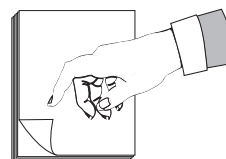


Pharmacotherapeutic management of depression

Aims of the clinical audit

- To review your management of patients with depression.
- To review antidepressant therapy:
 - dose and duration
 - response
 - adverse effects and possible interactions.
- To reflect on education provided to patients.

Please tear off each section. Registration/summary form and clinical audit forms to be returned to NPS. Please tear off forms carefully.



How to participate

1. Select patients

Prospectively as patients present for consultation or retrospectively from a search of electronic/paper medical records, identify 20 patients aged 18 years or over receiving an antidepressant for:

- mild major depression or adjustment disorder with depressed mood
- moderate or severe major depression
- dysthymia.

Exclude patients:

- using antidepressants for conditions other than depression.

Patient privacy

Patients must be informed that data from their medical records may be used for the purposes of clinical audits, and **written consent obtained**.

Please:

- display the enclosed poster in your practice
- ask patients who present to the practice to read and sign a copy of the enclosed *Patient information and consent form*, or
- send the enclosed *Patient information and consent form* to patients whose records you wish to use retrospectively, asking them to sign and return it to the practice.

Use the *Patient record form* to record the patients you have included for your future reference.

Do NOT send in the *Patient record form* or the *Patient information and consent form*. Keep these in your files.

2. Collect data and review

Complete the clinical audit form for each patient. See notes on pages 2–5.

Please note:

- Patient information must only be collected and recorded by the participating doctor.
- Both full-time and part-time GPs are required to submit 20 completed clinical audit forms.

3. Send in the clinical audit forms

Return the 20 clinical audit forms and *Registration/summary form* to:

**NPS Clinical Audit: Depression
Locked Bag 4888
STRAWBERRY HILLS NSW 2012**

**To be received at NPS not later than:
Friday 19th November 2004**

Please note: Unfortunately, late submissions cannot be accepted.

4. When you receive your results

You will be required to answer and return a set of review questions. See back page for details.

Professional development

This clinical audit:

- qualifies as an activity for the Quality Prescribing Initiative (QPI) of the Practice Incentives Program (PIP).

The NPS has applied for clinical audit points in the 2005–2007 triennium of the:

- Royal Australian College of General Practitioners (RACGP) Quality Assurance & Continuing Professional Development (QA&CPD) Program (Group 1 points), and
- Australian College of Rural and Remote Medicine (ACRRM) Professional Development Program (practice improvement category points).

Further information

Telephone NPS on (02) 8217 8700; for

Therapeutic enquiries

Kylie Easton
Judith Mackson

Audit and QPI enquiries

Cris Abbu

Clinical audit: background information

Additional information to assist you to review management.
Use it to complete the clinical audit form.

Patient details

(Q1) Your patient code

Choose your own unique identifying code for the patient e.g. sequential number or the patient's initials (please do not use the patient's name).

Diagnosis

(Q3) Depressive disorder

Mark the main indication for current antidepressant therapy.

Major depression diagnostic criteria are shown in Box 1.¹ An episode of major depression can be classified as mild, moderate or severe²:

- Mild – Few symptoms beyond minimum required to make diagnosis. Mild disability.
- Moderate – More than minimum criteria met. Greater functional impairment.
- Severe – Most criteria present. Marked interference with social and/or occupational functioning.

Box 1. DSM-IV diagnostic criteria for major depression¹

- A. At least 5 of the following symptoms for 2 weeks (criteria 1 or 2 essential):
1. depressed mood
 2. loss of interest or pleasure
 3. significant appetite or weight loss or gain
 4. insomnia or hypersomnia
 5. psychomotor agitation or retardation
 6. fatigue or loss of energy
 7. feelings of worthlessness or excessive guilt
 8. impaired thinking or concentration; indecisiveness
 9. suicidal thoughts/thoughts of death.
- B. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
- C. Do not include symptoms that are clearly due to a general medical condition.

Adjustment disorder with depressed mood includes symptoms of depression that do not meet criteria for major depression.¹ Symptoms may resolve spontaneously or benefit from counselling or supportive psychotherapy.¹ Pharmacotherapy is not first line.^{1,3}

Dysthymia is a chronic depressive state of more than 2 years' duration, which does not meet the full criteria for major depression and is not the consequence of a partially resolved major depression.⁴ Dysthymia responds to antidepressants less predictably than major depression.¹

(Q4) Does the patient have a coexisting psychiatric disorder(s)?

