# Fetroja – Skin Penetration/Use in Skin Infections and Wounds

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 U.S. 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.**

## 1. SUMMARY

- In **preclinical** studies, cefiderocol penetration into the skin of rats was negligible, based on quantitative whole-body autoradiography[1]
- **Clinical** studies to evaluate the safety and efficacy of cefiderocol to treat skin infections or wounds have not been conducted
- A **retrospective study** evaluated 30-day all-cause mortality (ACM) in 41 patients with various infection types, including 9 patients with skin and soft tissue infections, treated with cefiderocol in Italy. *Acinetobacter baumannii* isolates accounted for most of the infections (n=8), followed by *Klebsiella pneumoniae* (n=3), and *Pseudomonas aeruginosa* (n=2). The ACM rate was 11.1% (n=1). Microbiological eradication at end-of-therapy (EOT), clinical cure at EOT, and clinical response in the first 72 hours (h) were all 88.9%[2]
- **Marcella S et al** evaluated interim data from the PROVE (ie, Retrospective Cefiderocol Chart Review Study) real-world evidence study, which included patients with *A. baumannii* and *P. aeruginosa* infections who were treated with cefiderocol. Clinical cure and 30-day ACM were reported for patients with *A. baumannii* and *P. aeruginosa* with either monomicrobial or polymicrobial infections[3,4]
    - In patients with *A. baumannii* skin and skin structure infections (SSSI), the clinical cure and 30-day ACM rates for patients with monomicrobial infections (n=6) was 83% and 0%, respectively. For those with polymicrobial infections (n=7) the clinical cure rate was 57% and 30-day ACM was 29%
    - The clinical cure and 30-day ACM for patients with *P. aeruginosa* monomicrobial SSSIs (n=3) was 67% and 0%, respectively. In 8 patients with polymicrobial infections, the clinical cure rate was 50% and the 30-day ACM was 38%
- 3 published case reports are described:
    - A 78-year-old hospitalized female who was successfully treated with cefiderocol for a multidrug-resistant (MDR) *Acinetobacter* species (spp.)-infected decubitus ulcer[5]
    - A 33-year-old hospitalized male soldier with a wound due to an explosive device, was successfully treated with cefiderocol and tigecycline. 2 distinct carbapenem-resistant (CR) *Escherichia coli* isolates harboring New Delhi metallo-β-lactamase-5 (*bla*NDM-5) were cultured, each with a cefiderocol minimum inhibitory concentration (MIC) of 2 µg/mL. Prior to treatment with cefiderocol, empiric therapy was administered followed by treatment with amikacin and subsequently colistin and tigecycline[6]
    - A 65-year-old male was successfully treated for an extensively drug-resistant (XDR) *P. aeruginosa* infection (cefiderocol MIC of 0.5 µg/mL) of a neurological surgical wound after treatment failures with other agents[7]
- Numerous compassionate use cases of patients treated with cefiderocol and/or other antibiotics presenting with skin or wound infections are described in the **Appendix Table 1**. Among the cases are patients with infections due to different pathogens, including patients with various outcomes[8,9]

## 2. PRECLINICAL STUDIES

Studies evaluating the skin penetration of cefiderocol in humans have not been conducted.

The tissue distribution of cefiderocol was investigated using quantitative whole-body autoradiography (QWBA) after a single intravenous (IV) bolus of radiolabeled cefiderocol in rats under non-fasted conditions. In the 2 studies described below, radiolabeled cefiderocol hardly penetrated the skin.[1]

- In male pigmented rats (Long-Evans rats) administered [catechol-14-C]-cefiderocol sodium at 30 mg/kg, the concentrations of radioactivity in the melanin rich tissues (uveal tract/retina and pigmented skin) were below the lower limit of quantification (BLQ) by 120 h postdose
- In male and female albino rats (Sprague Dawley rats) and male pigmented rats (Long-Evans rats) administered [thiazole-14C]-cefiderocol sodium at 30 mg/kg, the levels of radioactivity in the melanin-rich tissues (uveal tract and pigmented skin) in pigmented rats had the same level of elevation as those observed in the uveal tract and skin in albino rats
    - Tissue elimination half-lives of radioactivity in the melanin-rich tissues in pigmented rats and those in non-melanin tissues in albino rats were similar

## 3. CLINICAL STUDIES

The efficacy and safety of cefiderocol in treating patients with infections originating from the skin such as skin, soft tissue infections, cellulitis and wounds have not been evaluated in our clinical trial program.

