

Omeprazol + Rifampicine/Hypericum

M1223

OH-omeprazol: inactieve metaboliet, gevormd via CYP2C19 (hoofdroute)
omeprazolsulfon: inactieve metaboliet, gevormd via CYP3A4

Onderbouwend	Stof	Effect	Code
Inui N. Clin Pharmacol Ther 2013;94:702-8. doi: 10.1038/clpt.2013.167. Epub 2013 Aug 23. * Inje cocktail: combinatie van CYP-specifieke probes voor fenotypering CYP2C9 (losartan), CYP3A (oraal midazolam), CYP1A2 (coffeïne), CYP2C19 (omeprazol) en CYP2D6 (dextromethorfan)	omeprazol + rifampicine	ratio omeprazol/1'-OH-omeprazol na 4 uur: voor start rifampicine: 0.90 (0.41–1.96) na 7 dagen rifampicine: 0.35 (0.19–0.64) 4 dagen na staken rifampicine: 0.32 (0.16–0.65) 8 dagen na staken rifampicine: 1.11 (0.41–3.02) Regime: rifampicine 450 mg 1dd gedurende 7 dagen, en omeprazol 20 mg in Inje cocktail* voor start, na 7 dagen rifampicine, en 4 en 8 dagen na staken rifampicine bij 13 vrijwilligers Auteurs: omeprazol wordt via 2C19 omgezet in 5'-OH-omeprazol. GIC: vervolgens geeft men getallen op voor 1'-OH-omeprazol, terwijl op p.5 bij Measurements of probe drugs and their metabolites weer 5' wordt genoemd	3A
Kanebratt KP. Clin Pharmacol Ther 2008;84:589-94. ** Karolinska cocktail: combinatie van CYP-specifieke probes voor fenotypering van CYP2C9 (losartan), CYP1A2 (coffeïne), CYP2C19 (omeprazol)	omeprazol + rifampicine	inductieratio* P450-enzymen na rifampicine: -inductieratio CYP2C19: 4.2 (bepaald mbv omeprazol:5'-OH-omeprazol) -inductieratio CYP3A4: 2.6 (bepaald mbv omeprazol:omeprazolsulfon) Regime: rifampicine 500 mg/dag gedurende 14 dagen, omeprazol 20 mg in Karolinska** cocktail voor start rifampicine en op dag 15; 6 vrijwilligers Omeprazol wordt hoofdzakelijk door CYP2C19 omgezet tot OH-omeprazol, en voor een kleiner deel door CYP3A4 tot omeprazolsulfon. Deze metabolieten zijn inactief. De metabolieten worden verder gemetaboliseerd door 2C19 resp. 3A4 * inductieratio = MR vóór rifampicine : MR na rifampicine MR = metabolic ratio = omeprazol : OH-omeprazol (igv CYP2C19) MR = omeprazol : omeprazolsulfon (igv CYP3A4).	3A
Wang L-S. Clin Pharmacol Ther 2004;75:191-7.	omeprazol + hypericum	EM (wild genotype) voor CYP2C19 omeprazol AUC -43.9%, Cmax -49.6% 5-OH-omeprazol AUC +37.2%, Cmax +38.1% omeprazolsulfon AUC +158.7%, Cmax +155.5% PM (mutant genotype) voor CYP2C19 omeprazol AUC -37.9%, Cmax -37.5% 5-hydroxyomeprazol AUC -9.9%, Cmax -5.9% omeprazolsulfon AUC +136.6%, Cmax +160.3% Regime: hypericum 300 mg 3dd gedurende 14 dagen of placebo, omeprazol 20 mg op dag 15 bij 12 vrijwilligers (6 EM en 6 PM); 2-fase crossover studie met washout van 5 weken	3A
Overig	Stof	Effect	
SPC Losec	omeprazol + rifampicine/hypericum	Werkzame stoffen waarvan bekend is dat ze CYP2C19, CYP3A4 of beide induceren (zoals rifampicine en Sint-Janskruid) kunnen leiden tot een daling van de concentratie omeprazol in het serum.	

Opmerkingen

WFG: bij CYP2C19 inductoren koppelen op basis van bewijs (rifampicine, hypericum), en niet extrapoleren naar andere inductoren.

Stockley online 2024: a pharmacokinetic interaction is established. The effect of rifampicin on omeprazole exposure appears to be marked, although note that in one of the two studies showing a marked effect the dose of omeprazole was very low (only 5 mg), and in the other the dose of rifampicin was low (150 mg rather than 600 mg). The clinical importance of such dramatic decreases in omeprazole exposure is unclear, however it would be reasonable to predict that efficacy might be greatly reduced resulting in the need for a dose increase to achieve symptom control or in certain situations (such as during short courses of *H. pylori* eradication), it might be prudent to avoid concurrent use. The effect of rifampicin on other proton pump inhibitors does not appear to have been studied, however all proton pump inhibitors are primarily metabolised by CYP2C19 and therefore their exposure might also be reduced by rifampicin, although to varying extents. Similar precautions as for omeprazole would seem prudent.

Stockley: St. John's wort induces the metabolism of omeprazole, and this might result in reduced efficacy. Other proton pump inhibitors are likely to be similarly affected.

Hansten: St. John's wort substantially reduced omeprazole plasma concentrations in healthy subjects, but the clinical importance of this effect is not established. Monitor for reduced omeprazole response.

Risicogroep	
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	Interactie	Actie	Datum
Beslissing WFG	Ja	Ja	1 juli 2014