Consider if the depression is secondary to another psychiatric condition such as an anxiety disorder or substance abuse.¹ If it is secondary, the major focus of management should be the primary condition.¹

Consider whether treatable organic causes or medications that may cause depression have been treated or reviewed.

Organic causes may include: cerebrovascular disease or hypothyroidism.¹ Medications that may cause depression include: corticosteroids, levodopa, interferon or isotretinoin.¹

Diagnosis (cont'd)

(Q5) Have you made a systematic assessment of suicide risk?

A careful assessment of the patient's risk for suicide is crucial.⁵ Although actual risk is very difficult to assess, a guide is given in Box 2.¹ Patients should be admitted to hospital if they are at significant risk for suicide.¹

Box 2. Guide to assessment of suicide risk¹

1. Key clinical questions:

- Have you got or had suicidal thoughts?
If 'yes':
 - Have you ever made or got close to making a suicide attempt?
 - Have you made detailed plans?
 - Do you feel you can keep in control of your suicidal thoughts?

2. Clinical assessment might also include the following questions:

- Do you think things will ever get better?
- Are you feeling hopeless?
- Do you have feelings of sadness, numbness or emptiness?
- Does anything give you any pleasure?
- Do you feel like you are a burden on people?
- Have you recently settled your financial affairs or changed your will?

3. Previous suicide attempt(s)

4. High-risk groups:

- Men

5. High-risk diagnoses:

- major depression
- bipolar disorder
- schizophrenia
- schizoaffective disorder
- alcohol or drug abuse or dependence
- personality disorder
- current psychosis

6. Other risk factors:

- ready access to means of suicide (e.g. tablets, firearms)
- social isolation
- chronic medical illness

Non-pharmacological strategies

(Q6) What non-pharmacological strategies have been implemented?

Non-pharmacological strategies that might be applied in general practice include⁶:

- support, understanding, encouragement and explanation
- meeting with other members of the family or friends
- advising environmental change
- recommending self-help groups
- contacting governmental and other agencies (e.g. housing departments) on behalf of the patient
- helping the patient with problem-solving skills
- discussing chronic social difficulties with the patient.

More formal psychotherapies such as cognitive behavioural therapy (CBT) are often useful.¹ Referral to a suitably trained psychologist or psychiatrist will usually be necessary.¹

Review of CURRENT antidepressant therapy

**Use Tables 1 and 2
in the separate piece
following this guide.**

(Q7) Specify the CURRENT drug, dose and frequency.

Record the dose and frequency for the patient's current antidepressant therapy.

All antidepressants are approximately equal in efficacy, although individual patient response may vary markedly.⁷ The choice of medication is determined on the basis of¹:

- adverse effect profile of the antidepressant (See Table 1)
- prior response to medication
- risks of drug interaction (See Table 2)
- safety in overdose
- simplicity of administration.

Combinations of antidepressants have not been shown to be more effective than monotherapy and there is a very significant risk of serious adverse effects. In addition, the risk of dying in the event of overdose is increased.¹

(Q8) Is the dose within the recommended usual TOTAL daily dose range?

Table 1 shows the usual total daily dose ranges.

Note: This question refers to TOTAL daily dose (e.g. venlafaxine 37.5 mg twice daily equates to a total daily dose of 75 mg).

(Q9) Is the patient using any medications or complementary medicines that may interact with current antidepressant therapy?

Refer to Table 2 for list of selected drug interactions.

(Q10) How long has the patient been using the current antidepressant?

A delay in onset of antidepressant response of at least 1–2 weeks occurs with all antidepressants, and the full benefit may not occur for up to 6–8 weeks.⁷

(Q11) What response has there been to date for the current antidepressant?

Where a **good clinical response** occurs continue antidepressant for at least 6 months, and preferably up to 12 months, after a single episode of major depression.¹

If the patient experiences **partial or no response, or relapse**, check the adequacy of treatment:

- duration
- dosage and compliance.

