

**Appendix 1: Grapefruit Interacting Drugs and Associated Oral Bioavailability, Adverse Event(s), Risk Ranking and Potential Alternative Medications**

<b>Interacting Drugs</b>	<b>Innate Oral Bioavailability*</b>	<b>Dose-Related Drug Adverse Event(s)</b>	<b>Predicted Interaction Risk Rank **</b>	<b>Potential Alternative Medication(s)***</b>
<b>Anti-Cancer Agents</b>				
crizotinib	intermediate	torsade de pointes, myelotoxicity	high	
cyclophosphamide	high	loss of efficacy	intermediate	
dasatinib	not known	torsade de pointes, myelotoxicity	high	<i>imatinib</i>
erlotinib	intermediate	myelotoxicity	high	
everolimus	low	myelotoxicity, nephrotoxicity	high	
imatinib	high	myelotoxicity	intermediate	
lapatinib	incomplete	torsade de pointes, myelotoxicity	high	
nilotinib	intermediate	torsade de pointes, myelotoxicity	high	<i>imatinib</i>
pazopanib	incomplete	torsade de pointes, myelotoxicity	high	<i>sorafenib</i>
sorafenib	intermediate	myelotoxicity	intermediate	
sunitinib	not known	torsade de pointes, myelotoxicity	high	<i>sorafenib</i>
vandetanib	not known	torsade de pointes, myelotoxicity	high	
venurafenib	not known	torsade de pointes, myelotoxicity	high	
<b>Anti-Diabetic Agents</b>				
repaglinide	intermediate	hypoglycemia	intermediate	glyburide, <i>metformin</i> , <i>sitagliptin</i>
saxagliptin	intermediate	hypoglycemia	intermediate	glyburide, <i>metformin</i> , <i>sitagliptin</i>
<b>Anti-Infective Agents</b>				
albendazole	low	dizziness, headache, nausea	intermediate	
artemether	low	enhanced anti-malarial efficacy	low	
erythromycin	intermediate	torsade de pointes	high	clarithromycin
etravirine	not known	skin rash	low	
halofantrine	low	torsade de pointes	very high	<i>doxycycline</i>
maraviroc	low	postural hypotension, syncope	very high	<i>enfuvirtide</i>
praziquantel	low	dizziness, headache, somnolence	intermediate	
primaquine	intermediate	myelotoxicity	high	<i>doxycycline</i>
quinine	intermediate	torsade de pointes	high	<i>doxycycline</i>

rilpivirine	not known	torsade de pointes	high	<i>nevirapine</i>
saquinivir	very low	enhanced HIV efficacy	low	amprenavir, indinivir
<b>Anti-Inflammatory Agents</b>				
budesonide – oral	intermediate	hyperglycemia, Cushingoid features	intermediate	
colchicine	not known	neutropenia, neuropathy	intermediate	prednisone, <i>ibuprofen</i>
methylprednisolone -oral	intermediate	hyperglycemia, Cushingoid features	intermediate	prednisone
<b>Anti-Lipemic Agents</b>				
atorvastatin	low	rhabdomyolysis	high	pravastatin, <i>rosuvastatin</i> , <i>fluvastatin</i>
lovastatin	very low	rhabdomyolysis	very high	pravastatin, <i>rosuvastatin</i> , <i>fluvastatin</i>
simvastatin	very low	rhabdomyolysis	very high	pravastatin, <i>rosuvastatin</i> , <i>fluvastatin</i>
<b>Cardiovascular Agents</b>				
amiodarone	intermediate	torsade de pointes	high	<i>sotalol</i>
amlodipine	high	hypotension, peripheral edema	low	
apixaban	intermediate	GI bleeding	high	warfarin
cilostazol	not known	GI bleeding	high	<i>acetylsalicylic acid</i>
clopidogrel	very low	loss of efficacy	high	<i>acetylsalicylic acid</i>
dronedarone	low	torsade de pointes	very high	<i>sotalol</i>
eplerenone	intermediate	hyperkalemia, serious arrhythmias	high	<i>spironolactone</i>
ergotamine	very low	gangrene, stroke	very high	<i>a triptan class drug</i>
felodipine	low	hypotension, peripheral edema	intermediate	amlodipine
losartan	intermediate	loss of efficacy	intermediate	
manidipine	low	hypotension, peripheral edema	intermediate	amlodipine
nicardipine	low	hypotension, peripheral edema	intermediate	amlodipine
nifedipine	intermediate	hypotension, peripheral edema	intermediate	amlodipine
nimodipine	very low	hypotension, peripheral edema	intermediate	
nisoldipine	very low	hypotension, peripheral edema	intermediate	amlodipine
nitrendipine	low	hypotension, peripheral edema	intermediate	amlodipine
propafenone	low	bradycardia, conduction disorders	intermediate	
quinidine	high	torsade de pointes	intermediate	

