Fetcroja® ▼
cefiderocol for injection

Dosing and administration guide for Fetcroja®

Fetcroja®

Fetcroja® is indicated for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options.[1]

The active substance in Fetcroja® is cefiderocol, a siderophore cephalosporin.[1]

Considerations before prescribing

In prescribing Fetcroja®, consideration should be given to official guidance on the use of antimicrobial agents. It is recommended that Fetcroja® should be used to treat patients who have limited treatment options only after consultation with a physician with appropriate experience in the management of infectious diseases.[1]

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk. Adverse events should also be reported to Shionogi on Tel: +44 (0)20 3053 4190 or via contact@shionogi.eu.

Prescribing information is available on the final page.

Recommended dosage*

In patients with normal renal function[1]			
Renal function	**Dose**	**Frequency**	**Duration of treatment**
CrCL ⩾90 to <120 mL/min[†]	2 g	Every 8 hours	Duration in accordance with the site of infection[‡]

In patients with augmented renal function[1]			
Renal function	**Dose**	**Frequency**	**Duration of treatment**
CrCL ⩾120 mL/min[†]	2 g	Every 6 hours	Duration in accordance with the site of infection[‡]

In patients with impaired renal function[1]		
Renal function	**Dose**	**Frequency**
Mild renal impairment (CrCL ⩾60 to <90 mL/min)[†]	2 g	Every 8 hours
Moderate renal impairment (CrCL ⩾30 to <60 mL/min)[†]	1.5 g	Every 8 hours
Severe renal impairment (CrCL ⩾15 to <30 mL/min)[†]	0.75 g	Every 8 hours
End stage renal disease (CrCL <15 mL/min)[†]	0.75 g	Every 12 hours
Patient with intermittent haemodialysis[§]	0.75 g	Every 12 hours

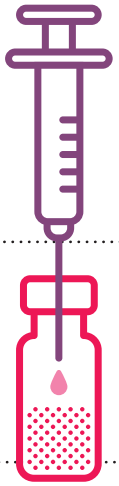
- No dose adjustment is required in patients with hepatic impairment or in elderly patients; no data are available in those <18 years[1]

* To be used in combination with antibacterial agents active against anaerobic pathogens and/or Gram-positive pathogens when these are known or suspected to be contributing to the infectious process.
[†] Creatinine clearance calculated using the Cockcroft-Gault formula.
[‡] For example, for complicated urinary tract infections including pyelonephritis and complicated intra-abdominal infections the recommended treatment duration is 5 to 10 days. For hospital-acquired pneumonia including ventilator-associated pneumonia the recommended treatment duration is 7 to 14 days. Treatment up to 21 days may be required.
[§] As cefiderocol is removed by haemodialysis, administer cefiderocol at the earliest possible time after haemodialysis on haemodialysis days.

Reconstitution

Fetcroja® is supplied as single use vials containing cefiderocol sodium tosylate, equivalent to 1 g cefiderocol. Excipients include sucrose, sodium chloride and sodium hydroxide (pH adjustment).[1]

Standard aseptic techniques should be used for solution preparation and administration.[1]

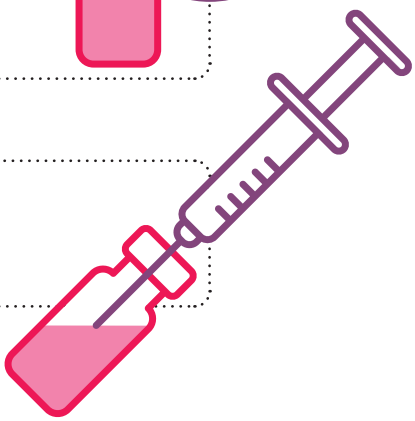


1. Reconstitute the powder with 10 mL of either sodium chloride 9 mg/mL (0.9%) solution for injection or 5% dextrose injection taken from the 100 mL bags that will be used to prepare the final infusion solution. Shake gently to dissolve.[1]

2. The vial(s) should be allowed to stand until the foaming generated on the surface has disappeared (typically within 2 minutes). The final volume of the reconstituted solution in the vial will be approximately 11.2 mL.[1]

   (Caution: the reconstituted solution is not for direct injection).

