-dose phase							
3 h infusion duration	**N=1**	**N=2**	**N=3**	**N=0**	**N=3**	**N=3**	**N=12**
3 h (end of infusion)							
N	1	1	3	0	3	3	11
Geometric mean (geometric CV %)	61.9 (N/A)	47.8 (N/A)	48.1 (8)	N/A	66.9 (15.5)	35.5 (24.5)	49.5 (29.5)
8 h (after infusion)							
N	1	2	3	0	2	3	11
n	1	2	3	N/A	2	3	11
Geometric mean (geometric CV %)	12.6 (N/A)	15.6 (0.2)	13.4 (16.4)	N/A	28.2 (33.4)	15.3 (44)	16.3 (37.5)
Multiple-dose phase							
1 h infusion duration	**N=0**	**N=6**			**N=2**	**N=4**	**N=18**
End of infusion							
N	0	3			2	2	9
Geometric mean (geometric CV %)	N/A	113.3			59 (22.3)	128.2 (110.8)	94.7 (47.7)
8 h (after infusion)							
N	0				2	2	10
Geometric mean (geometric CV %)	N/A	27.7			8 (41.5)	19.8 (21.2)	19.8 (56.8)
CSF timepoint							
N	0	1			0	0	2
n	N/A	2			0	0	3
Geometric mean (geometric CV %)	N/A	50.6 (2.6)		(N/A)	N/A	N/A	24.7 (192.2)
Multiple-dose phase							
3 h infusion duration	**N=0**	**N=6**	**N=1**	**N=5**	**N=2**	**N=4**	**N=18**
End of infusion							
N	0	2	0	2	0	2	6
Geometric mean (geometric CV %)	N/A	129.1 (185.2)	N/A	76.7 (128.9)	N/A	70.3 (25.7)	88.6 (89.9)
8 h (after infusion)							
N	0	3	0	2	0	2	7
Geometric mean (geometric CV %)	N/A	47 (112.3)	N/A	43.1 (280.9)	N/A	34.1 (37.2)	41.8 (98.6)

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Clinical Studies

Table 9. Summary of Plasma Cefiderocol Concentration by Timepoint and Infusion Duration (Single-Dose and Multiple-Dose Phases – PKCS Population)[5]

	Total Cefiderocol Concentration (µg/mL) / Geometric Mean (Geometric CV %)						
	Subgroup 1	Subgroup 2	Subgroup 3	Subgroup 4	Subgroup 5	Subgroup 6	Overall
Single-dose phase							
3 h infusion duration	**N=1**	**N=2**	**N=3**	**N=0**	**N=3**	**N=3**	**N=12**
3 h (end of infusion)							
N	1	1	3	0	3	3	11
Geometric mean (geometric CV %)	61.9 (N/A)	47.8 (N/A)	48.1 (8)	N/A	66.9 (15.5)	35.5 (24.5)	49.5 (29.5)
8 h (after infusion)							
N	1	2	3	0	2	3	11
n	1	2	3	N/A	2	3	11
Geometric mean (geometric CV %)	12.6 (N/A)	15.6 (0.2)	13.4 (16.4)	N/A	28.2 (33.4)	15.3 (44)	16.3 (37.5)
Multiple-dose phase							
1 h infusion duration	**N=0**	**N=6**	**N=1**	**N=5**	**N=2**	**N=4**	**N=18**
End of infusion							
N	0	3	0	2	2	2	9
Geometric mean (geometric CV %)	N/A	113.3 (14.5)	N/A	85.8 (0.3)	59 (22.3)	128.2 (110.8)	94.7 (47.7)
8 h (after infusion)							
N	0	3	0	3	2	2	10
Geometric mean (geometric CV %)	N/A	27.7 (14.2)	N/A	26 (16.7)	8 (41.5)	19.8 (21.2)	19.8 (56.8)
CSF timepoint							
N	0	1	0	1	0	0	2
n	N/A	2	0	1	0	0	3
Geometric mean (geometric CV %)	N/A	50.6 (2.6)	N/A	5.9 (N/A)	N/A	N/A	24.7 (192.2)
Multiple-dose phase							
3 h infusion duration	**N=0**	**N=6**	**N=1**	**N=5**	**N=2**	**N=4**	**N=18**
End of infusion							
N	0	2	0	2	0	2	6
Geometric mean (geometric CV %)	N/A	129.1 (185.2)	N/A	76.7 (128.9)	N/A	70.3 (25.7)	88.6 (89.9)
8 h (after infusion)							
N	0	3	0	2	0	2	7
Geometric mean (geometric CV %)	N/A	47 (112.3)	N/A	43.1 (280.9)	N/A	34.1 (37.2)	41.8 (98.6)

Subgroup 1: GA ≥37 weeks and PNA 28 days to <3 months; Subgroup 2: GA ≥37 weeks and PNA 0 to <28 days; Subgroup 3: GA ≥32 to 36 weeks and PNA ≥14 days; Subgroup 4: GA ≥32 to 36 weeks and PNA <14 days; Subgroup 5: GA ≥26 to <32 weeks and PNA ≥14 days; Subgroup 6: GA ≥26 to <32 weeks and PNA <14 days.
N is the number of participants with samples collected at each timepoint. n is the number of samples collected at each timepoint. Concentrations below the lower limit of quantitation were treated as 0 for calculations of mean, SD, CV (%), median, minimum, and maximum, and treated as missing for calculations of geometric mean and geometric CV (%).
Note: In the multiple-dose phase, plasma concentration data from 2 participants were deemed anomalous and excluded from the concentration summary. 1 participant's plasma concentrations at 3 h (end of infusion) and 8 h were 0.407 and 0.168 µg/mL, respectively, which were considerably lower than those of other participants in the same subgroup; no dosing deviations from the protocol-specified dose were identified. A second participant's plasma concentration at end of infusion was 986.514 µg/mL, which was considerably higher than those of other participants; however, the 8 h plasma concentration in this participant was comparable to those of other participants and was retained in the summary.
Abbreviations: CSF, cerebrospinal fluid; CV, coefficient of variation; GA, gestational age; N/A, not applicable; PKCS, pharmacokinetic concentration summary; PNA, postnatal age (chronological age); SD, standard deviation.

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Clinical Studies

The NEO-CEFI Study (Cont.)

Outcomes[5]

Clinical Outcomes (Multiple-Dose Phase; ITT Population)[5]

- EOT: clinical cure was achieved by 16 (88.9%) patients, with clinical failure in 1 (5.6%) patient and indeterminate outcomes in 1 (5.6%) patient
- TOC (7 [± 4] days after the EOT): clinical cure was achieved by 15 (83.3%) patients, clinical failure was observed in 1 (5.6%) patient, and 2 (11.1%) patients had indeterminate outcomes
- EOS (28 [±7] days after the last dose of cefiderocol): clinical cure was achieved by 3 (16.7%) patients, clinical failure was observed in 1 (5.6%) patient, and 14 (77.8%) patients had indeterminate outcomes – see **Table 10**
- Indeterminate outcomes included patients that were missing or lost to follow-up such that a determination of clinical cure/failure could not be made

Microbiological Outcomes (Multiple-Dose Phase; ITT Population)[5]

- EOT: microbiological eradication was achieved by 16 (88.9%) patients, with no persistence observed and indeterminate outcomes in 2 (11.1%) patients
- TOC (7 [± 4] days after the EOT): eradication was achieved by 15 (83.3%) patients, with no persistence and 3 (16.7%) indeterminate outcomes
- EOS (28 [±7] days after the last dose of cefiderocol): eradication was achieved by 3 (16.7%) patients, with no persistence and 15 (83.3%) indeterminate outcomes – see **Table 10**
- Indeterminate microbiological outcomes included patients that were missing or source specimen was unavailable for culture, and the patient's clinical outcome was assessed as indeterminate

Table 10. Summary of Clinical and Microbiological Outcomes by Timepoint (Multiple-Dose Phase; ITT Population)[5]

Timepoint Outcome	Sub group 1 (N=0)	Sub group 2 (N=6)	Sub group 3 (N=1)	Sub group 4 (N=5)	Sub group 5 (N=2)	Sub group 6 (N=4)	Overall [95% CI][a]
Clinical outcomes[b]							
EOT							
Clinical cure, n (%)	0	6 (100)	1 (100)	5 (100)	1 (50)	3 (75)	16 (88.9) [65.29; 98.62]
Clinical failure, n (%)	0	0	0	0	0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0	0	0	0	1 (50)	0	1 (5.6) [0.14; 27.29]
Posttreatment							
Clinical cure, n (%)	0	6 (100)			2 (100)	3 (75)	15 (83.3) [58.58; 96.42]
Clinical failure, n (%)	0	0			0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0				0	0	2 (11.1) [1.38; 34.71]
EOS							
Clinical cure, n (%)	0				0	0	3 (16.7) [3.58; 41.42]
Clinical failure, n (%)	0				0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0				(100)	3 (75)	14 (77.8) [52.36; 93.59]
Microbiological outcomes[c]							
EOT							
Eradication, n (%)	0	6 (			1 (50)	3 (75	16 (88.9) [65.29; 98.62]
Persistence, n (%)	0	0			0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	0		0	1 (50)	1 (25)	2 (11.1) [1.38; 34.71]
Posttreatment							
Eradication, n (%)	0	6 (100)	1 (100)	3 (60)	2 (100)	3 (75)	15 (83.3) [58.58; 96.42]
Persistence, n (%)	0	0	0	0	0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	0	0	2 (40)	0	1 (25)	3 (16.7) [3.58; 41.42]
EOS							
Eradication, n (%)	0	2 (33.3)	1 (100)	0	0	0	3 (16.7) [3.58; 41.42]
Persistence, n (%)	0	0	0	0	0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	4 (66.7)	0	5 (100)	2 (100)	4 (100)	15 (83.3) [58.58; 96.42]

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Clinical Studies

Table 10. Summary of Clinical and Microbiological Outcomes by Timepoint (Multiple-Dose Phase; ITT Population)[5]

