Alectinib/Asciminib + Rifampicine MFB 6375

Onderbouwend	Stof	Effect	Code
Morcos PN. Clin Pharmacol Drug Dev 2017;6:280-91. doi: 10.1002/cpdd.298.	alectinib + rifampicine	alectinib: ↓ AUC met 74% (3990→1020 ng.h/ml), Cmax met 52% (212→102 ng/ml); ↓ t½ 19.2 → 11.0h actieve M4-metaboliet: ↑ AUC 1.8x (2250→3970 ng.h/ml), Cmax 2.1x (90.5→194 ng/ml); t½ vrijwel niet gewijzigd. Regime: alectinib 600 mg op dag 1 en dag 17, rifampicine op dag 8 t/m dag 20; 24 vrijwilligers Auteurs: Consistent with the observations for alectinib and M4 alone, the M/P ratio was markedly altered following coadministration of alectinib with rifampin: alectinib alleen: M/P ratio Cmax 0.424, AUC 0.593; icm rifampicine: M/P ratio Cmax 1.92, AUC 3.96, Coadministration with rifampin resulted in only a minor effect on the combined exposure of alectinib and M4, with ratios for Cmax 96.1% and AUC 81.6%.	3A
SPC Alesenca	alectinib + rifampicine	zelfde getallen als Morcos 2017 netto effect op alectinib+M4 is gering: ↓ AUC alectinib+M4 met 18% en Cmax met 4%.	2A
Hoch M. Clin Transl Sci. 2022;15:1698-1712.	asciminib + rifampicine	↓ AUCinf asciminib met 14.9% en ↑ Cmax 1.09x. Regime: asciminib 40 mg eenmalig, rifampicine 600 mg 1 dd meerdere dagen, 18 gezonde personen. Auteurs: taking into account the large therapeutic window of asciminib, the observed changes in asciminib PK following multiple doses of CYP3A inducers are not considered to be clinically meaningful.	3A
SPC Scemblix	asciminib + rifampicine	getallen als Hoch 2022. ↓ AUCinf asciminib met 15% en ↑ Cmax met 9%.	2A

Overig	Stof	Effect
SPC Alesenca EPAR Alesenca	alectinib + inductoren	Aanpassen dosering alectinib niet nodig bij combinatie met sterke CYP3A-inductoren (oa carbamazepine, fenobarbital, fenytoïne, rifabutine, rifampicine en hypericum). p.46: Results from the human mass balance study demonstrated that alectinib and M4 were the main circulating moieties in plasma with 76% of the total radioactivity in plasma. The geometric mean Metabolite/Parent (M/P) ratio at steady state is 0.399. p. 51: The MP ratio of M4 and alectinib is 0.3-0.5 at normal conditions. However, when alectinib is coadministrated with the potent CYP3A inducer rifampin the M/P of M4 is altered to 3.74.
SPC Scemblix	asciminib + CYP3A4-inductoren	voorzichtig bij combinatie met sterke CYP3A4-inductoren, kan resulteren in een verminderde werkzaamheid van asciminib.
SPC + EPAR Scemblix	asciminib	in human plasma, parent drug was the predominant drug related component, with an average mean contribution to plasma radioactivity exposure of 92.7%. No metabolite with mean contribution to plasma radioactivity exposure ≥ 10% was detected. Circulating metabolites found were the direct O-glucuronide (4.93%), the ketone product of alcohol oxidation (1.88%), and the alcohol formed from oxidative opening of the pyrrolidinol ring (0.39%).

Opmerkingen
Werkgroep Interacties oncologische middelen 15-3-23: asciminib koppelen.

Stockley: -
PubMed: verder niks behalve Hoch 2022.

Risicofactoren	
Mitigerende factoren	

	Interactie	**Actie**	**Datum**
Beslissing WG OncoIA	Ja	Nee	15 maart 2023