3. To prepare the required doses, withdraw the appropriate volume of reconstituted solution from the vial, as shown in the table.[1]



Cefiderocol dose	Number of 1 g cefiderocol vials to be reconstituted	Volume to withdraw from reconstituted vial(s)	Total volume of cefiderocol solution required for further dilution in at least 100 mL of 0.9% sodium chloride injection or 5% dextrose injection
2 g	2 vials	11.2 mL (entire contents) from both vials	22.4 mL
1.5 g	2 vials	11.2 mL (entire contents) from first vial AND 5.6 mL from second vial	16.8 mL
1 g	1 vial	11.2 mL (entire contents)	11.2 mL
0.75 g	1 vial	8.4 mL	8.4 mL

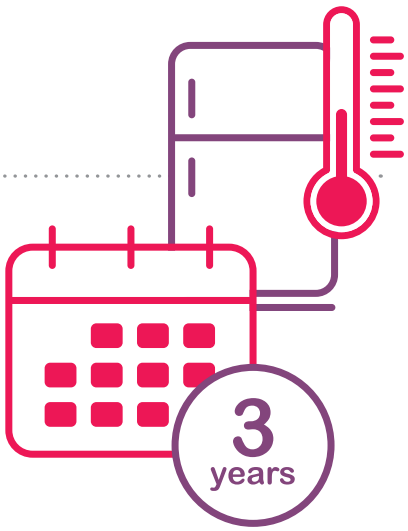
4 Add the withdrawn volume to the infusion bag containing the remainder of the 100 mL of sodium chloride 9 mg/mL (0.9%) solution for injection, or 5% dextrose injection.[1]

5 Visually inspect the diluted drug solution in the infusion bag for particulate matter and discolouration prior to use. Do not use discoloured solutions or solutions with visible particles.[1]

6 Fetcroja® is administered by intravenous infusion over 3 hours.[1]

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.[1]

Storage



Unopened vials

The powder has a shelf life of 3 years.
The product should be stored in a refrigerator (2 to 8°C) in the original carton, to protect it from light.[1]

Reconstituted Fetcroja®

The chemical and physical in-use stability of the reconstituted solution in the vial has been demonstrated for 1 hour at 25°C.[1]

- From a microbiological point of view, unless the method of opening/reconstitution precludes the risk of microbial contamination, the reconstituted product should be used immediately
- If not used immediately, in-use storage times and conditions are the responsibility of the user and should not be more than 1 hour at 25°C

Chemical, microbiological and physical in-use stability of the diluted solution in the infusion bag has been demonstrated for 6 hours at 25°C and for 24 hours at 2 to 8°C protected from light, followed by 6 hours at 25°C. [1]

- From a microbiological point of view, diluted products should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 6 hours at 25°C or 24 hours at 2 to 8°C protected from light, followed by 6 hours at 25°C, unless dilution has taken place in controlled and validated aseptic conditions
- The 6-hour period at 25°C should be inclusive of the product administration period of 3 hours
- If storing the infusion solution in the refrigerator, the infusion bag should be removed and allowed to reach room temperature prior to use

Pharmacokinetics

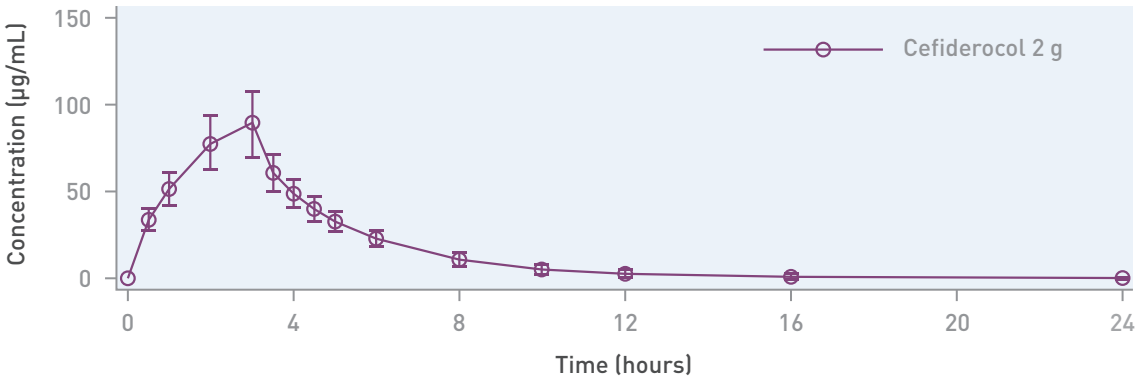
- Fetcroja® exhibits linear pharmacokinetics[1]

