Fetroja® – Activity Against *Stenotrophomonas Maltophilia*

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Phase 3 Clinical Studies

CREDIBLE-CR, a Phase 3, multicenter, randomized, prospective, open-label, parallel-group, descriptive study assessed the efficacy and safety of cefiderocol or BAT in patients with HABP/VABP/HCABP, BSI/sepsis, or cUTI caused by CR Gram-negative pathogens, with no prespecified statistical hypothesis. Clinical, microbiological outcomes and ACM were assessed in both treatment arms.[1]

- A total of 5 patients (all with HABP/VABP/HCABP) in the cefiderocol CR-Micro-ITT population had *Stenotrophomonas maltophilia* as a baseline pathogen[1]
- At the TOC visit, there were 3 clinical failures and 2 indeterminate outcomes. Additionally, there were 5 indeterminate microbiological outcomes at TOC[2]
- The 30-day mortality rate for the 5 patients in the cefiderocol treatment group with *S. maltophilia* infection was 80%[3]

APEKS-NP, a Phase 3, multicenter, randomized, double-blind, non-inferiority trial, assessed the efficacy and safety of cefiderocol in patients with HABP, VABP or HCABP caused by suspected Gram-negative pathogens. Patients were randomized to receive 3 h IV infusions of either cefiderocol 2 g or meropenem 2 g q8h for 7–14 days, in addition to adjunctive linezolid (600 mg q12h for at least 5 days).[4]

- 1 patient (0.8%) in the cefiderocol group and 3 patients (2.4%) in the meropenem group were diagnosed with a Gram-negative infection caused by *S. maltophilia*[5]
- The patient treated with cefiderocol showed clinical cure and microbiological eradication at the TOC visit[5]

Real-World Evidence

Torre-Cisneros et al (2025) reported on a subgroup analysis of the PERSEUS study – a retrospective, observational, multicenter study conducted in centers across Spain designed to assess the safety and effectiveness of cefiderocol treatment (administered for ≥72 h for up to 28 days) in patients hospitalized with rare glucose non-fermenting Gram-negative pathogens (including *S. maltophilia*, N=20).[6]

- Overall, the clinical cure rate was 70% in patients with *S. maltophilia* infections (63.6% of the 11 patients hospitalized specifically with *S. maltophilia*-related RTIs)
- Overall, the mortality rate was 30% in patients with *S. maltophilia* infections (36.4% of the 11 patients with *S. maltophilia*-related RTIs)

Clancy et al (2024) reported the final results of the PROVE study (Retrospective Cefiderocol Chart Review Study) that included 1075 patients hospitalized with a documented Gram-negative bacterial infection across the US and Europe who had been treated for ≥72 hours with cefiderocol for the first time.[7]

- 63 (5.9%) of the 1075 patients were infected with *S. maltophilia*
- Among these patients, the clinical cure rate was 66.7% and the 30-day ACM rate was 36.5%

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Real-World Evidence (Cont.)

Marcella et al (2023) also evaluated interim data from the PROVE study, in patients with *S. maltophilia* infections who were treated with cefiderocol in real-world settings. Of the 54 patients who received cefiderocol, the clinical cure rate was 64.8% and 30-day ACM rate was 18.5%[8]

Cai et al (2023) performed a retrospective evaluation of 19 patients hospitalized in the US with monomicrobial *S. maltophilia* and treated with cefiderocol for at least 3 days for respiratory, blood, urine, and wound infections. Patients were evaluated from the Premier HealthCare Database between January 2020 and June 2022.[9]

- In the 19 patients with monomicrobial *S. maltophilia* infections, 2 (10.5%) and 4 (21.1%) patients had died by Day 14 and Day 28, respectively

Published Case Reports

Vena et al (2025) reported details of 4 cases of BSI resulting from *S. maltophilia* infection treated with cefiderocol for ≥72 h (as part of a retrospective cohort study conducted from January 2021 to December 2022 across 14 Italian hospitals), as well as describing an additional 4 case reports of *S. maltophilia* BSI managed with cefiderocol identified from the medical literature.[10]

- *In vitro* susceptibility to cefiderocol was demonstrated regardless of testing methodology (reported in 6 of the 8 cases)
- A successful clinical outcome was achieved for 5 patients (62.5%) by the end of treatment, while microbiological eradication was demonstrated in 7 out of 8 cases (87.5%)
- Clinical failure occurred in 3 patients (37.5%) and was due to death in all cases (only 1 of which could be attributed to *S. maltophilia* infection)

Lupia et al (2024) reported a case series of 10 patients with hematologic malignancies infected with *S. maltophilia* in Italy between January 2021 and June 2023. Of the 4 patients treated with cefiderocol, the clinical improvement and microbiological eradication rates were 100% and 75%, respectively.[11]

- The 30-day mortality and in-hospital mortality rates were 30% and 50%, respectively

Patient case reports by **Zappulo**, **Martínez**, and **Falcone** (adult patients), as well as **Trauth**, and **Hsu** (pediatric patients) described the outcomes with cefiderocol for the treatment of *S. maltophilia* infections. The patients had a variety of infections, including VAP, septic shock, and bacteremia.[12–16]

- Cefiderocol was well tolerated, and all patients experienced clinical improvement after treatment

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Surveillance Studies

Onishi et al (2024) described the *in vitro* activity of cefiderocol and comparator antimicrobial agents against a total of 1781 *S. maltophilia* clinical isolates collected as part of the SENTRY Antimicrobial Surveillance Program between 2020 and 2023.[17]

- According to CLSI breakpoints, 99.3%, 83.1%, 97%, and 93% of isolates were susceptible to cefiderocol, levofloxacin, trimethoprim-sulfamethoxazole, and minocycline, respectively
- According to both CLSI and EUCAST breakpoints, cefiderocol retained activity (>98% susceptibility), against isolates NS to levofloxacin, trimethoprim-sulfamethoxazole or minocycline, whereas comparator agents were shown to be much less active (<90% susceptibility)

Sakoh et al (2024) conducted a retrospective study assessing the *in vitro* cefiderocol susceptibility of *S. maltophilia* samples shown to have previously caused invasive bacteremia infection. A total of 146 strains from 2 Japanese hospitals between April 2013 and December 2023 were tested.[18]

- 145 out of the 146 *S. maltophilia* isolates were susceptible to cefiderocol (99.3%) with a MIC_{50} and MIC_{90} of 0.06 and 0.25 µg/mL, respectively
- The single isolate resistant to cefiderocol (MIC ≥64 µg/mL) was also shown to possess resistance to trimethoprim–sulfamethoxazole (MIC ≥4/76 µg/mL), levofloxacin (MIC ≥8 µg/mL), and ceftazidime (MIC ≥32 µg/mL), but showed susceptibility to minocycline (MIC ≤2 µg/mL)

Nguyen et al (2023) compared the *in vitro* activity of cefiderocol and comparator antibiotics against Gram-negative bacterial clinical isolates including *S. maltophilia* collected in US hospitals in the ongoing multinational SENTRY surveillance program in 2020 to 2022. Susceptibility rates for cefiderocol in *S. maltophilia* were interpreted using CLSI 2023 breakpoints.[19]

- 657 *S. maltophilia* isolates were tested, all of which were meropenem NS due to intrinsic resistance
- Of the *S. maltophilia* isolates, 98.5% were susceptible to cefiderocol with a MIC_{50} of 0.06 µg/mL and MIC_{90} of 0.25 µg/mL

Karlowsky et al (2022) showed a detailed analysis of the multinational SIDERO-WT 2014–2019 surveillance studies. Among 2031 clinical *S. maltophilia* isolates collected over 5 years, the annual susceptibility rates ranged between 96.4% and 100% for US isolates and between 95.6% and 100% for European isolates. CLSI 2022 susceptibility breakpoints were used (ie, susceptible ≤1 µg/mL, NS >1 µg/mL).[20]

In the **SIDERO-WT 2014, 2015, 2016, 2018 and 2019, and Proteeae** multinational surveillance studies, analysis of 47,615 Gram-negative bacterial isolates demonstrated that 99.3% were susceptible to cefiderocol based on a MIC ≤4 µg/mL.[21]

- Based on CLSI breakpoints (susceptible ≤1 µg/mL), 98.6% of *S. maltophilia* were susceptible to cefiderocol

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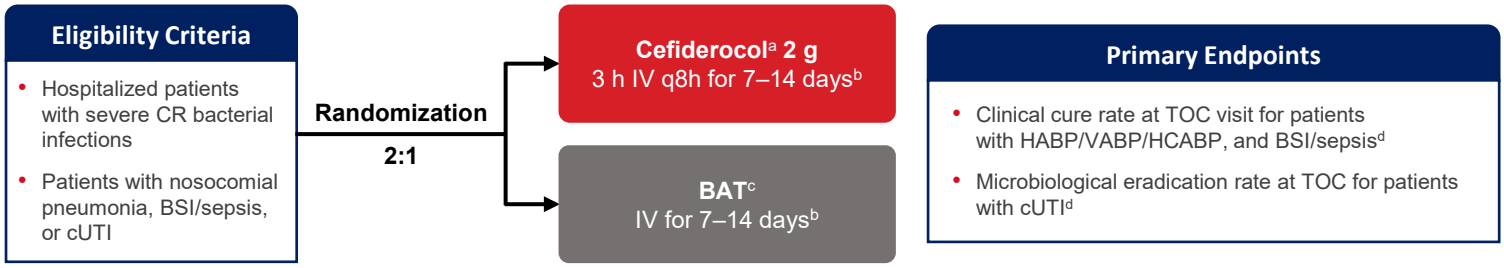
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Phase 3 Clinical Studies

