Effect of Co-medications on Rapamycin (Sirolimus)

 $0 = \text{no effect expected}; \downarrow = \text{decreased rapamycin exposure (induction)}; \uparrow = \text{increased exposure (inhibition)}; values are approximate fold-changes.}$

Substance	Prior days	Together	Subsequent days	Notes
Baclofen	0	0	0	Renal elimination
Daridorexant	0	0	0	CYP3A4 substrate; no inhibition/induction
Dextromethorphan	0	0	0	CYP2D6/3A4 substrate; no clinical induction/inhibition
Domperidone	0	0	0	CYP3A4/P-gp substrate; no perpetrator role
Duloxetine	0	0	0	CYP1A2/2D6 substrate; no 3A4/P-gp effect
Lercanidipine	0	0	0	CYP3A4 substrate only; no perpetrator role
Levothyroxine	0	0	0	Absorption issue only; no CYP3A4 effect
Lorazepam	0	0	0	UGT substrate
Metamizole	↓ (0.5–0.8×)	↓ (0.5–0.8× Cmax; 0.4–0.7× AUC)	↓ (persists up to a week)	CYP3A4 inducer; ↓ calcineurin inhibitor levels; offset may take ~1 week
Modafinil	↓ (0.7–0.9×)	↓ (0.7–0.9× Cmax; 0.6–0.8× AUC)	↓ (persists for days)	Moderate CYP3A4 inducer; onset ≥3–5 days; persists after stop
Nebivolol	0	0	0	CYP2D6 substrate
Paracetamol	0	0	0	UGT metabolism; no 3A4/P-gp effect
Pramipexole	0	0	0	Renal elimination
Prucalopride	0	0	0	Weak P-gp substrate; no meaningful effect
Rabeprazole	0	0	0	CYP2C19/non-enzymatic; minimal 3A4 effect
Sildenafil	0	0	0	CYP3A4 substrate only; no perpetrator role
Tizanidine	0	0	0	CYP1A2 substrate
Tramadol	0	0	0	CYP2D6 + 3A4 substrate; not perpetrator
Vortioxetine	0	0	0	CYP2D6 substrate; no 3A4/P-gp effect
Zolpidem	0	0	0	CYP3A4 substrate; no meaningful perpetrator effect
Zopiclone	0	0	0	CYP3A4 substrate; not a relevant perpetrator