Apremilast + Ketoconazol M1285

Onderbouwend	Stof	Effect	Code
Liu Y. Br J Clin Pharmacol 2014;78:1050-7. doi: 10.1111/bcp.12448.	apremilast + ketoconazol	kleine afname klaring apremilast (Cl/F van 10.2 naar 7.5 l/h), t1/2 van 7.6 naar 8.1h; toename AUC met 36% (van 2180 naar 2982 ng*h/ml) en Cmax met 5% (van 246 naar 259 ng/ml) → GIC: hier de getallen uit tabel 1 gevolgd, deze zijn net iets anders dan de getallen uit de abstract/ discussie Regime: dag 1 apremilast 20 mg 1x; wash out; vervolgens 7 dagen ketoconazol 400 mg 1dd en op dag 5 apremilast 20 mg 1x; single centre, open label, sequential treatment studies bij 18 vrijwilligers. Conclusie: ketoconazole slightly decreased apremilast clearance, resulting in a small increase in AUC which is probably not meaningful clinically.	3A
EPAR Otezla	apremilast + ketoconazol	→ GIC: getal AUC uit Liu 2014. p. 79 Study- CC-10004-PK-005: toename AUC met 36% en Cmax met 5%. Regime: multiple doses ketoconazole. Therefore while ketoconazole did reduce the apparent clearance of apremilast, and increase its AUC by 36%, this does not appear to be clinically meaningful. This was agreed by the CHMP. p.39 studie in cellijnen: ketoconazole inhibited apremilast transport by 92%. These results further support the evidence that apremilast is actively transported by P-gp.	1A

Overig	Stof	Effect
SPC Otezla	apremilast + ketoconazol	geen klinisch betekenisvolle geneesmiddelinteractie met ketoconazol; apremilast kan worden gecombineerd met een krachtige CYP3A4-remmer, zoals ketoconazol.
Otezla Prescribing Information. www.otezla.com/otezla-prescribing-information.pdf. Geraadpleegd 1-6-2015.	apremilast + ketoconazol	zelfde info als SPC.
EPAR Otezla	apremilast	p.186 - Plaque Psoriasis: as a higher dose than 30 mg BID was not studied in the phase 2 dose finding study a full characterisation of the dose response has not been shown, however as a clinically relevant effect was demonstrated this does not impact on the B/R (Benefit-Risk Balance) of apremilast. p.187 The most frequently reported treatment related adverse events were diarrhoea, nausea, headache, respiratory tract infection and nasopharyngitis. A dose effect was observed for diarrhoea, nausea and headache. The majority of adverse events were of mild to moderate intensity.

Opmerkingen
PubMed: verder niets.
Stockley/Hansten: apremilast niet genoemd.

Risicogroep	

	Interactie	Actie	Datum
Beslissing WFG	Ja	Nee	14 juli 2015