Drug Interactions with Antidepressants

These tables contain information on some of the important drug interactions with the SSRIs and other antidepressants. It is not fully comprehensive or inclusive and it is especially important to check out the possibility of an interaction occurring with drug combinations that you are not familiar with. Individual susceptibility and response to a drug interaction can be quite variable and the clinical significance is often approached on a case by case basis. The notes on importance and management give some advice but specialised texts such as Stockley's should be consulted for detailed information on clinical significance and management.

Fluoxetine, paroxetine and citalopram are metabolised by the cytochrome P-450 system in the liver but are substrates for different isoenzymes and vary in their potential to inhibit the metabolism of other drugs. In general, citalopram is less likely to cause drug interactions due to enzyme inhibition than fluoxetine or paroxetine. Drug interactions due to enzyme inhibition or induction are pharmacokinetic drug interactions. SSRIs (and other antidepressants) can also cause pharmacodynamic drug interactions where there is no change in the drug concentration of the interacting drug but the effects are additive or antagonistic due to the drug's pharmacological properties. Examples include additive sedation with CNS depressants and serotonin syndrome with other serotonergic drugs.

In Table 1 "All' refers to the three SSRIs available in New Zealand; paroxetine, fluoxetine and citalopram. Table 2 refers to TCAs in general although individual drugs have different properties which can increase the risk of an interaction; for example amitriptyline is one of the most sedative TCAs and clomipramine has marked serotonergic properties which increase the risk of serotonin syndrome if given with SSRIs.

Table 1: Some important drug interactions with Antidepressants

SSRI	Interacting Drug	Possible Effect(s)	Importance and Management
All	Alcohol	Increased CNS sedation	Advise vigilance in early stages of treatment
All	Benzodiazepines	Increased sedation possible. Fluoxetine and paroxetine may reduce metabolism of some benzodiazepines	Warn that increased sedation is possible
All	Warfarin	Increased INR and increased bleeding risk due to antiplatelet effect	Monitor INR and advise patients to report signs of bleeding
Fluoxetine & paroxetine	Metoprolol and propranolol	Increased beta-blocking effects, bradycardia	Monitor heart rate. Interaction not reported with citalopram
All	Buspirone	Serotonin syndrome and lowering of seizure threshold theoretically possible	Monitor concurrent use
All	Antiepileptics	SSRIs may lower the seizure threshold	Unlikely to be a problem if epilepsy well controlled. Observe seizure frequency
Fluoxetine	Antiepileptics, carbamazepine and phenytoin	Increased plasma concentrations of carbamazepine and phenytoin with fluoxetine	Monitor plasma concentrations of carbamazepine and phenytoin. Adjust dose if necessary. No similar reports with paroxetine and an interaction appears unlikely with citalopram.
Paroxetine	Antiepileptics, carbamazepine and phenytoin	Reported to decrease plasma concentration of paroxetine	Clinical significance not clear. Monitor clinical response
All	NSAIDs including aspirin	Increased risk of GI bleeding	Concurrent use not contraindicated but be aware of increased risk of bleeding especially in those with additional risk factors
All	Monoamaine oxidase inhibitors (MAOIs), including moclobemide	Hypertensive crisis	Avoid concurrent use. Washout periods essential when switching. Refer to product prescribing information and reference texts.
Fluoxetine & paroxetine (possibly citalopram)	Clozapine, haloperidol and risperidone	Increased plasma concentrations of antipsychotics	Monitor for dose related adverse effects and reduce dose of antipsychotic if necessary

All	Tramadol	Both tramadol and SSRIs lower seizure threshold. Serotonin syndrome reported with concurrent use	Use the combination of tramadol and an SSRI very cautiously especially at high doses. Alternative analgesic may be preferable
All	Tricyclic antidepressants	Increased plasma concentrations of TCA and increased adverse effects. Risk of serotonin syndrome especially with clomipramine	Increases are variable but can be in the order of 3–4 times and more. Increases usually less significant or negligible with citalopram. If the combination is judged necessary, start with the lowest dose of TCA and monitor for dose related adverse effects, e.g sedation, or anticholinergic symptoms
All	Sibutramine	Increased risk of CNS toxicity	Avoid
All (especially fluoxetine & paroxetine)	Perhexilene, flecainide and other antiarrhythmic drugs	Plasma concentrations can be increased leading to toxicity.	Refer to individual product prescribing information and reference texts
Fluoxetine & paroxetine	Protease inhibitors (ritonavir)	Fluoxetine increases ritonavir concentrations and ritonavir may increase fluoxetine and paroxetine concentrations. Cases of serotonin syndrome with fluoxetine reported	Monitor for symptoms of serotonin syndrome. Reduce dose if necessary
All	Lithium	Neurotoxic symptoms and serotonin like syndrome occasionally reported	Addition of lithium to an SSRI can be beneficial and is usually uneventful. Observe for adverse effects
All	Selegiline	Hypertension, CNS excitation, serotonin syndrome	Avoid this combination as serious interactions have been reported. Manufacturers advise to avoid. N.B. apparent safe use of this combination has also been reported in the literature
All	St John's Wort	Serotonin syndrome	Avoid this combination
All	Sumatriptan	A few cases of dyskinesias with fluoxetine. Occasional reports of serotonin syndrome	Concurrent use of sumatriptan and SSRIs not usually a problem but monitor for any adverse effects when the combination is started

Table 2: Some important drug interactions with tricyclic antidepressants (TCAs)

Interacting drugs(s)	Possible effect(s)	Importance and management
SSRIs	Increased plasma concentrations of TCA causing increased adverse effects. Serotonin syndrome possible, especially with clomipramine	Increases are variable but can be in the order of 3 – 4 times and more. Increases usually less significant or negligible with citalopram. If the combination is judged necessary, start with the lowest dose of TCA and monitor for dose related adverse effects, e.g. sedation, or anticholinergic symptoms
Alcohol	Increased CNS depression, sedation	Warn patient about increased drowsiness. Limit alcohol intake
Antiarrhythmic drugs, e.g. amiodarone, flecainide, quinidine	Increased risk of ventricular arrhythmias	Avoid concurrent use. Refer to specialised texts.
CNS depressants e.g. Benzodiazepines Antihistamines Antipsychotics	Increased CNS depression, sedation	Warn patient about increased drowsiness
Clonidine	Antihypertensive effects of clonidine are reduced or abolished	Avoid concurrent use
Warfarin	Occasional reports of changes in INR	Evidence for an interaction is poor and inconclusive. Monitor INR as normal
Lithium	Neurotoxic symptoms and serotonin-like syndrome occasionally reported	Concurrent use can be beneficial and is usually uneventful. Observe for adverse effects
Antipsychotics	Increased sedation, additive anticholinergic effects Plasma concentrations of phenothiazines and/or the TCA may be increased	Often used together in clinical practice but be aware of the possibility of additive pharmacological and adverse effects
Selegiline	CNS excitation, serotonin syndrome	Interaction appears less likely than with an SSRI Caution and awareness of possible symptoms advised
Ritonavir	Plasma concentrations of TCAs may be increased.	Monitor for increased dose related adverse effects. Reduce dose of TCA if necessary.
Tramadol	Increased risk of seizures. Possibility of serotonin syndrome especially with clomipramine	Adverse effects unlikely but be aware of symptoms