

Providing best care for anxiety disorders in general practice

KEY MESSAGES

- Use key symptoms to differentiate between types of anxiety disorders and determine effective treatment
- Trial non-drug therapy including psychological therapy as first line
- Consider an antidepressant for those who do not respond adequately to psychological therapies, selecting on the basis of evidence of efficacy in the diagnosed anxiety disorder
- Reserve benzodiazepines for short-term use in selected circumstances

Use key symptoms to differentiate between types of anxiety disorders

Anxiety disorders are characterised by various combinations of key symptoms — excessive anxiety, fear, worry, avoidance, compulsive rituals — that are associated with impaired function or significant distress (see *NPS News 65* insert at www.nps.org.au/news_65).¹⁻³ The essential feature of generalised anxiety disorder (GAD) is excessive anxiety and worry about a number of events and activities.² Generalised social anxiety disorder* is characterised by a marked and persistent fear of social and performance situations.²

One type of anxiety disorder may co-exist with another or be present with other disorders (e.g. mood or substance use).¹ Anxiety disorders are usually chronic. Symptoms may be primary or secondary to other physical or psychiatric disorders.

Anxiety may be caused by a general medical condition

A variety of general medical conditions can cause clinically significant anxiety symptoms.² For example, people who have chronic obstructive pulmonary disease (COPD) often experience anxiety (and depression). Treat COPD symptoms as usual. Provide people with information about treatment for the anxiety disorder.^{4,5} Consider a multidisciplinary

care plan to document the various medical, paramedical and non-medical services required.[†]

Other general medical conditions that can cause anxiety include hypoglycaemia, hyper- or hypothyroidism, heart failure, arrhythmia and vitamin B₁₂ deficiency.²

Trial non-drug therapy including psychological therapy as first line

The benefits of psychological therapies (such as cognitive behavioural therapy [CBT]) for both GAD and generalised social anxiety disorder are maintained for ≥ 12 months after stopping treatment³, and could be expected to continue for as long as people apply the skills learned. Conversely, up to 40% of people relapse within 6–12 months after stopping drug therapy.³

Where possible, start with psychological therapies and non-drug strategies for GAD and generalised social anxiety disorder (see *NPS News 65* insert for more information).^{1,2,4} If choosing CBT, guidelines recommend starting with 8–20 hours.^{3,6} Choice of therapy may differ between anxiety disorders: people with generalised social anxiety disorder benefit from CBT, exposure-based interventions and social skills training.^{1,3}

* Sometimes called social phobia.

† See www.health.gov.au/epc for more information about the Enhanced Primary Care program which provides a framework for a multidisciplinary approach to health for people with chronic conditions and/or complex care needs, and older Australians.

Consider antidepressants if response to psychological therapies is inadequate

If psychological and other non-drug therapies are not sufficiently effective or are unsuitable, an antidepressant may be added (see Table 1). Assess efficacy of antidepressant therapy after at least 12 weeks (in contrast to 6–8 weeks for major depression).

Guidelines do not recommend starting with combined therapy (an antidepressant combined with psychological and other non-drug strategies) in adults because there is no evidence that combination therapies are more effective than either alone.^{3,6}

Which antidepressants have efficacy for what anxiety disorder?

Not all antidepressants have been assessed for efficacy in all anxiety disorders, nor can efficacy be generalised across an antidepressant class. Choose an antidepressant shown to have benefit for the anxiety disorder diagnosed (see Table 1). Consider the adverse effect profile and concomitant medicines before prescribing.

Antidepressants are more effective than benzodiazepines for treating the uncontrollable worry associated with GAD and they do not produce tolerance or dependence.^{1,3}

In short-term (12–24 weeks) trials in generalised social anxiety disorder, escitalopram, fluvoxamine, paroxetine, sertraline and venlafaxine appear to be similarly effective but differ in their adverse effects.⁷ Long-term therapy with escitalopram, paroxetine or sertraline has been shown to prevent relapse in generalised social anxiety disorder.⁶

Antidepressants have a limited role for children and adolescents with anxiety

Anxiety disorders are the most common mental disorder in children: CBT is first-line.^{1,2,6} Consider adding an SSRI when there is severe functional impairment (e.g. social, academic) that does not respond to psychological therapies.^{1,3,6,9}

A systematic review found that CBT was more effective than placebo for treating childhood anxiety disorders (pooled odds ratio 3.3; 95% confidence interval 1.9 to 5.6). However, children with co-morbidities (e.g. other anxiety disorders, depression) were excluded from most trials so it is possible that this estimate may not reflect the 'real life' effects of CBT.¹⁰

Evidence for antidepressants is mostly in children with obsessive–compulsive disorder for which fluoxetine, fluvoxamine, paroxetine and sertraline are subsidised on the PBS.^{1,11,12} Carefully monitor antidepressant therapy in children and consider a trial discontinuation within a year for those with markedly reduced symptoms.^{1,6}