Timepoint Outcome	Sub group 1 (N=0)	Sub group 2 (N=6)	Sub group 3 (N=1)	Sub group 4 (N=5)	Sub group 5 (N=2)	Sub group 6 (N=4)	Overall [95% CI][a]
Clinical outcomes[b]							
EOT							
Clinical cure, n (%)	0	6 (100)	1 (100)	5 (100)	1 (50)	3 (75)	16 (88.9) [65.29; 98.62]
Clinical failure, n (%)	0	0	0	0	0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0	0	0	0	1 (50)	0	1 (5.6) [0.14; 27.29]
Posttreatment							
Clinical cure, n (%)	0	6 (100)	1 (100)	3 (60)	2 (100)	3 (75)	15 (83.3) [58.58; 96.42]
Clinical failure, n (%)	0	0	0	0	0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0	0	0	2 (40)	0	0	2 (11.1) [1.38; 34.71]
EOS							
Clinical cure, n (%)	0	2 (33)	1 (100)	0	0	0	3 (16.7) [3.58; 41.42]
Clinical failure, n (%)	0	0	0	0	0	1 (25)	1 (5.6) [0.14; 27.29]
Indeterminate (LTFU), n (%)	0	4 (66.7)	0	5 (100)	2 (100)	3 (75)	14 (77.8) [52.36; 93.59]
Microbiological outcomes[c]							
EOT							
Eradication, n (%)	0	6 (100)	1 (100)	5 (100)	1 (50)	3 (75)	16 (88.9) [65.29; 98.62]
Persistence, n (%)	0	0	0	0	0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	0	0	0	1 (50)	1 (25)	2 (11.1) [1.38; 34.71]
Posttreatment							
Eradication, n (%)	0	6 (100)	1 (100)	3 (60)	2 (100)	3 (75)	15 (83.3) [58.58; 96.42]
Persistence, n (%)	0	0	0	0	0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	0	0	2 (40)	0	1 (25)	3 (16.7) [3.58; 41.42]
EOS							
Eradication, n (%)	0	2 (33.3)	1 (100)	0	0	0	3 (16.7) [3.58; 41.42]
Persistence, n (%)	0	0	0	0	0	0	0 (0) [0; 18.53]
Indeterminate, n (%)	0	4 (66.7)	0	5 (100)	2 (100)	4 (100)	15 (83.3) [58.58; 96.42]

Subgroup 1: GA ≥37 weeks and PNA 28 days to <3 months; Subgroup 2: GA ≥37 weeks and PNA 0 to <28 days; Subgroup 3: GA ≥32 to 36 weeks and PNA≥14 days; Subgroup 4: GA ≥32 to 36 weeks and PNA <14 days; Subgroup 5: GA ≥26 to <32 weeks and PNA ≥14 days; Subgroup 6: GA ≥26 to <32 weeks and PNA <14 days.
Abbreviations: CI, confidence interval; EOS, end of study; EOT, end of treatment; GA, gestational age; LTFU, lost to follow-up; PNA, postnatal age.
[a]The 95% CI was calculated using the Clopper-Pearson method; [b]*Clinical Cure*: Participants who improved ≥1 baseline sign with no new or worsening signs of infection, but had insufficient improvement to allow switch to oral therapy (standard-of-care); *Clinical Failure*: No apparent response to therapy; persistence or worsening of baseline signs or reappearance of signs; development of new signs requiring antibiotic therapy other than, or in addition to, study treatment therapy; or death; *Indeterminate (Clinical)*: Missing or lost to follow-up such that a determination of clinical cure/failure could not be made; [c]*Eradication*: All baseline Gram-negative pathogens eradicated or presumed eradicated. If it was not possible to obtain an appropriate clinical culture and the participant had a successful clinical outcome, the response was presumed to be eradication. In the presence of colonizing Gram-negative pathogens and the participant had a successful clinical outcome, the response was presumed to be eradication; *Persistence*: Any baseline Gram-negative pathogen with persistence, presumed persistence, or persistence with increasing minimum inhibitory concentration; *Indeterminate (Microbiological)*: Missing or source specimen unavailable for culture and the participant's clinical outcome was assessed as indeterminate.

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Clinical Studies

The NEO-CEFI Study (Cont.)

Safety[5]

- In the single-dose phase (N=12), 5 (41.7%) patients experienced ≥1 TEAE
  - 2 (16.7%) patients experienced serious TEAEs
  - No treatment-related AEs, treatment-related SAEs, or TEAEs leading to discontinuation of cefiderocol were reported
  - 1 (8.3%) patient experienced Grade 4 multiple organ dysfunction syndrome and Grade 5 sepsis (both considered unrelated to study intervention), resulting in death on Day 39 of the study
- In the multiple-dose phase (N=18), 16 (88.9%) patients experienced at least 1 TEAE
  - 5 (27.8%) patients experienced serious TEAEs
  - Treatment-related AEs were reported in 2 (11.1%) patients (leukopenia and oral candidiasis, 1 patient each)
  - No treatment-related SAEs, TEAEs leading to study discontinuation, or TEAEs leading to death were reported
  - 1 (5.6%) patient discontinued cefiderocol due to a TEAE (candida infection, considered unrelated to cefiderocol)
- No all-cause mortality was observed through Day 28 in either phase

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Real-World Data: Case Series

Mantsiou et al (2026) published the combination of a multicenter case series plus a systematic review of previously published case reports/series of cefiderocol use in pediatric patients for the treatment of Gram-negative bacterial infections.[6]

- The case series was a retrospective, observational, multicenter study across 3 hospitals in Greece, involving all neonatal and pediatric patients (<18 years old) who received ≥1 dose of cefiderocol for the treatment of suspected or confirmed infections due to Gram-negative bacteria
  - Clinical response was defined by resolution of fever and/or other signs and symptoms of infection, while laboratory response was defined by the minimum time required for a reduction in CRP of ≥50%
- The systematic literature review element involved a search of articles published between 2015 and June 2025, and cases were included if patients were ≤18 years of age and sufficient clinical, laboratory and microbiological data were available

Results[6]

Case Series:

- Between February 2023 and August 2025, 21 courses of IV cefiderocol were administered to a total of 15 pediatric patients – 5 infants (>3 months of age); 6 children, and 4 adolescents (median age: 65 months [range: 4–183])
- Cefiderocol was used as a salvage therapy (due to prior treatment failure/limited options) in 38% of cases, or as empiric treatment (in high-risk patients with MDR pathogen colonization) in 62% of cases – see **Table 11**
  - Of 23 isolated pathogens, 4 were classified as MDR and 20 as XDR – 8 of which retained sensitivity to cefiderocol
  - Of those treated with cefiderocol as first-line therapy (n=13), MDR infection was detected in 9 cases
  - Cefiderocol was administered for proven/suspected BSIs (12 courses), UTIs (5 courses), HABP (2 courses) and hospital-acquired meningitis (2 courses)

Table 11. Multicenter Case Series: Cefiderocol Use, Outcomes, and AEs in Pediatric Patients[6]

Characteristic	Courses of Treatment (n=21)
Number of cefiderocol doses, median (range)	24 (4–88)
Cefiderocol dosage (mg/kg), median (range)	60 (24–70)
Indication to start cefiderocol, n (%)	
Prior treatment failure	8 (38)
First choice treatment	13 (62)
Prior administration of antibiotics, n (%)	15 (71)
Coadministration of antibiotics, n (%)	18 (86)
Clinical response, n (%)	17 (81)
Time-to-response (h), median (range)	72 (24–240)
Laboratory response, n/N' (%)	15/16 (93.8)
Time-to-response (h) , median (range)	72 (24–168)
Microbiologic clearance, n/N' (%)	7/9 (77.8)
Time-to-response (h) , median (range)	96 (72–264)
AEs	
Urine discoloration	5 (24)[a]
Outcome at Day 30, n (%)	
Discharged from hospital	14 (67)
Remains hospitalized	1 (5)
Transferred to another hospital	1 (5)
Death	5 (24)

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Real-World Data: Case Series

Table 11. Multicenter Case Series: Cefiderocol Use, Outcomes, and AEs in Pediatric Patients[6]

Characteristic	Courses of Treatment (n=21)
Number of cefiderocol doses, median (range)	24 (4–88)
Cefiderocol dosage (mg/kg), median (range)	60 (24–70)
Indication to start cefiderocol, n (%)	
Prior treatment failure	8 (38)
First choice treatment	13 (62)
Prior administration of antibiotics, n (%)	15 (71)
Coadministration of antibiotics, n (%)	18 (86)
Clinical response, n (%)	17 (81)
Time-to-response (h), median (range)	72 (24–240)
Laboratory response, n/N' (%)	15/16 (93.8)
Time-to-response (h) , median (range)	72 (24–168)
Microbiologic clearance, n/N' (%)	7/9 (77.8)
Time-to-response (h) , median (range)	96 (72–264)
AEs	
Urine discoloration	5 (24)[a]
Outcome at Day 30, n (%)	
Discharged from hospital	14 (67)
Remains hospitalized	1 (5)
Transferred to another hospital	1 (5)
Death	5 (24)

N'=number of patients with available information.
Abbreviations: AE, adverse event; h, hours.
[a]1 patient had the AE on 4 occasions.
Table adapted from Mantsiou et al. *Pediatr Infect Dis J*. 2026.