CREDIBLE-CR

CREDIBLE-CR (NCT02714595) was a prospective, randomized, open-label, multicenter, parallel-group, descriptive Phase 3 trial that assessed the efficacy and safety of cefiderocol and BAT in hospitalized patients with severe CR bacterial infections. CREDIBLE-CR was a descriptive study with no hypothesis testing or formal inferential analysis. Please see **Figure 1** for the study design.[1]

Figure 1. CREDIBLE-CR Study Design[1]



Abbreviations: BAT, best available therapy; BSI, bloodstream infection; CR, carbapenem-resistant; cUTI, complicated urinary tract infection; g, grams; h, hours; HABP, hospital-acquired bacterial pneumonia; HCABP, healthcare-associated bacterial pneumonia; IV, intravenous; q8h, every 8 hours; TOC, test of cure; VABP, ventilator-associated bacterial pneumonia.
[a]Could be complemented with 1 adjunctive antibiotic therapy, excluding polymyxins, cephalosporins, and carbapenems and combinations with a β-lactamase inhibitor.
[b]Could be extended up to 21 days at the discretion of the investigator.
[c]Selected before randomization and could consist of up to 3 systemic antibiotics.
[d]Defined as all patients with a confirmed CR Gram-negative pathogen who received at least 1 dose of study drug.

Results

- A total of 5 patients (6.3%; all with HABP/VABP/HCABP) in the CR-Micro-ITT population had *S. maltophilia* as a baseline pathogen, all belonging to the cefiderocol treatment group[2]
- Among the 5 patients, an indeterminate clinical outcome occurred in 2 (40%) patients and clinical failure occurred in 3 (60%) patients[2]
- All 5 patients experienced an indeterminate microbiological outcome[2]
- 30-day ACM occurred in 4 (80%) patients[3]
- An analysis has not been conducted to evaluate safety outcomes in patients based on baseline pathogen (eg, *S. maltophilia*)

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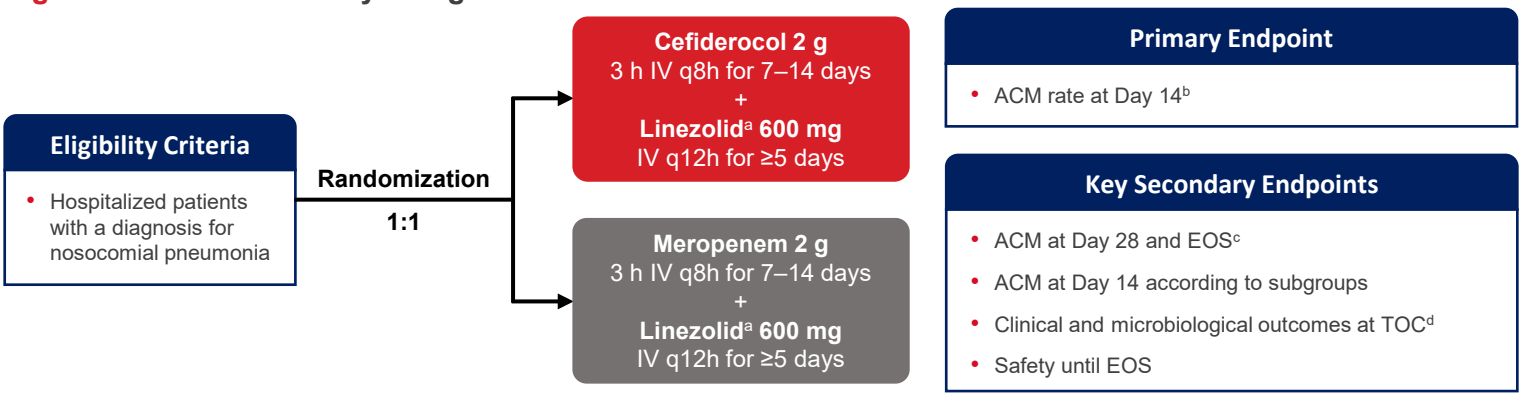
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Phase 3 Clinical Studies (Cont.)

APEKS-NP

APEKS-NP (NCT03032380) was a Phase 3, multicenter, randomized, double-blind, non-inferiority study that assessed the efficacy and safety of cefiderocol in VABP, HABP, or HCABP caused by suspected Gram-negative pathogens. Please see **Figure 2** for the study design.[4]

Figure 2. APEKS-NP Study Design[4]



Abbreviations: ACM, all-cause mortality; EOS, end of study; EOT, end of treatment; g, grams; h, hours; IV, intravenous; LRTI, lower respiratory tract infection; mITT, modified intention-to-treat; q8h, every 8 hours; q12h, every 12 hours; TOC, test of cure.
[a]Administered to cover Gram-positive bacteria.
[b]In the mITT population (non-inferiority margin, -12.5%), defined as all randomized patients who received ≥1 dose of a study drug and had evidence of a Gram-negative LRTI.
[c]EOT+28 days (±3 days).
[d]EOT+7 days (±2 days).

Results[5]

- 1 patient (0.8%) in the cefiderocol group and 3 patients (2.4%) in the meropenem group were diagnosed with a Gram-negative infection caused by *S. maltophilia*
- 1 patient (100%) achieved clinical cure in the cefiderocol group, and 2 patients (66.7%) achieved clinical cure in the meropenem group
- 1 patient (100%) achieved microbiological eradication in the cefiderocol group, and 1 patient (33.3%) achieved microbiological eradication in the meropenem group
  - From the meropenem group, 1 patient (33.3%) had persistence, and 1 patient (33.3%) had an indeterminate outcome
- The rates of ACM were not analyzed in patients with *S. maltophilia*
- An analysis has not been conducted to evaluate safety outcomes in patients based on baseline pathogen (eg, *S. maltophilia*)

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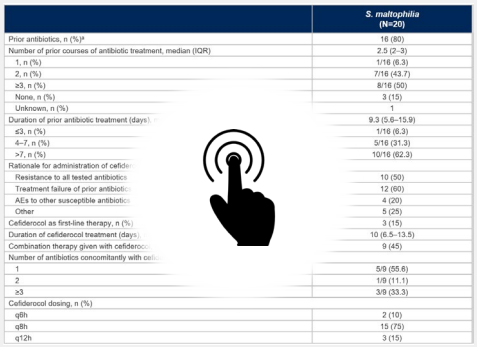
Real-World Evidence

Torre-Cisneros et al (2025) reported on a subgroup analysis of the PERSEUS study. This study was a retrospective, observational, multicenter study conducted in centers across Spain that was designed to assess the safety and effectiveness of cefiderocol treatment (administered for ≥72 h for up to 28 days) in patients hospitalized with rare glucose non-fermenting Gram-negative pathogens (including *S. maltophilia*). Of the 261 patients included in the primary analysis, a total of 20 patients were included with *S. maltophilia* infections. The main outcomes were clinical cure and ACM at Day 28 from treatment initiation in patients treated with cefiderocol for ≥72 h and up to 28 days. Clinical cure was defined as the cessation treatment with cefiderocol due to the resolution of symptoms and clinical signs of infection. Clinical success was the composite outcome of clinical cure or survival at Day 28[6]

Results[6]

- The median (IQR) age of the 20 patients infected with *S. maltophilia* was 60.5 (48–65.5) years, the median (IQR) CCI was 3 (2–5)
- 15 (75%) patients were in the ICU, 11 (55%) received ventilation at baseline, 11 (55%) were immunosuppressed, and 9 (45%) were transplant recipients
- The most common primary infection sites were respiratory (55%), CRBSI (20%), and IAIs (10%)
  - Secondary bacteremia occurred in 4 (20%) patients and polymicrobial infection occurred in 3 (15%) patients
- 80% of these patients had received prior antibiotics, with trimethoprim–sulfamethoxazole the most commonly prescribed treatment regimen
  - Cefiderocol was not commonly used as a first-line therapeutic choice, rather as a result of reported resistance following treatment failure with other antimicrobials
- The overall pattern of prior, concomitant and cefiderocol use for patients with confirmed *S. maltophilia* infection is presented **Table 1**

Table 1. Treatment of Patients with *S. maltophilia* Infection in the PERSEUS Study[6]



	S. maltophilia (N=20)
Prior antibiotics, n (%)[a]	16 (80)
Number of prior courses of antibiotic treatment, median (IQR)	2.5 (2–3)
1, n (%)	1/16 (6.3)
2, n (%)	7/16 (43.7)
≥3, n (%)	8/16 (50)
None, n (%)	3 (15)
Unknown, n (%)	1
Duration of prior antibiotic treatment (days)	9.3 (5.6–15.9)
≤3, n (%)	1/16 (6.3)
4–7, n (%)	5/16 (31.3)
>7, n (%)	10/16 (62.3)
Rationale for administration of cefid	
Resistance to all tested antibiotics	10 (50)
Treatment failure of prior antibiotic	12 (60)
AEs to other susceptible antibiotic	4 (20)
Other	5 (25)
Cefiderocol as first-line therapy, n (%)	3 (15)
Duration of cefiderocol treatment (days)	10 (6.5–13.5)
Combination therapy given with cefidero	9 (45)
Number of antibiotics concomitantly with cef	
1	5/9 (55.6)
2	1/9 (11.1)
≥3	3/9 (33.3)
Cefiderocol dosing, n (%)	
q8h	2 (10)
q8h	15 (75)
q12h	3 (15)

