Generalised anxiety disorder in adults

Anxiety disorders are the most prevalent mental health condition in the community. Generalised anxiety disorder (GAD) is a predominant form, and often co-occurs with depression and other anxiety disorders. Psychological, e.g. cognitive behavioural therapy (CBT), and pharmacological, e.g. selective serotonin reuptake inhibitors, treatments are equally effective in the management of GAD, but patients engaging with CBT may be less likely to relapse.

KEY PRACTICE POINTS:

- Generalised anxiety disorder (GAD) is characterised by persistent and uncontrollable worry present for at least six months that causes distress or impairment in important areas of functioning, e.g. social, occupational. Associated symptoms include muscle tension, restlessness, difficulty sleeping and concentrating, fatigue and irritability.
- GAD can usually be diagnosed clinically based on the presence of characteristic symptoms (as above). Perform a physical examination and request laboratory testing or other investigations as indicated to exclude alternative causes, e.g. hyperthyroidism.
  - A formal diagnosis can be made based on the criteria for GAD in the DSM-5-TR. Use the GAD-7 (or local grading tools) to assess the severity of the patient's symptoms, which can guide management decisions.
  - Consider discussion with, or referral to, a psychiatrist or other mental health specialist for patients where there is diagnostic uncertainty, safety concerns or significant co-morbidities, e.g. substance misuse, complex mental or physical health conditions
- Risk factors and associated conditions for GAD include co-morbid mental health conditions or a family history of mental health conditions, people who are neurodivergent with presentations such as ADHD and Autism spectrum disorder (ASD), substance use/recreational drug use, stressful life circumstances, e.g. illness, unemployment
- Psychological and pharmacological treatments are equally effective in the management of GAD but the relapse rate for psychological therapies may be lower
  - Cognitive behavioural therapy (in person or online) is first-line psychotherapy
  - Selective serotonin reuptake inhibitors and venlafaxine are first-line medicines, initiated at a low dose. Second- and third-line options include other antidepressants, buspirone, pregabalin and benzodiazepines (short-term use only).
- When deciding on psychological or pharmacological treatment, consider factors such as patient preference, co-morbidities, availability and cost, possible adverse effects and current or prior response to treatments
  - Recommend self-directed strategies alongside psychotherapy and pharmacotherapy, e.g. exercise, yoga, mindfulness, sleep hygiene techniques, journaling
- Follow up with the patient regularly, e.g. initially within two to four weeks, (either in person or via phone) and then with decreasing frequency as they stabilise; monitor adherence, symptoms/response and adverse effects, including self-harm/suicidal ideation
- Modify the patient's treatment regimen if there is inadequate response after an appropriate trial (at least four to six weeks) of psychological and/or pharmacological treatment. Discuss with or refer the patient to a psychiatrist (or other mental health specialist) if there is insufficient response after modifying treatment.
- Continue pharmacological treatment for 6 – 12 months after symptoms have resolved to reduce the risk of relapse

This is a revision of a previously published article.
What's new for this update:

- General article revision and update of evidence
- Section added on the management of GAD during pregnancy
- Section added on online cognitive behavioural therapy
- Section added on follow-up and ongoing monitoring

Generalised anxiety disorder (GAD) is one of the most common anxiety disorders

Anxiety is a normal human emotion that affects most people at some time.[1] It becomes a disorder when it is of greater intensity and duration than expected and if it leads to impairment/avoidance behaviours or disability.[1] Anxiety disorders are the most prevalent mental health condition in the community, yet many people do not seek treatment (see: "The prevalence of anxiety disorders in New Zealand").[1, 2] It is estimated that one in five patients in primary care meet diagnostic criteria for an anxiety disorder.[3]