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Real-World Data: Case Series

Results (Cont.)[6]

Case Series (Cont.):

- The median dose of cefiderocol was 60 mg/kg (range: 24–70 mg/kg), while the median treatment duration was 8 days (range: 2–30 days; 4–88 doses)
- Clinical response was achieved in 10 (76.2%) patients (16 of 21 courses) with a median time to clinical response of 72 h (range: 24–240)
  - The remaining 5 patients died, but none of these deaths were associated with cefiderocol administration or treatment failure (as assessed by the investigator)
- Laboratory response (defined as ≥50% CRP reduction) was achieved in 15/16 (93.8%) courses within a median of 72 h (range: 24–240), while CRP values normalized within a median of 9.5 days
  - Of the 9 patients with available data, microbiologic clearance was achieved in 7 (77.8%) patients within a median of 84 h (range: 72–264)
- Grade 1 chromaturia occurred following 5 treatment courses (4 in the same patient), appearing within 24 hours of cefiderocol initiation and all resolving quickly after ending therapy
- No pediatric patients discontinued treatment due to AEs

Systematic Literature Review:

- Out of the 243 reports identified, 17 were included describing 32 pediatric patients receiving 37 courses of cefiderocol (many of which are also summarized individually in **Table 12**)
  - 3 patients received 2 courses, and 1 patient received 3 courses
- Cefiderocol was most commonly utilized for BSIs (35.1%) and febrile neutropenia in pediatric oncology patients with previous MDR colonization (18.9%)
  - Treatment of pneumonia accounted for 9 (24.3%) courses of cefiderocol (including 3 HABP and 2 VABP cases)
  - 6 (16.2%) courses of cefiderocol were administered for pulmonary exacerbations in children with CF
- Dosing of cefiderocol ranged from 30–100 mg/kg (usually 60 mg/kg), with dosing intervals of 6 or 8 h, often administered as extended infusions over 3 h
- The median duration of treatment was 12 days (range: 1–98 days)
- Cefiderocol was initiated a median of 7 days (range: 3–26) after previous antibiotic therapy for the index indication out of 13 courses in which prior antimicrobial treatment duration had been reported
  - Cefiderocol was administered as initial empiric monotherapy, without prior or concomitant antibiotics, in 2 courses
- Cefiderocol was administered in combination with other antimicrobials in 28 (75.7%) courses of treatment
- In the majority of cases, clinical effectiveness was reported following cefiderocol treatment (although, due to heterogeneity of outcomes, data were inconsistently provided)
  - Clinical response occurred in all 5 instances of cefiderocol use for the treatment of either VABP or HABP
- Among the 37 cefiderocol treatment courses, no safety data were provided in 18 cases (48.6%). Of the remaining 19 courses, 15 (78.9%) reported no AEs
  - AEs included chromaturia (n=3) and transient leukopenia (n=1)
  - No treatment discontinuations occurred as a result of drug-related toxicity

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Real-World Data: Case Series

Schmid et al (2024) described a retrospective case series review, involving the real-world use of cefiderocol in the treatment of pediatric patients with infection or colonization with MDR Gram-negative bacteria at the Great Ormond Street Hospital (GOSH) in the UK (between January 2021 and February 2023). A standard dose of cefiderocol was considered to be 60 mg/kg q8h infused over 3 h, capped at a maximum of 2 g/dose.[7]

- Clinical response was defined as resolution/significant improvement in symptoms (based on chart review including clinical/biochemical parameters, including CRP)

Results[7]

- In total, 18 courses of cefiderocol were administered to 14 pediatric patients (age range: 0.6–15.8 years, 33% female)
- 56% of patients were immunocompromised at cefiderocol initiation, and 33% were admitted to the ICU
- 10 courses in 9 patients represented serious or invasive infections with MDR Gram-negative bacteria, including *S. maltophilia* (n=6), *A. baumannii* (n=1), *P. aeruginosa* (n=1), *Pseudomonas putida* (n=1), and *K. pneumoniae* (n=1)
- Co-infection was almost universally present alongside the index pathogen, including *Pseudomonas* spp., *Enterococcus faecium*, coagulase-negative *Staphylococci* and fungi (all patients received co-administration of other antimicrobial agents)
- Infection sites were pulmonary (n=6), BSI (n=3), and SSSI (n=1), with the most frequent treatment indications being HABP (n=6), sepsis (n=4), and neutropenic fever (n=2)
- Median treatment duration for cefiderocol was 11 days (IQR: 7–14), with a favorable clinical response observed in 6 of the 10 cases
- In a further 8 episodes (across 6 patients), cefiderocol was administered either empirically or prophylactically, due to known MDR Gram-negative bacteria
- Overall, 30-day mortality was 12% – 1 death in both the infection group and colonization group, with both cases being attributed primarily to the underlying disease state
- Only 1 case of microbiological failure (persistently positive blood culture with *A. baumannii* at 96 h) and 1 case of recurrence (BSI due to *S. maltophilia* 27 days after previous bacteremia) was recorded
- Cefiderocol was generally well tolerated
  - 1 case of mild transaminitis (<5x ULN for serum ALT) and 1 case of chromaturia were recorded (neither AE leading to treatment discontinuation, and both resolving after the end of cefiderocol treatment)
  - 2 patients developed desquamating skin changes while receiving cefiderocol, both of which discontinued treatment early

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Real-World Data: Individual Case Reports

Use of cefiderocol in pediatric patients has been further described in various case studies and case reports (**Table 12**).[8–18]

- Patients ranged in age from 5 weeks to 17 years
- Treatment duration ranged from 7 to 42 days
- Cefiderocol was generally well-tolerated and was associated with positive clinical and microbiological outcomes
- Definitions and methods of reporting outcomes were not standardized and varied by study

Table 12. Individual Case Reports[8–18]

Case Author	Age, y/sex	Infection Type	Pathogen	Treatment	AEs	Patient Outcomes
Mori et al (2026)[8]	6/M	Inherited glycosylphosphatidylinositol deficiency and multiple relapsed B-cell ALL undergoing chemotherapy who developed persistent BSI	IMP-producing *K. pneumoniae* MIC=0.5 µg/mL Co-infection with MRSE managed with vancomycin, rifampin, and then daptomycin	**Cefiderocol:** 180 mg/kg/day for a total of 14 days Concomitant therapy: gentamicin (5 mg/kg/day) – discontinued after Day 8	None reported	Following cefiderocol discontinuation, several blood cultures remained negative for *K. pneumoniae* 10 days after completion of cefiderocol treatment, the patient died as a result of relapsed ALL
Trauth et al (2024)[9]	36 + 2-week gestational age/F	Preterm infant, delivered via secondary emergency caesarean section, who developed VAP	MDR *S. maltophilia* with secondary pathogen *Klebsiella oxytoca* Disc zone diameter of inhibition=29 mm^2	**Cefiderocol:** 100 mg/kg tid for 14 days Concomitant therapy: TMP/SMX (dose-escalated to 12 mg/kg bid) plus tigecycline (1.5 mg/kg bid)	None reported	Swabs and tracheal aspirates became sterile after 5 days of treatment Clinical and microbiological cure was achieved after 2 weeks of treatment By Day 70, patient was extubated, all antibiotic therapy was ceased, and there were no further serological or clinical signs of infection
Funiciello et al (2023)[10]	1 month/M	Meningoencephalitis	DTR VIM-producing *P. aeruginosa*	**Cefiderocol:** 60 mg/kg q8h (over 3 h) for 8 weeks	None reported	Complete microbiological response (negative CSF cultures at 8 weeks and 30 months after treatment) Progressive improvement in MRI images
Hsu et al (2023)[11]	5 weeks/M	Bacteremia BSI	*S. maltophilia*	**Cefiderocol:** 40 mg/kg q8h (over 1 h)	None reported	Clearance of *S. maltophilia* growth and resolution of BSI within 24 h Negative blood cultures 30 days post-treatment

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Real-World Data: Individual Case Reports

Table 12. Individual Case Reports (Cont.)[8–18]

Case Author	Age, y/sex	Infection Type	Pathogen	Treatment	AEs	Patient Outcomes
Koirala et al (2023)[12]	26 + 6-week gestational age/F	Recurrent apneas with associated abdominal distension leading to intubation and mechanical ventilation Increased gastric nonbilious aspirates	MDR *S. maltophilia* Disc zone diameter of inhibition=28 mm^2	**Cefiderocol:** 30 mg/kg q8h (over 1 h) for 10 days	Mild abdominal distension, controlled with short-course antibiotics No AEs related to cefiderocol treatment	Improvement in clinical condition Decreased need for oxygen and reduced ETT secretions after 48 h Successful extubation Hospital discharge
Mercadante et al (2023)[13]	8 months/F	VAP complicated by BSI	VIM-producing *P. aeruginosa* MIC=1 µg/mL	**Cefiderocol:** 60 mg/kg q8h (over 3 h) for 14 days CRRT support for severe acute kidney injury	None reported	Withdrawal of CRRT after 4 days of cefiderocol treatment and normalization of renal clearance Discharge from pediatric ICU Good clinical condition 3 months after discharge (VIM-producing *P. aeruginosa* in stool)
Monari et al (2023)[14]	Neonate, 31 weeks gestation + 1 day/F	BSI	VIM-producing *K. pneumoniae* MIC=0.125 mg/L	**Cefiderocol:** loading dose 60 mg/kg; maintenance dose 40 mg/kg q8h (over 3–4 h) for 9 days	None reported	Clinical improvement within 48 h Negative inflammatory markers within 5 days Negative blood cultures at follow up
Grasa et al (2021)[15]	2/F	Febrile neutropenia Pulmonary tuberculosis BSI	VIM-producing *P. aeruginosa* Disk zone diameter of inhibition=22 mm^2	**Cefiderocol:** 60 mg/kg q8h for 7 days Concomitant therapy: Teicoplanin	None reported	Improved clinical signs and symptoms within 48 h Increased neutrophil count to >500 cells/µL Hospital discharge
Warner et al (2021)[16]	17/NR	CF and bilateral orthotopic lung transplantation	*A. xylosoxidans* MIC=1 m/L	**Cefiderocol:** 60 mg/kg q8h for 42 days Concomitant therapy: Meropenem Trimethoprim-sulfamethoxazole Inhaled tobramycin	None reported	Improved clinical outcome at Day 30; patient discharged in good condition following BOLT Microbiological relapse with *A. xylosoxidans* occurred following treatment discontinuation

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Real-World Data: Individual Case Reports

Table 12. Individual Case Reports (Cont.)[8–18]

