



National Prescribing Service Limited



9 September 2004

000001

Dr Sam Sample
99 Sample Street
SAMPLETOWN NSW 0000

Prescribing
Practice Review

Dear Dr Sample,

Depression is the fourth most frequently managed problem in Australian general practice. Antidepressant drugs are an appropriate treatment for many patients with major depression. This *Prescribing Practice Review* provides some **key messages** for optimising use of antidepressants.

Use an effective drug treatment for at least 6 months in major depression

A recent Australian study found that many patients who start antidepressants do not take them for long enough. Ensure an adequate treatment to reduce the risk of relapse and recurrence. For first episodes of major depression, 6–12 months treatment is recommended, with longer durations for people with a more enduring history of depression.

Remember that the efficacy of drug treatment is not established for milder depressive episodes.

4–6 weeks of drug treatment may be needed before an effect is seen

During the first 4–6 weeks of antidepressant drug treatment, monitor adverse effects and support treatment adherence. After 4–6 weeks of drug treatment, assess whether the patient is responding to treatment. Patients who do not respond to adequate doses at this stage are unlikely to respond to this drug.

Depression-specific psychological therapies are first-line in mild depression and effective adjuncts in more severe depression

The effectiveness of depression-specific psychological therapies is increasingly supported by evidence. Consider psychological therapy as initial treatment in mild depression or as an adjunct to drug treatment in more severe depression.

Ask about suicidal thoughts and assess risk, especially during initial treatment

Depression is often associated with suicidal ideation, and major depression is a risk factor for suicide. Ask patients with depression about suicidal thoughts and be aware of the risk factors.

Advise patients what to expect from drug therapy: likely adverse effects, time to effect and the expected course of treatment

Patients may stop taking antidepressants because of adverse effects, a perceived or genuine lack of effect, misconceptions about antidepressant drugs, stigma associated with the diagnosis—or because they feel better. Advising patients about what to expect from treatment may aid adherence.

**No. 27
Managing
depression**

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An independent, Australian organisation for Quality Use of Medicines

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A guide to adverse effects, interactions and changeover periods for antidepressant drugs can be found at www.nps.org.au/healthpro > Topics and Resources > Topics > Depression.

An NPS clinical audit on management of depression is also available to help you review your own approach to antidepressant drug prescribing—an enrolment form is enclosed.

Yours sincerely,



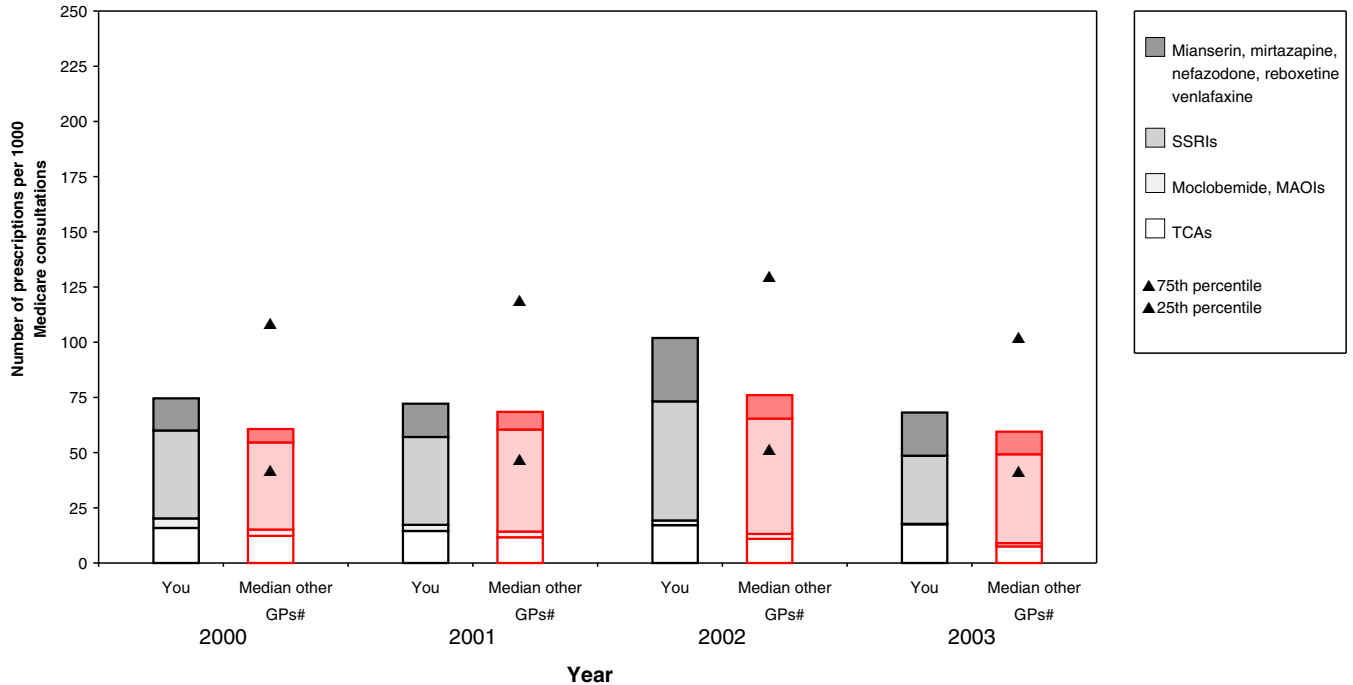
Dr Stephen Phillips
Chair, National Prescribing Service