Review the diagnosis including the possibility of additional organic causes or psychiatric conditions.⁴

If failure to respond despite an adequate dose and duration of treatment, switch to another antidepressant class.⁴

Psychological treatment or a psychiatric referral should be considered if the person fails to respond to a second antidepressant.⁴

(Q12) Has the patient experienced an adverse effect(s) with the current antidepressant?

Table 1 outlines common adverse effects of antidepressants at usual therapeutic doses.

Many adverse effects of antidepressants (e.g. nausea with selective serotonin reuptake inhibitors [SSRIs] or sedation with tricyclic antidepressants [TCAs]) settle within the first one or two weeks of treatment.⁶

If adverse effects are severe or persistent, it is best to switch classes of antidepressants, since classes such as SSRIs share adverse effect profiles.⁶

Patient education and compliance

Patient education may help improve compliance.

Doctor/patient discussion points for depression may include the following.⁴

- **Depression is common.** Most people recover but treatment speeds recovery.
- **Talking things through** with family, friends or a counsellor is often helpful.
- **Antidepressants** are usually effective. They take 6–8 weeks to work fully. A course for at least 6 months after symptoms improve is usual.
- **The choice of antidepressant** may depend on your age, previous use of antidepressants, possible adverse effects, other medications that you take, other medical conditions that you have, and personal preference. If one antidepressant does not suit at first, a change to a different one is an option.
- **Adverse effects** are often minor or improve in time. The **Consumer Medicine Information** leaflet lists possible adverse effects. (These are available at www.nps.org.au)
- **Talking treatments**, such as cognitive therapy, psychotherapy or counselling for specific problems such as relationship difficulties, may be options in some cases.
- See a doctor if you get worse, feel suicidal, or develop persistent troublesome adverse effects.

Previous antidepressant therapy

(Q16) Was the patient prescribed a different antidepressant(s) previously during THIS episode of depression?

When stopping antidepressants, gradual tapering of the dose should be considered to reduce the risk of withdrawal symptoms (see Table 1).¹

When changing antidepressants, an appropriate interval ('washout period') should be observed between medications to avoid interactions (See Antidepressant Changeover Category in Table 1).¹

References

1. Writing Group for Therapeutic Guidelines: Psychotropic. Therapeutic Guidelines: Psychotropic, Version 5, 2003. Melbourne:Therapeutic Guidelines Limited, 2003.
2. Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for Depression. Australian and New Zealand clinical practice guidelines for the treatment of depression. *Aust N Z J Psychiatry* 2004;38:389–407.
3. Ellis PM, Smith DAR. Treating depression: the beyondblue guidelines for treating depression in primary care. *Med J Aust* 2002;176:S77–83.
4. Anonymous. PRODIGY Guidance — Depression. Vol. 2004: www.prodigy.nhs.uk/guidance.asp?gt=depression, 2003 (accessed July 2004).
5. American Psychiatric Association Practice Guidelines. Practice guideline for the treatment of patients with major depressive disorder (revision). *Am J Psychiatry* 2000;157:S1–45.
6. Mitchell PB. Managing depression in a community setting. *Med J Aust* 1997;167:383–8.
7. Australian Medicines Handbook. 2004.

5. Completing the clinical audit cycle

Review questions which allow you to reflect on your prescribing practice will be sent to you along with:

- your original clinical audit forms
- feedback on your individual results
- the aggregate results of all participants' management practices
- commentary on the aggregate results.

Review questions must be completed and returned to NPS for the clinical audit to qualify for the Quality

Prescribing Initiative (QPI) of the Practice Incentives Program (PIP). You will then be sent a certificate of completion for step 4 of the audit cycle.

Step 5

Details of step 5 of the clinical audit will be provided with the review questions.

Step 5 requires further review of patient management to determine whether any changes made have resulted in improved patient management.

Confidentiality

Patient information must only be collected and recorded by the participating doctor. Individual results of your clinical audit and responses to review questions are kept confidential by NPS.

What will happen to

Your patient data:

- Your de-identified patient data forms are returned to you.
- Your individual results are provided to you only.
- Your data are aggregated with that of other participants and the de-identified aggregate results:
 - are provided to all participants
 - may be used in NPS evaluation and reports
 - are provided to the RACGP and ACRRM.

The RACGP has advised that program information may be shared with researchers and interested general practitioners for the purpose of continuing education coordination at the discretion of the QA&CPD Program.