Case Author	Age, y/sex	Infection Type	Pathogen	Treatment	AEs	Patient Outcomes
Alamarat et al (2020)[17]	15/M	Chronic osteomyelitis of left femur, following surgery for fracture	XDR *P. aeruginosa* harboring NDM-1 MIC=4 µg/mL ESBL-producing *K. pneumoniae* MIC=0.5 µg/mL	**Cefiderocol:** 2 g q8h (over 3 h) for 14 weeks Concomitant therapy: Aztreonam Bone implant	Intermittent episodes of reduced WBC count, spontaneously resolved	Hospital discharge Apparent clinical cure Avoided amputation
Gainey et al (2020)[18]	10/F	CF with multiple acute pulmonary exacerbations with hospitalizations Sustained decline in FEV_1	XDR *Achromobacter* spp. PDR *Achromobacter* spp. MIC=32 µg/mL Prior to initial treatment, *A. xylosoxidans* MIC=32 µg/mL Prior to second treatment, *A. xylosoxidans* MIC=16 µg/mL *A. ruhlandii* MIC=1 µg/mL	Treatment course 1 **Cefiderocol:** 60 mg/kg/dose q8h Concomitant therapy: IV meropenem/vaborbactam Treatment course 2 **Cefiderocol:** 60 mg/kg/dose q8h (over 3 h) for 14 days Concomitant therapy: IV meropenem/vaborbactam 2 g q8h (over 3 h) and IV bacteriophages (Ax2CJ45Φ2)	None reported	Treatment course 1 Improved clinical outcome after 30 days of treatment Treatment course 2 FEV_1 increase from 33% to 60% on Day 12 of therapy Hospital discharge Microbiological eradication (no additional *Achromobacter* spp. infection at 8- or 16-weeks post-treatment) Further increase in FEV_1 to 65% after 8 weeks of therapy

Abbreviations: AE, adverse event; ALL, acute lymphoblastic leukemia; bid, twice a day; BOLT, bilateral orthotopic lung transplantation; BSI, bloodstream infection; CF, cystic fibrosis; CRRT, continuous renal replacement therapy; CSF, cerebrospinal fluid; DTR, difficult-to-treat resistant; ESBL, extended-spectrum β-lactamase; ETT, endotracheal tube; F, female; FEV1, forced expiratory volume in one second; h, hours; ICU, intensive care unit; IMP, imipenemase; IV, intravenous; M, male; MBL, metallo-β-lactamase; MDR, multidrug-resistant; MIC, minimum inhibitory concentration; MRI, magnetic resonance imaging; MRSE, methicillin-resistant Staphylococcus epidermidis; NDM-1, New Delhi metallo-β-lactamase-1; NR, not reported; PDR, pandrug-resistant; q8h, every 8 hours; tid, three times a day; TMP/SMX: trimethoprim–sulfamethoxazole; VAP, ventilator-associated pneumonia; VIM, Verona integron-encoded metallo-β-lactamase; WBC, white blood cell; XDR, extensively drug-resistant; y, years.

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Surveillance Studies

Nguyen et al (2024) evaluated the *in vitro* activity of cefiderocol and comparator agents against bacterial isolates from pediatric patients (0–17 years old) hospitalized with pneumonia between 2020 and 2022 as part of the SENTRY Antimicrobial Surveillance Program.[19]

- A total of 1389 isolates were collected (318 from Europe and 1071 from the US), that included Enterobacterales (N=608), *P. aeruginosa* (N=459), *S. maltophilia* (N=161), *Acinetobacter* spp. (N=124), as well as other species (N=37)
- MICs were determined according to CLSI guidelines using broth microdilution with ID-CAMHB, and evaluation of nonsusceptibility was interpreted according to 2023 CLSI, FDA, and EUCAST breakpoints
- Carb-NS isolate subsets were defined as being nonsusceptible to meropenem and imipenem

Results[19]

- Carb-NS was detected in all 161 (100%) *S. maltophilia* isolates, 48 *P. aeruginosa* and 13 *Acinetobacter* spp. isolates (10.5% each), and 2 (0.3%) Enterobacterales isolates
- The organism prevalence and the *in vitro* activity of cefiderocol against these isolates is shown in **Figure 1** and **Table 13**, respectively

Figure 1. Prevalence of the Various Organisms Isolated from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020–2022)[19]

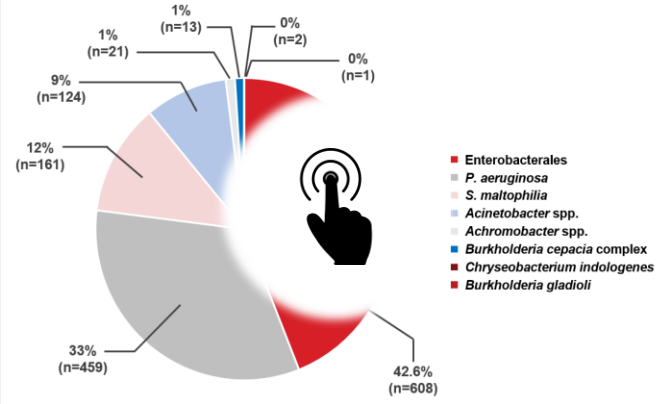
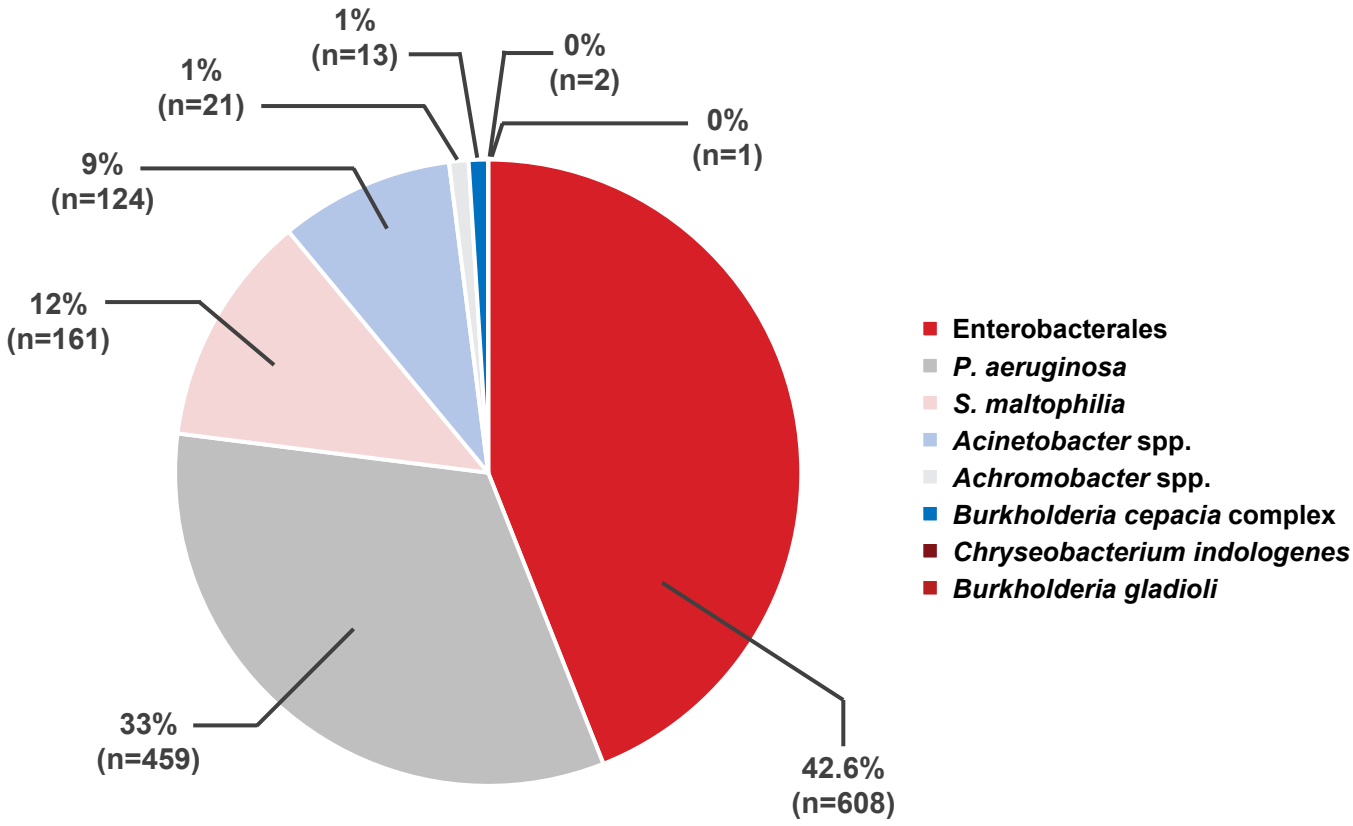


Table 13. *In Vitro* Activity of Cefiderocol and Comparator Agents against Isolates from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020–2022)[19]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
Enterobacterales (N=608)						
Cefiderocol	0.06	0.5	≤0.004 to 16	99.7	99.7	99.3
Meropenem	0.03	0.06	≤0.015 to >32	99.5	99.5	99.5
Imipenem–relebactam	0.12	0.5	0.06 to 4	97.7	97.7	99.3
Meropenem–vaborbactam	0.03	0.06	≤0.015 to 4	100	100	100
Ceftazidime–avibactam	0.12	[illegible]	[illegible] to >32	99.8	99.8	99.8
Ceftolozane–tazobactam	0.25	[illegible]	[illegible]	96.1	96.1	96.1
Carb-NS Enterobacterales (n=2)						
Cefiderocol	N			100	100	100
Imipenem–relebactam				0	0	0
Meropenem–vaborbactam				100	100	100
Ceftazidime–avibactam				50	50	50
Ceftolozane–tazobactam				50	50	50
***P. aeruginosa* (N=459)**						
Cefiderocol	0	[illegible]		99.8	98.9	99.8
Meropenem	0	[illegible]		86.9	86.9	86.9
Imipenem–relebactam	0.25	[illegible]		98.3	98.3	98.3
Meropenem–vaborbactam	0.5	[illegible]	[illegible]>8	NA	NA	95.8
Ceftazidime–avibactam	2	[illegible]	[illegible].12 to >32	98.7	98.7	98.7
Ceftolozane–tazobactam	0.5	1	≤0.12 to >16	98	98	98
Carb-NS *P. aeruginosa* (n=48)						
Cefiderocol	0.06	0.25	≤0.004 to 0.5	100	100	100
Imipenem–relebactam	1	4	0.12 to >16	83.3	83.3	83.3
Meropenem–vaborbactam	8	>8	2 to >8	NA	NA	60.4
Ceftazidime–avibactam	4	16	0.5 to >32	87.5	87.5	87.5
Ceftolozane–tazobactam	1	8	0.25 to >16	89.6	89.6	89.6