## 4. RETROSPECTIVE STUDY

**Palermo et al (2023)** conducted a retrospective study which included 9 patients with skin and soft tissue infections (SSTIs) treated with cefiderocol between September 2021 and July 2022 in Palermo, Italy.[2]

- Cefiderocol 2 g every 8 hours (q8h) over 3 h (with adjustments for renal impairment) was administered as monotherapy in 6 (66.7%) patients or as combination treatment in 3 (33.3%) patients
- The primary outcome was 30-day ACM. Secondary outcomes included clinical cure at EOT, clinical response in the first 72 h of treatment, and microbiological eradication

***Results***

- Of the 41 patients included in the study, 9 (21.9%) had a SSTI[2]
- Polymicrobial infections were identified in 3 (33.3%) patients. 8 (88.9%) CR *A. baumannii* isolates, 3 *K. pneumoniae* isolates, and 2 *P. aeruginosa* isolates were identified[2]
- Outcome details are provided in **Table 1**

**Table 1. 30-Day All-Cause Mortality and Secondary Outcomes in Patients with Skin and Soft Tissue Infections Treated with Cefiderocol[2]**

| Study Population n (%) N=41 | Monotherapy n (%) (n=9) | Combination Therapy n (%) (n=9) | 30-Day ACM n (%) (n=9) | Microbiological Eradication at EOT[a] n (%) (n=9) | Clinical Cure at EOT[b] n (%) (n=9) | Clinical Response in First 72 h[c] n (%) (n=9) | Days of Therapy Median (IQR) |
|---|---|---|---|---|---|---|---|
| 9 (21.9%) | 6 (66.7%) | 3 (33.3%) | 1 (11.1%) | 8 (88.9) | 8 (88.9) | 8 (88.9) | 11 (8-22) |

**Abbreviations:** ACM, all-cause mortality; EOT, end-of-therapy; h, hours; IQR, interquartile range.
[a]Defined as documented or presumed eradication of isolated bacteria at EOT.
[b]Defined as symptom resolution and clearance of inflammatory markers.
[c]Defined as an initial clinical response in which it was not necessary to switch therapy or the patient did not die.

## 5. REAL-WORLD EVIDENCE

**Marcella S et al (2022)** evaluated interim data from the PROVE study (i.e. Retrospective Cefiderocol Chart Review Study), which was a multicenter, retrospective, chart review study in patients treated with cefiderocol in the United States (US) and European hospitals. The analyses described the outcomes of cefiderocol treatment in subsets of patients with *A. baumannii*, most of which were carbapenem-resistant *A. baumannii* (CRAB), and *P. aeruginosa*.[3,4]

***Methods***

- The primary objectives of PROVE include describing the clinical and microbiological characteristics of infections treated with cefiderocol, in addition to assessment of patient outcomes, and safety[3,4]
- Patients with a documented Gram-negative bacterial infection are eligible for enrollment if they received cefiderocol treatment for the first time for ≥72 hours. Patients who received cefiderocol prior to local commercial availability were excluded from the study[3,4]
- Included in the outcomes are clinical resolution of Gram-negative bacterial infection (clinical signs and/or symptoms have resolved or improved without relapse) at EOT, 30-day ACM, and safety[3,4]
- Index culture samples were obtained before starting cefiderocol treatment or after cefiderocol treatment, if used empirically[3,4]
- Susceptibility to carbapenems was determined using local antibiotic susceptibility testing (AST). AST results included MICs or zone sizes based on reports generated by each site's laboratory. Recommended breakpoints, as outlined by the Clinical and Laboratory Standards Institute (CLSI) and the FDA were used to determine susceptibility[3,4]
- Descriptive statistics were used to describe all collected data[3,4]

