Ator/Prava/Rosuvastatine + Bempedoïnezuur | M 8546

ESP15228: actieve metaboliet van bempedoïnezuur

Onderbouwend	Stof	Effect	Code
Spc + EPAR Nilemdo	atorvastatine, pravastatine, rosuvastatine + bempedoïnezuur	↑AUC atorvastatine, pravastatine, rosuvastatine en/of metabolieten 1.4-1.5x (90% CI 1.24-1.67x resp. 1.22-1.74x resp. 1.21-1.75x) na statine 1x + bempedoïnezuur 180 mg; studie met 12 subjects. bij combi met bempedoïnezuur 240 mg (supra-therapeutische dosis): ↑AUC pravastatine 2x, rosuvastatine 1.7x (90% CI 1.60-2.46x resp 1.53-1.87x).	2A
Stockley online mei 2025	statines + bempedoïnezuur	getallen als SPC Nilemdo, obv data UK and US manufacturers. Atorvastatine: nothing expected, no action (obv Lalwani 2019). Rosuva: idem. Pravastatin: moderate, adjust (obv prod.info)	1-2A
Lalwani ND. J Clin Lipidol 2019;13:568–79.	atorvastatine + bempedoïnezuur	↑AUC atorvastatine en/of metabolieten 1.2-1.3x ('mild increase') Regime: 4 weken atorvastatine 80 mg, daarna 4 weken atorvastatine 80 mg + placebo (n=23) of atorvastatine 80 mg + bempedoïnezuur 180 mg (n=45); studie in patienten. The aim of the study was to assess the LDL-C-lowering efficacy of bempedoic acid added to stable high-intensity atorvastatin background therapy and multiple-dose plasma pharmaco-kinetics of atorvastatin alone and combined with steady-state bempedoic acid. Conclusie: bempedoic acid added to atorvastatin effectively lowers LDL-C without causing clinically important increases in atorvastatin exposure. Results showed mild increases in AUC, with test/reference ratios and 90% CIs that were outside the predefined 80-125% range and encompassed unity. For the Cmax of atorvastatin and ortho-hydroxy atorvastatin, the 90% CIs were outside the 80-125% range; however, the test/reference ratios were 99% resp. 103%, which suggests that the Cmax of atorvastatin and its major active metabolite were generally unchanged. The increased exposure to atorva-statin did not result in increases in blood concentrations that could be considered clinically meaningful for causing any adverse effects and did not warrant adjustment of the atorvastatin dose.	3A

Overig	Stof	Effect
Spc + EPAR Nilemdo CPK: creatinefosfokinase	atorvastatine, pravastatine, rosuvastatine	bempedoïnezuur als aanvullende therapie bij een statine: monitor op bijwerkingen die gepaard gaan met het gebruik van hoge doses statines, en informeer patiënt over het potentieel verhoogde risico op myopathie en direct melden van eventuele onverklaarde spierpijn, -gevoeligheid of -zwakte. Bij dergelijke symptomen moet een lagere dosering van dezelfde statine of een alternatieve statine, of staken van bempedoïnezuur en opstarten van een alternatieve lipidenverlagende behandeling worden overwogen onder monitoring van het lipidengehalte en de bijwerkingen.

ULN: bovengrens van normaal		Staak bempedoïnezuur en statine bij bevestigde myopathie (CPK-spiegel > 10x ULN). Mechanisme: bempedoïnezuur en de glucuronide zijn zwakke remmers van OATP1B1 en 1B3. Combinatie met substraten van OATP1B1 of OATP1B3 (oa atorvastatine, pravastatine, rosuvastatine) kunnen leiden tot hogere plasmaconcentraties van deze middelen. EPAR: statin Cmax were also increased by a similar extent, suggesting that not only the excretion but also the first pass effect of statins is affected. According to the applicant, the interaction can probably be attributed to inhibition of OATP transport.
Jadhav SB. Eur Heart J Cardiovasc Pharmacother 2022;8:578-6.	atorvastatine, rosuvastatine, pravastatine + bempedoïnezuur	Dose-response models predicted that combining bempedoic acid with the lowest statin dose would achieve a similar degree of LDL-C lowering as quadrupling that statin dose; for example, the predicted LDL-C lowering was 54% with atorvastatin 80 mg compared with 54% with atorvastatin 20 mg + bempedoic acid 180 mg. Methods: bempedoic acid and statin dosing and LDL-C data were pooled from clinical studies. Dose-response models were developed for bempedoic acid monotherapy and bempedoic acid-statin combinations using previously published statin parameters. Conclusion: these findings suggest bempedoic acid combined with lower statin doses offers similar LDL-C lowering compared with statin monotherapy at higher doses.
Thirumalai A. Endocrine Practice 2022;28:S61. *niet in bezit* AACE Annual Meeting 2022 Abstract #1164309 AT: atorvastatine BA: bempedoïnezuur	atorvastatine + bempedoïnezuur	abstract: female (88) on AT 80mg and ezetimibe 10mg once daily, LDL-C 100-150 mg/dL. BA 180mg daily was added to her regimen. After 2 months, patient presented with significant bilateral muscle cramps in arms and legs. Labs showed elevated CK levels (643 U/L). AT was then decreased to 20mg once daily. Symptoms resolved and CK levels normalized within one week of AT dose reduction. LDL-C had dropped to 1 mg/dL initially on BA addition but was 37 mg/dL 4 weeks after AT dose adjustment. Discussion: starting BA in patients without dose limitation of simvastatin and pravastatin resulted in a higher incidence of myalgias. In clinical trials, BA added to high-dose AT has not shown an increased risk of muscle-related adverse events, however, our patient developed this, possibly related to increased AT concentrations. Our patient also showed a profound lowering of LDL-C and it remained at target levels even after lowering the dose of AT. This case illustrates the possibility of an interaction between BA and high-dose AT and the potential need to consider a dose reduction of all statins when adding BA. →GIC: gebruik 3 middelen, statine hoge dosis+ezetimib+bempedoinezuur.

Opmerkingen
Stockley: zie tabel.

PubMed: verder niets, behalve Jadhav 2022.

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG IA	Ja	Nee	2-6-2025