Your confidential prescribing data

The data includes all prescriptions dispensed for your patients if the drug is above the patient co-payment or, if the drug is below the patient co-payment, it includes only those prescriptions dispensed for concession cardholders.**

Antidepressant[^] use 2000 - 2003



Practice Points

- Increased use of antidepressants probably reflects increased recognition and treatment of depression.
- Although no drug or class has greater efficacy than any other, it is estimated that only 50% of patients respond to initial drug treatment.¹

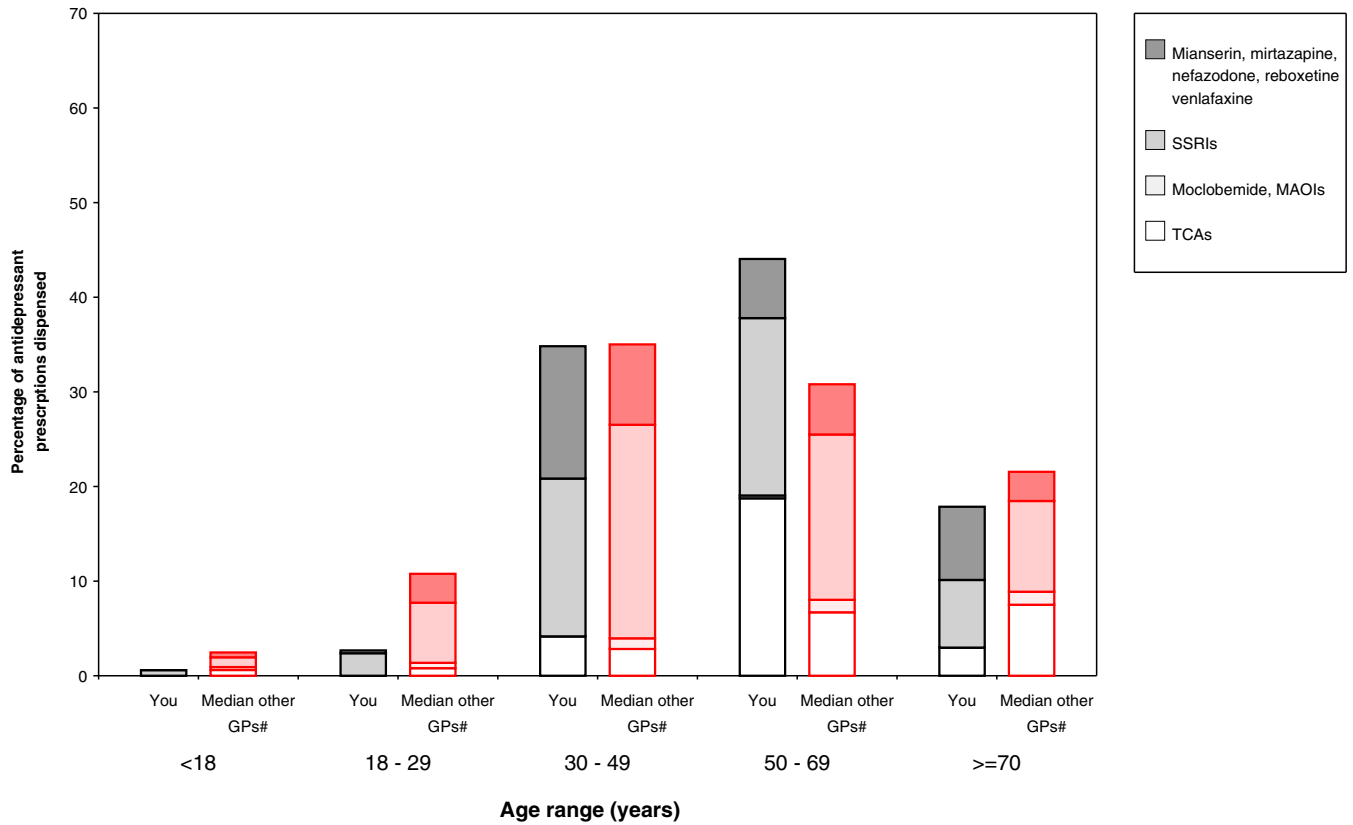
[^]All antidepressants

Tricyclic antidepressants** (TCAs):	Selective serotonin reuptake inhibitors (SSRIs):	Other antidepressants:	Monoamine oxidase inhibitors (MAOIs):
Amitriptyline**	Citalopram	Mirtazapine	Reversible Moclobemide
Clomipramine**	Escitalopram	Nefazodone**	Irreversible** Phenzelzine Tranlycypromine
Desipramine ⁺ **	Fluoxetine	Reboxetine	
Dothiepin**	Fluvoxamine	Venlafaxine	
Doxepin**	Paroxetine	Tetracyclic Mianserin**	
Imipramine**	Sertraline		
Nortriptyline**			
Trimipramine**			

⁺ Deleted from PBS November 2000.

** Below the patient co-payment in 2003: all TCAs, irreversible MAOIs, mianserin 10mg, nefazodone 100mg.

Your antidepressant prescribing by patient age 2003



Practice Points