***Results***

- Patients (n=220) from 21 sites were enrolled as of August 9, 2022. Of these, 26 had a SSSI[3,4]

<u>*Acinetobacter baumannii*</u>[4]

- These results include data from 76 patients with *A. baumannii* infections of various infection types. Most infections were monomicrobial (63%), while 37% were polymicrobial
- The study included a total of 14 (18%) patients with SSSI; 6/76 (8%) patients had monomicrobial SSSI and 7/76 (9%) patients had polymicrobial SSSI. Additionally, 1 patient had a SSSI with *A. baumannii* as co-infection, not the primary infection. See **Table 2** for outcome data

<u>*Pseudomonas aeruginosa*</u>[3]

- Data from 120 patients with *P. aeruginosa* infections from various infection sites were included. Monomicrobial infections accounted for 64% of infections, while 32.5% were polymicrobial
- A total of 12/120 (10%) patients had a SSSI with *P. aeruginosa*. 3 patients (3%) had a monomicrobial SSSI infection and 8 (7%) had polymicrobial infections. 1 patient had a SSSI with *P. aeruginosa* as co-infection, not the primary infection. See **Table 2** for outcome data

**Table 2. Outcomes by Key Characteristics of Patients with *Acinetobacter baumannii* or *Pseudomonas aeruginosa* Skin and Skin Structure Infections[3,4]**

| Characteristic | Overall | Clinical Cure[a] | 30-Day Mortality |
|---|---|---|---|
| | Number of isolates | n (%) | n (%) |
| ***Acinetobacter baumannii*** | | | |
| Overall Number of Patients (various infection sites)[b] | 76 | 48 (63) | 16 (21) |
| Monomicrobial– Primary Infection Site<br>Skin and skin structure | 6 | 5 (83) | 0 (0) |
| Polymicrobial – Primary Infection Site<br>Skin and skin structure | 7 | 4 (57) | 2 (29) |
| *Acinetobacter baumannii* as co-infection, not primary<br>Skin and skin structure | 1 | 1 (100) | 0 (0) |
| ***Pseudomonas aeruginosa*** | | | |
| Overall Number of Patients (various infection sites)[b] | 120 | 76 (63) | 25 (21) |
| Monomicrobial – Primary Infection Site<br>Skin and skin structure | 3 | 2 (67) | 0 (0) |
| Polymicrobial – Primary Infection Site<br>Skin and skin structure | 8 | 4 (50) | 3 (38) |
| *Pseudomonas aeruginosa* as co-infection, not primary<br>Skin and skin structure | 1 | 1 (100) | 0 (0) |

[a]Clinical cure based on answer to the clinical assessment question: resolved, improved = cured; resolved then relapse, failure, or unknown = not cured.
[b]Various infection sites include blood, bone/joint, intra-abdominal, respiratory, skin and skin structure, urine, and other sites.

## 6. CASE REPORTS

**DiTursi and Gilotra (2021)** described a 78-year-old female who was hospitalized for debridement of an extensive decubitus ulcer.[5]

- After debridement, an MDR *Acinetobacter* spp. was grown from a wound culture on Day 3. Serial debridements were continued in addition to treatment with meropenem
- An *Acinetobacter* spp. resistant to all agents tested was isolated on Day 31. Cefiderocol was initiated along with the continuation of local wound care. No additional surgical debridements were conducted
- Cefiderocol treatment ended on Day 49 of her hospital stay, and no additional *Acinetobacter* spp. was isolated. The patient was clinically stable during treatment with cefiderocol

**Carney et al (2021)** reported on a 33-year-old male soldier who underwent an amputation and hemipelvectomy subsequent to a serious blast injury. He was left with a large soft tissue wound on the right flank. 2 genetically distinct isolates of CR *E. coli* that possessed a variant NDM-MBL (*bla*NDM-5) were isolated from blood and deep wound cultures.[6]