There are a range of anxiety disorders, including generalised, social, panic, phobias, separation anxiety and selective mutism, and patient presentation varies.[1, 4] One of the predominant forms is generalised anxiety disorder (GAD), which is characterised by excessive and uncontrollable worry about multiple aspects of everyday life, e.g. employment, education, relationships.[1, 3, 5] It is common for people with GAD to have mixed anxiety and depression and other co-morbid anxiety disorders (see: "Associations between GAD, depression and suicide risk").[5] An anxiety disorder can be a long-term condition and symptoms will fluctuate in intensity over time; however, symptoms can be managed and complete recovery is possible for some people.[1, 6, 7]

Factors that can increase the risk of GAD

The median age of onset of GAD is 32 years.[1, 15] This is later than the onset of anxiety disorders in general, which typically begin early in life (median age 17 years) and prevalence tends to reduce with age.[6, 15]

GAD is more prevalent in females than males.[1] Demographic factors also influence the development of GAD, which is more common in people who are separated, divorced or widowed, who have a lower level of education and who are unemployed.[1]

Other potential predictors of GAD include:[5–7]

- Low socioeconomic status
- Certain co-morbidities, e.g. long-term medical or other mental health conditions or people who are neurodivergent with presentations such as ADHD and Autism spectrum disorder (ASD)[16]
- Substance use/recreational drug use
- Family history of anxiety, depression or other mental health conditions
- Stressful life circumstances, e.g. trauma, illness, financial pressures, the impact of social media and "the complexity of living in a fragile and uncertain world"

Associations between GAD, depression and suicide risk

People with GAD are often frequent users of medical services, including primary care, and are at increased risk of depression, substance dependence/misuse and suicidal ideation and attempts.[5, 17] Over half of people with GAD also have a co-morbid mood or other anxiety disorder, e.g. depression (mixed anxiety and depression), social anxiety disorder.[5] A meta-analysis found that people with panic disorder, social anxiety disorder or GAD were 50% more likely to experience suicidal ideation and attempt suicide.[1] Co-morbid mental health conditions, e.g. depression, further increases suicide risk.[1]

The prevalence of anxiety disorders in New Zealand

It is estimated that 15% of people in New Zealand experience an anxiety disorder per year; similar to the global prevalence (14%).[1, 6] Many patients presenting to general practice will have anxiety (either reported or unreported).[3, 8] The prevalence of anxiety disorders is estimated to have risen markedly during the COVID-19 pandemic.[9, 10]

Data from the New Zealand Health Survey show that between 2021 and 2023, the prevalence of "mild or greater anxiety symptoms in the last two weeks" (GAD-7 score 5 – 21) was approximately 27%; an increase of 8% since 2016/17.[11] Prevalence was highest among Māori (35.5%), followed by Pacific peoples (31.5%), Asian (23.4%) and Europeans/Other (26.8%).[11] However, there is inconsistent evidence that Māori and Pacific peoples experience a higher rate of anxiety disorders.[12, 13] Further research is required to understand the reasons for disparities in anxiety symptoms and anxiety disorders between populations; however in general, factors such as low socioeconomic status (including deprivation, housing, education, employment) and discrimination influence mental wellbeing.[14]

Diagnostic work-up of a patient with suspected GAD

Patients with GAD typically present with significant worry or stress and/or non-specific symptoms, including fatigue, sleep disturbance, headache, dizziness, restlessness, irritability, difficulty concentrating, gastrointestinal disturbances (e.g. diarrhoea), tachycardia, chest pain or muscle tension.[3, 18] Also consider the possibility of GAD in patients who attend primary care frequently and have a chronic medical condition, or in those who often seek reassurance about somatic symptoms or repeatedly worry about a range of issues.[19] Anxiety may also be identified in patients during screening for depression or psychological distress, e.g. a low score on the **Patient Health Questionnaire-9 (PHQ-9)** or high score on the **Kessler-10 (K10)**.

