Voclosporine + CYP3A4-remmers | M 8379

Onderbouwend	Stof	Effect	Code
Ling SY. Br J Clin Pharmacol 2014;77:1039-50.	voclosporine + ketoconazol, verapamil	-ketoconazol : ↑AUC voclosporine 18x en Cmax 6.4x -verapamil: ↑AUC voclosporine 2.7x en Cmax 2.1x Regime: voclosporine 0.4 mg/kg 2dd op dag 1-20, ketoconazol 400 mg 1dd op dag 11-20 met de ochtenddosis voclosporine, of met verapamil 80 mg 3dd op dag 11-20 met de ochtenddosis voclosporine; studie met 24 gezonde personen.	3A
Spc + EPAR Lupkynis Getallen als Ling 2014	voclosporine + ketoconazol voclosporine + verapamil	↑AUC voclosporine 18.6x en Cmax 6x door ketoconazol 400 mg/dag ged. 10 dagen ↑AUC voclosporine 2.7x en Cmax 2x door verapamil 80 mg 3dd ged. 10 dagen	2A

Overig	Stof	Effect
Spc + EPAR Lupkynis	voclosporine + CYP3A4-remmers	- sterke CYP3A4-remmers: combi gecontraindiceerd - matige CYP3A4-remmers: verlaag dosis tot 15.8 mg in de ochtend en 7.9 mg in de avond bij combinatie - zwakke CYP3A4-remmers: kunnen de blootstelling aan voclosporine verhogen, maar er is geen in-vivo onderzoek uitgevoerd; geen dosisaanpassing noodzakelijk. EPAR: due to the poor prediction of voclosporin PK, the simulated Cmax and AUC-values under a DDI scenario are not considered reliable and cannot be used to support dosing recommendations.
Lupkynis FDA label	voclosporine + diltiazem, fluconazol	co-administration of multiple doses of fluconazole or diltiazem is predicted to increase voclosporin Cmax and AUC0-12 approximately 2- and 3-fold, respectively. Verder zelfde data en advies als spc.
Yu J. Clin Ther 2022;44:1536-44.	voclosporine + ketoconazol, verapamil, diltiazem, fluconazol	review: data uit product label Lupkynis. PBPK modeling/simulations predicted that multiple doses of diltiazem and fluconazole increased the voclosporin AUC 3.24- resp. 3.05-fold., 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.
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
Werkgroep Interacties & MFB's: naast standaardlijst CYP3A4-remmers ook verapamil, diltiazem en fluconazol koppelen.

Stockley: niet in.

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG IA	Ja	Ja	8 april 2024