Surveillance Studies

Figure 1. Prevalence of the Various Organisms Isolated from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020−2022)[19]



Enterobacterales organisms include: *Citrobacter freundii* species complex (10), *C. koseri* (4), *Cronobacter sakazakii* (1), *Enterobacter asburiae* (2), *E. cloacae* (15), *E. cloacae* species complex (73), *E.* (88), *Klebsiella aerogenes* (26), *K. oxytoca* (67), *K. pneumoniae* (136), *K. variicola* (4), *Morganella morganii* (1), *Pantoea calida* (1), *P. piersonii* (1), *Pluralibacter gergoviae* (5), *Proteus mirabilis* (8), *P. vulgaris* group (1), *Providencia rettgeri* (3), *Raoultella ornithinolytica* (2), *Serratia liquefaciens* (5), *S. liquefaciens* complex (2), *S. marcescens* (150), unspeciated *Providencia* (1), unspeciated *Raoultella* (2).
Figure adapted from Nguyen et al. ESCMID. 2024.

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Surveillance Studies

Table 13. ***In Vitro*** **Activity of Cefiderocol and Comparator Agents against Isolates from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020–2022)**[19]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
Enterobacterales (N=608)						
Cefiderocol	0.06	0.5	≤0.004 to 16	99.7	99.7	99.3
Meropenem	0.03	0.06	≤0.015 to >32	99.5	99.5	99.5
Imipenem–relebactam	0.12	0.5	0.06 to 4	97.7	97.7	99.3
Meropenem–vaborbactam	0.03	0.06	≤0.015 to 4	100	100	100
Ceftazidime–avibactam	0.12	0.25	≤0.015 to >32	99.8	99.8	99.8
Ceftolozane–tazobactam	0.25	1	≤0.12 to >16	96.1	96.1	96.1
Carb-NS Enterobacterales (n=2)						
Cefiderocol	NA	NA	0.03 to 0.5	100	100	100
Imipenem–relebactam	NA	NA	4 to 4	0	0	0
Meropenem–vaborbactam	NA	NA	0.06 to 4	100	100	100
Ceftazidime–avibactam	NA	NA	0.25 to >32	50	50	50
Ceftolozane–tazobactam	NA	NA	0.5 to >16	50	50	50
P. aeruginosa **(N=459)**						
Cefiderocol	0.06	0.25	≤0.004 to 16	99.8	98.9	99.8
Meropenem	0.5	4	≤0.015 to >32	86.9	86.9	86.9
Imipenem–relebactam	0.25	1	≤0.03 to >16	98.3	98.3	98.3
Meropenem–vaborbactam	0.5	4	≤0.015 to >8	NA	NA	95.8
Ceftazidime–avibactam	2	4	≤0.12 to >32	98.7	98.7	98.7
Ceftolozane–tazobactam	0.5	1	≤0.12 to >16	98	98	98
Carb-NS *P. aeruginosa* **(n=48)**						
Cefiderocol	0.06	0.25	≤0.004 to 0.5	100	100	100
Imipenem–relebactam	1	4	0.12 to >16	83.3	83.3	83.3
Meropenem–vaborbactam	8	>8	2 to >8	NA	NA	60.4
Ceftazidime–avibactam	4	16	0.5 to >32	87.5	87.5	87.5
Ceftolozane–tazobactam	1	8	0.25 to >16	89.6	89.6	89.6

Abbreviations: Carb-NS, carbapenem nonsusceptible; CLSI, Clinical Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MIC, minimum inhibitory concentration; $MIC_{50/90}$, minimum inhibitory concentration required to inhibit the growth of 50% and 90% of organisms; NA, not applicable; S, susceptible.
[a]According to 2023 CLSI, FDA, and EUCAST breakpoints.
Table adapted from Nguyen et al. ESCMID. 2024.

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Table 13 (Cont.). ***In Vitro*** **Activity of Cefiderocol and Comparator Agents against Isolates from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020–2022)**[19]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
Acinetobacter **spp. (N=124)**						
Cefiderocol	0.06	1	0.015 to 8	98.4	96	98.4
Meropenem	0.5	8	0.06 to >32	87.9	87.9	87.9
Imipenem–relebactam	0.12	>8	≤0.03 to >8	NA	89.5	89.5
Ampicillin–sulbactam	2	32	≤0.5 to >64	83.1	83.1	NA
Colistin	0.5	2	0.12 to >8	NA	NA	94.4
Carb-NS ***Acinetobacter*** **spp. (n=13)**						
Cefiderocol	0.25	2	0.03 to 8	92.3	84.6	92.3
Imipenem–relebactam	>8	>8	>8 to >8	NA	0	0
Ampicillin–sulbactam	64	>64	4 to >64	15.4	15.4	NA
Colistin	0.5	>8	0.25 to >8	NA	NA	84.6
S. maltophilia **(all Carb-NS) (N=161)**						
Cefiderocol	0.06	0.25	0.008 to 1	100	NA	100
Levofloxacin	1	4	0.12 to >32	86.9	NA	NA
Trimethoprim–sulfamethoxazole	≤0.12	0.5	≤0.12 to >4	96.9	NA	NA
Minocycline	0.5	1	≤0.06 to 4	100	NA	NA

Abbreviations: Carb-NS, carbapenem nonsusceptible; CLSI, Clinical Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, US Food and Drug Administration; MIC, minimum inhibitory concentration; $MIC_{50/90}$, minimum inhibitory concentration required to inhibit the growth of 50% and 90% of organisms; NA, not applicable; S, susceptible.
[a]According to 2023 CLSI, FDA, and EUCAST breakpoints.
Table adapted from Nguyen et al. ESCMID. 2024.

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Surveillance Studies

Results (Cont.)[19]

- Most isolates were shown to be susceptible to cefiderocol (including Carb-NS isolates), with 99.5% and 99.6% of isolates having MIC values of ≤2 and ≤4 µg/mL, respectively – see **Figure 2**
- 95.2% and 100% of *Achromobacter* isolates had a MIC≤2 µg/mL and MIC ≤4 µg/mL, respectively, while 100% of *Burkholderia cepacia* complex isolates had a MIC≤4 µg/mL – see **Table 14**

Figure 2. MIC Distribution for Cefiderocol against Enterobacterales, *P. aeruginosa*, *Acinetobacter* spp., and *S. maltophilia* Isolates from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020−2022)[19]

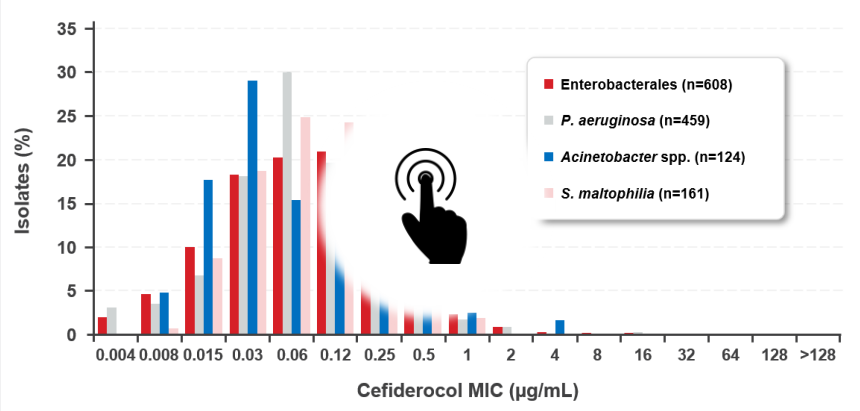


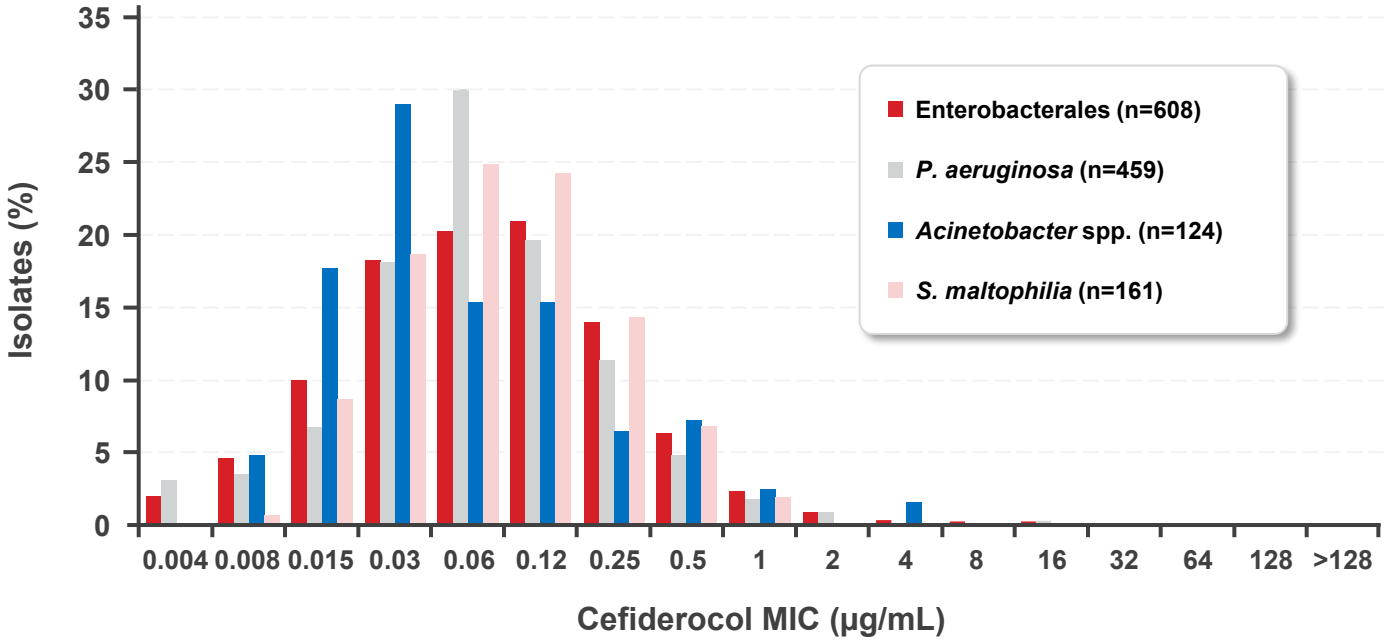
Table 14. *In Vitro* Activity of Cefiderocol and Comparator Agents against Pediatric Respiratory Isolates of *Burkholderia cepacia* complex and *Achromobacter* spp. from the SENTRY Antimicrobial Surveillance Program (2020−2022)[19]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)
***Burkholderia cepacia* complex (n=13)**			
Cefiderocol	0.06	0.25	≤0.004 to 0.5
Ceftazidime		8	1 to 8
Meropenem		4	0.25 to 4
Levofloxacin		32	0.5 to >32
Trimethoprim–sulfamethoxazole		>4	≤0.12 to >4
Minocycline		16	0.25 to 32
***Achromobacter* spp. (n=21)**			
Cefiderocol		0.25	0.008 to 4
Ceftazidime		16	2 to >32
Cefepime		>32	8 to >32
Meropenem	0.12	4	0.06 to >32
Ciprofloxacin	4	>4	1 to >4
Trimethoprim–sulfamethoxazole	≤0.12	1	≤0.12 to 2
Minocycline	1	2	0.5 to 4