- The patient was initially treated with ertapenem and subsequently broadened to empiric therapy. After antibiotic susceptibilities were determined on post-injury day (PID) 7, he continued on amikacin and was subsequently treated with colistin. On PID 13 tigecycline was added (*E. coli* was isolated again from an intraoperative culture)
- Due to the potential for colistin-induced neurotoxicity, treatment with cefiderocol (through compassionate use) was pursued. Both *E. coli* isolates had a cefiderocol MIC of 2 µg/mL and therefore, treatment with cefiderocol (in addition to tigecycline), was started on PID 22

- After treatment with cefiderocol and tigecycline for 4 weeks, wound cultures were negative. As the patient's surgical course improved, skin grafting, and wound closure was accomplished. During the patient's approximately 4-month hospitalization, he did not have a re-infection

**Bavaro et al (2021)** reported on the successful compassionate use of cefiderocol to treat a 64-year-old male who developed an infection caused by XDR *P. aeruginosa* at a neurological surgical wound site that had not responded to several antibiotic regimens and right parietal bone excision. A MIC for cefiderocol of 0.5 µg/mL against *P. aeruginosa* was determined by broth microdilution and considered susceptible based on the susceptibility breakpoint of ≤2 µg/mL established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Additional details are provided in **Table 3**.[7]

**Table 3. Compassionate use of Cefiderocol to Treat a Patient with a Recurring Neurosurgical Infection due to XDR-*Pseudomonas aeruginosa*[7]**

| Infection Type | Causative Pathogen | Concomitant Antibiotics | Cefiderocol Dose and Regimen | Cefiderocol Treatment Duration, Days | Reported SAEs | Patient Outcome |
|---|---|---|---|---|---|---|
| Recurrent neurosurgical site infection of the right parietal bone | XDR-*Pseudomonas aeruginosa* | Fosfomycin, 6 g q8h | 2 g q8h infused over 3 h TID | 14 | None | Success; after 30 days from discharge, no relapse of infection was reported |

**Abbreviations:** q8h, every 8 hours; SAE, serious adverse event; TID, 3 times daily; XDR, extensively drug-resistant.

## 7. ADDITIONAL COMPASSIONATE USE

Prior to the approval of cefiderocol in the United States by the FDA and in European countries by the European Commission, Shionogi has provided cefiderocol through compassionate use upon unsolicited request from attending physicians to patients with serious carbapenem resistant (CR) Gram-negative infections who have no other treatment options. All other available treatments must be ruled out through susceptibility testing and/or evidence of treatment failure in efficacy or safety, and patients must be unable to enroll in clinical studies of cefiderocol.[8,9]

Of the patients that completed cefiderocol therapy through compassionate use (as of November 2020), there were several patients that presented with infections originating from the skin or wounds (see Appendix Table 1).[8,9]

## RELEVANT PRESCRIBING INFORMATION

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[10]

- Complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *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*, and *Serratia marcescens*

Fetroja is contraindicated in:[10]

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

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

**LITERATURE SEARCH**

As of December 2025, a computerized search of the published medical literature using internal and external databases (ie, Medline® and Embase®) has identified additional relevant references regarding the penetration of cefiderocol in the skin or use in treating skin or would infections. For your review, these references are listed in the bibliography that follows:


Kirkegaard-Biosca C, del Barrio-Tofino E, Villamarin M, et al. Cefiderocol for the treatment of infections by VIM-type-producing Gram-negative bacteria. *Antibiotics*. 2024;13(9):874. doi:10.3390/antibiotics13090874

Marino A, Rullo EV, Russotto Y, et al. Real-world effectiveness and safety of cefiderocol in critically ill patients with MDR Gram-negative infections: results from a retrospective study. Biomed Rep. 2025;23(4):156. doi:10.3892/br.2025.156

