SILDENAFIL and POSSIBLE DRUG INTERACTIONS (Jan 2007)

Background Sildenafil is metabolised in the liver by cytochrome P450 isoenzymes CYP3A4 (major pathway) and CYP2C9 to the N-desmethyl metabolite, which has approximately 50% of the activity of the parent compound. Excretion is predominantly in the faeces. It is a weak inhibitor of cytochrome P450 isoenzymes but is not thought to be an inducer (unlike Bosentan). The major drug interaction is likely to be with inhibitors of CYP3A4 and/or CYP2C9. Inducers of these two enzymes may increase the clearance of Sildenafil (e.g. Rifampicin, Bosentan)

Vasodilators (Potentiation)

Nitrates*
Nicorandil*
Alpha-blockers*

BOSENTAN ↓ SILDENAFIL AUC 63%
SILDENAFIL ↑ BOSENTAN AUC 50%
SITAXENTAN ↑SILDENAFIL AUC 28%

Inhibitors CYP3A4

Miconazole ●
Ketoconazle *
Itraconazole *
Voriconazole●
Erythromycin 1
Cimetidine ●
Grapefruit Juice
Amiodarone●
Ciprofloxacin
Clarithromycin 2
Diltiazem
Fluconazole●
Fluvoxamine
Nefazodone 2
Verapamil
Nifedipine
Fluoxetine●
Glibenclamide
Ciclosporin
Atorvastatin.●
Isoniazid
Nicardipine
Omeprazole
Sertraline
Metronidazole
Quinine
Reboxetine

HIV Antivirals

Protease Inhibitors

Ritonavir *
Saquainavir 1
Nelfinavir
Indinavir
Lopinavir
Amprenavir
Atazanavir
(Efavirenz)†

NNRTIs

Delaviridine

*SmPC recommends avoid

● Also inhibits CYP2C9

† Has been shown to both induce and inhibit this enzyme

1. SmPC rec.20mg bd

2. SmPC rec. 20mg od.

OMISSION FROM THIS TABLE DOES NOT IMPLY THAT THE COMBINATION IS SAFE. AS KNOWLEDGE PROGRESSES FURTHER ADDITIONS ARE LIKELY.