There are few data on the relative or combined efficacy of psychological therapies and/or drug therapy for anxiety disorders in children and adolescents. However, a recent 12-week, small (n = 488) placebo-controlled trial found that CBT combined with sertraline in children (aged 7–17 years) with a diagnosis of generalised, social or separation anxiety disorder was significantly more effective than monotherapy with either CBT or sertraline (NNT* = 1.7). The trial also showed that monotherapy with either CBT or sertraline was significantly more effective than placebo (NNT = 2.8 and 3.2 respectively).¹³

Table 1: Guideline recommendations for drug therapy for GAD and generalised social anxiety disorder^{†1,3,6,8}

Anxiety disorder	If adding drug therapy, start with a 12 week trial of:	After 12 weeks of therapy	
GAD	<ul style="list-style-type: none"> an SSRI (escitalopram, paroxetine, sertraline) OR imipramine[†] OR venlafaxine 	If there is improvement, continue for at least 6 months, then slowly taper the dose and stop.	If there is no improvement or the first antidepressant is not suitable, switch to another antidepressant
Generalised social anxiety disorder	<ul style="list-style-type: none"> an SSRI (escitalopram, fluvoxamine, paroxetine, sertraline) OR venlafaxine 	If there is improvement, continue for at least 6 months (up to 12–24 months), then slowly taper the dose and stop.	

[†] In practice the use of imipramine for GAD is limited by its adverse effects and the risk of death in overdose.³

Concerns have been raised about the increased risk of suicidal ideation and behaviours in children and adolescents who take antidepressants. The Australian Adverse Drug Reactions Advisory Committee recommends case-by-case SSRI prescribing with careful monitoring.¹⁴ A British guideline suggests that children and adolescents

with anxiety disorders are at lower risk of self-harm and gain more therapeutic benefit with SSRI therapy compared with children with depression.⁶ The main indications for SSRIs in children and adolescents include obsessive-compulsive disorder, GAD and generalised social anxiety disorder.¹⁵

* NNT = the number of children who needed to be treated for 1 child to benefit (rated as 'very much' or 'much' improved on the Clinical Global Impressions – Improvement scale).

Reserve benzodiazepines for short-term use in selected circumstances

In general, **reserve benzodiazepine use to the short-term**³ for people who have not responded to at least 2 therapies (e.g. psychological therapy, antidepressant).⁶ Short-term therapy may be useful for an acute exacerbation of GAD refractory to non-drug strategies and psychological therapies. Gradually reduce the dose to zero within 6 weeks.¹ Short-term therapy may also be useful before the social event or performance for people with **non-generalised social anxiety disorder** who cannot use propranolol (e.g. those with asthma, severe peripheral vascular disease).¹ Use may be limited by adverse effects such as sedation, impaired coordination or disinhibition.¹

Limitations of long-term benzodiazepine use

Benzodiazepines may cause dependence — particularly in those with a history of dependence

on alcohol and/or other drugs — and a withdrawal syndrome. Up to a third of people taking a benzodiazepine long-term have difficulty withdrawing or stopping.^{1,3,6,16}

For GAD, limit long-term use for people for whom non-drug strategies, psychological therapies and alternative drug therapies (e.g. SSRI) have failed to provide significant improvement.¹ Try to wean every 6–12 months by gradually reducing the dose and increasing the focus on psychological therapy (to manage symptom exacerbation).¹

For generalised social anxiety disorder, limit long-term use to people who have unsuccessfully trialled at least 2 antidepressants, and only when there is no history of alcohol and/or other drug abuse or depression (common co-morbidities).^{1,3}

Diagnose premenstrual dysphoric disorder according to criteria

Figure 1: Research criteria for premenstrual dysphoric disorder (PMDD)²

<p>A Symptoms begin 1 week before menses and resolve in the first few days after menses (over most cycles in the past 12 months)</p> <p>B Five of the following symptoms, one of which must be a mood symptom</p> <p>Mood symptoms (at least 1 must be present)</p> <ul style="list-style-type: none"> – Depressed mood, feelings of hopelessness or self-deprecating thoughts – Anxiety/tension – Mood swings – Irritability/anger or increased interpersonal conflict <p>Other symptoms</p> <ul style="list-style-type: none"> – Decreased interest in usual activities – Difficulty concentrating – Fatigue or lack of energy 	<ul style="list-style-type: none"> – Appetite changes – Hypersomnia or insomnia – Feeling out of control or overwhelmed – Somatic symptoms (e.g. bloating, mastalgia, headache) <p>C Symptoms must be severe enough to interfere with work, school, usual activities or interpersonal relationships</p> <p>D Symptoms may be superimposed on an underlying psychiatric disorder, although they should not be an exacerbation of another condition</p> <p>E Criteria A, B, C, and D must be confirmed by prospective daily charting for ≥ 2 consecutive symptomatic menstrual cycles</p>
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Treating premenstrual dysphoric disorder

