

Roxadustat + Gemfibrozil / Probenecide	M 8262
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Onderbouwend	Stof	Effect	Code
SPC + EPAR Evrenzo	Roxadustat + Gemfibrozil / Probenecide	↑roxadustat AUC 2.3x en Cmax 1.4x. Regime: roxadustat 100 mg, gemfibrozil (remt CYP2C8 en OATP1B1) en probenecide (remt UGT en OAT1/3) enkele dosis; studie met 18 gezonde vrijwilligers.	2A

Overig	Stof	Effect
SPC + EPAR Evrenzo	Roxadustat + CYP2C8-remmers of UGT1A9-remmers	monitor het Hb-gehalte bij combinatie met gemfibrozil, probenecide, andere sterke remmers CYP2C8 [of andere sterke remmers van UGT1A9] EPAR: a clinically relevant interaction with clopidogrel is not expected, based on the lower interaction potential of clopidogrel compared to gemfibrozil, clopidogrel was not identified as a significant factor on roxadustat pharmacokinetics in patients with chronic kidney disease by the population modeling analyses and the overall decreased metabolic and transporter function in the CKD population.
Rekic D. Clinical Pharmacokinetics 2021;60:759–73.	Roxadustat en CYP2C8	Roxadustat is predominantly eliminated by phase I oxidation (CYP2C8) and phase II conjugation (glucuronidation via UGT1A9 and glucosidation), and therefore roxadustat may be affected by modulators of CYP2C8 and UGT1A9. Co-administration of a single dose of roxadustat 100 mg with probenecid 500 mg twice daily (UGT inhibitor) or gemfibrozil 600 mg twice daily (CYP2C8 inhibitor) increased roxadustat area under the curve (AUC) by 2.3-fold. Clopidogrel and its glucuronide metabolite are categorized as strong inhibitors of CYP2C8 and OATP1B1. In a previous study, the CYP2C8 inhibitor gemfibrozil increased roxadustat AUC by 2.3-fold. In our PopPK analysis, the effect of clopidogrel on AUC and Cmax was small (~3%), statistically insignificant, and within the determined no-effect boundaries.

Opmerkingen

Werkgroep Interacties: Ja/Ja na enige discussie (enerzijds vinden artsen het klinisch relevant, anderzijds is er al enorme variatie in onderhoudsdosering dus is het effect van de interactie niet zo spannend). Actie: monitor Hb-gehalte extra bij starten, dosiswijziging en na staken remmer. Bij start roxadustat, overweeg lagere startdosering.

Risicofactoren	
Mitigerende factoren	

	Interactie	Actie	Datum
Beslissing WG IA	Ja	Ja	5 oktober 2023