Table 2. Outcomes in Patients with *S. maltophilia* Infection in the PERSEUS Study[6]



	S. maltophilia (N=20)
Clinical cure, n (%)	14 (70)
Patients with prior trimethoprim–sulfame	7/10 (70)
Patients without prior trimethoprim–su	7/10 (70)
28-day mortality, n (%)	6 (30)
Patients with prior trimethoprim–sulfa	3/10 (30)
Patients without prior trimethoprim–sulfa	3/10 (30)
Clinical success, n (%)	14 (70)
Patients with prior trimethoprim–sulfamethoxazole	7/10 (70)
Patients without prior trimethoprim–sulfamethoxazole treatment	7/10 (70)

Clinical Outcomes[6]

- The clinical cure rate was 70% in patients with *S. maltophilia* infections overall (**Table 2**)
  - 63.6% of the 11 patients hospitalized specifically with *S. maltophilia*-related RTIs
- The mortality rate was 30% in patients with *S. maltophilia* infections overall (**Table 2**)
  - 36.4% of the 11 patients with *S. maltophilia*-related RTIs
- Prior treatment with trimethoprim–sulfamethoxazole did not appear to significantly affect rates of either clinical cure or mortality among patients with *S. maltophilia* infections (**Table 2**)

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Real-World Evidence

Table 1. Treatment of Patients with *S. maltophilia* Infection in the PERSEUS Study[6]

	***S. maltophilia* (N=20)**
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Number of prior courses of antibiotic treatment, median (IQR)	2.5 (2–3)
1, n (%)	1/16 (6.3)
2, n (%)	7/16 (43.7)
≥3, n (%)	8/16 (50)
None, n (%)	3 (15)
Unknown, n (%)	1
Duration of prior antibiotic treatment (days), median (IQR)	9.3 (5.6–15.9)
≤3, n (%)	1/16 (6.3)
4–7, n (%)	5/16 (31.3)
>7, n (%)	10/16 (62.3)
Rationale for administration of cefiderocol, n (%)[b]	
Resistance to all tested antibiotics	10 (50)
Treatment failure of prior antibiotics	12 (60)
AEs to other susceptible antibiotics	4 (20)
Other	5 (25)
Cefiderocol as first-line therapy, n (%)	3 (15)
Duration of cefiderocol treatment (days), median (IQR)	10 (6.5–13.5)
Combination therapy given with cefiderocol, n (%)[c]	9 (45)
Number of antibiotics concomitantly with cefiderocol, n (%)	
1	5/9 (55.6)
2	1/9 (11.1)
≥3	3/9 (33.3)
Cefiderocol dosing, n (%)	
q6h	2 (10)
q8h	15 (75)
q12h	3 (15)

Abbreviations: AE, adverse event; IQR, interquartile range; q6h, every 6 hours; q8h, every 8 hours; q12h, every 12 hours.
[a]Data are shown for patients with a full dataset.
[b]Not mutually exclusive; physicians could select ≥1 option.
[c]Includes antibiotics with Gram-negative coverage that have been started before, concomitantly, or during the same treatment period.
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025.

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Real-World Evidence

Table 2. Outcomes in Patients with *S. maltophilia* Infection in the PERSEUS Study[6]

	***S. maltophilia* (N=20)**
Clinical cure[a], n (%)	14 (70)
Patients with prior trimethoprim–sulfamethoxazole treatment	7/10 (70)
Patients without prior trimethoprim–sulfamethoxazole treatment	7/10 (70)
28-day mortality, n (%)	6 (30)
Patients with prior trimethoprim–sulfamethoxazole treatment	3/10 (30)
Patients without prior trimethoprim–sulfamethoxazole treatment	3/10 (30)
Clinical success[b], n (%)	14 (70)
Patients with prior trimethoprim–sulfamethoxazole treatment	7/10 (70)
Patients without prior trimethoprim–sulfamethoxazole treatment	7/10 (70)

[a]Clinical cure was defined as the cessation treatment with cefiderocol due to the resolution of symptoms and clinical signs of infection.
[b]Clinical success was the composite outcome of clinical cure or survival at Day 28.
Table adapted from Torre-Cisneros et al. *Eur J Clin Microbiol Infect Dis*. 2025.

use for patients with confirmed *S. maltophilia* infection is presented **Table 1**

Clinical Outcomes[6]

- The clinical cure rate was 70% in patients with *S. maltophilia* infections overall (**Table 2**)
  - 63.6% of the 11 patients hospitalized specifically with *S. maltophilia*-related RTIs
- The mortality rate was 30% in patients with *S. maltophilia* infections overall (**Table 2**)
  - 36.4% of the 11 patients with *S. maltophilia*-related RTIs
- Prior treatment with trimethoprim–sulfamethoxazole did not appear to significantly affect rates of either clinical cure or mortality among patients with *S. maltophilia* infections (**Table 2**)

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Real-World Evidence (Cont.)

PROVE (Retrospective Cefiderocol Chart Review Study)

Clancy et al (2024) reported the final results of the PROVE study, a multicenter, retrospective medical chart review study in patients treated with cefiderocol in European and US hospitals. Patients were eligible if they had a documented Gram-negative infection along with the first-time use of cefiderocol for ≥72 h. Clinical cure was defined by resolution or improvement in infection signs and symptoms, without evidence of a later relapse and/or reinfection. ACM at Days 14 and 30 were also analyzed.[7]

Results[7]

- Among the 1075 total patients enrolled, there were 63 (5.9%) with *S. maltophilia*
- The clinical cure and 30-day ACM rates for patients with *S. maltophilia* were 66.7% and 36.5%, respectively

Marcella et al (2023) also retrospectively evaluated **interim** data from the PROVE study. This analysis described the outcomes of cefiderocol treatment in a subset of 54 patients with *S. maltophilia*.[8]

Methods[8]

- Hospitalized patients were eligible if they had a documented *S. maltophilia* infection along with the first-time use of cefiderocol for ≥72 h
- Clinical cure was defined by resolution or improvement in infection signs and symptoms, without evidence of a later relapse and/or reinfection
- Clinical cure and ACM at Day 30 were analyzed

Results[8]

- The most common infection sites included respiratory (65%), skin and skin structure (15%), and intra-abdominal (7%)
- Mechanical ventilation was required for 31 (57.4%) patients, and 39 (72.2%) patients were admitted to the ICU
- The median treatment duration for cefiderocol was 11 days. Infections were polymicrobial for 31 (57.4%) patients, with 38.9% of the co-infections involving *Pseudomonas aeruginosa*
- Of the 54 patients with *S. maltophilia*, 35 (64.8%) achieved clinical cure and 10 (18.5%) had died by Day 30
  - Among the 23 monomicrobial *S. maltophilia* infections, 15 (65.2%) achieved clinical cure and 7 (30.4%) had died by Day 30
  - Among the 31 polymicrobial *S. maltophilia* infections, 20 (64.5%) achieved clinical cure and 3 (9.7%) had died by Day 30

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Real-World Evidence (Cont.)

Cai et al (2023) assessed the usage of cefiderocol in 19 US patients hospitalized with microbiologically confirmed *S. maltophilia*, taken from the Premier HealthCare Database between January 2020 and June 2022.[9]

- Hospitalized patients were eligible if they had laboratory-confirmed *S. maltophilia* infection without other Gram-negative pathogens within 3 days of receiving cefiderocol as part of routine care for ≥3 consecutive days. Patients presented with respiratory, blood, urine, wound, and other infection types
- Patients with COVID-19 were excluded. In addition to patient and clinical characteristics, the total treatment duration for cefiderocol and the number of other antibiotics used before cefiderocol treatment were evaluated as well. In-hospital ACM at Days 14 and 28 were also evaluated

Results[9]

- The median age was 66 years and the median CCI was 4
- Mechanical ventilation was required for 13 (68.4%) patients and 15 (79%) patients were admitted to the ICU
- The median treatment duration for cefiderocol was 8 days, and cefiderocol was monotherapy for 7 (36.8%) patients
- Of the 19 patients with monomicrobial *S. maltophilia*, 2 (10.5%) and 4 (21.1%) had died in-hospital by Days 14 and 28, respectively

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Published Case Reports

Adult Patients (≥18 years old)

Vena et al (2025) reported details of 4 cases of BSI resulting from *S. maltophilia* infection treated with cefiderocol for ≥72 h (as part of a retrospective cohort study conducted from January 2021 to December 2022 across 14 Italian hospitals), as well as describing an additional 4 case reports of *S. maltophilia* BSI managed with cefiderocol identified from the medical literature.[10]

Methods[10]

- Antibiotic susceptibility testing was performed *in vitro* with susceptibility patterns reported, as appropriate, according to EUCAST or CLSI recommendations for 2023
- Clinical case reports of interest were identified in the scientific literature by searching Embase® and Medline® and included only reports describing patients ≥18 years of age who received cefiderocol treatment for a minimum of 72 h as a result of BSI caused by *S. maltophilia*
- Clinical outcome definitions:
  - **Successful** – complete resolution of the signs and symptoms of *S. maltophilia* infection without the need for additional antibiotic therapy during follow-up (except when de-escalation therapy was required)
  - **Failure** – absence of clinical response, infection recurrence, and/or all-cause in-hospital mortality

Results[10]