Start with non-drug strategies and lifestyle changes

PMDD is a chronic condition, with symptoms lasting possibly until menopause. Start with non-drug strategies (e.g. CBT, relaxation training) and lifestyle changes (e.g. exercise)¹⁷: see the *NPS RADAR* review for more information.¹⁸

Fluoxetine or sertraline may be beneficial for some women suffering from PMDD

Consider adding fluoxetine or sertraline for women who still have PMDD symptoms after 2–3 months of non-drug strategies and lifestyle changes.^{17,19}

Fluoxetine and sertraline are TGA-approved for PMDD as defined by DSM-IV research criteria (see Figure 1) but are not subsidised on the PBS for this indication.^{12,20,21} The efficacy of antidepressants for PMDD has not been directly compared with that of other drugs (e.g. oral contraceptives, gonadotrophin-releasing hormone agonists). Uncertainties remain about the efficacy, tolerability and safety of long-term SSRI therapy because of a lack of long-term trials.

Oral contraceptives may be an option for women who only have physical symptoms¹⁷ but trials have conflicting results.^{19,22}

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References

1. Therapeutic Guidelines: Psychotropic. Version 6 Updated March 2009 [eTG complete CD-ROM]. Melbourne: Therapeutic Guidelines Ltd, 2008.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders DSM-IV-TR. 4th (text revision) ed. Washington, DC: American Psychiatric Association, 2000.
3. Canadian Psychiatric Association. *Can J Psychiatry* 2006;51:1–92S.
4. Therapeutic Guidelines: Respiratory. Version 3 Updated March 2009 [eTG complete CD-ROM]. Melbourne: Therapeutic Guidelines Ltd, 2005.
5. McKenzie DK, et al. The COPD-X plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease. Lutwyche: The Australian Lung Foundation, 2009. <http://www.copdx.org.au/guidelines/index.asp> (accessed 22 July 2009).
6. Baldwin DS, et al. *J Psychopharmacol* 2005;19:567–96.
7. Hansen RA, et al. *Int Clin Psychopharmacol* 2008;23:170–9.
8. National Institute for Health and Clinical Excellence. Anxiety (amended): management of anxiety (panic disorder, with or without agoraphobia, and generalized anxiety disorder) in adults in primary, secondary or community care. NICE Clinical Guideline 22 (amended). London: National Institute for Health and Clinical Excellence, 2007. <http://www.nice.org.uk/nicemedia/pdf/CG022NICEguidelineamended.pdf> (accessed 7 April 2009).
9. Royal Australian College of General Practitioners. Clinical guidance on the use of antidepressant medications in children and adolescents. South Melbourne: Royal Australian College of General Practitioners, 2005. <http://www.racgp.org.au/guidelines/antidepressants> (accessed 6 April 2009).
10. Cartwright-Hatton S, et al. *Br J Clin Psychol* 2004;43:421–36.
11. Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd, 2009.
12. Department of Health and Ageing. PBS for Health Professionals. Canberra, 2009. www.pbs.gov.au (accessed 21 April 2009).
13. Walkup JT, et al. *N Engl J Med* 2008;359:2753–66.
14. Adverse Drug Reactions Advisory Committee. Use of SSRI antidepressants in children and adolescents. Canberra: Therapeutics Goods Administration, 2004. http://www.tga.gov.au/adr/adrac_ssri.htm (accessed 6 April 2009).
15. The Royal Australian and New Zealand College of Psychiatrists. Clinical guidance on the use of antidepressant medications in children and adolescents. Melbourne: The Royal Australian and New Zealand College of Psychiatrists, 2005. http://www.ranzcp.org/images/stories/ranzcp-attachments/Resources/College_Statements/Practice_Guidelines/Clinical_Guidance_on_the_use_of_Antidepressant_medications_in_Children_and_Adolescents.pdf (accessed 1 April 2009).
16. Anderson I. *Int J Psychiatry Clin Pract* 2006;10 (Suppl 3):10–7.
17. National Prescribing Centre. Tackling premenstrual syndrome. *MeReC Bulletin* 2003;13:9–12. http://www.npc.co.uk/ebt/merec/therap/other/resources/merec_bulletin_vol13_no3.pdf (accessed 30 March 2009).
18. National Prescribing Service. Sertraline (Zoloft), fluoxetine (Lovan, Prozac) for premenstrual dysphoric disorder (PMDD). *NPS RADAR*, December 2004. Sydney: National Prescribing Service, 2004. http://nps.org.au/health_professionals/publications/nps_radar/issues/archive/december_2004/sertraline (accessed 30 March 2009).
19. Kaur G, et al. *Cleve Clin J Med* 2004;71:303–22.
20. Eli Lilly Australia Pty Ltd. Prozac product information. 11 September 2006.
21. Pfizer Australia Pty Ltd. Zoloft product information. 15 August 2008.
22. Rapkin AJ, Winer SA. *Expert Opin Pharmacother* 2008;9:429–45.

Online citations available at:
www.nps.org.au/ppr_48

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 clinical circumstances of each patient.



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