Your personal details:

- are provided to the RACGP QA&CPD Program and/or ACRRM Professional Development Program for point allocation (if applicable)
- are recorded for the purpose of PIP and NPS evaluation.

Individual clinical audit results will not be available after potentially identifying data are removed from NPS records at the close of the clinical audit cycle, i.e. completion by participants in step 5.

Please note: You are responsible for advising NPS of any changes of address during the audit cycle. You can obtain a record of your personal details from NPS by request in writing.

Important: please sign the confidentiality agreement on the enclosed *Registration/summary form*.

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the individual clinical circumstances of each patient.



National Prescribing Service Limited

National Prescribing Service Limited ACN 082 034 393
An independent, Australian organisation for Quality Use of Medicines

Level 7 / 418A Elizabeth Street Surry Hills NSW 2010
Phone: 02 8217 8700 | Fax: 02 9211 7578 | email: info@nps.org.au | web: www.nps.org.au



National Prescribing Service Limited

Tables 1 and 2

- 1. Antidepressant therapy: doses, adverse and withdrawal effects, monitoring and changeover categories**
- 2. Selected antidepressant drug interactions**

Please use these tables to complete the clinical audit form.
Keep for future reference.

National Prescribing Service Limited ACN 082 034 393
An independent, Australian organisation for Quality Use of Medicines
Level 7 / 418A Elizabeth Street Surry Hills NSW 2010
Phone: 02 8217 8700 | Fax: 02 9211 7578 | email: info@nps.org.au | web: www.nps.org.au

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence.
Any treatment decisions based on this information should be made in the context of the individual clinical circumstances of each patient.

08/04

Table 1: Antidepressant therapy: doses, adverse and withdrawal effects, monitoring and changeover categories^{1,2}

Drug	Usual total daily dose range	Common adverse effects	Monitoring, withdrawal effects and antidepressant changeover category
Monoamine oxidase inhibitors (MAOIs)			
phenelzine <i>Nardil</i>	45–60 mg	orthostatic hypotension, sleep disturbances, headache, drowsiness, fatigue, weakness, agitation, tremors, twitching, myoclonus, hyperreflexia, constipation, dry mouth, weight gain, impotence, loss of libido, ↑ serum transaminases	Antidepressant changeover category: Category A
tranylcypromine <i>Parnate</i>	30–40 mg		
Reversible inhibitors of monoamine oxidase A			
moclobemide <i>Arima, Aurorix, Clobemix, Maosig, Mohexal</i>	300–600 mg*	nausea, dry mouth, constipation, diarrhoea, anxiety, restlessness, insomnia, dizziness, headache	Antidepressant changeover category: Category C
Selective serotonin reuptake inhibitors (SSRIs)			
citalopram <i>Celapram, Cipramil, Talam, Talohexal</i>	20–40 mg*	nausea, agitation, insomnia, drowsiness, tremor, dry mouth, diarrhoea, dizziness, headache, sweating, asthenia, anxiety, weight gain or loss, sexual dysfunction, rhinitis, myalgia, rash	Withdrawal effects: dizziness, nausea, paraesthesia, anxiety, agitation, tremor, sweating, confusion, electric shock-like sensations. More common with paroxetine and least likely with fluoxetine. Antidepressant changeover category: Category B – EXCEPT fluoxetine which is Category A
escitalopram <i>Lexapro</i>	10–20 mg*		
fluoxetine <i>Auscap, Fluohexal, Lovan, Prozac, Zactin</i>	20–40 mg*		
fluvoxamine <i>Faverin, Luvox, Movox</i>	100–200 mg*		
paroxetine <i>Aropax, Oxetine, Paxtine</i>	20–40 mg*		
sertraline <i>Zoloft</i>	50–100 mg*		
Tricyclic antidepressants (TCAs)			
amitriptyline <i>Endep, Tryptanol</i>	75–150 mg	sedation, dry mouth, blurred vision, constipation, weight gain, orthostatic hypotension, urinary hesitancy or retention, reduced GI motility, anticholinergic delirium, impotence, loss of libido, other sexual adverse effects, tremor, dizziness, sweating, agitation, insomnia	Monitoring: Blood pressure: before and after starting treatment and after each dose change. ECG to detect heart block or pre-existing prolonged QT interval in adults < 60 years for TCA doses > 200 mg daily, and in older patients at doses > 100 mg daily. Withdrawal effects: cholinergic rebound: hypersalivation, runny nose, abdominal cramping, diarrhoea, sleep disturbance. More common with amitriptyline, doxepin, trimipramine. Antidepressant changeover category: Category B
clomipramine <i>Anafranil, Placil</i>	75–150 mg		
dothiepin <i>Dothep, Prothiaden</i>	75–150 mg		
doxepin <i>Deptran, Sinequan</i>	75–150 mg		
imipramine <i>Melipramine, Tofranil</i>	75–150 mg		
nortriptyline <i>Allegron</i>	75–150 mg		
trimipramine <i>Surmontil</i>	75–150 mg		
Other antidepressants			
mianserin <i>Lumin, Tolvon</i>	60–90 mg*	sedation, dry mouth, dizziness, vertigo	Monitoring: Full blood examination at baseline, then every 4 weeks during the first 3 months. Stop if signs of agranulocytosis. Hepatic function tests at baseline; test periodically if known liver disease; stop if jaundice occurs. Antidepressant changeover category: Category B
mirtazapine <i>Avanza, Axit 30, Mirtazon, Remeron</i>	30–45 mg*	increased appetite, weight gain, sedation, asthenia, peripheral oedema	Antidepressant changeover category: Category B Whenever practical withdraw over at least 1–2 weeks to minimise risk of withdrawal symptoms.
reboxetine <i>Edronax</i>	8–10 mg*	urinary retention, dry mouth, sweating, paraesthesia, constipation, ↑ in diastolic blood pressure, ↑ in heart rate, impotence, insomnia, headache	Monitoring: Blood pressure and heart rate at baseline, then each week until stable, then as clinically indicated. Antidepressant changeover category: Category C
venlafaxine <i>Efexor, Efexor-XR</i>	75–150 mg*	nausea, vomiting, anorexia, headache, sweating, rash, anxiety, dizziness, fatigue, syncope, hypertension (dose-related), orthostatic hypotension, tremor	Monitoring: Blood pressure: more frequently when starting, then periodically, especially with doses > 200 mg daily. Withdrawal effects: May cause a syndrome similar to that seen with SSRIs. Antidepressant changeover category: Category C