- The age of the 8 patients included in the analysis ranged from 18 to 82 years (median [IQR], 52.5 [27.5–61] years). Cardiovascular disease was the most common underlying condition (66.7%) followed by onco-hematological disease (50%), and the median CCI (calculated for 6 of 8 patients) was 3.5 (IQR, 0.5–5.8)
- A cumulative summary of the 8 patient cases, including outcomes, is shown in **Table 3** (4 from the **Italian hospital cohort** and 4 identified in the **scientific literature**)
- All but 1 of the 8 *S. maltophilia* isolates (87.5%) were susceptible to trimethoprim–sulfamethoxazole at elevated doses per EUCAST breakpoints, 3 (37.5%) were susceptible to levofloxacin per CLSI breakpoints, while *in vitro* susceptibility to cefiderocol was demonstrated regardless of testing methodology (reported in 6 of the 8 cases)
- 7 patients (87.5%) were treated with cefiderocol as first-line therapy, the mean duration of cefiderocol therapy was 14 days, and combination antimicrobial therapy was used in 5 cases (62.5%)
- A successful clinical outcome was achieved for 5 patients (62.5%) by the end of treatment, while microbiological eradication was demonstrated in 7 out of 8 cases (87.5%)
- No statistically significant differences were observed in clinical success between those patients treated with cefiderocol as monotherapy versus combination therapy, or as first-line versus second-line therapy
- Clinical failure occurred in 3 patients (37.5%) and was due to death in all cases (only 1 of which could be attributed to *S. maltophilia* infection)

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Published Case Reports

Table 3. Clinical Presentation, Antimicrobial Treatment, and Clinical Course[10,11,22,23]

Case	Age	Infection Type	Poly-microbial	Cefiderocol Susceptibility	Treatment[a]	Treatment After Cefiderocol	Micro-biological Eradication	In-Hospital Mortality	SM Infection Relapse
Patients from the Italian Hospital Cohort[10]									
1	47	CVC-BSI[b]	No	MD, MIC = 0.016 mg/L	Cefiderocol + levofloxacin for 3 days	TMP-SMX for 15 days	Yes	No	No
2	82	CVC-BSI[b]	No	MD, MIC = 0.016 mg/L	Cefiderocol for 7 days	None	Yes	No	No
3	21	Wound infection[b]	No	MD, MIC ≤2 mg/L	Cefiderocol + TMP-SMX for 14 days	None	Yes	Yes	No
4	18	CVC-BSI[b]	No	MD, MIC = 0.062 mg/L	Cefiderocol for 4 days	None	Unknown	Yes	No

Abbreviations: CVC-BSI, central venous catheter-related blood stream infection; MD, microdilution method; MIC, minimum inhibitory concentration; SM, *S. maltophilia*; TMP-SMX, trimethoprim–sulfamethoxazole.
[a]Administration of cefiderocol was in accordance with the prescribing information at a dose of 2 g IV over 3 h q8h (dose adjustments were required only for patients with moderate to severe renal dysfunction [CrCl <60 mL/min] or for those with augmented renal clearance [CrCl ≥120 mL/min]).
[b]Source control has been achieved in these patients.
Table adapted from Vena et al. *Infect Dis Ther*. 2025.

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Published Case Reports

Table 3 (Cont.). Clinical Presentation, Antimicrobial Treatment, and Clinical Course[10,11,22,23]

Case	Age	Infection Type	Poly-microbial	Cefiderocol Susceptibility	Treatment[a]	Treatment After Cefiderocol	Micro-biological Eradication	In-Hospital Mortality	SM Infection Relapse
Patients Identified by Literature Search									
5[22]	62	CVC-BSI[b] with septic thrombosis	No	DD, MIC = 25mm	Cefiderocol + levofloxacin for 22 days + intra-lock therapy with TMP-SMX for 14 days	Minocycline + intra-lock therapy with TMP-SMX as a chronic suppressive therapy	Yes	No	No
6[23]	58	Bacteremic VAP	Yes (+ ESBL-producing *E. coli*)	MD, MIC = 0.125 mg/L	Cefiderocol for 14 days + tigecycline for 10 days	None	Yes	Yes	No
7[11]	NA	Bacteremic HAP	No	DD (MIC not specified)	Cefiderocol for 22 days	None	Yes	No	No
8[11]	NA	CVC-BSI[b]	Yes (+ pathogen not specified)	DD (MIC not specified)	Cefiderocol + TMP-SMX for 14 days	None	Yes	No	No

Abbreviations: CVC-BSI, central venous catheter-related blood stream infection; DD, disk diffusion method; ESBL, extended-spectrum β-lactamase; HAP, hospital-associated pneumonia; MD, microdilution method; MIC, minimum inhibitory concentration; NA, not available; SM, *S. maltophilia*; TMP-SMX, trimethoprim–sulfamethoxazole; VAP, ventilator-associated pneumonia.

[a]Administration of cefiderocol was in accordance with the prescribing information at a dose of 2 g IV over 3 h q8h (dose adjustments were required only for patients with moderate to severe renal dysfunction [CrCl <60 mL/min] or for those with augmented renal clearance [CrCl ≥120 mL/min]).

[b]Source control has been achieved in these patients.

Table adapted from Vena et al. *Infect Dis Ther*. 2025.

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Published Case Reports (Cont.)

Lupia et al (2024) presented a case series of 10 adult patients with *S. maltophilia* infections and hematologic malignancies from 2 hematological centers in Northern Italy between January 2021 and June 2023. Patients included had at least 1 *S. maltophilia* isolate cultured from blood or respiratory tract and clinical signs of infection.[11]

- Cefiderocol MIC testing was completed using disk diffusion methods and interpreted according to EUCAST PK/PD non-species-related breakpoints

Results[11]

- Nosocomial pneumonia was the most frequent source of *S. maltophilia* infection, either with (20%) or without associated BSI (40%), followed by CRBSI at 30%
- All patients had prior exposure to β-lactams, β-lactam/β-lactamase inhibitors, cephalosporins, or carbapenems <30 days before infection
- Cefiderocol susceptibility was tested in 7 of the 10 strains and was susceptible in all samples
- Among the 4 patients treated with cefiderocol, 2 received monotherapy and 2 received combination therapy with trimethoprim–sulfamethoxazole
  - There were no AEs in the patients treated with cefiderocol
- The case details of the 4 patients treated with cefiderocol are summarized in **Table 4**

Table 4. Case Details of Hospitalized Patients with Hematological Malignancies Infected with *S. maltophilia* Treated with Cefiderocol[11]

Infection Type	Treatment	Duration	Septic Shock	Clinical Improvement	Microbiological Eradication	30-Day Mortality	In-Hospital Mortality
Nosocomial pneumonia + BSI	Cefiderocol	22	Yes	Yes	Yes	No	No
Hemorrhagic pneumonia	Cefiderocol + trimethoprim–sulfamethoxazole	14	Yes	Yes	No	No	Yes
Hemorrhagic pneumonia	Cefiderocol	18	No	Yes	Yes	No	Yes
CRBSI	Cefiderocol + trimethoprim–sulfamethoxazole	14	Yes	Yes	Yes	No	No

Abbreviations: BSI, bloodstream infection; CRBSI, catheter-related bloodstream infection.
Table adapted from Lupia et al. *Medicina*. 2024.

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Published Case Reports (Cont.)

Zappulo et al (2022) presented a case of a 69-year-old male with AML who presented with *S. maltophilia* pneumonia determined to be intermediate to trimethoprim–sulfamethoxazole, and resistant to ciprofloxacin, colistin, levofloxacin, and tigecycline, but susceptible to cefiderocol (MIC <0.5 µg/mL), according to EUCAST.[12]

- Treatment with IV cefiderocol (2 g q8h) and levofloxacin daily was initiated. After 1 week of treatment with the cefiderocol-based regimen, a progressive improvement of respiratory distress was observed
- Eradication of *S. maltophilia* from respiratory samples was reported after 2 weeks
- After 21 days of treatment with the cefiderocol-based regimen, the patient left the hospital with complete clinical resolution of the infection
- At a 2-week follow-up visit, there were no signs of relapse reported
- The patient died the following month as a result of hematologic disease recurrence

Martínez et al (2022) described a case of a 72-year-old male with sepsis due to acute lithiasic pancreatitis initially treated with the combination of piperacillin–tazobactam, meropenem and linezolid. Thirty days later, the patient developed septic shock with retroperitoneal collection (fluid) in the pararenal space and drainage cultured *S. maltophilia* from the fluid.[13]

- Treatment with the combination of levofloxacin and meropenem was started for 20 days. On Day 60 following admission, another episode of septic shock occurred and PDR *S. maltophilia* was isolated from the retroperitoneal collection
- Cefiderocol 2 g q8h was then initiated as monotherapy and continued for a duration of 21 days
- After Day 3 of cefiderocol treatment, *S. maltophilia* was not isolated from the extracted material during surgical drainage
- On Day 7 of cefiderocol treatment, the patient became afebrile, had clinical improvement and showed improvement in laboratory parameters
- *S. maltophilia* was not isolated again during the remainder of the hospital admission and the patient did not experience an AE related to cefiderocol

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Published Case Reports (Cont.)