Torre-Cisneros J, Almirante B, Martos CF, et al. Effectiveness and safety of cefiderocol treatment in patients with Gram-negative bacterial infections in Spain in the early access programme: results of the PERSEUS study. *Eur J Clin Microbiol Infect Dis*. 2025;44(6):1375-1390. doi: 10.1007/s10096-025-05108-6

Kung F, Nguyen ST, DeJonge BLM, et al. *In vitro* activity of cefiderocol and comparator agents against non-fermentative Gram-negative bacilli Isolated from patients hospitalized with pneumonia as part of the SENTRY global surveillance program (2020-2022) Poster presented at: IDWeek 2024. October 16 - 19, 2024. Los Angeles, CA.

Petrucci F, Perciballi B, Rivano Capparuccia M, et al. Compassionate use of cefiderocol in a complex case of extensively drug-resistant *Acinetobacter baumannii* fracture-related infection: a comprehensive approach and multidisciplinary management. *Infection*. 2024;52(6):2487-2493. doi: 10.1007/s15010-024-02294-x

Sanz-Codina M, van Os W, Pham AD, et al. Target-site cefiderocol pharmacokinetics in soft tissues of healthy volunteers. *J Antimicrob Chemother*. 2024;79(12):3281-3288. doi: 10.1093/jac/dkae359

Nguyen ST, Valencia CV, Bryowsky JJ, et al. Antimicrobial activity of cefiderocol and comparator agents against isolates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii-calcoaceticus* species complex, and *Stenotrophomonas maltophilia* by infection type from United States hospitals in the SENTRY Antimicrobial Surveillance Program (2020-2022). Poster presented at: IDWeek 2023. October 11 – 15, 2023; Boston, MA.

Bryowsky JJ, DeJonge BLM, Nguyen ST, et al. *In vitro* activity of cefiderocol and comparator agents against Enterobacterales from United States hospitals stratified by infection type (2020-2022). Poster presented at: IDWeek 2023. October 11 – 15, 2023; Boston, MA.

Gavaghan V, Miller JL, Dela-Pena J. Case series of cefiderocol for salvage therapy in carbapenem-resistant Gram-negative infections. *Infection*. 2023;51(2):475-482. doi:10.1007/s15010-022-01933-5

Pallett SJC, Trompeter A, Basarab M, Moore LSP, Boyd SE. Multidrug-resistant infections in war victims in Ukraine. *Lancet Infect Dis*. 2023;23(8):e270-e271. doi: 10.1016/S1473-3099(23)00391-2.

**REFERENCES**

1. Data on File 35. Shionogi Inc.
2. Palermo G, Medaglia AA, Pipitò L, et al. Cefiderocol efficacy in a real-life setting: single-centre retrospective study. *Antibiotics (Basel)*. 2023;12(4). doi:10.3390/antibiotics12040746
3. Marcella S, Carr AL, Kobic E, S. N, Zhou A. Real-world experience of cefiderocol with *Pseudomonas aeruginosa* in the PROVE (Retrospective Cefiderocol Chart Review) study. Poster presented at: IDWeek 2022. October 19 - 23, 2022; Washington, DC.
4. Marcella S, Kobic E, Carr AL, Georgiades B, C. M. Outcomes using cefiderocol for the treatment of *Acinetobacter baumannii* infections from the PROVE (Real-World Evidence) study. Poster presented at: IDWeek 2022. October 19 - 23, 2022; Washington, DC.
5. DiTursi S, Giltra T. Successful use of cefiderocol for a decubitus ulcer infected with carbapenem-resistant *Acinetobacter*: A case report. *J Am Coll Clin Pharm*. 2021;4(12):1743. doi:10.1002/jac5.1561.
6. Carney BW, Rizzo JA, Alderete JF, Cindass R, Markelz AE, Cancio LC. Carbapenem-resistant enterobacterales infection after massive blast injury: use of cefiderocol based combination therapy. *Mil Med*. 2021;186(11-12):1241-1245. doi:10.1093/milmed/usab350
7. Bavaro DF, Romanelli F, Stolfa S, et al. Recurrent neurosurgical site infection by extensively drug-resistant *P. aeruginosa* treated with cefiderocol: a case report and literature review. *Infect Dis*. 2021;53(3):206-211. doi:10.1080/23744235.2020.1856921
8. Shionogi Inc. Cefiderocol Briefing Document. U.S. Food and Drug Administration. https://www.fda.gov/advisory-committees/advisory-committee-calendar/october-16-2019-antimicrobial-drugs-advisory-committee-meeting-announcement-10162019-10162019. Published October 11, 2019. Accessed September 23, 2022.
9. Clinical and Laboratory Standards Institute. Subcommittee on Antimicrobial Susceptibility Testing (AST): 2021 Winter BPWG 12B Cefiderocol Briefing Book. https://clsi.org/meetings/ast-file-resources/. Published February 25, 2021. Accessed August 11, 2022.
10. Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.

