Voclosporine + CYP3A4-Inductoren | M 8356

Onderbouwend	Stof	Effect	Code
Ling SY. Br J Clin Pharmacol 2014;77:1039-50. doi: 10.1111/bcp.12309.	voclosporine + rifampicine	↓AUC voclosporine met 87.7% en Cmax met 70%, t1/2 met 85% (4.96→0.82h) Regime: voclosporine 0.4 mg/kg 1x op dag 1 en 16, rifampicine 600 mg/dag op dag 6-15; studie met 24 gezonde personen).	3A
Spc + EPAR Lupkynis getallen als Ling 2014	voclosporine + rifampicine	↓AUC voclosporine met 87% en Cmax met 68% door rifampicine 600 mg 1dd gedurende 10 dagen.	2A

Overig	Stof	Effect
Spc + EPAR Lupkynis	voclosporine + CYP3A4-inductoren	Sterke en matige CYP3A4-inductoren: combinatie niet aanbevolen. Zwakke inductoren kunnen ook leiden tot een verminderde blootstelling, maar de klinische relevantie is niet bekend. EPAR: a mild CYP3A4 inducer may according to definition result in up to 50% decrease in AUC of a sensitive substrate. As previously concluded, there is not much data to support the lower range of the therapeutic window and to conclude that a 50% decrease in exposure would not be clinically relevant (especially for patients already having an exposure in the lower range). It is not necessary to have a recommendation that concomitant use is not recommended (as for moderate/strong inducers); however, this has been added to the SmPC and endorsed by the CHMP.
Lupkynis FDA label	voclosporine + efavirenz	multiple doses of efavirenz is predicted to decrease voclosporin Cmax and AUC0-12 by 61% resp. 70%.
Yu J. Clin Ther 2022;44:1536-44.	voclosporine + rifampicine, efavirenz	review: data uit product label Lupkynis. 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 (AUCRs) ≥5 for inhibition DDIs (ie, strong interactions) were then fully analyzed. Conclusion: voclosporin is sensitive to CYP3A induction.
Chong KM. J Clin Med 2024;13:451.	voclosporine	review. There is no need for TDM when using voclosporin as it has a predictable pharmacokinetic profile. A population pharmacokinetic analysis in patients with lupus nephritis showed that voclosporin has a linear pharmacokinetic profile. Factors such as sex, body weight, age, serum albumin, total bilirubin and eGFR did not have any significant or clinically relevant effect on its pharmacokinetic parameters. This enables a pharmacodynamic rather than pharmacokinetic approach to dosing, with the dose adjusted in response to decreases in the eGFR.

Opmerkingen
Stockley:

Risicofactoren	
Mitigerende factoren	

	Interactie	Actie	Datum
Beslissing WG IA	Ja	Ja	8 april 2024