Falcone et al (2021) described the case of a polymicrobial infection due to NDM-producing *Klebsiella pneumoniae* and *S. maltophilia* as part of a case series report. A total of 10 patients admitted to the ICU were treated with cefiderocol under the compassionate use program between April 2020 and May 2020. Clinical success was defined as the composite of resolution of signs and symptoms, survival, and absence of microbiological recurrence or recurrent infection within 30 days.[14]

- In this series, a 79-year-old female patient with history of hypertension and COVID-19 had been diagnosed with secondary VAP due to NDM-producing *K. pneumoniae* and *S. maltophilia*
  - Her SOFA score was 10 and APACHE II score was 39
- The patient failed the initial treatment with ceftazidime–avibactam plus aztreonam, and fosfomycin
  - Both *K. pneumoniae* and *S. maltophilia* were susceptible to cefiderocol (MICs of 1 and 0.5 µg/mL, respectively)
- The patient received cefiderocol monotherapy, 2 g q6h, and achieved clinical success by Day 30 and survived

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Published Case Reports

Pediatric Patients (<18 years old)

Trauth et al (2024) reported the case of a preterm infant who, after being treated for a *S. maltophilia* infection with a variety of combination antimicrobial treatments, was switched to a regimen containing cefiderocol.[15]

- After several operations, VABP was diagnosed on Day 30. Although initially thought to be a colonizer pathogen, *S. maltophilia* was then isolated in tracheal aspirates, and by Day 40 the patient presented to the hospital with fever and high oxygen demand
- Antibiotic therapy was switched to levofloxacin in combination with trimethoprim–sulfamethoxazole, but serological signs of infection showed insufficient improvement
  - The tracheal aspirate revealed that the S. *maltophilia* isolate was resistant to levofloxacin and ceftazidime, and susceptible to cefiderocol
  - *Klebsiella oxytoca* was also detected that was susceptible to piperacillin–tazobactam, trimethoprim–sulfamethoxazole, and levofloxacin, prompting a switch to piperacillin–tazobactam plus trimethoprim–sulfamethoxazole
- Following clinical deterioration by Day 57, the decision was made to change the antimicrobial regimen to cefiderocol (100 mg/kg tid) in addition to dose-escalated trimethoprim–sulfamethoxazole (12 mg/kg bid) plus tigecycline (1.5 mg/kg bid)
  - After 5 days – various swabs and tracheal aspirates became sterile
  - After 2 weeks – clinical and microbiological cure was achieved
  - By Day 70 – the patient had been successfully extubated, and all antibiotic therapy was withdrawn
  - No toxicities were apparent throughout this treatment period, and there were no further clinical or serological signs of infection up to Day 81 when the patient died under palliative care as a result of her underlying genetic condition

Hsu et al (2023) described a 5-week-old infant who required multiple procedures in their first days of life and who developed *S. maltophilia* bacteremia isolated on DoL 30 that received cefiderocol for approximately 30 days.[16]

- The patient was empirically treated with meropenem on DoL 30 to 34 and after the strain was identified as *S. maltophilia*, high-dose trimethoprim–sulfamethoxazole was started on DoL 32
  - After 6 days of therapy with trimethoprim–sulfamethoxazole, repeat peripheral blood cultures remained positive
- The source of bacteremia was presumed to be endovascular and cefiderocol monotherapy at 40 mg/kg over 1 h infusion, q8h was started on DoL 37
  - No combination therapy with other anti-infectives or surgical interventions were initiated
- 1 day after cefiderocol initiation (DoL 38), repeat blood cultures showed no growth and remained negative for the next 30 days of cefiderocol treatment
- No AEs were documented

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Surveillance Studies

Onishi et al (2024) described the *in vitro* activity of cefiderocol and comparator antimicrobial agents against 1781 *S. maltophilia* isolates collected from medical centers across the US and Europe as part of the SENTRY Antimicrobial Surveillance Program between 2020 and 2023.[17]

Methods[17]

- MICs were determined according to CLSI broth microdilution methodology using ID-CAMHB for cefiderocol and CAMHB for comparator agents. CLSI and EUCAST PK and PD breakpoints were used to determine susceptibility

Results[17]

- A total of 1781 isolates were collected (57% from the US; 43% from across Europe), with the most common infection types being pneumonia (67%), bloodstream (12%), and skin/skin structure (9%)
- Cefiderocol was the most active agent against *S. maltophilia* isolates ($MIC_{50/90}$, 0.06/0.25 µg/mL) – Figure 3 and Table 5
- According to CLSI breakpoints, 99.3%, 83.1%, 97%, and 93% of isolates were susceptible to cefiderocol, levofloxacin, trimethoprim–sulfamethoxazole, and minocycline, respectively – Table 5
- According to both CLSI and EUCAST breakpoints, cefiderocol retained activity (>98% susceptibility), against isolates NS to levofloxacin, trimethoprim–sulfamethoxazole or minocycline, whereas comparator agents were shown to be much less active (<90% susceptibility) – Table 5

Figure 3. Cumulative MIC Distributions of Cefiderocol and Comparator Agents against *S. maltophilia* Isolates[17]

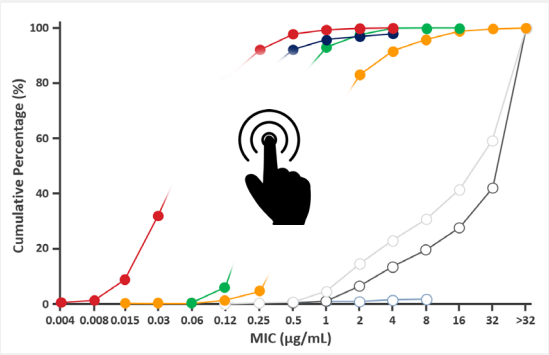


Table 5. *In Vitro* Activity of Cefiderocol and Comparator Agents against *S. maltophilia* Isolates from the US and Europe between 2020 and 2023[17]

Isolate Set	MIC_{50}	MIC_{90}	MIC Range	%S	
Antimicrobial Agents	µg/mL			CLSI[b]	EUCAST[b]
All (N=1781)					
Cefiderocol (n=1781)	0.06	0.25	≤0.004 to 8	99.3	99.7
Levofloxacin (n=1779)	1	4	≤0.015 to >32	83.1	27.3
Trimethoprim–sulfamethoxazole (n=1780)			≤0.12 to >4	97.0	N/A
Minocycline (n=1780)			≤0.06 to 16	93	N/A
Ceftazidime (n=1779)			1 to >32	N/A	13.5
Imipenem–relebactam (n=1781)			1 to >8	N/A	0.8
Ceftazidime–avibactam (n=1779)			2 to >8	N/A	30.6
Levofloxacin-NS[a] (n=301)					
Cefiderocol (n=301)				99.7	99.7
Trimethoprim–sulfamethoxazole (n=				88.7	N/A
Minocycline (n=301)				65.6	N/A
Trimethoprim–sulfamethoxazole-NS[a]					
Cefiderocol (n=53)			0.5 to 2	98.1	100
Levofloxacin (n=53)			2 to >32	35.8	9.4
Minocycline (n=53)			0.12 to 16	62.3	N/A
Minocycline-NS[a] (n=125)					
Cefiderocol (n=125)	0.06	0.25	0.008 to 1	99.7	100
Levofloxacin (n=125)	8	32	0.06 to >32	16.8	1.6
Trimethoprim–sulfamethoxazole (n=125)	0.5	>4	≤0.12 to >4	84	N/A

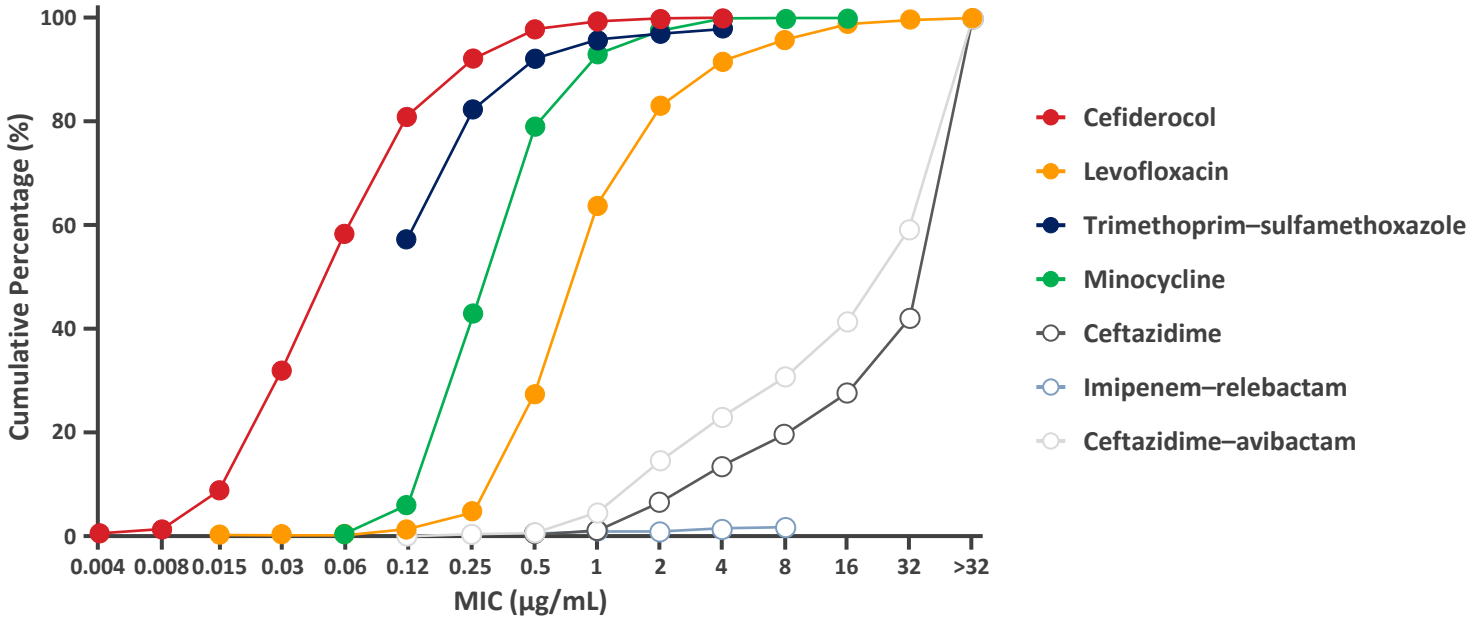
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Surveillance Studies

Figure 3. Cumulative MIC Distributions of Cefiderocol and Comparator Agents against *S. maltophilia* Isolates[17]



Abbreviation: MIC, minimum inhibitory concentration.
Figure adapted from Onishi et al. IDWeek. 2024.