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Surveillance Studies

Figure 2. MIC Distribution for Cefiderocol against Enterobacterales, *P. aeruginosa*, *Acinetobacter* spp., and *S. maltophilia* Isolates from Pediatric Patients Hospitalized with Pneumonia from the SENTRY Antimicrobial Surveillance Program (2020−2022)[19]



Abbreviation: MIC, minimum inhibitory concentration
Figure adapted from Nguyen et al. ESCMID. 2024.

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Surveillance Studies

Table 14. ***In Vitro*** **Activity of Cefiderocol and Comparator Agents against Pediatric Respiratory Isolates of** ***Burkholderia cepacia*** **complex and** ***Achromobacter*** **spp. from the SENTRY Antimicrobial Surveillance Program (2020−2022)**[19]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)
Burkholderia cepacia **complex (n=13)**			
Cefiderocol	0.06	0.25	≤0.004 to 0.5
Ceftazidime	4	8	1 to 8
Meropenem	2	4	0.25 to 4
Levofloxacin	2	32	0.5 to >32
Trimethoprim–sulfamethoxazole	1	>4	≤0.12 to >4
Minocycline	2	16	0.25 to 32
Achromobacter **spp. (n=21)**			
Cefiderocol	0.03	0.25	0.008 to 4
Ceftazidime	4	16	2 to >32
Cefepime	32	>32	8 to >32
Meropenem	0.12	4	0.06 to >32
Ciprofloxacin	4	>4	1 to >4
Trimethoprim–sulfamethoxazole	≤0.12	1	≤0.12 to 2
Minocycline	1	2	0.5 to 4

Abbreviations: MIC, minimum inhibitory concentration; MIC50/90, minimum inhibitory concentration required to inhibit the growth of 50% and 90% of organisms.
Table adapted from Nguyen et al. ESCMID. 2024.

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Surveillance Studies

In a separate analysis, **Nguyen et al (2023)** reported the *in vitro* activity of cefiderocol and comparator agents against bacterial isolates obtained from pediatric patients (0–17 years old) between 2020 and 2022 as part of the SENTRY Antimicrobial Surveillance Program. The study also examined cefiderocol activity against MDR isolate phenotypes, defined as resistant to >1 microbial agent in ≥3 antimicrobial categories, and against Carb-NS isolates, defined as nonsusceptible to imipenem and meropenem.[20]

- Isolates included Enterobacterales (N=2249), *P. aeruginosa* (N=707), ABC (N=194), and *S. maltophilia* (N=220)
- Evaluation of nonsusceptibility was interpreted according to 2023 CLSI, FDA, and EUCAST breakpoints

Results[20]

- Cefiderocol was highly active against all pediatric isolates of Enterobacterales, *P. aeruginosa*, ABC, and *S. maltophilia*, including against MDR and Carb-NS isolates – see **Figure 3**, **Figure 4**, and **Table 15**
- Susceptibility of MDR isolates of Enterobacterales and *P. aeruginosa* to cefiderocol was 96.3% and 98.4%, respectively

Figure 3. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested Against Resistant Phenotypic Subsets of Enterobacterales[20]

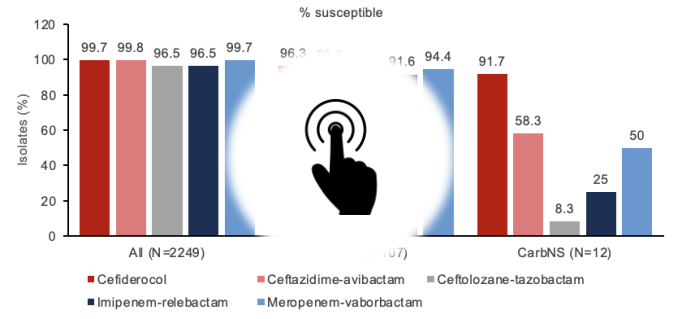


Figure 4. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested against Resistant Phenotypic Subsets of *P. aeruginosa*[20]

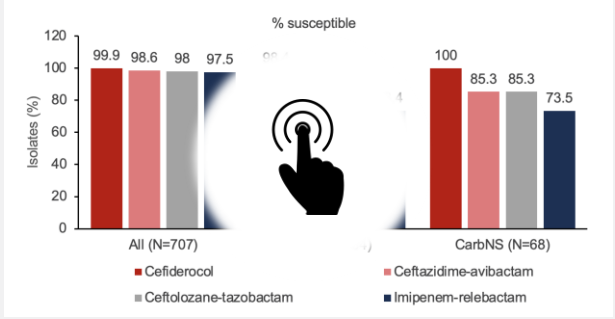


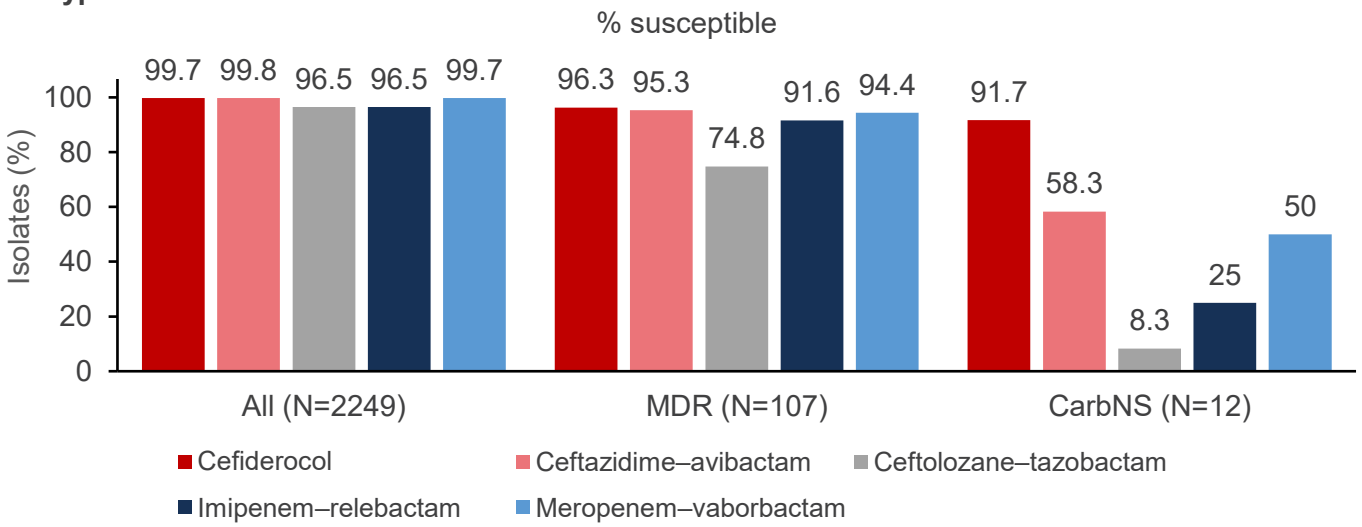
Table 15. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested Against Pediatric Isolates from the SENTRY Antimicrobial Surveillance Program (2020–2022)[20]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
Enterobacterales (N=2249)						
Cefiderocol	0.06	0.5	≤0.004 to 32	99.7	99.7	99.2
Meropenem	0.03	0.06	≤0.015 to >32	99.3	99.3	99.4
Imipenem–relebactam	0.12	0.5	≤0.03 to >8	96.5	96.5	99
Meropenem–vaborbactam	0.03	0.12	≤0.015 to >8	99.7	99.7	99.7
Ceftazidime–avibactam	0.12	0.5	≤0.03 to >8	99.8	99.8	99.8
Ceftolozane–tazobactam	0.5	1	≤0.03 to >8	96.5	96.5	96.5
Carb-NS – Enterobacterales (N=12)						
Cefiderocol	1	4	0.25 to >16	91.7	91.7	58.3
Imipenem–relebactam	>8	>8	2 to >8	25	25	33.3
Meropenem–vaborbactam	>8	>8	2 to >8	50	50	50
Ceftazidime–avibactam	16	>32	0.5 to >32	58.3	58.3	58.3
Ceftolozane–tazobactam	8	>16	0.25 to >16	8.3	8.3	8.3
***P. aeruginosa* (N=707)**						
Cefiderocol	0.5	2	≤0.004 to >32	98.7	99.7	98.7
Meropenem	0.5	4	≤0.015 to >8	88.1	88.1	88.1
Imipenem–relebactam	1	4	≤0.03 to >8	97.5	97.5	97.5
Meropenem–vaborbactam	2	8	≤0.015 to >8	NA	95.6	95.6
Ceftazidime–avibactam	2	8	0.5 to >32	98.6	98.6	98.6
Ceftolozane–tazobactam	2	8	0.5 to >32	98	98	98
Carb-NS – *P. aeruginosa* (N=68)						
Cefiderocol	0.12	4	≤0.004 to >16	100	98.5	98.5
Imipenem–relebactam	1	>8	0.12 to >8	73.5	73.5	73.5
Meropenem–vaborbactam	8	>8	2 to >8	NA	NA	54.4
Ceftazidime–avibactam	4	16	0.5 to >32	85.3	85.3	85.3
Ceftolozane–tazobactam	1	8	0.25 to >16	85.3	85.3	85.3