Antidepressant changeover category

Note: Consider hospitalisation during washout/changeover if severely depressed.

Drug	Recommendation	
	Withdrawal period when switching	Drug-free interval
Category A changeover (longest washout period)		
fluoxetine, phenelzine, tranylcypromine	<i>fluoxetine</i> —gradual withdrawal generally unnecessary; withdrawal symptoms very unlikely. <i>phenelzine</i> and <i>tranylcypromine</i> —withdraw gradually to minimise withdrawal effects. Maintain drug and diet restrictions for 2–3 weeks after stopping.	Wait for at least 2 weeks after stopping before starting next antidepressant. Wait 5 weeks after stopping fluoxetine before starting MAOI.
Category B changeover (intermediate washout period)		
TCAs, SSRIs (except fluoxetine), mianserin, mirtazapine	Withdraw gradually to prevent withdrawal symptoms (particularly if higher dose or long term use). Of the SSRIs, withdrawal symptoms most likely with paroxetine. Usually reduce dose by 25% per day (when switching).	Wait for 2–4 days after stopping before starting next antidepressant.
Category C changeover (shortest washout period)		
moclobemide, reboxetine, venlafaxine	<i>venlafaxine</i> —withdraw gradually to prevent withdrawal symptoms. <i>moclobemide</i> —withdrawal symptoms not reported.	Wait for 1–2 days after stopping before starting next antidepressant.

* Lower doses are usually sufficient to treat depression in most people.

1. Australian Medicines Handbook 2004

2. Therapeutic Guidelines: Psychotropic, Version 5, 2003. North Melbourne:Therapeutic Guidelines Ltd;2003.

Table 2: Selected antidepressant drug interactions¹

Note: Table is not an exhaustive list. Interactions selected are generally only those known to occur in humans and are likely to be of clinical importance.