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Surveillance Studies

Table 5. ***In Vitro*** **Activity of Cefiderocol and Comparator Agents against** ***S. maltophilia*** **Isolates from the US and Europe between 2020 and 2023**[17]

Isolate Set	MIC_{50}	MIC_{90}	MIC Range	%S	
Antimicrobial Agents	**µg/mL**			**CLSI[a]**	**EUCAST[b]**
All (N=1781)					
Cefiderocol (n=1781)	0.06	0.25	≤0.004 to 8	99.3	99.7
Levofloxacin (n=1779)	1	4	≤0.015 to >32	83.1	27.3
Trimethoprim–sulfamethoxazole (n=1780)	≤0.125	0.5	≤0.12 to >4	97.0	N/A
Minocycline (n=1780)	0.5	1	≤0.06 to 16	93	N/A
Ceftazidime (n=1779)	>32	>32	0.12 to >32	N/A	13.5
Imipenem–relebactam (n=1781)	>8	>8	0.12 to >8	N/A	0.8
Ceftazidime–avibactam (n=1779)	32	>32	0.06 to >32	N/A	30.6
Levofloxacin-NS[a] (n=301)					
Cefiderocol (n=301)	0.06	0.25	≤0.004 to 4	99.7	99.7
Trimethoprim–sulfamethoxazole (n=301)	0.25	4	≤0.12 to >4	88.7	N/A
Minocycline (n=301)	1	4	0.12 to 16	65.6	N/A
Trimethoprim–sulfamethoxazole-NS[a] (n=53)					
Cefiderocol (n=53)	0.125	0.5	0.008 to 2	98.1	100
Levofloxacin (n=53)	8	32	0.5 to >32	35.8	9.4
Minocycline (n=53)	1	4	0.12 to 16	62.3	N/A
Minocycline-NS[a] (n=125)					
Cefiderocol (n=125)	0.06	0.25	0.008 to 1	99.7	100
Levofloxacin (n=125)	8	32	0.06 to >32	16.8	1.6
Trimethoprim–sulfamethoxazole (n=125)	0.5	>4	≤0.12 to >4	84	N/A

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration; $MIC_{50/90}$, minimum inhibitory concentration to inhibit 50% and 90% of growth; N/A, not applicable; NS, non-susceptible; PD, pharmacodynamic; PK, pharmacokinetic; S, susceptibility.

[a]Cefiderocol S ≤1, levofloxacin S ≤2, trimethoprim–sulfamethoxazole S ≤2/38, minocycline S ≤1, breakpoints as published by CLSI (2024).

[b]Cefiderocol S ≤2, levofloxacin S ≤0.5, ceftazidime S≤4, imipenem–relebactam S ≤2, ceftazidime–avibactam S ≤8, PK-PD breakpoints as published by EUCAST (2023).

Table adapted from Onishi et al. IDWeek. 2024.

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Surveillance Studies (Cont.)

Sakoh et al (2024) conducted a retrospective study assessing the *in vitro* cefiderocol susceptibility of stored samples of *S. maltophilia* shown to have previously caused invasive bacteremia infection.[18]

Methods[18]

- In total, the drug susceptibility of 146 *S. maltophilia* strains (isolated from blood culture samples from 2 Japanese hospitals between April 2013 and December 2023) were tested
- For cefiderocol, susceptibility was determined according to CLSI broth microdilution methodology using ID-CAMHB, as well as a disk diffusion test using 30 µg disks and Mueller Hinton agar in accordance with EUCAST guidance. But with a MIC breakpoint of ≤1 µg/mL considered as susceptible, consistent with CLSI guidelines
- CLSI broth microdilution methodology using CAMHB was used for the other agents tested

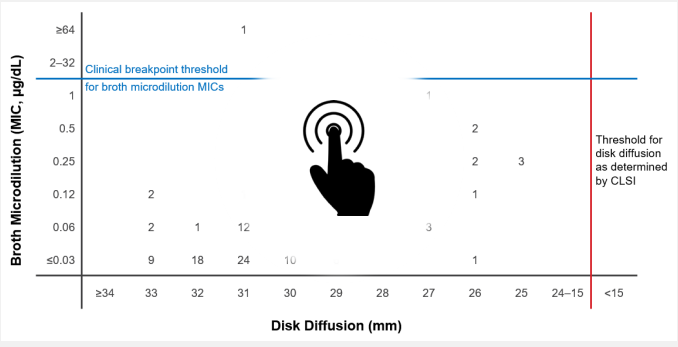
Results[18]

- Antimicrobial susceptibility testing results are presented in **Table 6**, and a comparison of the broth microdilution and disk diffusion results for cefiderocol is shown in **Figure 4**

Table 6. Antimicrobial Susceptibility Testing Results for All 146 *S. maltophilia* Isolates[18]

Antibiotic	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	Susceptibility Rate (%)
Cefiderocol		0.25	99.3 (145/146)
Trimethoprim–sulfamethoxazole		≤8	94.5 (138/146)
Levofloxacin		>8	78.1 (114/146)
Minocycline		≤2	100 (146/146)
Ceftazidime	>32	≥32	38.4 (56/146)

Figure 4. Comparison of Broth Microdilution and Disk Diffusion Testing Results for Cefiderocol[18]



- The single isolate resistant to cefiderocol (MIC ≥64 µg/mL) was also shown to possess resistance to trimethoprim–sulfamethoxazole (MIC ≥4/76 µg/mL), levofloxacin (MIC ≥8 µg/mL), and ceftazidime (MIC ≥32 µg/mL), but showed susceptibility to minocycline (MIC ≤2 µg/mL)
- Results from disk diffusion testing demonstrated that all 146 *S. maltophilia* isolates were susceptible to cefiderocol (based on CLSI interpretative criteria, with a disk diffusion diameter of ≥15 mm considered susceptible)

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Surveillance Studies (Cont.)

Table 6. Antimicrobial Susceptibility Testing Results for All 146 *S. maltophilia* Isolates[18]

Antibiotic	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	Susceptibility Rate (%)
Cefiderocol	0.06	0.25	99.3 (145/146)
Trimethoprim–sulfamethoxazole	≤2/38	≤2/38	94.5 (138/146)
Levofloxacin	≤1	≥8	78.1 (114/146)
Minocycline	≤2	≤2	100 (146/146)
Ceftazidime	16	≥32	38.4 (56/146)

Abbreviation: $MIC_{50/90}$, minimum inhibitory concentration to inhibit 50% and 90% of growth.
Table adapted from Sakoh et al. *Eur J Clin Microbiol Infect Dis*. 2024.

Table 6. Antimicrobial Susceptibility Testing Results for All 146 *S. maltophilia* Isolates[18]

Figure 4. Comparison of Broth Microdilution and Disk Diffusion Testing Results for Cefiderocol[18]

- The single isolate resistant to cefiderocol (MIC ≥64 µg/mL) was also shown to possess resistance to trimethoprim–sulfamethoxazole (MIC ≥4/76 µg/mL), levofloxacin (MIC ≥8 µg/mL), and ceftazidime (MIC ≥32 µg/mL), but showed susceptibility to minocycline (MIC ≤2 µg/mL)
- Results from disk diffusion testing demonstrated that all 146 S. maltophilia isolates were susceptible to cefiderocol (based on CLSI interpretative criteria, with a disk diffusion diameter of ≥15 mm considered susceptible)