If GAD is suspected in a patient, discuss:[1, 18, 19]

- The nature of symptoms, e.g. worry, avoidance, obsession
- Symptom severity, e.g. impact on daily functioning, relationships, employment
- Symptom duration
- Triggers or precipitants. Is there an association with specific life events or trauma?
- Any underlying conditions (including co-morbid mood or anxiety disorders, or whether there is a family history of mental health conditions), medicines (including over-the-counter) or illicit drug use. Also ask about alcohol and caffeine intake.
- Social life and circumstances, e.g. relationships, living conditions, employment status
- Self-harm or suicidal ideation
- Any past treatments for anxiety (or other mental health condition) and response to these, including adverse effects

Differential diagnosis of GAD

There are various conditions that can cause symptoms of anxiety, and these should be excluded as a possible cause of the patient's symptoms. For example, thyroid disorders, e.g. hyper- or hypothyroidism, angina, arrhythmias, asthma, depression, other anxiety disorders, ADHD/spectrum disorders and bodily distress disorder/somatic symptom disorder.[3, 5, 6]

Medicines such as sympathomimetics, stimulants, digoxin, anticholinergics and corticosteroids, and substance misuse/withdrawal should also be considered as a possible cause of the patient's symptoms.[3, 5, 6]

Perform a physical examination and request laboratory testing (e.g. thyroid function, full blood count, creatinine, electrolytes) or other investigations (e.g. ECG) as indicated to exclude alternative causes.[3, 5, 6]

Symptoms of GAD overlap with bodily distress disorder/somatic symptom disorder. For information on somatisation, see: **bpac.org.nz/2019/somatisation.aspx**

Screening for GAD using the GAD-2 screening questionnaire (Table 1) may be appropriate in certain patient groups, e.g. those with frequent presentations to primary care, multiple co-morbidities or substance misuse. There is some evidence from the United States that screening in people aged 64 years and under can improve treatment outcomes in those subsequently diagnosed with an anxiety disorder.[3]

Table 1. Generalised Anxiety Disorder-2 (GAD-2). An online calculator is available from: **medscape.com/calculator/570/generalized-anxiety-disorder-2-gad-2**.

Over the last two weeks, how often have you been bothered by the following?				
	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3

A score of ≥ 3 may indicate GAD and should prompt further investigation.

Diagnosing GAD

Most patients can be diagnosed with GAD in primary care, but there are some patients for whom discussion with, or referral to a psychiatrist or other mental health specialist, should be considered, e.g. if there is diagnostic uncertainty or other significant factors, such as suicidal ideation, substance misuse, complex co-morbid mental or physical health conditions.[5, 19] The DSM-5-TR classifies and defines mental disorders and can be used to make a formal diagnosis of GAD (see: "DSM-5-TR: diagnostic criteria for GAD and the GAD-7"). The GAD-7 (Table 2) is a tool that can be used to screen for GAD or to measure severity which can guide management decisions; some HealthPathways also have local grading tools.[3, 9] Some patients may already have completed the GAD-7 at home, and their score can be discussed.

The ICD-11 also has diagnostic criteria for GAD, see: **icd.who.int/browse/2024-01/mms/en#1712535455**

Management of GAD

Treatment for GAD aims to reduce symptom severity, improve overall functioning and achieve remission. In clinical trials, around one in two people who undergo treatment for anxiety (psychological or pharmacological) report an improvement in symptoms and no longer meet criteria for the anxiety disorder.[1] However, an anxiety disorder can be a long-term condition and symptoms will fluctuate in intensity over time.[1, 6, 7]

Management of anxiety can usually take place in primary care unless the patient has very severe GAD (request acute or non-acute mental health assessment) or complex co-morbidities, e.g. suicidal ideation, substance use disorder, significant mental or physical health conditions.[5, 20] A step-based approach to management is generally recommended:[1, 19]

1. Education about anxiety and advice on lifestyle factors (see: "Prioritise education and lifestyle changes")
2. Specific psychological or pharmacological treatment(s) as needed (see: "Psychological versus pharmacological treatment")

Some patients, e.g. those with mild anxiety, may only require education and self-management strategies, while others, e.g. those with more severe symptoms or co-morbid depression,

DSM-5-TR diagnostic criteria for GAD and the GAD-7

DSM-5-TR[4]