- Not all antidepressant use will be for treatment of depression. TCAs may be used for enuresis in children or for pain management. Sedative TCAs are sometimes used as hypnotics, but should generally be avoided in the absence of a depressive disorder.¹
- TCAs are no better than placebo for childhood depression.²
The benefit-harm ratio for SSRIs in children and adolescents is uncertain - there is little evidence of benefit and a possible harm through increased suicidal ideation.³
- Older people may respond more slowly to antidepressants. Consider a lower starting dose with more gradual increases.

Duration of antidepressant therapy

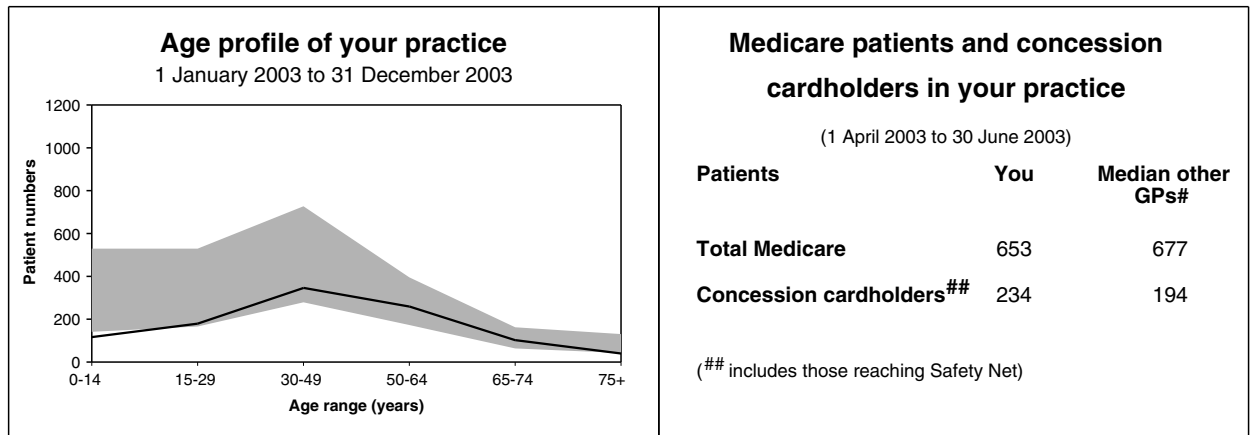
	You	Median other GPs#
Number and percentage of patients using any antidepressant who had less than 6 prescriptions for antidepressants dispensed in 2003	51 (68%)	51 (70%)
Total number of patients dispensed any antidepressant in 2003	75	73
Total number of antidepressant prescriptions dispensed from your prescriptions in 2003	338	295

Practice Points

- Many patients discontinue treatment early. Review patients to ensure an adequate duration of therapy i.e. 6-12 months in first episodes of major depression.
- Note that patients dispensed less than 6 prescriptions in 2003 may have commenced prior to 2003 or continued into 2004.

