Fetroja® – Continuous Infusion and Extended Stability

SHIONOGI

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 | Case Series/ Case Studies | Individual Case Reports | Stability Studies | Relevant Prescribing Information | Literature Search | Abbreviations & References

Summary

Shionogi has not conducted studies assessing the safety or efficacy of administering cefiderocol with an infusion time beyond 3 h. The published case series/case studies/individual case reports below were described by external authors. Shionogi does not recommend the administration of cefiderocol with an infusion time longer than 3 hours

- **Prinz et al (2023)** evaluated quasi-continuous infusion of cefiderocol in 6 patients. Patients were treated with cefiderocol 2 g q8h over a 3 h infusion for 24 h followed by treatment with continuous infusion 6 g over 24 h (3 doses of 2 g over 8 h)[1]
- **Gatti et al (2023)** analyzed the PK/PD of cefiderocol administered via continuous infusion in 5 critically ill patients undergoing CVVH with CRAB infections. All patients received a cefiderocol loading dose of 2 g infused over 2 h followed by a maintenance dose of 2 g (over 8 h) q8h[2]
- **Babich et al (2025)** assessed the suitability of the administration of cefiderocol 6 g/day for 62 days administered as a 24 h continuous infusion via elastomeric pumps in a 31-year-old patient with NDM-producing *Klebsiella pneumoniae* otomastoiditis in conjunction with TDM[3]
- **Möhlman et al (2023)** described a 37-year-old female patient with abdominal sepsis and respiratory insufficiency due to MDR *Pseudomonas aeruginosa*, treated with cefiderocol 4 g daily via continuous infusion (1 g over 6 h QID) while receiving CVVH[4]
- **Ziegler et al (2021)** described a 46-year-old patient with MDR *P. aeruginosa* who received cefiderocol 2 g TID over a 4 h infusion[5]

Shionogi does not have additional data to support the extended stability of the reconstituted Fetroja vial or diluted Fetroja infusion solution beyond the storage and stability recommendations that are provided in the Fetroja Full Prescribing Information

- **Stability studies were conducted by external investigators (see Reference List). Shionogi does not recommend the storage of cefiderocol based on the findings of these external studies**

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Case Series/Case Studies

Shionogi has not conducted studies assessing the safety or efficacy of administering cefiderocol with an infusion time beyond 3 h. The published case series/case studies below were described by external authors. Shionogi does not recommend the administration of cefiderocol with an infusion time longer than 3 h.

Prinz et al (2023) conducted a study of 6 patients treated with cefiderocol via quasi-continuous infusion:[1]

- All patients received cefiderocol 2 g q8h over a 3 h infusion for 24 h
  - After 24 h, plasma samples were collected to measure trough concentrations
- Administration was changed to continuous infusion of 6 g over 24 h (3 doses of 2 g over 8 h)
- 4 of the 6 patients received a 2 g bolus followed immediately by continuous infusion; however, 2 patients did not receive the bolus dose
- XDR *K. pneumoniae* expressing NDM-type and OXA-48-like carbapenemases were isolated from respiratory samples in all 6 patients (intra-abdominal infection was the initial infection site in 1 patient)
- All strains were susceptible to cefiderocol (MIC range from 0.75 to 1 mg/L)

Gatti et al (2023) presented a retrospective case series assessing the PK/PD of cefiderocol administered via continuous infusion in 5 critically ill patients undergoing CVVHDF with CRAB infections:[2]

- All patients received a loading dose of cefiderocol (2 g over 2 h infusion) followed by a maintenance dose of 2 g (over 8 h) q8h
- Blood samples were collected after 24 h from the initiation of CVVH to measure cefiderocol C_{ss}
- The time with unbound serum cefiderocol above MIC (fC_{ss}/MIC) ratio was defined as optimal if ≥4
- Infection types included BSI with VAP (n=2), only VAP (n=2), BSI and cIAI (n=1 each)

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Individual Case Reports

Shionogi has not conducted studies assessing the safety or efficacy of administering cefiderocol with an infusion time beyond 3 h. The published individual case reports below were described by external authors. Shionogi does not recommend the administration of cefiderocol with an infusion time longer than 3 h.