1. Excessive anxiety and worry about a number of events or activities, occurring more days than not for at least six months
2. Worry is difficult to control
3. Anxiety and worry are associated with at least three of the following symptoms (with at least some of the symptoms present for more days than not in the past six months):
   - Restlessness or feeling keyed up or on edge
   - Being easily fatigued
   - Difficulty concentrating or mind going blank
   - Irritability
   - Muscle tension
   - Sleep disturbance
4. Anxiety, worry or physical symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning
5. The disturbance is not caused by the physiological effects of a substance or medicine or another medical condition
6. The disturbance is not better explained by another mental disorder

Table 2. Generalised Anxiety Disorder-7 (GAD-7). An online calculator is available from: **www.mdcalc.com/calc/1727/gad7-general-anxiety-disorder7**.

Over the last two weeks, how often have you been bothered by the following?				
	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Score: 5 – 9 Mild anxiety; 10 – 14 Moderate anxiety; 15 – 21 Severe anxiety

may require a combination of treatment options.[1, 3, 6] Involve the patient's family/whānau or support people in the management plan (where appropriate); it is important to ask about and consider the cultural or spiritual beliefs held by the patient and their family/whānau about anxiety and mental illness.[1]

For patients with GAD and co-morbid depression, the National Institute for Health and Care Excellence (United Kingdom) recommends treating the mental health condition that is more severe first.[19] Other sources, including local HealthPathways, suggest treating the mood disorder (or other primary disorder, e.g. substance misuse) first, as this will also help to improve the patient's symptoms of anxiety.[5] In practice, a combined approach to both conditions is usually helpful.

Prioritise education and lifestyle changes

As part of initial management, provide the patient with education about anxiety, including reassurance that it affects many people and is manageable. Recommend self-directed activities/coping skills and lifestyle changes as appropriate, e.g. (also see: "Brief anxiety reduction techniques for patients"):[1, 10, 18]

- Exercise/physical activity
- Yoga
- Mindfulness, meditation or other relaxation techniques
- Breathing techniques
- Journaling or reading self-help books/apps
- Dietary factors, e.g. limiting caffeine and alcohol consumption
- Good sleep hygiene practices

Expert advice: Be aware that mindfulness is not effective or acceptable for everyone, and is more difficult when anxiety symptoms are prominent. It can also be more challenging for people with certain co-morbidities, e.g. ADHD. Tailor recommendations about lifestyle and self-directed strategies to each patient depending on their co-morbidities or individual circumstances.

There is some evidence that behavioural and lifestyle interventions are effective at managing anxiety, either alone or alongside more intensive treatment.[3, 18] Re-enforcing these strategies can also be useful to support patients if they experience a relapse of symptoms.

Some patients may benefit from engaging with community mental health services or peer support groups; see local HealthPathways for details. Health improvement practitioners can also provide support, if available at your practice, or patients may wish to engage with other allied health services, e.g. psychology, counselling, physiotherapy, occupational therapy, dietitian. Some patients may be interested in trialling acupuncture, as there is some evidence that it is effective at managing the symptoms of GAD.[10, 21]

Brief anxiety reduction techniques for patients

There are many anxiety reduction techniques that clinicians can direct patients to, or that patients can find by searching online. During a consultation, it can sometimes be useful and more engaging for clinicians to briefly discuss a few simple anxiety reduction techniques that patients can try. These are known as grounding techniques which provide acute relief of anxiety symptoms. Depending on the technique, these can relieve anxiety in many ways, including by distracting thinking, engaging senses, helping people to practice self-compassion or become calmer. **For example**:

- **3-3-3** – think of three things you can see, hear and touch
- **5-4-3-2-1** – identify five things you can see, four things you can touch, three things you can hear, two things you can smell and one thing you can taste
- **Slow breathing**[1] – breathe in for four seconds, hold your breath for two seconds, breath out slowly for six seconds. Repeat for one minute, and then as necessary, repeat the whole technique again.
- **R**ecognise, **A**llow, **I**nvestigate, **N**urture (**RAIN**) – Recognise – notice that you are feeling anxious; Allow – give yourself permission to have that feeling; Investigate – get curious, e.g. how does the anxiety feel in your body? what do you need?; Nurture – be gentle and kind to yourself, offer yourself what you need, e.g. self-care.