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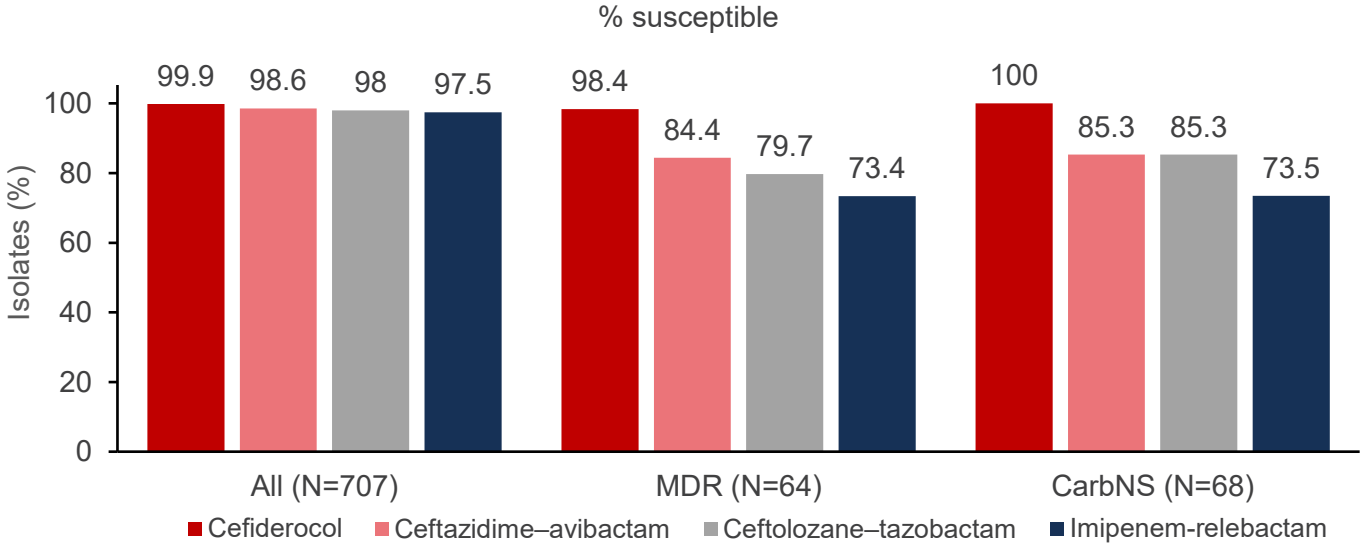
Surveillance Studies

Figure 3. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested Against Resistant Phenotypic Subsets of Enterobacterales[20]



Abbreviations: Carb-NS, carbapenem nonsusceptible; CLSI, Clinical and Laboratory Standards Institute; MDR, multidrug resistant.
Figure adapted from Nguyen et al. IDWeek. 2023.

Figure 4. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested against Resistant Phenotypic Subsets of *P. aeruginosa*[20]



Abbreviations: Carb-NS, carbapenem nonsusceptible; CLSI, Clinical and Laboratory Standards Institute; MDR, multidrug resistant.
Figure adapted from Nguyen et al. IDWeek. 2023.

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Surveillance Studies

Table 15. Activity of Cefiderocol and Comparator Antimicrobial Agents Tested against Pediatric Isolates from the SENTRY Antimicrobial Surveillance Program (2020–2022)[20]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
Enterobacterales (N=2249)						
Cefiderocol	0.06	0.5	≤0.004 to 32	99.7	99.7	99.2
Meropenem	0.03	0.06	≤0.015 to >32	99.3	99.3	99.4
Imipenem–relebactam	0.12	0.5	≤0.03 to >8	96.5	96.5	99
Meropenem–vaborbactam	0.03	0.06	≤0.015 to >8	99.7	99.7	99.7
Ceftazidime–avibactam	0.12	0.25	≤0.015 to >32	99.8	99.8	99.8
Ceftolozane–tazobactam	0.25	1	≤0.12 to >16	96.5	96.5	96.5
Carb-NS – Enterobacterales (N=12)						
Cefiderocol	2	4	0.03 to 8	91.7	91.7	58.3
Imipenem–relebactam	4	>8	0.06 to >8	25	25	33.3
Meropenem–vaborbactam	4	>8	0.06 to >8	50	50	50
Ceftazidime–avibactam	2	>32	0.25 to >32	58.3	58.3	58.3
Ceftolozane–tazobactam	>16	>16	0.5 to >16	8.3	8.3	8.3
***P. aeruginosa* (N=707)**						
Cefiderocol	0.06	0.25	≤0.004 to 16	99.9	98.7	99.7
Meropenem	0.5	4	≤0.015 to >32	88.1	88.1	88.1
Imipenem–relebactam	0.25	0.5	≤0.03 to >8	97.5	97.5	97.5
Meropenem–vaborbactam	0.5	4	≤0.015 to >8	NA	NA	95.6
Ceftazidime–avibactam	2	4	0.12 to >32	98.6	98.6	98.6
Ceftolozane–tazobactam	0.5	1	≤0.12 to >16	98	98	98
Carb-NS – *P. aeruginosa* (N=68)						
Cefiderocol	0.12	0.25	≤0.004 to 4	100	98.5	98.5
Imipenem–relebactam	1	>8	0.12 to >8	73.5	73.5	73.5
Meropenem–vaborbactam	8	>8	2 to >8	NA	NA	54.4
Ceftazidime–avibactam	4	16	0.5 to >32	85.3	85.3	85.3
Ceftolozane–tazobactam	1	8	0.25 to >16	85.3	85.3	85.3

Abbreviations: CAMHB, cation-adjusted Mueller–Hinton broth; Carb-NS, carbapenem non-susceptible; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; MIC, minimum inhibitory concentration; N, number of isolates; NA, not applicable (no breakpoint established or not tested); S, susceptible.
[a]According to 2023 CLSI, FDA, and EUCAST breakpoints.
Figure adapted from Nguyen et al. IDWeek. 2023.

Table 15 (Cont.). Activity of Cefiderocol and Comparator Antimicrobial Agents Tested against Pediatric Isolates from the SENTRY Antimicrobial Surveillance Program (2020–2022)[20]

Organism Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	MIC Range (µg/mL)	%S[a] CLSI	%S[a] FDA	%S[a] EUCAST
***A. baumannii-calcoaceticus* complex (N=194)**						
Cefiderocol	0.06	1	0.008 to >64	97.9	95.4	97.4
Meropenem	0.5	32	0.06 to >32	87.1	87.1	87.1
Imipenem–relebactam	0.12	>8	≤0.03 to >8	NA	NA	88.1
Ampicillin–sulbactam	2	32	≤0.5 to >64	80.9	80.9	NA
Colistin	0.5	1	0.12 to >8	NA	NA	95.4
Carb-NS – *A. baumannii-calcoaceticus* complex (N=23)						
Cefiderocol	0.25	1	0.03 to 8	95.7	91.3	95.7
Imipenem–relebactam	>8	>8	>8 to >8	NA	NA	0
Ampicillin–sulbactam	32	>64	4 to >64	17.4	17.4	NA
Colistin	0.5	>8	0.25 to >8	NA	NA	78.3
***S. maltophilia* (N=220)**						
Cefiderocol	0.06	0.25	0.008 to 1	100	NA	100
Levofloxacin	1	4	0.12 to >32	88.1	NA	NA
Trimethoprim–sulfamethoxazole	≤0.12	0.5	≤0.12 to >4	96.4	NA	97.7

Abbreviations: CAMHB, cation-adjusted Mueller–Hinton broth; Carb-NS, carbapenem non-susceptible; CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; MIC, minimum inhibitory concentration; N, number of isolates; NA, not applicable (no breakpoint established or not tested); S, susceptible.
[a]According to 2023 CLSI, FDA, and EUCAST breakpoints.
Figure adapted from Nguyen et al. IDWeek. 2023.

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PK/PD Studies

A PK modeling study was conducted to identify dosing regimens in pediatric patients (from birth to <18 years of age) based on PK predictions and an evaluation of PD results.[21,22]

Methods

- A PK model for pediatric patients was developed by utilizing data from 54 healthy adult patients and 37 adults with varying degrees of renal function. Allometric relationships developed for parenteral β-lactam antibiotics were used to scale the total clearance and V_{ss} in pediatric patients. Additionally, in neonates and infants with immature glomeruli, the maturation factor of renal function was used to predict clearance[21,22]
- Monte-Carlo simulations were conducted to determine the PTA for 75% of the $fT_{>MIC}$, C_{max}, and AUC[21,22]
- Simulations for patients aged 3 months to <18 years were conducted in 6 different age groups:[22]
  - 3 months to <6 months
  - 6 months to <12 months
  - 12 months to <2 years
  - 2 years to <6 years
  - 6 years to <12 years
  - 12 years to <18 years
- Cefiderocol dosage regimens included a single dose or q8h dosing of 60 mg/kg with an infusion time of 3 h. See **Table 16** for the proposed dosing of cefiderocol for pediatric patients[22]

Table 16. Proposed Dosing of Cefiderocol for Pediatric Patients (3 Months to <18 Years of Age)[22]

PNA (Chronological)	Dose	
	Body Weight <34 kg	Body Weight ≥34 kg
3 months to <18 years	60 mg/kg	2 g
The infusion time is 3 h		

Abbreviations: g, grams; h, hours; PNA, postnatal age.
Table adapted from Katsube et al. IDWeek. 2019.