Practice profile

The data below, based on Medicare claims, are provided to help you review your prescribing data within the profile of your practice.



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs# fall within the shaded area.

Concession card holders include patients who have reached the Safety Net. Data from a three month period (1 Apr - 30 Jun 2003) that best represents your patient mix have been provided.

Notes:

This data is provided confidentially for your own personal review. All data has been extracted from the HIC PBS claims database.

@ Data shown are an aggregate for all your provider locations.

The comparator group "other GPs#" includes all prescribers who are currently located in a similar geographical region i.e capital city, other metropolitan area, small rural centre, large rural centre, other rural area, remote centre and other remote area.

▲ 25% to 75% of all doctors in the comparator group fall in the range shown by the triangular symbols.

References

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2. Hazell P, O'Connell D, Heathcote D, et al. BMJ 1995;310:897-901.
3. Adverse Drug Reactions Advisory Committee: Use of SSRI antidepressants in children and adolescents - updated 17 June 2004. www.tga.gov.au/adr/adrac_ssri.htm. Accessed July 2004.

Managing depression

Key messages

- Use an effective drug treatment for at least 6 months in major depression.
- 4–6 weeks of drug treatment may be needed before an effect is seen.
- Depression-specific psychological therapies are first-line in mild depression and effective adjuncts in more severe depression.
- Ask about suicidal thoughts and assess risk, especially during initial treatment.
- Advise patients what to expect from drug therapy: likely adverse effects; time to effect; and the expected course of treatment.

Assess the severity of depression to determine whether drug treatment is required

Drug treatment guidelines are based on evidence in people with major depression

Severity of major depression depends on the

- number of depressive symptoms
- degree of impaired functioning
- history of depression
- risk of suicide^{1–3}

Table 1: Severity of depression and treatment recommendations^{1–3}

Type of depression and severity	Diagnosis*	Treatment recommendations
Milder depression or adjustment disorder [†]	Do not meet criteria for major depression	Little evidence to guide treatment choices May resolve spontaneously or with supportive psychotherapy, counselling, or problem-solving
Chronic milder depression (dysthymia)	Repeated episodes of milder depression that do not meet criteria for major depression	Antidepressants can be effective but response is unpredictable
Major depression— <i>mild</i>	Meet minimum criteria for major depression	Initial drug therapy not well supported by evidence Consider supportive therapy or problem-solving techniques, or CBT If symptoms persist beyond 8 weeks, consider drug treatment
Major depression— <i>moderate</i>	More than minimum criteria met, greater degree of impairment to functioning	Drug treatment and depression specific psychological therapy have equal efficacy
Major depression— <i>severe or with high suicide risk</i>	Most diagnostic criteria met Marked impairment in ability to function	Consult with or refer to specialised mental health services/psychiatrist

*Major depression diagnosed according to DSM-IV – see *Therapeutic Guidelines Psychotropic* 2003¹

[†]Adjustment disorder refers to depressed mood in response to a stressful life event (e.g. bereavement)

4–6 weeks of drug treatment may be needed before an effect is seen

Use response after 4–6 weeks to guide ongoing management

During initial treatment, follow up to encourage medication use and adjust treatment as necessary

Although no drug or class is more efficacious than any other, it is estimated that only 50% of patients respond to initial drug treatment.¹

If there is no response after 4–6 weeks, response is unlikely.^{1,4,5} (Note that older people should be started at a lower dose and may take longer to respond).

If there is a partial response after 4–6 weeks, then a longer trial or increased dose of the same drug is reasonable. However note the following.

- In antidepressant trials, around 50% of patients respond to active treatments in the first 4–6 weeks of treatment. However 30% of patients on placebo respond to a similar degree.⁶ Such effects may account for early but unsustainable improvement.
- Higher doses of selective serotonin reuptake inhibitors (SSRIs) increase adverse effects with uncertain benefit.⁷ It is prudent to remain within doses recommended in the drug's product information.