A sheet on grounding techniques can also be provided to patients, e.g. from **Just a Thought**, the **University of Sydney** or **John Hopkins University of Medicine**.

Patient resources:

- Information and education:
  - Your Health in Mind **www.yourhealthinmind.org**
  - Anxiety New Zealand Trust **anxiety.org.nz/** (including a 24/7 helpline)
  - Mental Health Education and Resource Centre **mherc.org.nz**
  - Healthify **healthify.nz/health-a-z/a/anxiety/**
- Breathing techniques: **calming breathing techniques**, **three-minute breathing exercise**, **breathing apps**
- Mindfulness: **mindfulness and meditation apps**, **mindfulness techniques**, **mindfulness to get through tough moments**
- Journaling: **journaling to cope with anxiety**, **journaling prompts**

Psychological versus pharmacological treatment

The management of GAD may involve psychotherapy (e.g. cognitive behavioural therapy [CBT]), medicines (e.g. antidepressants) or a combination of both.[1, 19] Psychotherapy and pharmacological treatment are similarly effective;[3, 18] although the relapse rate for psychological therapies may be lower, and many patients prefer this to taking medicines.[5, 22] Evidence is inconsistent as to whether combined psychotherapy and pharmacotherapy is more effective than either alone.[1, 19]

The choice of which treatment to start with should be discussed as part of a shared decision-making process with the patient, and guided by the following factors:[1, 3]

- Patient preference, motivation and ability to engage
- Co-morbidities, age and pregnancy (psychotherapy is usually preferred in older patients and during pregnancy [see: "Management of GAD during pregnancy]")
- Possible adverse effects
- Availability and cost of treatment
- Current and prior treatments and response

Continue behavioural interventions alongside treatment

Behavioural interventions should continue alongside the chosen treatment regimen.[1]

Throughout treatment, encourage patients to gradually increase exposure to situations that cause anxiety, particularly if it has resulted in an avoidance behaviour due to a past experience.[1, 3] This may temporarily increase anxiety, but over time leads to a reduction in symptoms and improvement in social and daily functioning.[3]

Cognitive behavioural therapy is first-line psychotherapy

A range of behavioural and psychological therapies are available for people with anxiety disorders.[1, 5] Cognitive behavioural therapy (CBT) is the most widely used and effective form of psychotherapy for GAD, however, access can be limited due to wait times for both public and private services and cost for private services.[1, 5] Online therapy can be useful for some people, e.g. Just a Thought, and is considered to be as effective as face-to-face CBT (see: "Online cognitive behavioural therapy").[1, 10] Some primary care clinicians may also be skilled in simple CBT techniques that they can guide patients through, however, consultation time is often a limiting factor.

CBT sessions are typically conducted over many weeks and involve strategies for patients to change their emotions, ways of thinking and behaviours in response to fears and worries, e.g. psychoeducation, cognitive restructuring, exposure therapy.[1, 5] It can take up to six sessions of weekly CBT for the patient to experience symptom improvement (see: "Follow-up and ongoing monitoring").[1] CBT is effective in the short-term (i.e. within one year of completion), and people may be more likely to recover and have a lower risk of relapse than with antidepressants, however, long-term efficacy data is lacking.[1, 5, 22]

Other forms of psychotherapy for anxiety disorders include acceptance and commitment therapy (ACT; may be difficult for severe GAD), psychodynamic and interpersonal therapy. In general, these may be less effective than CBT for people with GAD, but can be successful in some cases.[1, 6]

Best Practice Tip: Where possible, ensure patients are referred to a provider that offers CBT, and that it is suggested in the referral that you think the patient might benefit from this type of therapy. If a patient has previously engaged with a counsellor or psychologist, but did not benefit (or are reluctant to return as they think they have already trialled this type of treatment), then explain that directed CBT is not the same as general counselling or psychology and that it is more successful for GAD. There are several websites where patients can search for a private CBT-trained therapist (in person or online), e.g. **www.psychologytoday.com/nz/counselling**.

