Finerenon + CYP3A4-Inductoren | M 8410

Onderbouwend	Stof	Effect	Code
Wendl T. CPT Pharmacometrics Syst Pharmacol 2022;11:199-211. PBPK: Physiologically-based pharmacokinetic model	finerenon + efavirenz, rifampicine	PBPK model finerenone was applied to predict clinically untested DDI studies with CYP3A4 modulators. *predicted ratio AUC resp.* Cmax - efavirenz 0.19 0.32 - rifampicin 0.07 0.14	1A
Spc/EPAR Kerendia	finerenon + inductor	Geen getallen in spc EPAR p.67 simulated data (table 7): 'R'= ratio Perpetrator in combination with finerenone / AUCR geo. mean / AUCR geo. CV / C_{max}R geo. mean / C_{max}R geo. CV Efavirenz 400 mg SD simulated 0.58 0.13 0.69 0.10 Efavirenz 400 mg OD simulated 0.20 0.21 0.34 0.18 Efavirenz 600 mg OD simulated 0.19 0.21 0.32 0.18 Rifampicin 600 mg OD simulated 0.07 0.25 0.14 0.20	1A
Kerendia usa https://www.kerendia-us.com/	finerenon + efavirenz, rifampicine	Drug Interaction Clinical Studies and Model-Informed Approaches: - efavirenz (moderate CYP3A4 inducer) and rifampicin (strong CYP3A4 inducer) ↓ finerenone AUC by 80% and 90%, respectively.	1A

Overig	Stof	Effect
Spc/EPAR Kerendia	finerenon + CYP3A4-inductoren	substraat voor CYP3A4 (hoofdroute, 90%) en 2C8 (10%). Advies: niet combineren met krachtige en matige CYP3A4-inductoren. De verwachting is dat deze CYP3A4-inductoren leiden tot een aanzienlijke daling van de plasma-concentratie en tot een verminderd therapeutisch effect. EPAR p.66 The applicant has also applied the same PBPK model to predict the magnitude of finerenone interaction with CYP3A4 inducers rifampicin (strong) and efavirenz (moderate). However, the number of selected compounds was considered insufficient to qualify the PBPK platform for the intended purpose, i.e. CYP3A4 induction prediction. Furthermore, there were no clinically observed data available with finerenone as a "victim" of CYP3A4 induction in order to verify the model predictive performance. Therefore, PBPK predicted numerical values for CYP3A4 inducers were considered unreliable and removed from the initially proposed SmPC text. Importantly, it is agreed that the expected magnitude of interaction between finerenone and strong and moderate CYP3A4 inducers is high when considering the elimination pathway of finerenone and the key role of CYP3A4 enzyme in this process.
Yu J. Clin Ther 2022;44:1536-44.	finerenon + rifampicine, efavirenz	review: ratio AUC 0.07 (= afname met 93%) (Cmax niet bekend) obv PBPK model met finerenon 10 mg 1-malig en rifampicine 600 mg/dag tot steady state (data uit product label Kerendia. - efavirenz (moderate CYP3A inducer) was predicted to decrease the finerenone AUC by up to 81% using PBPK analysis. Methods: DDI data for small molecular drugs approved by the FDA in 2021 were analyzed using the University of Washington Drug Interaction Database. The mechanism(s) and clinical magnitude of these interactions were characterized based on information available in the new drug application reviews. Clinical studies and simulation results with mean AUC ratios ≤0.2 for induction (ie, strong interactions) were then fully analyzed. Conclusion: finerenone is a sensitive substrate of CYP3A.

Opmerkingen
Werkgroep Interacties & MFB's 18-11-24: nogmaals gekeken naar het advies, dit wordt 'houd rekening met verminderd effect finerenon (was monitor effect finerenon). Het valt verder niet te specificeren, als behandelaar weet je wat je moet doen; het gaat meer om bewustwording dat effect kan veranderen. Niet K monitoren.

Idem 27-6-24: advies vermijd combinatie, als dit niet kan monitor effect finerenon. Discussie over wat te monitoren, er is een slechte relatie spiegel ~ effect; klinisch gezien zou je proteïnurie moeten volgen (maar nogal ongrijpbaar en moeilijk te monitoren).

Stockley online feb 2024: 'severe, avoid, Rifampicin very markedly decreases the exposure to finerenone'.

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG IA	Ja	Ja	27 juni 2024