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PK/PD Studies

Methods (Cont.)

- Simulations for patients from birth to <3 months were performed in 6 age groups:[22]
  - 0 months to <1 month, GA 22 weeks to <32 weeks
  - 0 months to <1 month, GA 32 weeks to 44 weeks
  - 1 month to <2 months, GA 22 weeks to <32 weeks
  - 1 month to <2 months, GA 32 weeks to 44 weeks
  - 2 months to <3 months, GA 22 weeks to <32 weeks
  - 2 months to <3 months, GA 32 weeks to 44 weeks
- Tested dosage regimens included a single dose or q8h dosing of 30 to 60 mg/kg. A 1-h infusion time was used for patients from birth to <3 months of age – see **Table 17**[22]

Table 17. Proposed Dosing of Cefiderocol for Pediatric Patients (<2–3 Months of Age)[22]

PNA (Chronological)	Dose	
	GA <32 Weeks	GA ≥32 Weeks
<2 months	30 mg/kg	40 mg/kg
2 to <3 months	40 mg/kg	60 mg/kg
The infusion time is 1 h		

Abbreviations: GA, gestational age; h, hour; PNA, postnatal age.
Table adapted from Katsube et al. IDWeek. 2019.

- There were 1000 virtual pediatric patient simulations for each age group. Individual cefiderocol plasma concentrations were simulated to calculate the C_{max}, AUC, and PTA for 75% $fT_{>MIC}$ in a MIC range from 0.25 to 16 µg/mL. The unbound fraction of 0.422 was used[22]

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PK/PD Studies

Results

PK[22]

- In patients aged 3 months to <18 years, the predicted plasma concentration profiles of cefiderocol with a 3-h infusion were comparable to adults. Predicted C_{max} in patients from birth to <3 months of age with a 1-h infusion were lower than adult concentrations. Simulated AUC ratios in pediatric patients relative to adults ranged from 0.81 to 1.18 in all age groups

PD[22]

- The q8h dosing of 60 mg/kg (2 g for body weight ≥34 kg) with a 3-h infusion achieved >90% of PTA for 75% $fT_{>MIC}$ against strains with MICs ≤4 µg/mL in patients aged 3 months to <18 years – see **Table 18**
- The q8h administration of age- and body-weight-adjusted dosing (30 to 60 mg/kg) with a 1-h infusion in patients aged birth to <3 months provided >90% of PTA for 75% fT>MIC against strains with an MIC of ≤4 µg/mL – see **Table 19**

Table 18. PTA for 75% $fT_{>MIC}$ Following q8h Dosing of 60 mg/kg (2 g for Body Weight ≥34 kg) Over a 3-h Infusion in Patients Aged from 3 Months to <18 Years[22]

Age	MIC (µg/mL)						
	0.25	0.5	1	2	4	8	16
3 to <6 months	100	100	100	100	98.9	79.5	15.3
6 to <12 months	100	100	100	99.6	93.6	54.7	3.6
12 months to 2 years	100	100	100	99.8	91.9	48.0	3.1
2 to <6 years	100	100	100	99.8	93.1	52.1	4.2
6 to <12 years	100	100	100	100	97.5	73.2	14.4
12 to <18 years	100	100	100	99.9	96.5	66.9	8.7

Note: There were 1000 simulations for each age group.
Abbreviations: $fT_{>MIC}$, the fraction of time where the free plasma concentrations exceed the MIC over the dosing interval; MIC, minimum inhibitory concentration; PTA, probability of target attainment; q8h, every 8 hours.
Table adapted from Katsube et al. IDWeek. 2019.

Table 19. PTA for 75% $fT_{>MIC}$ Following q8h Dosing of Age- and Body-Weight-Adjusted Dosing Over a 1-h Infusion in Patients Aged from Birth to <3 Months[22]

CA (Months)	GA (Weeks)	MIC (µg/mL)						
		0.25	0.5	1	2	4	8	16
0 to <1	32 to 44	100	100	100	99.9	97.9	78.0	19.9
0 to <1	22 to <32	100	100	100	100	99.9	95.9	49.8
1 to <2	32 to 44	100	100	100	99.6	94.4	58.7	10.3
1 to <2	22 to <32	100	100	100	100	99.6	86.8	23.0
2 to <3	32 to 44	100	100	100	99.8	96.2	69.3	18.4
2 to <3	22 to <32	100	100	100	100	99.1	87.0	31.5

Note: There were 1000 simulations for each age group.
Abbreviations: CA, chronological age; fT>MIC, the fraction of time where the free plasma concentrations exceed the MIC over the dosing interval; GA, gestational age; MIC, minimum inhibitory concentration; PTA, probability of target attainment; q8h, every 8 hours.
Table adapted from Katsube et al. IDWeek. 2019.

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Relevant Prescribing Information

Fetroja is indicated in patients ≥18 years for the treatment of:[23]

- Complicated UTI, including pyelonephritis caused by the following susceptible Gram-negative microorganisms:
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*
  - *Pseudomonas aeruginosa*
  - *Enterobacter cloacae* complex

- Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible Gram-negative microorganisms:
  - *Acinetobacter baumannii* complex
  - *Escherichia coli*
  - *Enterobacter cloacae* complex
  - *Klebsiella pneumoniae*
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*

Fetroja is contraindicated in:[23]

- Patients with a known history of severe hypersensitivity to cefiderocol or other β-lactam antibacterial drugs, or any other component of Fetroja

Please read the attached Fetroja **Full Prescribing Information**

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Literature Search

As of February 2026, a computerized search of the published medical literature using internal and external databases (eg, PubMed®) has identified additional relevant references regarding the use of cefiderocol in pediatric patients. For your review, these references are listed in the bibliography that follows:

- Russo C, Mesini A, Mariani M, et al. Reduce susceptibility to cefiderocol in gram negative bacteria in children: is hope already lost before it's even arrived? *J Infect Public Health*. 2024;17(4):624-631. [Web Link]
- Shapiro K, Ungar SP, Krugman J, et al. Cefiderocol red wine urine syndrome in pediatric patients: a multicenter case series. *Pediatr Infect Dis J*. 2024;43(2):142-144. [Web Link]
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Please keep in mind that medical literature databases, while considered a major source of biomedical information, are selective in their sources, and the information derived from them should not be considered all-inclusive.

This medical response contains information in addition to that provided in the Fetroja® (cefiderocol) for injection, for intravenous use Full Prescribing Information approved by the US Food and Drug Administration (FDA). Shionogi does not recommend the use of Fetroja in any manner other than as described in the Full Prescribing Information. **Please read the attached Fetroja Full Prescribing Information.**

Abbreviations

ABC	*Acinetobacter baumannii-calcoaceticus* complex	eGFR	estimated glomerular filtration
AE	adverse event	EOS	end of study
ALL	acute lymphoblastic leukemia	EOT	end of treatment
ALT	alanine aminotransferase	ESBL	extended-spectrum β-lactamase
AUC	area under the time-concentration curve	ETT	endotracheal tube
bid	twice a day	EUCAST	European Committee on Antimicrobial Susceptibility Testing
BOLT	bilateral orthotopic lung transplantation	F	female
BSI	bloodstream infection	FDA	US Food and Drug Administration
C	cohort	FEV_1	forced expiratory volume in one second
CA	chronological age	$fT_{>MIC}$	fraction of time where the free plasma concentrations exceed the MIC over the dosing interval
Carb-NS	carbapenem nonsusceptible	g	gram
CF	cystic fibrosis	GA	gestational age
cIAI	complicated intra-abdominal infection	H	hour
CLSI	Clinical Laboratory Standards Institute	HABP	hospital-acquired bacterial pneumonia
C_{max}	peak plasma concentration	HAP	hospital-acquired pneumonia
CNS	central nervous system	ICU	intensive care unit
CRP	C-reactive protein	IMP	imipenemase
CRRT	continuous renal replacement therapy	IQR	interquartile range
CSF	cerebrospinal fluid	ITT	intent-to-treat
cUTI	complicated urinary tract infection	IV	intravenous
CV	coefficient of variation	LTFU	lost to follow-up
DTR	difficult-to-treat resistant	M	male

Abbreviations (Cont.)

max	maximum	R	resistant
MBL	metallo-β-lactamase	S	susceptible
MDR	multidrug resistant	SCr	standardized serum creatinine
MIC	minimum inhibitory concentration	SD	standard deviation
MIC_{50}	minimum inhibitory concentration that inhibits 50% of isolates	SOC	standard of care
MIC_{90}	minimum inhibitory concentration that inhibits 90% of isolates	SSSI	skin and skin structure infection
min	minimum	TEAE	treatment-emergent adverse event
mITT	modified intent-to-treat	tid	three times a day
MRI	magnetic resonance imaging	TMP/SMX	trimethoprim–sulfamethoxazole
MRSE	methicillin-resistant *Staphylococcus epidermidis*	TOC	test of cure
NA	not applicable	UK	United Kingdom
NDM-1	New Delhi metallo-β-lactamase-1	ULN	upper limit of normal
NR	not reported	US	United States
PD	pharmacodynamics	VABP	ventilator-associated bacterial pneumonia
PDR	pandrug-resistant	VAP	ventilator-associated pneumonia
PK	pharmacokinetics	VIM	Verona integron-encoded metallo-β-lactamase
PNA	postnatal age	V_{SS}	volume of distribution at steady state
PT	post-treatment	WBC	white blood cell
PTA	probability of target attainment	XDR	extensively drug-resistant
q8h	every 8 hours	y	years

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ENCLOSURE

Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.