Online cognitive behavioural therapy

Self-directed online CBT programmes can also be effective for people with GAD.[1, 10] Programmes may contain modules, assessments, games and other activities, with the overall aim of teaching people cognitive behavioural techniques to manage their anxiety.

Just a Thought, is a New Zealand organisation that offers free online CBT courses and hosts other resources for a range of mental health conditions, including generalised, social and health anxiety, obsessive compulsive disorder, depression, mixed depression and anxiety. The courses have been adapted for New Zealand from Australian online CBT courses by **This Way Up**. Courses can either be completed by the patient in a self-guided manner or through prescription by a clinician; patient progress can be monitored through the clinician dashboard.

An analysis of the Just a Thought generalised anxiety and depression courses, published in 2024, showed that while course adherence was low, there were significant reductions in mental distress; people aged 25 years and over, those with a higher level of distress at baseline and those who had completed more sessions were most likely to show clinically meaningful reductions in mental distress.[23] Adherence rates were higher when a healthcare professional prescribed the course.

Beating the Blues, is also a New Zealand-based online CBT course that is funded for adults aged 18 years and over with mild to moderate anxiety or depression. The course is conducted over eight sessions (50 minutes per week). To enrol patients, clinicians must be registered to "prescribe" the course on ManageMyHealth through Medtech or via the Beating the Blues website. Access can be provided through some PHOs. Guidance for clinicians is available here: **beatingtheblues.co.nz/clinicians/**.

Other New Zealand-based CBT courses and resources include **Groov app**, **Headstrong** and **SPARX** (aimed at younger people). Australian-based courses and resources include **moodgym**, **e-couch**, **MentalHealthOnline** and **Centre for Clinical Interventions**.

Pharmacological treatment of GAD

First-line medicines for people with GAD are selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs).[1] Second- and third-line medicines include other antidepressants (e.g. imipramine, mirtazapine), buspirone, pregabalin and benzodiazepines (e.g. clonazepam); see sections below for details.[1, 2] GAD is often an unapproved indication for these medicines.

Selective serotonin reuptake inhibitors and venlafaxine are first-line options

The first-line pharmacological treatment for patients with GAD is a SSRI or SNRI (i.e. venlafaxine), as these are generally well tolerated and have fewer long-term risks compared to other anxiolytic medicines; they are also effective at treating co-morbid depression.[1, 2] In practice, SSRIs are often trialled first as venlafaxine is difficult to withdraw and may be less tolerated.[1, 19] However, there is insufficient evidence to favour a SSRI over a SNRI.[1]

Selecting a SSRI

There is no evidence supporting use of one particular SSRI over another; choice should be individualised to the patient, considering factors such as co-morbidities, possible adverse effects, medicine interactions, patient preference and likely adherence, past history and response.[1, 18] Some guidelines recommend escitalopram, paroxetine or sertraline (unapproved indication) as first-line SSRIs.[1, 2, 19]

For information on the comparative advantages and disadvantages of individual SSRIs, see: **bpac.org.nz/2021/depression.aspx**

Management of GAD during pregnancy

Clinicians should have a higher suspicion of anxiety in patients who are pregnant as the prevalence of anxiety symptoms and disorders (new-onset or worsening of pre-existing anxiety), including GAD, may be higher during pregnancy and post-partum.[9, 18] Non-pharmacological management, particularly CBT, is usually recommended first line.[1, 2] However, some patients will require pharmacological treatment, e.g. those with severe symptoms or who are unable to engage in CBT.[1, 18]

The decision to start or continue pharmacological treatment during pregnancy and the post-partum period should take into consideration the possible benefits and risks to the mother (e.g. risk of untreated GAD) and fetus/infant (e.g. adverse effects of medicines during pregnancy and breast-feeding).[9, 18] SSRIs are generally recommended first line on the basis of safety and efficacy; sertraline or escitalopram are usually preferred, however, prescribe the same SSRI if prior treatment has been successful.[1, 18] See the **NZF** for information on the compatibility of specific medicines during pregnancy and breast-feeding.

