DRUG INTERACTIONS

Drug	Possible mechanism/ onset and severity	Adverse effects	Management
Drugs that DECREASE Sirolimus levels			
Anticonvulsants: • Phenytoin • Carbamazepine • Phenobarbital, primidone	↑Enzyme induction, ↑sirolimus metabolism • delayed / major • delayed/ moderate • delayed / major	↓ effectiveness of sirolimus which may lead to rejection	↑sirolimus dose by 30% and monitor levels following addition, dose change or discontinuation.
Antimicrobial: Rifampin	Induction of hepatic enzymes delayed / major	Same as above	Monitor sirolimus levels following addition, dose change or discontinuation
Drugs that INCREASE Sirolimus levels			
Antimicrobials: • Erythromycin, clarithromycin • Azole antifungals	↓sirolimus metabolism • delayed / major • delayed/ moderate	↑ sirolimus levels, ↑ risk of toxicity	Monitor sirolimus levels following addition, dose change or discontinuation. Monitor serum creatinine
Antidepressants: fluoxetine, fluvoxamine	↓ sirolimus metabolism delayed/ moderate	↑ sirolimus levels, ↑ risk of toxicity	Consider another antidepressant (citalopram, escitalopram) and/or monitor sirolimus levels closely
Cardiovascular: diltiazem, verapamil, amiodarone	May inhibit hepatic metabolism of sirolimus delayed / major	↑ sirolimus levels, ↑ risk of toxicity	Monitor sirolimus levels following addition, dose change or discontinuation
HMG-CoA Reductase Inhibitors: lovastatin, simvastatin, atorvastatin	sirolimus may ↓ metabolism of these agents	accumulation of statin and toxicity Myalgia, myopathy, rhabdomyolysis	Start with low dose of these agents and monitor very closely for toxicity
Digoxin	↓ volume of distribution of digoxin by 50-70%, ↑digoxin half-life by 30-40%, and increased digoxin levels	digoxin toxicity such as vomiting, cardiac arrhythmia's	Initiate low dose and follow up with serum digoxin levels Closely monitor for symptoms of digoxin toxicity

(1) BC Transplant. (2021, May 13). MEDICATION GUIDELINES FOR SOLID ORGAN TRANSPLANTS. BC Transplant. (http://www.transplant.bc.ca/Documents/Health%20Professionals/Clinical%20guidelines/Clinical%20Guidelines%20for%20Transplant%20Medications.pdf)