If response to an adequate trial of the initial medication is poor, switching to a different drug class is recommended after checking compliance.¹ If depression persists after 3 months of therapy, consider referral or consultation with a specialist colleague.² Consider adjunctive psychological therapy. (See page 3.)

Use antidepressants for at least six months in major depression to prevent relapse or recurrence

Continued drug therapy for 6–12 months is recommended for all episodes of major depression^{1,2,5}

Only 40% of patients in Australia who start on an antidepressant* are still using antidepressants 6–8 months later.⁸

Aim to achieve a stable symptom-free period of 4–6 months before the depression is considered to be in remission. Suboptimal treatment durations increase the likelihood of relapse or recurrence.^{1,2,5}

Maintenance doses should be the same as doses used to achieve initial control.^{1,2,5}

A history of depression increases the likelihood of relapse and recurrence

For first episodes of major depression, continue antidepressant treatment for 6–12 months.^{1,2,5}

As depression is a relapsing condition, ask about previous episodes in any patient presenting with a new episode.² Patients with a history of major depression and/or chronic milder depression (dysthymia) have a higher risk of relapse or recurrence than those with a single episode of major depression.

Guidelines suggest that 2 episodes of major depression within 5 years or 3 prior episodes may indicate a need for maintenance treatment of 3–5 years.¹

* Note: This includes antidepressants prescribed for other problems, including milder depressive illness.⁸ Recommended treatment durations are based on evidence for major depression.

Medication advice can improve compliance and outcome

Be aware of possible reasons that patients stop treatment early

Address potential concerns about adverse effects, lack of effect, perceived stigma of antidepressant drug use, and educate patients about duration of treatment.^{9,10} Advise patients that

- adverse effects may occur—what these are and their expected duration
- mood may not improve immediately
- not all people respond to the first drug chosen, and there are other treatment options
- missing doses may reduce effectiveness
- even when they feel better, they should continue drug treatment for at least 6 months
- drugs should not be ceased abruptly, but tapered gradually because of possible 'rebound' symptoms.

Provide advice about what to expect from medications, address concerns and follow up to improve compliance

Follow-up patients to monitor for adverse effects and to support compliance—this may improve treatment adherence.²

Psychological treatments are effective for many patients with depression

Consider psychological therapy as initial treatment in mild depression or as an adjunct to drug therapy in more severe depression

Non-drug interventions in depression range from supportive counselling, education and information, through to more structured depression-specific psychological therapies.

Non-directive counselling may reduce symptoms in the short-term and is associated with patient satisfaction.^{11,12}

Specific psychological therapies such as cognitive behavioural therapy (CBT) and interpersonal therapy (IPT) are recommended as:²

- first-line treatment for mild or moderate depression
- adjunctive therapy if response is not achieved with a drug alone (in moderate to severe major depression)
- preventive therapy to prevent recurrence when a patient is in remission.

Psychological therapy may prevent relapse

Specific cognitive therapies have been shown to prevent relapse

- after successful acute treatment with cognitive therapy¹³
- in those with residual symptoms after a period of optimum drug treatment¹⁴
- and in patients with a high risk of recurrence.¹⁵

There is limited evidence comparing combined treatment (antidepressants plus psychological therapy) with antidepressant drugs and usual care. However a recent review found that drugs-plus-psychotherapy was associated with an increased likelihood of response and a decreased likelihood of long-term dropout than drugs alone.¹⁶

If access to psychological services is problematic, look into low-cost programs or other delivery options

Cost, availability and patient preference may limit the use of psychological therapies. Consider:

- the range of options available through the Commonwealth-funded *Better Outcomes in Mental Health Care Initiative* including: low-cost or free access to approved psychological services, upskilling of GPs, new Medicare item numbers for trained GPs and service incentive payments. Contact your local division of general practice or see the Australian Divisions of General Practice (ADGP) website (www.adgp.com.au/site/index.cfm?display=2550).
- computer based interactive CBT programs^{17,18} that are being evaluated—for example MoodGYM, a free web-based intervention initially designed for young people¹⁸ (www.moodgym.anu.edu.au).

Consider adverse effects and interactions when prescribing antidepressants to older people

Start at a lower dose and increase slowly

Both SSRIs and tricyclic antidepressants (TCAs) are effective treatments in late-life depression,¹⁹ but SSRIs are generally first-line because they are better tolerated.