Plasma pharmacokinetic parameters for Fetcroja®[2]	
Parameter	**Single dose, 2 g, 3 hour IV infusion (N=43)***
C_{max} (µg/mL)	89.7 (20.5)
T_{max} (h†)	2.90 (2.08–4.58)
AUC_{0-last} (µg.h/mL)	384.8 (17.3)
$AUC_{0-\infty}$ (µg.h/mL)	386.1 (17.2)
$t_{1/2}z$ (h)	2.41 (14.0)
Total clearance (L/h)	5.18 (17.2)
Vz (L)	18.0 (18.1)

* Data are given as geometric mean (%CV) unless otherwise noted.
† Median (range).
CV, coefficient of variation; $t_{1/2}z$, terminal elimination half life; Vz, volume of distribution in the terminal elimination phase.

- The majority of Fetcroja® is renally eliminated[1]
- The terminal elimination half-life in healthy adult subjects was 2 to 3 hours[1]

Plasma concentration following IV administration of 2 g cefiderocol in healthy adult subjects[2]



Mean (SD) plasma concentration in healthy adult subjects (N=48) after a single IV dose of 2 g cefiderocol.

- In a population pharmacokinetic analysis, no clinically relevant effect on the pharmacokinetics of Fetcroja® was observed with respect to age, gender or race[1]

Interactions, contraindications and safety

Drug–drug interactions

Cefiderocol induces CYP3A4 *in vitro*. Therefore, the metabolism of CYP3A4 substrates can be increased and lead to decreased systemic exposure of these products.[1]

- In the event of co-administration, monitoring is recommended to detect decreased efficacy of the concomitant drug

The *in vitro* CYP3A4 induction by cefiderocol is mediated by PXR, therefore other PXR inducible proteins may also be induced, e.g. the CYP2C family and PgP. The clinical relevance of this induction is unknown.[1]

- If cefiderocol is administered together with substrates of the CYP2C family or PgP, monitoring is recommended to detect decreased efficacy of the concomitant drug

Based on *in vitro* studies and one phase 1 clinical evaluation, no significant drug–drug interactions are anticipated between cefiderocol and substrates, inhibitors, or inducers of cytochrome P450 enzymes (CYPs) or gut, renal or hepatic drug transporters.[1]

Contraindications

Cefiderocol is contraindicated in patients with hypersensitivity:[1]

- to the active substance
- to any of the excipients
- to any cephalosporin antibacterial.

It is also contraindicated in those with severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of betalactam antibacterial agent (e.g. penicillins, monobactams or carbapenems).[1]

Adverse events summary

The most common adverse reactions were diarrhoea (8.2%), vomiting (3.6%), nausea (3.3%) and cough (2%).[1]

Reporting suspected adverse reactions after authorisation of the medicinal product is important to continuously monitor the benefit/risk balance of every medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via their national reporting system. Please refer to page 8 for more information.

For full information on Fetcroja®, please see the Summary of Product Characteristics

Shionogi Europe Medical Information service

If you have any medical questions about cefiderocol, please contact Shionogi Medical Information at:

English language
contact@shionogi.eu
Tel: +44 (0)20 3053 4190

German language
kontakt@shionogi.eu
Tel: +49 (0)89 2109 3049

Spanish language
contacta@shionogi.eu
Tel: +34 911 239 258

Italian language
contattaci@shionogi.eu
Tel: +39 06 94 805 118

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Fetcroja® prescribing information

Insert local API

April 2020
PP-EU-FDC-0006

CrCL, creatinine clearance; IV, intravenous; SD, standard deviation.

References

1. Fetcroja® (cefiderocol) Summary of Product Characteristics, March 2020.
2. Sanabria C *et al*. Effect of Cefiderocol, a Siderophore Cephalosporin, on QT/QTc Interval in Healthy Adult Subjects. *Clin Ther*. 2019;41:1724–1736.

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