Nierfunctie: nalmefeen 5696

Clcr = creatinineklaring, GFR = glomerulaire filtratie snelheid

Onderbouwend	Bewijs	Effect	Opmerkingen
SPC Selincro 8 juli 2015.	1	Na nalmefeen 1 mg intraveneus blootstelling 1,6x hoger, C_{max} 2,1-4,6x lager en t½ langer (26 uur ipv 10 uur) bij patiënten met ernstige nierinsufficiëntie vergeleken met gezonde personen. Er zijn geen gegevens beschikbaar over orale toediening bij patiënten met nierinsufficiëntie	gecontraïndiceerd bij eGFR < 30 ml/min per 1,73 m^2 geen aanpassing dosering nodig bij licht tot matig verminderde nierfunctie. Omdat nalmefeen voornamelijk via de nieren wordt uitgescheiden, is voorzichtigheid geboden, bijv. vaker monitoren.

Overig	Opmerkingen
EPAR	Following administration of a single dose of 18 mg ^{14}C-nalmefene to healthy subjects in distribution study 12393A, renal excretion represented the main route of elimination, with a mean of 71% of total radioactivity excreted in urine compared to a mean of 20% in faeces. Nalmefene 3-O-glucuronide was the major metabolite in urine, accounting for approximately 54% of the administered dose, while only trace amounts of intact nalmefene (3%) were excreted in urine. Nornalmefene was the predominant metabolite in faeces. The elimination half-life is about 12.5 hours.

Risicogroep	

Opmerkingen:

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Clcr < 10 ml/min:

- EPAR Selincro: In study 22 (an early open-label, single-dose study), eight patients with ESRD were administered 1 mg NMF as i.v. bolus injection over 15 seconds on two occasions: one time the day after a haemodialysis session and once four hours before the next scheduled haemodialysis with a wash-out of 1-2 weeks in-between. Exposure to nalmefene-conjugates was largely increased in ESRD (AUC values more than eight times higher). De-conjugation (and consequently re-institution of pharmacological activity) of metabolites or parent compounds has been reported if conjugated molecules cannot be eliminated. Healthy subjects were not directly involved in study 22. Instead, healthy subject data were taken from study 21, conducted in 1993 in order to examine the influence of hepetic impairment after 2 mg i.v. bolus administration of NMF.
  Overall, there was a higher exposure to nalmefene and nalmefene conjugates in a very limited number of patients with ESRD administered 1 mg intravenously.
- Matzke GR ea. The effect of renal insufficiency and hemodialysis on the pharmacokinetics of nalmefene J Clin Pharmacol 1996;36:144-51: The disposition of nalmefene, an opioid antagonist intended for the reversal of opioid-induced respiratory depression, and its primary metabolite nalmefene glucuronide, were characterized in adult volunteers with normal renal function and in patients with end-stage renal disease (ESRD). The effect of hemodialysis on the elimination of nalmefene and nalmefene glucuronide also was assessed. Participants with normal renal function received a single intravenous dose of 2 mg, and patients with ESRD received two separate doses of 1 mg nalmefene hydrochloride. Terminal elimination half-life (t1/2) of both nalmefene and nalmefene glucuronide was prolonged in patients with ESRD compared with that in participants with normal renal function. The steady-state volume of distribution (Vdss) of nalmefene was significantly higher and total body clearance lower in patients with ESRD than in participants with normal renal function. Hemodialysis clearance of nalmefene was approximately 3.3% of total body clearance. Although the hemodialysis clearance of nalmefene glucuronide was 179.3 +/- 24.1 mL/min and its t1/2 was significantly reduced during dialysis to 5.2 +/- 2.3 hours, a dramatic rebound of nalmefene glucuronide concentrations of 75.7% was observed 7.7 +/- 5.4 hours after the end of hemodialysis. Thus, hemodialysis does not result in clinically significant alterations in the disposition of nalmefene or its primary metabolite, nalmefene glucuronide. These data suggest that there is no pharmacokinetic basis for modification of the initial dosage, but maintenance doses, if needed, should be administered less frequently due to the prolonged elimination of the active moiety, nalmefene.

	Wijziging kinetiek	Actie	Clcr grens	Datum
Beslissing werkgroep	Ja	Ja	30 ml/min	16 februari 2016