rivaroxaban	high	GI bleeding	intermediate	warfarin
sibutramine	not known	hypertension	intermediate	
sildenafil	intermediate	hypotension	intermediate	
tadalafil	intermediate	hypotension	intermediate	
ticagrelor	intermediate	GI or kidney bleeding	high	<i>acetylsalicylic acid</i>
vardenafil	intermediate	hypotension	intermediate	
verapamil	intermediate	complete heart block	high	diltiazem
<b>CNS Agents</b>				
aprepitant	intermediate	drowsiness, headache	low	
alfentanil – oral	intermediate	respiratory depression	high	<i>hydromorphone, morphine</i>
bupirone	very low	dizziness, sedation	high	<i>oxazepam, tamazepam</i>
carbamazepine	high	ataxia	low	<i>phenytoin, clonazepam</i>
dextromethorphan	very low	hallucinations, somnolence	high	
diazepam	low	sedation	intermediate	<i>alprazolam, oxazepam, tamazepam</i>
fentanyl – oral	intermediate	respiratory depression	high	<i>hydromorphone, morphine</i>
fluvoxamine	not known	adverse change in mood	intermediate	<i>citralopram, paroxetine, escitalopram</i>
ketamine – oral	low	respiratory depression	very high	<i>hydromorphone, morphine</i>
lurasidone	low	torsade de pointes, orthostatic hypotension, syncope	very high	<i>haloperidol, risperidone, olanzapine</i>
methadone	high	respiratory depression	intermediate	
midazolam – oral	intermediate	sedation	intermediate	<i>alprazolam, lorazepam</i>
oxycodone	intermediate	respiratory depression	high	<i>hydromorphone, morphine</i>
pimozide	intermediate	torsade de pointes	high	<i>haloperidol, risperidone, olanzapine</i>
quazepam	intermediate	sedation	low	<i>alprazolam, oxazepam, temazepam</i>
quetiapine	very low	dizziness, somnolence	high	<i>haloperidol, risperidone, olanzapine</i>
sertraline	intermediate	dizziness, somnolence	intermediate	<i>citralopram, paroxetine, escitalopram</i>
triazolam	intermediate	sedation	intermediate	<i>alprazolam, lorazepam</i>
ziprasidone	intermediate	torsade de pointes	high	<i>haloperidol, risperidone</i>

				<i>olanzapine</i>
<b>Estrogens</b>				
estradiol	low	breast cancer risk, thrombosis	intermediate	
ethinylestradiol	intermediate	breast cancer risk, thrombosis	intermediate	
<b>Gastrointestinal Agents</b>				
cisapride	intermediate	torsade de pointes	high	<i>metoclopramide</i>
domperidone	low	torsade de pointes	very high	<i>metoclopramide</i>
<b>Immunosuppressant Agents</b>				
cyclosporine	low	nephrotoxicity	high	
everolimus	low	myelotoxicity, nephrotoxicity	high	
sirolimus	low	myelotoxicity, nephrotoxicity	high	
tacrolimus	low	nephrotoxicity	high	
<b>Urinary Tract Agents</b>				
darifenacin	low	urinary retention, constipation	intermediate	
fesoterodine	intermediate	urinary retention, constipation	intermediate	
solifenacin	high	torsade de pointes	intermediate	
silodosin	intermediate	postural hypotension, dizziness	intermediate	
tamsulosin	intermediate	postural hypotension, dizziness	intermediate	

\* Innate oral drug bioavailability is the population average: very low (<10%), low (>10-30%), intermediate (>30 – 70%), high (>70%)

\*\* Predicted Risk Rank is based initially upon the seriousness of the dose-related adverse drug effect and then adjusted dependent upon the innate oral bioavailability of the drug, which is used to determine the potential magnitude of increase in systemic drug concentration (see text). There are four categories of risk ranking: very high, high, intermediate, low. It is recommended for older patients, particularly the elderly, that drugs in the very high or high category that consumption of grapefruit or other interacting citrus fruits should be contraindicated during pharmacotherapy until proven safe or that a suggested alternative non-interacting drug be employed when available.

\*\*\* Potential alternative medication(s) include established or predicted (*italics*) commonly prescribed drugs (Top 100 prescribed in 2011 in Canada) with the same therapeutic indication that have no or minor pharmacokinetic interaction with grapefruit or other interacting citrus fruits.