Atorvastatine/metoprolol + Dulaglutide M1287

Onderbouwend	Stof	Effect	Code
SPC Trulicity	atorvastatine + dulaglutide	afname AUC atorvastatine en hydroxyatorvastatine met 21% en Cmax met 70% bij combinatie met dulaglutide; dit is niet klinisch relevant Gemiddelde t½ atorvastatine en *o*-hydroxyatorvastatine resp. 17% en 41 % verhoogd WFG: vreemd, waarop baseert fabrikant 'niet klinisch relevant?' GIC heeft nagevraagd bij fabrikant. Q1. Op basis waarvan is geconcludeerd dat afname Cmax atorvastatine met 70% (en AUC met 21%) “niet klinisch relevant” is. A: “these changes in the pharmacokinetics of atorvastatin and its active metabolite were not considered to be of clinical significance, as AUC (primary exposure parameter) was reduced by <30%. The known pharmacokinetic variability for atorvastatin is >30% (Narwal et al. 2010). “ Q2. Wat is het mogelijke mechanisme achter deze interactie? A: "The mechanism is most likely due to the known delayed gastric emptying effect, but this decrease in atorvastatin exposure was deemed not clinically significant. Narwal R ea. Development of a population pharmacokinetic model for atorvastatin acid and its lactone metabolite. Clin Pharmacokinet 2010;49:693-702.	1A
SPC Trulicity	metoprolol + dulaglutide	toename AUC metoprolol met 19% en Cmax met 32% na 1-malig dulaglutide; dit is niet klinisch relevant	1A

Overig	Stof	Effect
EPAR Trulicity	dulaglutide	The elimination of dulaglutide is expected to be through proteolytic degradation into its amino acid components and is not anticipated to be eliminated intact in the urine or to be metabolized by the CYP enzymes. Therefore, PK interactions with drugs primarily renally eliminated or metabolized by CYP enzymes are unlikely. However, dulaglutide causes a delay in gastric emptying, a well known effect of the class, which may alter the PK of orally co-administered drugs.
https://clinicaltrials.gov/ct2/show/results/NCT01250834	atorvastatine + dulaglutide	Period 1: a single 40-milligram (mg) oral dose of atorvastatin on Day 1, followed by a 7- to 10-day washout period . Period 2: a single 1.5-mg subcutaneous dose of LY2189265 on Day 1, followed by a single 40-mg oral dose of atorvastatin on Day 3.

Opmerkingen
PubMed search 9-4-2015: geen info.

Stockley, Hansten: --

Risicogroep	

	Interactie	Actie	Datum
Beslissing WFG	Ja	Nee	14 juli 2015