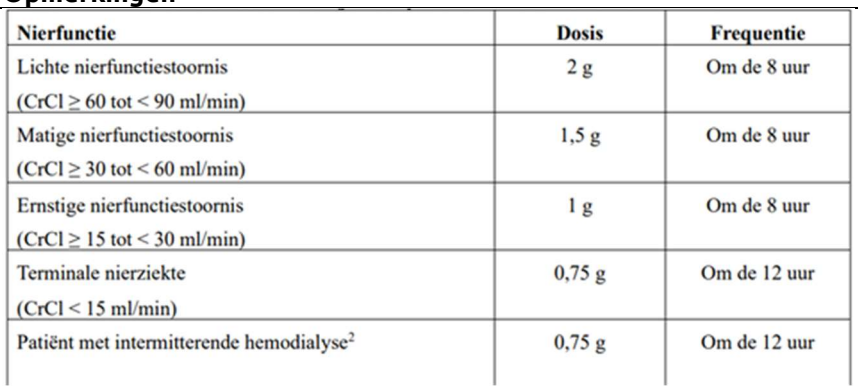
Nierfunctie: cefiderocol

	Wijziging kinetiek	Actie	Clcr grens	Datum
Beslissing werkgroep	Ja	Ja	50 ml/min	20 maart 2025

Literatuur

Onderbouwend	Bewijs	Effect	Opmerkingen
Katsube T ea. Cefiderocol, a Siderophore Cephalosporin for Gram-Negative Bacterial Infections: Pharmacokinetics and Safety in Subjects With Renal Impairment. J Clin Pharmacol. 2017;57:584-91.	3	De AUC van cefiderocol was 3%, 46% en 155% hoger en de t1/2 was 6%, 47% en 145% hoger bij patiënten met respectievelijk milde (n = 8) (eGFR 60-90 mL/min), matige (n = 7) (eGFR 30-60 mL/min) en ernstige (n = 6) (eGFR < 30 mL/min) nierfunctiestoornis vergeleken met patiënten met een normale nierfunctie (n = 8) (CLcr ≥ 90 mL/min, AUC = 213, t1/2 = 3 uur) na een eenmalige intraveneuze toediening van 1000 mg cefiderocol gedurende 1 uur. Verminderde nierfunctie had geen significante invloed op de Cmax.	Auteurs: Renal impairment impacted AUC, CL, and t1/2 without affecting Cmax. The results of this study suggested the need for dose adjustment based on renal function in patients with moderate and severe renal impairment.
SPC+EPAR Fetcroja Zelfde getallen als Katsube 2017	0	De AUC was 1.03x, 1.47x, 2.55x en 4.12x hoger en t1/2 was 1.06x, 1.47x, 2.45x, 3.41x hoger bij patiënten met resp. een milde, matige, ernstige nierfunctiestoornis en ESRD (zonder HD) t.o.v. patiënten met een normale nierfunctie na 1-malig 1 g cefiderocol i.v.	

Overig	Opmerkingen
SmPC Fetcroja (19-07-2024) + EPAR (27-02-2020) Zelfde getallen als Katsube 2016	 EPAR: “The results of the dedicated renal impairment study showed a significant effect of renal function on the pharmacokinetics of cefiderocol, which is expected for a substance that is predominantly renally excreted. The proposed dosage adjustment for renally impaired patients is not based directly on the results of the RI study but on

	population-PK models and Monte Carlo simulations of PTA. During model development, different renal function markers were tested (CrCL, adjusted eGFR and absolute eGFR) and were found to simulate similar PTA. The proposed posology in section 4.2. of the SPC is based on Cockcroft-Gault CrCL which is supported. Regarding safety in renally impaired patients, the prosed doses lead to similar AUC across the different renal impairment groups which is adequate from a PK perspective. Regarding efficacy in renally impaired patients, the reader is referred to the PD section where the PTA analyses are presented and assessed." "Based on plasma PTA simulations using relevant PDTs, the doses of cefiderocol in different renal function categories are predicted to be sufficient for the treatment of infections caused by pathogens having MICs up to 2 mg/L."
Katsube T ea. Pharmacokinetic/Pharmacodynamic Modeling and Simulation of Cefiderocol, a Parenteral Siderophore Cephalosporin, for Dose Adjustment Based on Renal Function. Antimicrob Agents Chemother. 2016;61:e01381-16.	Population PK model was developed for cefiderocol and dose adjustments were determined based on renal function. Plasma, urine, and dialysate concentration data were collected from two phase 1 studies involving healthy subjects and subjects with varying degrees of renal impairment. Monte Carlo simulations were conducted to calculate the probability of target attainment (PTA) for different dosing regimens. The PTA was based on the fraction of time during the dosing interval where the free drug concentration in plasma exceeds the minimum inhibitory concentration (MIC). Proposed dose regimens: **TABLE 6** Dose regimens based on renal function to provide similar cefiderocol exposure among renal function groups and >90% of PTA for 75% $T_{f>MIC}$ against an MIC of ≤4 μg/ml **Renal function** — **Dose regimen** Augmented (CG-CL_{CR}, ≥120 ml/min) — 2 g q6h, 3-h infusion Normal (MDRD-eGFR, ≥90 ml/min/1.73 m^2) — 2 g q8h, 3-h infusion Mild impairment (MDRD-eGFR, 60 to <90 ml/min/1.73 m^2) — 2 g q8h, 3-h infusion Moderate impairment (MDRD-eGFR, 30 to <60 ml/min/1.73 m^2) — 1.5 g q8h, 3-h infusion Severe impairment (MDRD-eGFR, 15 to <30 ml/min/1.73 m^2) — 1 g q8h, 3-h infusion ESRD (MDRD-eGFR, <15 ml/min/1.73 m^2) — 0.75 g q12h, 3-h infusion Requiring intermittent HD — 0.75 g q12h, 3-h infusion[a] [a]A supplemental (third) dose of 0.75 g with a 3-h infusion is administered after the completion of intermittent HD on dialysis days.

Zoektermen

Pubmed
Datum: 26-8-2024

Search #	Zoektermen
#1	("Renal Insufficiency"[Mesh] OR "Kidney Diseases"[Mesh] OR "Renal Dysfunction"[Title/Abstract] OR "Acute Kidney Injury"[Mesh] OR "Kidney Failure, Chronic"[Mesh]) AND ("Cefiderocol"[Supplementary Concept] OR "Cefiderocol"[Title/Abstract])