Drug	Drug interactions	Potential clinical effect		
Monoamine oxidase inhibitors (MAOIs)				
phenelzine tranylcypromine	Amphetamines, cocaine, methylphenidate, dopamine, adrenaline, noradrenaline, pseudoephedrine, ephedrine, phenylpropanolamine, methyl dopa, levodopa, phenylephrine, diethylpropion, phentermine, sibutramine	Increased risk of severe hypertension		
	Sumatriptan, zolmitriptan, naratriptan	Increased risk of cardiac toxicity		
	Antidiabetic drugs	Enhanced response to insulin and oral hypoglycaemic agents		
	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
Reversible inhibitors of monoamine oxidase A				
moclobemide	Cimetidine	Increased blood concentrations of moclobemide		
	Antihypertensives	Possible additive hypotensive effects		
	Sympathomimetics (including pseudoephedrine)	Possible risk of hypertension		
	Pethidine	Cumulative effects of amines (e.g. serotonin) may produce restlessness and agitation		
	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
	Drugs involved in cytochrome P450 enzyme inhibition interactions [†]			
Selective serotonin reuptake inhibitors (SSRIs)				
citalopram escitalopram fluoxetine fluvoxamine paroxetine sertraline	Bupropion	Increased risk of seizures		
	Pimozide	Increased risk of prolonged QT interval		
	TCAs	Increased risk of toxicity or serotonin syndrome		
	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
	Drugs involved in cytochrome P450 enzyme inhibition interactions [†]			
Tricyclic antidepressants (TCAs)				
amitriptyline clomipramine dothiepin doxepin imipramine nortriptyline trimipramine	Clonidine, methyl dopa	TCAs reduce their antihypertensive effects		
	Cimetidine, fluoxetine, fluvoxamine, sertraline	Increased risk of TCA adverse effects		
	Rifampicin, rifabutin, phenytoin, carbamazepine, phenobarbitone, primidone	Increased metabolism of TCAs resulting in reduced efficacy		
	Bupropion	Increased risk of seizures		
	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
Other antidepressants				
mirtazapine	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
reboxetine	Inhibitors of CYP3A4 (e.g. ketoconazole)	Increased risk of reboxetine toxicity		
	Inducers of CYP3A4 (e.g. carbamazepine)	May increase reboxetine clearance resulting in loss of efficacy		
	Sibutramine, MAOIs	Increased risk of adverse effects		
venlafaxine	Lithium	Increased risk of neurotoxicity or serotonin syndrome		
	Drugs that contribute to serotonin syndrome*	Increased risk of serotonin syndrome		
	Drugs involved in cytochrome P450 enzyme inhibition interactions [†]			
*Drugs that contribute to serotonin syndrome				
Antidepressants TCAs, MAOIs, SSRIs, mianserin, mirtazapine, moclobemide, reboxetine, venlafaxine, St John's Wort	Opioids Tramadol, pethidine, pentazocine, dextromethorphan	Stimulants Phentermine, diethylpropion, amphetamines	5HT₁ agonists Sumatriptan, naratriptan, zolmitriptan	Others Illicit drugs (e.g. 'ecstasy', LSD), selegiline, tryptophan, buspirone, lithium, carbamazepine
Serotonin syndrome can occur with: high doses of a single serotonergic agent; after adding a second serotonergic drug; or when drugs with different mechanisms of increasing serotonin are used together. Symptoms include: mental changes (confusion, agitation); hyperreflexia and clonus; flushing, shivering, sweating, hyperthermia.				
†Cytochrome P450 enzyme inhibition interactions				
CYP 450 isoform	Antidepressant	Some affected drugs		
CYP1A2	Fluvoxamine**	Theophylline, caffeine, methadone, clozapine, olanzapine, some TCAs, warfarin		
CYP2D6	Paroxetine**, fluoxetine**, other SSRIs***, venlafaxine***, moclobemide***	Flecainide, haloperidol, some TCAs, metoprolol, propranolol, perhexiline, thioridazine		
CYP3A4	Fluvoxamine**, norfluoxetine (metabolite of fluoxetine)** , other SSRIs***	Alprazolam, midazolam, triazolam, amiodarone, buspirone, carbamazepine, cisapride, cyclosporin, methadone, mycophenolate, tacrolimus, statins, zopiclone, quetiapine, zolpidem, warfarin		

Inhibition of other enzymes by antidepressants may enhance the effects of phenytoin or warfarin.

** = High risk, *** = Lower risk but interaction may still occur.