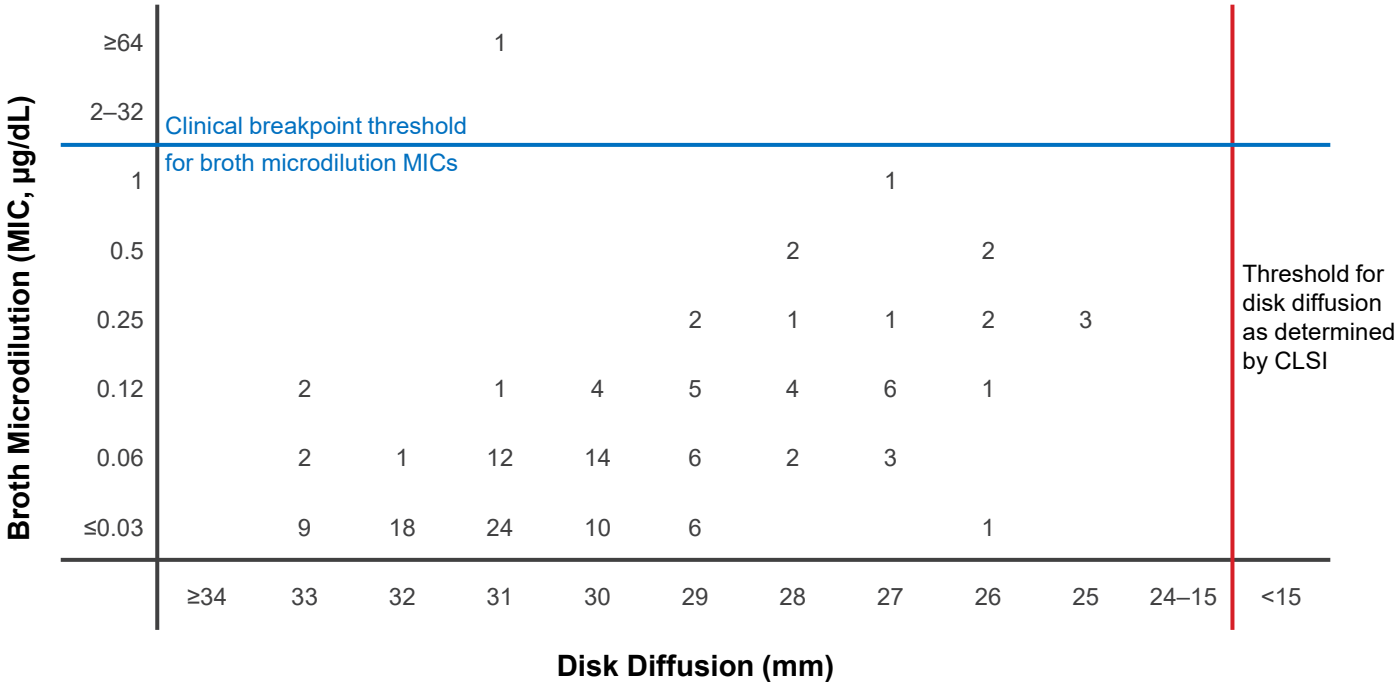
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Surveillance Studies (Cont.)

Figure 4. Comparison of Broth Microdilution and Disk Diffusion Testing Results for Cefiderocol[18]



Abbreviations: CLSI, Clinical Laboratory and Standards Institute; MIC, minimum inhibitory concentration.
Figure adapted from Sakoh et al. *Eur J Clin Microbiol Infect Dis*. 2024.

- The single isolate resistant to cefiderocol (MIC ≥64 µg/mL) was also shown to possess resistance to trimethoprim–sulfamethoxazole (MIC ≥4/76 µg/mL), levofloxacin (MIC ≥8 µg/mL), and ceftazidime (MIC ≥32 µg/mL), but showed susceptibility to minocycline (MIC ≤2 µg/mL)
- Results from disk diffusion testing demonstrated that all 146 *S. maltophilia* isolates were susceptible to cefiderocol (based on CLSI interpretative criteria, with a disk diffusion diameter of ≥15 mm considered susceptible)

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Surveillance Studies (Cont.)

Nguyen et al (2023) analyzed data from the ongoing SENTRY multinational surveillance program, which collects consecutive clinical isolates of Gram-negative bacterial pathogens from hospitalized patients with all infection types in US hospitals.[19]

Methods[19]

- The *in vitro* activity of cefiderocol and comparator antibiotics was determined by broth microdilution according to CLSI methods using ID-CAMHB for cefiderocol and CAMHB for other antibiotics
- Comparator antibiotics included levofloxacin, minocycline, and trimethoprim–sulfamethoxazole for *S. maltophilia*
- Susceptibility to cefiderocol was interpreted using CLSI 2023 breakpoints

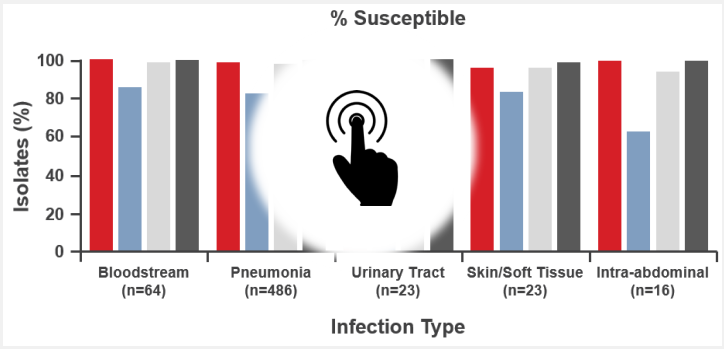
Results[19]

- Overall, 657 *S. maltophilia* isolates were collected and tested and 98.5% were susceptible per CLSI interpretive criteria
- Cefiderocol had the lowest MIC_{90} among comparator antibiotics (Table 7)
- Cefiderocol demonstrated high activity by infection type, with the most common infection sites being pneumonia (n=486), skin and soft tissue infection (n=68), and bloodstream infection (n=64), see Figure 5

Table 7. Activity of Cefiderocol and Comparator Agents Tested against *S. maltophilia* in the SENTRY Surveillance Program[19]

Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	CLSI[a]			FDA[a]		
					%R	%S	%I	%R
S. maltophilia (n=657)								
Cefiderocol	0.06				–	–	–	–
Levofloxacin	1				10.6	–	–	–
Trimethoprim–sulfamethoxazole	≤0.12				2.3	–	–	–
Minocycline	0.5	1		0	0.1	–	–	–

Figure 5. Activity of Cefiderocol and Comparator Agents Tested against *S. maltophilia* in the SENTRY Surveillance Program Stratified by Infection Type[19]



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Surveillance Studies (Cont.)

Table 7. Activity of Cefiderocol and Comparator Agents Tested against *S. maltophilia* in the SENTRY Surveillance Program[19]

Agent	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	CLSI[a]			FDA[a]		
			%S	%I	%R	%S	%I	%R
***S. maltophilia* (n=657)**								
Cefiderocol	0.06	0.25	98.5	–	–	–	–	–
Levofloxacin	1	8	82	7.4	10.6	–	–	–
Trimethoprim–sulfamethoxazole	≤0.12	0.5	97.7	–	2.3	–	–	–
Minocycline	0.5	1	99.9	0	0.1	–	–	–

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; FDA, US Food and Drug Administration; I, intermediate; MIC, minimum inhibitory concentration; MIC_{50}, MIC value at which concentration 50% of tested strains were inhibited; MIC_{90}, MIC value at which concentration 90% of tested strains were inhibited; R, resistant; S, susceptible; US, United States.
[a]Criteria as published by CLSI (2023), and FDA (2023).
Table adapted from Nguyen et al. IDWeek. 2023.

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Surveillance Studies (Cont.)

Figure 5. Activity of Cefiderocol and Comparator Agents Tested against *S. maltophilia* in the SENTRY Surveillance Program Stratified by Infection Type[19]

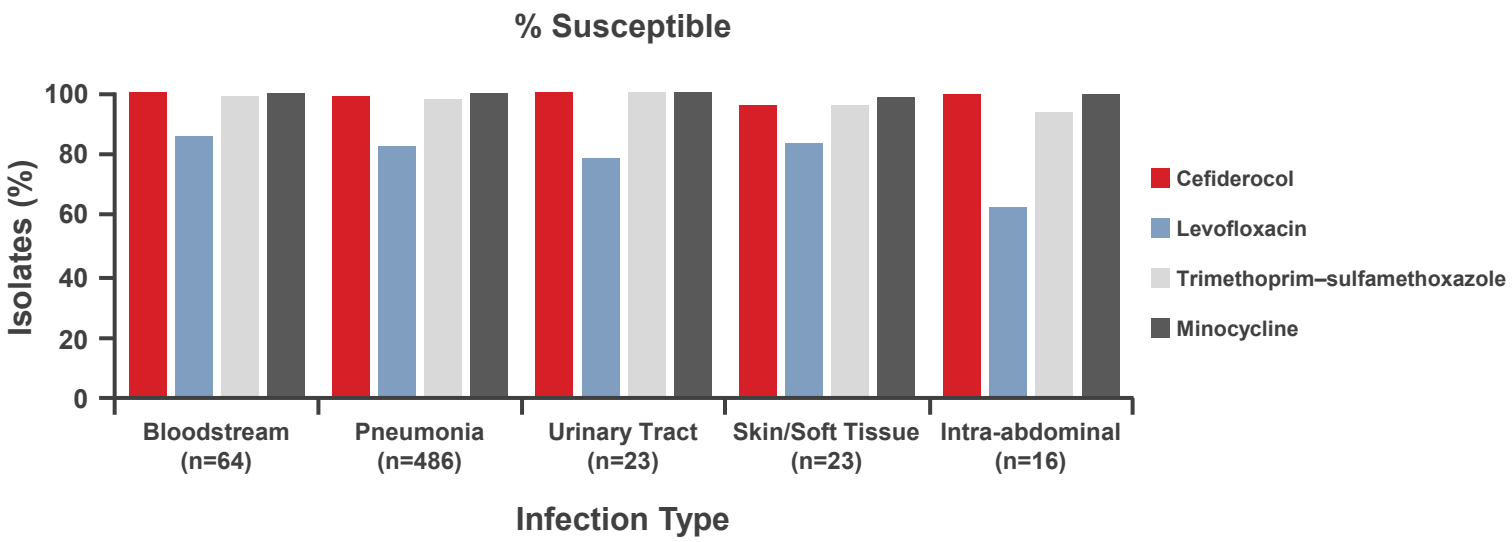


Figure adapted from Nguyen et al. IDWeek. 2023

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Surveillance Studies (Cont.)