**ENCLOSURE**

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

# APPENDIX

**Appendix Table 1. Compassionate Use Summary Information by Patient (Patients with Skin Infections and Wounds)[8,9]**

| Country | Age/ Gender | Relevant Medical History | Infection Type | Causative Pathogen | Concomitant Antibiotics | Cefiderocol Dose and Regimen | Total Days Cefiderocol Treatment MIC[a] | Reported SAEs | Patient Outcome |
|---|---|---|---|---|---|---|---|---|---|
| USA | 69 y/ Female | Lung transplant complicated by empyema, multilevel rib osteomyelitis, kidney injury, and steroid-induced diabetes | Chest wall soft tissue infection | MDR *Pseudomonas aeruginosa* | Vancomycin, sulfamethoxazole/ trimethoprim, valganciclovir | 1 g q8h | 56<br>1st<br>0.5 µg/mL<br>2nd<br>2 µg/mL | None reported | Recovered and discharged home. Survived. |
| Switzerland | 28 y/ Female | Postoperative wound infection with osteomyelitis after a complicated tibia fracture | Postoperative wound infection with osteomyelitis of tibia fracture | *Pseudomonas aeruginosa* VIM, *Acinetobacter baumannii* OXA-23, *Enterobacter cloacae* KPC, and *Achromobacter xylosoxidans* | Daptomycin, colistin, tigecycline, ceftazidime/ avibactam | 2 g q8h | 20 | None reported | Bone infection completely healed. |
| USA | 22 y/ Male | Cystic fibrosis, lung transplant, respiratory failure, leukopenia, post-transplant chest wall and bloodstream infection | Chest wall and BSI | *Burkholderia cepacia* | Vancomycin, levofloxacin, meropenem, metronidazole, minocycline, septra, tedizolid, tobramycin | 2 g q8h over 3 h (19 days)<br>1.5 g q12h over 3 h (2 days) | 21 | Sepsis (physician assessed as unrelated to cefiderocol) | Died due to *Burkholderia* bacteremia refractory to multiple agents. |