Selective serotonin reuptake inhibitors (SSRIs)

Of the SSRIs, fluoxetine, fluvoxamine and paroxetine have more potential drug interactions than sertraline or citalopram.

Be aware of the possibility of serotonin syndrome which can occur when multiple drugs are used which affect serotonin, or with high doses of a serotonergic drug (e.g. most antidepressants, tramadol, pethidine, buspirone, amphetamines and anorectics).²⁰

Common adverse effects

Initial adverse effects include nausea, insomnia, drowsiness, dizziness and agitation. These usually resolve within a few weeks. Sexual dysfunction and weight gain may continue long-term and affect compliance.⁷

Less common adverse effects

The elderly are vulnerable to **hyponatraemia** related to SIADH (syndrome of inappropriate ADH secretion) with SSRIs or venlafaxine. Being female, having a lower BMI and a lower baseline sodium level appear to increase risk.^{21,22} Adverse event reports have often noted concurrent use of thiazide diuretics.²¹

Decreases in plasma sodium levels can be seen within 2 weeks of starting SSRIs.²² Symptoms include confusion, lethargy and dizziness. Consider monitoring sodium levels during initial treatment.

There appears to be a small increase in the absolute risk of **gastrointestinal bleeding** (about 3 extra cases per 1000 patient-years of treatment) with SSRIs in patients aged ≥ 80 years, with previous gastrointestinal bleeding, or concurrent use of aspirin or another NSAID.²³

Consider adverse effects and interactions when prescribing antidepressants to older people (cont'd)

Tricyclic antidepressants TCAs are not first preference in older people because of their adverse effects—sedation increases the risk of falls. They should not be used in patients with cardiac disease due to their anticholinergic and proarrhythmic effects.^{7,24} Of all the TCAs, nortriptyline is least likely to cause hypotension, sedation or anticholinergic effects.⁷

Assess suicide risk in patients with depression

Asking about suicidal thoughts does not cause suicidal behaviour²⁵ Assessing the extent of the plan is an important part of assessing risk. Patients may be relieved to have the opportunity to discuss the issue.²⁵

Key clinical questions¹

'Have you got or had suicidal thoughts?'

If yes:

'Have you ever made or got close to making a suicide attempt?'

'Have you ever made detailed plans?'

'Do you feel you can keep in control of your suicidal thoughts?'

Risk factors for suicide^{1,25,26}

<ul style="list-style-type: none">■ A previous suicide attempt or acts of self-harm■ Being male■ Access to means of suicide (tablets, firearms)■ Social isolation■ Chronic medical illness■ Young people and older people have higher rates of suicide	<ul style="list-style-type: none">■ Diagnosis of:<ul style="list-style-type: none">○ major depression○ bipolar disorder○ schizophrenia or schizoaffective disorder○ alcohol/drug abuse○ personality disorder○ current psychosis
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Assess suicidal intent, but be aware that suicide risk is difficult, and protocols have low predictive value^{1,25,27}

The risk of suicide increases when the suicide plan is detailed, the method is readily available and likely to be lethal, and the plan minimises the possibility of help from others. The presence of aggressiveness, violence, hopelessness, impulsiveness or agitation are thought to be correlated with an increased risk of suicidal behaviours.²⁵

Eliciting guarantees of safety or 'no self-harm' contracts are not recommended as sole management strategies.^{25,27} Episodes of suicide attempts and deliberate self-harm require comprehensive psychiatric assessment.²⁷

Prescribing issues

Initial period of antidepressant treatment is recognised as a risk period for suicide attempts

Patients may act upon suicidal impulses in the early stages of treatment as energy improves before mood.¹

Some findings suggest that SSRIs may aggravate suicidal ideation in children and adolescents. These require further investigation but the Therapeutic Goods Administration has alerted practitioners to the possibility.²⁸

Consider prescribing a drug that is less toxic in overdose and limit quantities dispensed

TCA and monoamine oxidase inhibitors (MAOIs) are considered the most toxic in overdose.⁷ SSRIs are least toxic but consider the combinations of medicines that may be available to the patient.

Reviewer:

Dr Bill Lyndon
Chairman of the RANZCP Committee on Psychotropic
Drugs and Other Physical Treatments

References:

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*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

Our goal To improve health outcomes for Australians through prescribing that is: ■ safe ■ effective ■ cost-effective
Our programs To enable prescribers to make the best prescribing decisions for their patients, the NPS provides ■ information ■ education ■ support ■ resources

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