Karlowsky et al (2022) presented the results from the multinational SIDERO-WT 2014-2019 surveillance program, which collected clinical Gram-negative bacterial from US and European hospitals from patients with various infection types.[20]

Methods[20]

- MICs were determined using CLSI methods and interpreted according to CLSI 2022 susceptibility breakpoints for *S. maltophilia* (susceptible: MIC ≤1 µg/mL, NS: MIC >1 µg/mL)

Results[20]

- Of the 2031 *S. maltophilia* isolates, cefiderocol inhibited 98.6% of strains
- The MIC_{90} for cefiderocol was 0.25 µg/mL, while for all comparator antibiotics, including colistin, MIC_{90} was >8 µg/mL
- The variation in the annual susceptibility rates in North America and Europe did not exceed 3.6% and 4.4%, respectively
- The lowest susceptibility rate in North America was 96.4% in year 2015 and 95.6% in year 2014 in Europe (**Table 8**)

Table 8. Annual Cefiderocol Susceptibility Testing Results for *S. maltophilia* Isolates Collected Between 2014 and 2019[20]

	CLSI MIC Interpretation (% Susceptible/Intermediate/Resistant)						
S. maltophilia[a]	2014	2015	2016	2017	2018	2019	Maximum difference in annual % susceptible from 2014 to 2019
North America	(21) 100/NA/NA	(140) 96.4/NA/NA	(200) 99.0/NA/NA	(187) 100/NA/NA	(198) 98.5/NA/NA	(217) 99.5/NA/NA	3.6
Europe	(114) 95.6/NA/NA	(172) 100/NA/NA	(209) 99/NA/NA	(133) 99.2/NA/NA	(190) 96.8/NA/NA	(249) 98.4/NA/NA	4.4

Abbreviations: CLSI, Clinical Laboratory Standards Institute; MIC, minimum inhibitory concentration; NA, not available.
[a]CLSI MIC breakpoints for cefiderocol tested against *S. maltophilia*: susceptible, ≤1 µg/mL; NS, >1 µg/mL.
Table adapted from Karlowsky et al. *Antimicrob Agents Ch*emother. 2022.

Surveillance Studies (Cont.)

SIDERO-WT 2014–2016, 2018, 2019 and Proteeae

To investigate the *in vitro* activity of cefiderocol and comparators against Gram-negative bacterial isolates, data from SIDERO-WT, a multinational surveillance study conducted in North America and Europe, were analyzed.[21]

Methods[21]

- Broth microdilution was used to test susceptibility to cefiderocol and meropenem
- Meropenem CLSI breakpoints were used to define CR
- Susceptibility testing was conducted for all aerobic Gram-negative bacteria, including *S. maltophilia*, which is intrinsically resistant to carbapenems
- The susceptibility ratio of cefiderocol was calculated according to the CLSI breakpoint of ≤1 µg/mL for *S. maltophilia*

Results[21]

- 47,615 Gram-negative isolates were collected, among which 2031 isolates of *S. maltophilia* were isolated and tested. Susceptibility rates to cefiderocol and comparator antibiotics are shown in **Table 9**

Table 9. Percentage of Susceptible Strains against All Gram-Negative Bacteria Collected in Multinational Surveillance SIDERO-WT-2014–2016, -2018, -2019, and Proteeae[21]

Species (Number of Strains)	Percentage of Susceptible Strains (%)[a]						
	Cefiderocol	Ceftazidime–avibactam	Ceftolozane–tazobactam	Ciprofloxacin	Colistin	Meropenem–vaborbactam[c]	Imipenem–relebactam[d]
All Gram-negative (47,615)	99.3	89.5	(N=		95.3 (N=39,454)	87.7 (N=17,156)	78.2 (N=9327)
S. maltophilia (2031)	98.6[e]	40	32.5 (N=1565)	37.6	68.7	3.8 (N=858)	1.9 (N=466)

Surveillance Studies (Cont.)

Table 9. Percentage of Susceptible Strains against All Gram-Negative Bacteria Collected in Multinational Surveillance SIDERO-WT-2014–2016, -2018, -2019, and Proteeae[21]

Species (Number of Strains)	Percentage of Susceptible Strains (%)[a]						
	Cefiderocol	Ceftazidime–avibactam	Ceftolozane–tazobactam[b]	Ciprofloxacin	Colistin	Meropenem–vaborbactam[c]	Imipenem–relebactam[d]
All Gram-negative (47,615)	99.3	89.5	85.8 (N=45,868)	68.3	95.3 (N=39,454)	87.7 (N=17,156)	78.2 (N=9327)
S. maltophilia (2031)	98.6[e]	40	32.5 (N=1565)	37.6	68.7	3.8 (N=858)	1.9 (N=466)

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration.

[a]Ratios (%) of susceptible strains were calculated by using the following MIC criteria established by CLSI. If there was no CLSI criteria that met the combinations of drugs and species, the CLSI criteria for the closely related species or the criteria established by EUCAST were applied: cefiderocol ≤4μg/mL for all species, except *Burkholderia* spp. (CLSI), ceftazidime–avibactam MIC ≤8 μg/mL for Enterobacterales and *P. aeruginosa* (CLSI) and the same criteria were applied for non-fermenters except for *P. aeruginosa*, ceftolozane–tazobactam MIC ≤2 μg/mL for Enterobacterales (CLSI), ≤4μg/mL for *P. aeruginosa* (CLSI) and other non-fermenters, ciprofloxacin MIC ≤0.25 μg/mL for Enterobacterales (CLSI), ≤0.5 μg/mL for *P. aeruginosa* (CLSI), and ≤1 μg/mL for *Acinetobacter* spp. (CLSI) and other non fermenters, colistin MIC ≤2 μg/mL of intermediate criteria for all Gram-negatives (CLSI) was used as the susceptible breakpoint, meropenem–vaborbactam MIC ≤4 μg/mL for Enterobacterales (CLSI), and ≤8 μg/mL for non-fermenters (EUCAST's criteria for *P. aeruginosa*).

[b]Ceftolozane–tazobactam was tested for all Gram-negatives in SIDERO-WT-2014 to 2018 and Proteeae studies.

[c]Meropenem–vaborbactam was only tested in SIDERO-WT-2018 and 2019.

[d]Imipenem–relebactam was only tested in SIDERO-WT-2019.

[e]Susceptibility rate was calculated based on CLSI 2022 breakpoints (susceptible: ≤1 μg/mL, NS: >1 μg/mL).

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Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[24]

- Complicated urinary tract infections (cUTIs), 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:[24]

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

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Literature Search

As of April 2026, a computerized search of the published medical literature using internal and external databases (ie, PubMed®) has identified several additional relevant references regarding the activity of cefiderocol against resistant *S. maltophilia*. For your review, these references are listed in the bibliography below:

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- Kung F, Lentini S, Kunz Coyne AJ, Gray R, Do A. Activity of cefiderocol-based combinations against cefiderocol-resistant *Stenotrophomonas maltophilia* isolates. Poster presented at: IDWeek 2025; October 19–23, 2025; Atlanta, GA
- Nguyen ST, et al. Cefiderocol remains active against US clinical isolates of *Stenotrophomonas maltophilia* non-susceptible to comparator agents: results from the SENTRY Antimicrobial Surveillance Program (2020–2024). Poster presented at: IDWeek 2025; October 19–23, 2025; Atlanta, GA.
- Yamano Y, DeJonge BL, Nguyen Stet al. Analyzing trends of cefiderocol susceptibility across five years of the SENTRY surveillance program. Poster presented at: IDWeek 2025; October 19–23, 2025; Atlanta, GA.

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Literature Search

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- Wang Y, Li Y, Zhao J, Guan J, Ni W, Gao Z. Susceptibility of cefiderocol and other antibiotics against carbapenem-resistant, Gram-negative bacteria. *Ann Transl Med*. 2022;10(5):261. [Web Link]

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.

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Abbreviations

ACM	all-cause mortality	ICU	intensive care unit
AE	adverse event	ID-CAMHB	iron-depleted cation-adjusted Mueller Hinton broth
AML	acute myeloid leukemia	ITT	intent-to-treat
APACHE II	Acute Physiology and Chronic Health Evaluation II	IV	intravenous
BAT	best-available therapy	LRTI	lower respiratory tract infection
BSI	bloodstream infection	MDR	multi-drug resistant
CAMHB	Cation-adjusted Mueller Hinton broth	MIC	minimum inhibitory concentration
CCI	Charlson Comorbidity Index	mITT	modified intent-to-treat
CLSI	Clinical Laboratory Standards Institute	NDM	New Delhi metallo-β-lactamase
COVID-19	Coronavirus disease-19	NS	non-susceptible
CR	carbapenem-resistant	PD	pharmacodynamics
CrCl	creatinine clearance	PDR	pan-drug resistant
CRBSI	catheter-related bloodstream infection	PK	pharmacokinetics
CR-Micro-ITT	carbapenem-resistant bloodstream infection	q6h	every 6 hours
cUTI	complicated urinary tract infection	q8h	every 8 hours
DoL	day of life	q12h	every 12 hours
EOS	end of study	RTI	respiratory tract infection
EUCAST	European Committee on Antimicrobial Susceptibility Testing	SOFA	Sequential Organ Failure Assessment
FDA	US Food and Drug Administration	TOC	test of cure
g	grams	US	United States
h	hours	VABP	ventilator-associated bacterial pneumonia
HABP	hospital-acquired bacterial pneumonia	VAP	ventilator-associated pneumonia
HCABP	healthcare-associated bacterial pneumonia	y	years
HSCT	hematopoietic stem cell transplant		

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

Enclosure

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