Eravacycline + 3A4-inductoren | MFB 7972

TP-498, TP-6208, TP-034: inactieve metabolieten eravacycline

Onderbouwend	Stof	Effect	Code
Newman J. Antimicrob Agents Chemother 2019;63:e01810-18. doi: 10.1128/AAC.01810-18.	eravacycline + rifampicine	Eravacycline: ↓AUC met 25-35% en t1/2 met 26%; ↑Cmax 1.07x (vrijwel ongewijzigd) en Cl 1.5x door rifampicine; TP-498: ↓AUC ratio 35.2 en ↑Cmax, ratio 119.6 TP-6208: ↑AUC en Cmax, ratio 147 resp. 222.3 TP-034: ↑AUC en Cmax, ratio 138.3 resp. 200.8 Regime: eravacycline 1 mg/kg iv op dag 1 en op dag 17, rifampicine 600mg 1dd op dag 8 t/m dag 17; studie met 12 vrijwilligers. Auteurs: this interaction could lead to decreased efficacy, the dose of eravacycline should be increased to 1.5 mg/kg q12h when coadministered with a strong CYP3A inducer, such as rifampin or phenytoin.	3A
SPC + EPAR Xerava	eravacycline + rifampicine,	↓ eravacycline AUC met 32% en ↑Cl 1.54x door rifampicine → getallen uit Newman 2019 p.43: When co-administrating with a strong inducer (rifampicin) the exposure in terms of AUC decreased by ca. 30% while Cmax was unchanged. The epimer TP-498 behaved in a similar manner as parent compound, while TP-6208 and TP-034 increased considerably; Cmax approx. 2-fold and AUC0-t ca 1.4-1.5-fold for both metabolites.	1A
FDA Xerava	eravacycline + rifampicine	p.13: Concomitant use of rifampin (strong CYP3A4/3A5 inducer) decreased eravacycline AUC by 35% and increased eravacycline clearance by 54%	1A

Overig	Stof	Effect
SPC Xerava	eravacycline + CYP3A-inductoren	verhoog dosis eravacycline met ong. 50% (1,5 mg/kg i.v. om de 12 uur) bij combinatie met krachtige CYP3A-inductoren,
EPAR Xerava	eravacycline	p. 43: In vitro data indicate that eravacycline is a substrate of CYP3A4 and this was confirmed in vivo as the major metabolic pathway forming TP-6208. No other CYP enzyme was indicated to be involved in the metabolism. Other enzymes were investigated in vitro and flavin monooxygenases (FMO-1, -3, -5) was shown to form TP6208, while aldehyde oxidase (AO) and monoamine oxidases (MAO-A, MAO-B) were not involved in the metabolism of eravacycline.
FDA Xerava	eravacycline + CYP3A-inductoren	Zelfde advies: with concomitant use of a strong CYP3A inducer, administer XERAVA 1.5 mg/kg every 12 hours for a total duration of 4 to 14 days. No dosage adjustment is warranted in patients with concomitant use of a weak or moderate CYP3A inducer.

Opmerkingen
PubMed: verder geen hits behalve Newman 2019.
Stockley: niet genoemd

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG IA	Ja	Ja	19 mei 2022