Fetcroja®▼ (cefiderocol) 1 g powder for concentrate for solution for infusion

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing

Presentation: Each vial contains cefiderocol sulfate tosylate equivalent to 1 g of cefiderocol. **Indication(s):** Fetcroja is indicated for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options. **Dosage and administration:** Intravenous use. Follow reconstitution instructions exactly as per SmPC. Fetcroja is administered by intravenous infusion over 3 hours. Normal renal function (CrCL ≥90 to <120 mL/min): 2 g every 8 hours. Augmented renal clearance (CrCL ≥120 mL/min): 2 g every 6 hours. Duration of treatment is in accordance with the site of infection. For complicated UTIs 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. Special populations: *Renal impairment:* 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): 1 g every 8 hours. End stage renal disease (CrCL <15 mL/min): 0.75 g every 12 hours. Intermittent haemodialysis (administer Fetcroja at the earliest possible time after completion of haemodialysis on haemodialysis days): 0.75 g every 12 hours. *Hepatic impairment:* No dose adjustment is required in patients with hepatic impairment. *Elderly:* No dose adjustment is required. *Paediatric:* No data are available. The safety and efficacy of Fetcroja in children below 18 years of age has not yet been established. **Contraindications:** Severe hypersensitivity (e.g. anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins, monobactams or carbapenems). Hypersensitivity to the active substance or to any of the excipients. Hypersensitivity to any cephalosporin antibacterial medicinal product. **Special warnings and precautions:** Hypersensitivity has been reported with Fetcroja. Before initiating therapy with Fetcroja, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics. If a severe allergic reaction occurs, treatment with Fetcroja must be discontinued immediately and adequate emergency measures must be initiated. *Clostridioides difficile*-associated diarrhoea (CDAD) has been reported with Fetcroja. Discontinuation of therapy with Fetcroja and the use of supportive measures together with the administration of specific treatment for *Clostridioides difficile* should be considered. Medicinal products that inhibit peristalsis should not be given. Patients with known seizure disorders should continue anticonvulsant therapy. Patients who develop focal tremors, myoclonus, or seizures should be evaluated neurologically and placed on anticonvulsant therapy if not already instituted. If necessary, the dose of Fetcroja should be adjusted based on renal function or alternatively, Fetcroja should be discontinued. In clinical trials, Fetcroja has only been used to treat patients with the following types of infection: complicated urinary tract infections (cUTI); hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), healthcare-associated pneumonia (HCAP); sepsis and patients with bacteraemia (some with no identified primary focus of infection). Fetcroja has little or no activity against the majority of Gram-positive organisms and anaerobes. Additional antibacterial medicinal products should be used when these pathogens are known or suspected to be contributing to the infectious process. The use of Fetcroja may result in the overgrowth of non-susceptible organisms, which may require interruption of treatment or other appropriate measures. Cefiderocol may result in false-positive results in urine dipstick tests (urine protein, ketones, or occult blood). Alternative methods of testing should be used by the clinical laboratories to confirm positive tests. A positive direct or indirect Coombs test may develop during treatment with Fetcroja. **Drug interactions:** Fetcroja induces CYP3A4 *in vitro*. Therefore, the metabolism of co-administered medicinal products that are substrates of CYP3A4 can increase and lead to decreased systemic exposure of these medicinal products. If Fetcroja is administered together with substrates of CYP3A4, the patients should be monitored for decreased efficacy of the concomitant drug. As the *in vitro* CYP3A4 induction by Fetcroja is PXR mediated, other PXR inducible proteins may also be induced, for example the CYP2C family and PgP. The clinical relevance of this induction is unknown. As a consequence, if Fetcroja is administered together with substrates of the CYP2C family or PgP, the patients should be monitored for 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 Fetcroja and substrates or inhibitors of cytochrome P450 enzymes (CYPs) or gut, renal or hepatic drug transporters. **Pregnancy, breast-feeding and fertility:** There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of Fetcroja in pregnancy. As a precautionary measure, it is preferable to avoid the use of Fetcroja during pregnancy. It is unknown whether Fetcroja is excreted in human milk. Risk/benefit ratio should be considered, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. The effect of Fetcroja on fertility in humans has not been studied. **Undesirable effects:** See SmPC for full list of side effects. Common (≥1/100, <1/10): Candidiasis, *Clostridioides difficile* colitis, cough, diarrhoea, nausea, vomiting, rash, infusion site reaction and abnormal hepatic function. **Legal classification:** POM. **Pack size and basic NHS price:** Pack size of 10 vials: £1319.00. **Marketing Authorisation Number(s):** EU/1/20/1434/001. **Marketing Authorisation Holder:** Shionogi B.V, Kingsfordweg 151, 1043GR Amsterdam, The Netherlands. **Date of preparation:** April 2020

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse events should be reported. For Ireland, reporting forms and information can be found at www.hpra.ie. For the UK, reporting forms and information can be found at https://yellowcard.mhra.gov.uk or via the Yellow Card app (download from the Apple App Store/Google Play Store). Adverse events should also be reported to Shionogi on 02030534190 or via contact@shionogi.eu.