Babich et al (2025) evaluated the use of elastomeric pumps for 24 h continuous infusion of cefiderocol in a 31-year-old male patient in the OPAT setting to treat otomastoiditis caused by NDM-producing *K. pneumoniae*:[3]

- Cefiderocol was initiated at 6 g/day as a 24 h continuous infusion using an elastomeric pump (INFUSOR LV; product code 2C2063K, 10 mL/h; Baxter), diluted in 240 mL of NS
- The treatment duration for cefiderocol was 63 days
- TDM was used to ensure optimal treatment efficacy and PK/PD
  - Plasma concentrations were assessed on Days 17 and 45

Möhlman et al (2023) described a 37-year-old female patient on CVVH being treated for abdominal sepsis with respiratory insufficiency caused by MDR *P. aeruginosa*:[4]

- She was switched from ceftazidime–avibactam in combination with colistin to cefiderocol 2 g TID for 3 doses followed by 1 g (6 h infusion time) QID administered as a continuous infusion (at a rate of 8.4 mL/h)
- Liquid chromatography–tandem mass spectrometry was used to assess the total cefiderocol concentrations from intraperitoneal drain, pre-/postfilter ultrafiltrate and plasma collections

Ziegler et al (2021) described a 46-year-old patient who received various anti-infective regimens for pneumonia that was caused by MDR *P. aeruginosa*:[5]

- Due to acute renal injury, CRRT was required
- Cefiderocol was administered as 2 g TID with an infusion time of 4 h

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Stability Studies

Shionogi does not have additional data to support the extended stability of the reconstituted Fetroja vial or diluted Fetroja infusion solution beyond the storage and stability recommendations that are provided in the Fetroja Full Prescribing Information.

The following stability studies were conducted by external investigators. Shionogi does not recommend the storage of cefiderocol based on the findings of these external studies.

- d'Huart E, Boutouha I, Berardi C, Vigneron J, Demore B, Charmillon A. Stability of nine time-dependent antibiotics for outpatient parenteral antimicrobial therapy (OPAT) use. *Antibiotics (Basel)*. 2025;14(5):466. [Web Link]
- Fernández-Rubio B, Herrera-Hidalgo L, de Alarcón A, et al. Stability studies of antipseudomonal beta lactam agents for outpatient therapy. *Pharmaceutics*. 2023;15(12):2705. [Web Link]
- Loeuille G, Vigneron J, D'Huart E, Charmillon A, Demoré B. Physicochemical stability of cefiderocol, a novel siderophore cephalosporin, in syringes at 62.5 mg/mL for continuous administration in intensive care units. *Eur J Hosp Pharm*. 2023;30(e1):e29-e34. [Web Link]
- Loeuille G, D'Huart E, Vigneron J, et al. Stability studies of 16 antibiotics for continuous infusion in intensive care units and for performing outpatient parenteral antimicrobial therapy. *Antibiotics (Basel)*. 2022;11(4):458. [Web Link]

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Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[6]

- 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:[6]

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

Section 2.1 Recommended Dosage of the **Fetroja Full Prescribing Information** states the following:[6]

- The recommended dosage of Fetroja is 2 grams administered every 8 hours by intravenous (IV) infusion over 3 hours in adults with a creatinine clearance (CLcr) of 60 to 119 mL/min.
- Dosage adjustment of Fetroja is recommended for patients with CLcr less than 60 mL/min, including patients receiving intermittent hemodialysis (HD) or continuous renal replacement therapy (CRRT), and for patients with CLcr 120 mL/min or greater *[see Dosage and Administration (2.2)]*. The recommended duration of treatment with Fetroja is 7 to 14 days. The duration of therapy should be guided by the patient's clinical status.

Section 2.5 Storage of Reconstituted Solutions of the **Fetroja Full Prescribing Information** states the following:[6]

Diluted Fetroja Infusion Solution

- The diluted Fetroja infusion solution in the infusion bag is stable for up to 6 hours at room temperature.
- The diluted Fetroja infusion solution in the infusion bag may also be refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours, protected from light; and then the infusion should be completed within 6 hours at room temperature.

