

Cariprazine + CYP3A4-remmers

M6898

DCAR = desmethylcariprazine, DDCAR = didesmethylcariprazine (actieve metabolieten van cariprazine)

Onderbouwend	Stof	Effect	Code
EPAR Reagila	cariprazine + ketoconazol	cariprazine: ↑ AUC cariprazine 3.9x en Cmax 3.4x ; t1/2 67h vs 85h. DDCAR: ↑ AUC 1.4x en Cmax 1.4x, kleine ↑ t1/2. DCAR: ↓ blootstelling tot 65-68%, t1/2 74h vs 47h. Regime: cariprazine 0.5 mg/dag al dan niet i.c.m. ketoconazol 400 mg/dag gedurende 10 dagen, studie onder 36 gezonde personen, 1 groep cariprazine, 1 groep cariprazine + ketoconazol. →GIC: lage dosis cariprazine en ketoconazol. Studie met matige CYP3A4-remmers nog niet uitgevoerd, wel gepland.	2A
SPC Reagila	cariprazine + ketoconazol	toename plasmablootstelling totaal cariprazine (som cariprazine en werkzame metabolieten) 2x bij combinatie met ketoconazol gedurende 4 dagen.	1A

Overig	Stof	Effect
SPC + EPAR Reagila	cariprazine + CYP3A4-remmers	Vanwege lange t1/2 verdere verhoging blootstelling verwacht bij langere combinatie. Combinatie met matig sterke tot sterke remmers van CYP3A4 gecontraïndiceerd. Cariprazine is metabolized to its active metabolites DCAR and DDCAR with both CYP3A4 and CYP2D6 enzymes involved. Thus, inhibitors and inducers of CYP3A4 might influence the formation of the active metabolites, and elimination of the mother substance. However, there are uncertainties concerning how DCAR and DDCAR are eliminated. Therefore, based on current information available, the safety of drug interactions is not completely clear.
FDA Prescribing Information Vraylar	cariprazine + CYP3A4-remmers	dosisadvies bij combinatie met sterke CYP3A4-remmers: -start CYP3A4-remmer: halveer dosis cariprazine. Bij 4.5 mg/dag: dosis verlagen tot 1.5 of 3 mg/dag. Bij 1.5 mg/dag: dosis verlagen tot 1.5 mg om de dag. - start cariprazine: 1.5 mg op dag 1 en dag 3 (niet dag 2). Vanaf dag 4 1.5 mg 1dd, daarna zo nodig tot max 3 mg/dag.
EPAR Reagila	cariprazine	rubriek clinical safety: -For the claimed posology of 1.5-6 mg/day, dose dependency was observed for TEAEs blurred vision, CPK elevation, akathisia/restlessness, insomnia and anxiety. -The maximum tolerated dose of cariprazine was 18 mg/day. Few instances of overdose, in the clinical databases of the schizophrenia studies and none of the patients who received cariprazine greater than 18 mg/day experienced an adverse outcome. One accidental overdose of cariprazine with 48 mg experienced orthostatic dizziness and sedation, however fully recovered the same day.

Opmerkingen

Pubmed, Stockley: -

Risicofactoren	
Mitigerende factoren	

	Interactie	Actie	Datum
Beslissing WFG	Ja	Ja	11 december 2018