| Patient/ Country | Age/ Gender | Relevant Medical History | Infection Type | Causative Pathogen | Concomitant Antibiotics | Cefiderocol Dose and Regimen | Total Days Cefiderocol Treatment, MIC | Reported SAEs | Patient Outcome |
|---|---|---|---|---|---|---|---|---|---|
| Italy | 25 y/ Female | Extensive burns | cSSSI | Pan-resistant *Acinetobacter baumannii* | None reported | 2 g q6h | 10 | Anemia | Survived. |
| USA | 71 y/ Female | Asthma, 67% total body surface area burn, acute respiratory failure, leukocytosis | Wound; pneumonia; bacteremia | *Pseudomonas aeruginosa*; *Stenotropho-monas maltophilia* | Amphotericin B; minocycline; meropenem | 2 g q8h | 8 ≤0.03 µg/mL | Worsening sepsis; death | Patient move to comfort care by family. |
| United Kingdom | 84 y/ Male | Type 2 diabetes, severe atherosclerosis, stroke | Infected diabetic left foot, multi-organ failure, AKI and sepsis | *Klebsiella pneumoniae* (OXA-48 and NDM) | Piperacillin/ tazobactum | 1 g q8h | 15 | Elevated LFTs which decreased toward normal while on treatment | Patient died 17 days after discontinuation of cefiderocol and dialysis due to multiorgan failure. |
| United Kingdom | 66 y/ Female | Hypothyroidism, hypertension, bilateral knee replacements, and lower back surgery | Wound and elbow joint repair infection | *Acinetobacter baumannii*, *Acinetobacter nosocomialis* | Tigecycline | Initial dosage not reported (8 days), final dosage 1.5 g q8h (17 days) | 25 | Increased ALP thought by the treating physician to be related to bone damage | Discharged from Hospital. Survived. |
| Italy | 55 y/ Female | Surgery for scoliosis with prostheses implant | ABSSSI; prostheses related bone infection | XDR *Acinetobacter baumannii* | None reported | 2 g q8h | 21 | None reported | Favorable outcome achieved by 14 days of treatment and 7 more days of treatment for the bone infection. Survived. |

| Patient/ Country | Age/ Gender | Relevant Medical History | Infection Type | Causative Pathogen | Concomitant Antibiotics | Cefiderocol Dose and Regimen | Total Days Cefiderocol Treatment, MIC | Reported SAEs | Patient Outcome |
|---|---|---|---|---|---|---|---|---|---|
| Italy | 60 y/ Female | Post-traumatic paraplegia sacral-perineal and perianal pressure ulcers (stage IV) | Bone infection and cSSTI | MDR *Acinetobacter baumannii* | None reported | 2 g q8h; CrCl = 150 mL/min | 21 | None reported | Complete Recovery; Survived. |
| USA | 54y/ Female | Chemotherapy for peripheral T-cell lymphoma (Sezary Syndrome); hospital acquired MRSA tricuspid valve endocarditis | BSI Skin Infection | XDR *Acinetobacter baumannii* BSI; *Klebsiella pneumoniae* skin infection | Meropenem | 1.5 g q8h | 15 XDR *Acinetobacter baumannii* 0.25 µg/mL *K. pneumoniae* 2 µg/mL | None reported | Survival |
| Germany | 33y/ Female | Liver cirrhosis, primary sclerosing cholangitis, thrombosis of portal vein, total colectomy and colitis ulcerosa (ulcerative colitis) | Intra-abdominal wound infection | MDR *Pseudomonas aeruginosa* | Polymyxin B | 2 g q8h CrCl = 40 mL/min | 8 Disk diameter >19 mm | Renal insufficiency, pneumonia, and disease progression | Survived |
| Spain | 53y/ Male | Splenectomy; *Haemophilus influenzae* pneumonia | Multiorgan failure and soft tissue necrosis | *Pseudomonas aeruginosa* VIM | Not clearly stated, colistin, linezolid, aztreonam, rifampicin | Dose and regimen not stated (CrCl = 15 mL/min (CRRT) | 16 | Not reported | The infection responded to treatment, and the patient survived. |

**Abbreviations:** ABSSSI, acute bacterial skin and skin structure infection; AKI, acute kidney injury; ALP, alkaline phosphatase; BSI, blood stream infection; CrCl, creatinine clearance; cSSSI, complicated skin and skin structure infection; CRRT, continuous renal replacement therapy; cSSTI, complicated skin and soft tissue infection; KPC, *Klebsiella pneumoniae* carbapenemase; LFT, liver function test; MIC, minimum inhibitory concentration; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; NDM, New Delhi metallo-β-lactamase; OXA-oxacillinase; q8h, every 8 hours; q12 h, every 12 hours; SAE, serious adverse event; USA, United States of America; VIM, Verona-integron-encoded metallo-β-lactamase; XDR, extensively drug-resistant; y, year.

[a]MICs are not available for all pathogens.