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

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Literature Search

Sept 2026

As of September 2026, a computerized search of the published medical literature using internal and external databases (ie, Medline® and Embase®) has identified several additional relevant references regarding the continuous/extended/prolonged infusion of cefiderocol or for the extended stability of cefiderocol. For your review, these references are listed in the bibliography that follows:

- Goutelle S, Ammour N, Ferry T, Schramm F, Lepeule R, Friggeri A. Optimal dosage regimens of cefiderocol administered by short, prolonged or continuous infusion: a PK/PD simulation study. *J Antimicrob Chemother*. 2025;80(3):726-730. [Web Link]
- Granata G, Venditti C, Rotondo C, et al. Combating metallo-β-lactamase-producing *Pseudomonas aeruginosa*: the fractional inhibitory concentration index as a tool to evaluate antibiotic synergy. *Antibiotics (Basel)*. 2025;14(2):210. [Web Link]
- Parra-Plaza A, Ugarte A, Benavent E, et al. Use of cefiderocol for carbapenem-resistant Gram-negative infections in hospital at home: multicentric real-world experience. *Antibiotics (Basel)*. 2025;14(12):1216. [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

AE	adverse event	IV	intravenous
BSI	bloodstream infection	MDR	multidrug-resistant
CI	confidence interval	MIC	minimum inhibitory concentration
cIAI	complicated intra-abdominal infections	NA	not available
CLcr	creatinine clearance	NS	normal saline
CRAB	carbapenem-resistant *Acinetobacter baumannii*	NDM	New Delhi metallo-β-lactamase
CRRT	continuous renal replacement therapy	OPAT	outpatient parenteral antimicrobial therapy
C_{ss}	steady state concentration	OXA	oxacillinase
CVVH	continuous venovenous hemodiafiltration	PD	pharmacodynamics
D5W	dextrose 5% in water	PK	pharmacokinetics
fC_{ss}	free steady state concentration	q8h	every 8 hours
FDA	US Food and Drug Administration	QID	four times a day
g	grams	TDM	therapeutic drug monitoring
h	hours	TID	three times a day
HABP	hospital-acquired bacterial pneumonia	cUTI	complicated urinary tract infection
HD	hemodialysis	VAP	ventilator-associated pneumonia
ICU	intensive care unit	VABP	ventilator-associated bacterial pneumonia
IQR	interquartile range	XDR	extensively drug-resistant

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References

1. Prinz C, Streit F, Schumann C, et al. Feasibility of continuous infusion of cefiderocol in conjunction with the establishment of therapeutic drug monitoring in patients with extensively drug-resistant Gram-negative bacteria. *Clin Drug Investig*. 2023;43(4):307-314. [Web Link]

2. Gatti M, Rinaldi M, Tonetti T, et al. Pharmacokinetics/pharmacodynamics of cefiderocol administered by continuous infusion in a case series of critically ill patients with carbapenem-resistant *Acinetobacter baumannii* infections undergoing continuous venovenous haemodiafiltration (CVVHDF). *Int J Antimicrob Agents*. 2023;62(2):106852. [Web Link]

3. Babich S, Cojutti PG, Gatti M, Pea F, Di Bella S, Monticelli J. Feasibility of 24 h continuous-infusion cefiderocol administered by elastomeric pump in attaining an aggressive PK/PD target in the treatment of NDM-producing *Klebsiella pneumoniae* otomastoiditis. *JAC Antimicrob Resist*. 2025;7(3):dlaf066. [Web Link]

4. Möhlmann JE, van Luin M, Uijtendaal EV, Zahr N, Sikma MA. Continuous infusion of cefiderocol in a critically ill patient with continuous venovenous haemofiltration. *Br J Clin Pharmacol*. 2023;89(12):3753-3757. [Web Link]

5. Ziegler S, Kirsch M, Schmidt D, Sakka SG. Application of cefiderocol after identification of 4MRGN *Pseudomonas aeruginosa* in tracheal secretions associated with weaning failure and absent therapy alternatives. *Anästh Intensivmed*. 2021;62(9):421-425. [Web Link]

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

Enclosure

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