Fetroja (cefiderocol)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Fetroja
- **Generic name:** Cefiderocol
- **Pharmacologic class:** Cephalosporin antibacterial
- **Strength and Formulation:** 1gm; per vial; lyophilized powder for IV infusion after reconstitution and dilution; contains sodium 176mg/vial
- **Manufacturer:** Shionogi
- **How supplied:** Single-dose vials—10
- **Legal Classification:** Rx

Fetroja


1 gram
Rx ONLY
NDC 59630-266-10
Fetroja®
(cefiderocol) for injection
1 gram per vial
For Intravenous Infusion.
Must be reconstituted then diluted.
Contains 10 single-dose vials.
SHIONOGI INC.

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Indication

- For the treatment of **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*
  - For patients who have limited or no alternative treatment options

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Dosage and Administration

- Give by IV infusion over 3hrs
- Treat for 7–14 days
- **≥18yrs:**
  - (CrCl 60–119mL/min): 2g every 8hrs
  - (CrCl 30–59mL/min): 1.5g every 8hrs
  - (CrCl 15–29mL/min): 1g every 8hrs
  - ESRD (CrCl <15mL/min) with or without hemodialysis: 0.75g every 12hrs
  - (CrCl ≥120mL/min): 2g every 6hrs
- **<18yrs**: not established

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Considerations for Special Populations

- **Pregnancy:** no available data to evaluate for drug-associated risk
- **Nursing mothers**: drug detected in milk of lactating rats; likely present in human milk but effect unknown
- **Pediatric**: <18 years old: not established
- **Geriatric:** no overall differences in safety and efficacy observed; dose adjustment should be based on renal function

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Considerations for Special Populations

- **Renal impairment:**
  - *Patients with CrCl 60-89mL/min*: no dosage adjustment recommended
  - *Patients with CrCl <60mL/min*: dosage adjustment required with CrCl 15-59mL/min and in patients with ESRD or who are receiving hemodialysis; in patients requiring hemodialysis, complete hemodialysis at the latest possible time before the start of cefiderocol dosing
  - *Patients with CrCl ≥120mL/min*: may be seen in seriously ill patients who are receiving IV fluid resuscitation; dosage adjustment required
- **Hepatic impairment**: dosage adjustment not necessary

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Contraindications

- History of severe hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs

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Warnings/Precautions

- Increase in all-cause mortality (see full labeling)
- Reserve for use in those who have limited or no alternative treatment options
- Penicillin or other beta-lactam allergy
- Discontinue if an allergic reaction occurs
- Seizure disorder
- Other CNS reactions (eg, nonconvulsive status epilepticus, encephalopathy, coma)

Interactions

- May cause false (+) results in dipstick tests (urine protein, ketones, occult blood); use alternative methods to confirm (+) tests

Adverse Reactions

- **Most frequent (incidence ≥2%)**: diarrhea, infusion site reactions, constipation, rash, candidiasis, cough, elevations in liver tests, headache, hypokalemia, nausea, vomiting
- **Others**: *C. difficile*-associated diarrhea, hypersensitivity reactions

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Mechanism of Action

- Cefiderocol functions as a **siderophore** and binds to extracellular free ferric iron
- In addition to passive diffusion via porin channels, cefiderocol is actively transported across the outer cell membrane of bacteria into the periplasmic space using a siderophore iron uptake mechanism
- Cefiderocol exerts bactericidal action by inhibiting cell wall biosynthesis through binding to penicillin-binding proteins

Pharmacokinetics

- Terminal elimination half-life is 2-3 hours
- Minimally metabolized
- Primarily excreted by the kidneys

Clinical Trials

- 448 adults hospitalized with cUTI (including pyelonephritis) randomized 2:1 to Fetroja 2g IV every 8 hours or imipenem/cilastatin 1g/1g IV every 8 hours for 7-14 days
- No switch from IV to oral antibacterial therapy was permitted
- Efficacy assessed as a composite of microbiological eradication and clinical cure in the microbiological intent-to-treat population (Micro-ITT; included all patients who received at least a single dose of study medication and had at least one baseline Gram-negative uropathogen)

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Clinical Trials

- Micro-ITT included:
  - 371 patients of whom 25% had cUTI with pyelonephritis; 48% had cUTI without pyelonephritis; 27% had acute uncomplicated pyelonephritis
  - Complicating conditions: obstructive uropathy, catheterization, renal stones
  - Median age: 66 years; 55% female
  - 32% had CrCl >50-80mL/min; 17% had CrCl 30-50mL/min; 3% had CrCl <30mL/min
  - Most common baseline pathogens: *E. coli* and *K. pneumoniae*
- Median duration of therapy in both treatment groups: 9 days

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Clinical Trials

- Response rates for the composite endpoint of microbiological eradication (all Gram-negative uropathogens found at baseline at ≥ 10^5 CFU/mL reduced to < 10^4 CFU/mL) and clinical response (resolution or improvement of cUTI symptoms and no new symptoms assessed by the investigator) at the Test of Cure (TOC) visit were higher in the Fetroja arm compared with imipenem/cilastatin
  - **Composite response at TOC**: 72.6% vs 54.6%, respectively (treatment difference: 18.6 [95% CI, 8.2-28.9])

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Clinical Trials

- Clinical response rates at TOC visit were similar between Fetroja and imipenem/cilastatin
  - **Clinical response at TOC**: 89.7% vs 87.4% (treatment difference: 2.4 [95% CI, -4.7 to 9.4])
- Subgroup analyses examining outcomes by age, gender, and/or outcomes in patients with renal impairment, concomitant bacteremia, complicated UTI with or without pyelonephritis, or acute uncomplicated pyelonephritis demonstrated responses were consistent with the overall population

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/fetroja/