For further information on SSRIs during pregnancy, including the risks of taking SSRIs during the perinatal period, see: **bpac.org.nz/2019/perinatal-depression.aspx**

Prescribe low doses initially to reduce the risks of adverse effects and up-titrate as tolerated to an effective dose (see the **NZF** for dosing information).[5] There is usually a delay between initiation and the onset of anxiolytic effects; it can take up to six weeks of treatment for the patient to begin to experience symptom improvement (see: "Follow-up and ongoing monitoring").[1, 3] Augmentation with buspirone may be considered following discussion with a psychiatrist or other mental health specialist for patients who require more symptom relief but who do not want to increase the dose further or who are already taking the maximum dose of SSRI (see: "Buspirone"); however, there is limited evidence of benefit.[20, 24]

Possible adverse effects include a transient increase in anxiety on initiation, gastrointestinal disturbances (e.g. nausea, bleeding), headache, sleep disturbance and sexual dysfunction.[1, 2]

If the patient does not respond adequately after an appropriate trial of at least four to six weeks or experiences problematic adverse effects that cannot be managed (e.g. with a dose reduction or addition of another medicine), consider switching to an alternative SSRI (or to venlafaxine if taking a SSRI), stopping pharmacological treatment and changing to psychotherapy or trialling combination treatment (see: "Follow-up and ongoing monitoring").[1, 19]

Other antidepressants may be considered if first-line medicines are ineffective or poorly tolerated[1, 2]

Tricyclic antidepressants, e.g. imipramine (unapproved indication), have demonstrated some efficacy in people with GAD, but they are associated with more adverse effects, a greater risk of overdose and are less tolerated compared to other antidepressants.[1–3] There are limited studies assessing the effectiveness of **mirtazapine** (unapproved indication) for anxiety, however, it is reportedly well tolerated.[1, 18] **Bupropion** (unapproved indication) has limited evidence for GAD but may be considered for patients concerned about weight gain or sexual dysfunction with SSRIs.[9, 24]

Buspirone

Buspirone is a second-line treatment for the management of GAD and can also be used to augment treatment with an antidepressant if there has only been a partial response (after discussion with a psychiatrist or other mental health specialist).[1, 24]

Buspirone has similar effectiveness to benzodiazepines in the management of GAD, although it is possibly less effective if benzodiazepines have already been used,[3, 5] therefore, it may be preferable to trial it first. Buspirone is generally well tolerated, has a low potential for misuse and dependence and is relatively safe in overdose.[2, 5, 24] It is usually dosed three times daily, which may not be suitable for patients who have difficulty with adherence.[24] Possible adverse effects include drowsiness, dizziness, fatigue, nausea and headache.[2, 3]

Pregabalin

Pregabalin has shown some efficacy in GAD (unapproved indication) and is generally well tolerated, although has potential for addiction and misuse, therefore, is not a first-line option.[1–3] Adverse effects include sedation, dizziness, headache and dry mouth.[1–3] Pregabalin may be considered, following discussion with a psychiatrist or other mental health specialist for patients who have had inadequate response to a SSRI or SNRI, or who experienced intolerable adverse effects with these medicines.[1, 2] There are limited studies on the efficacy of gabapentin in people with an anxiety disorder.[3]

Benzodiazepines

Benzodiazepines have been widely used for GAD because they have a rapid onset of action and can be effective at managing the somatic symptoms of anxiety in the short-term (e.g. two to four weeks).[3, 20] However, benzodiazepines have less effect on the underlying psychological aspects of anxiety and are associated with tolerance, dependence and misuse; therefore, are not recommended first-line or for long-term use.[1, 3] Other common adverse effects include sedation, drowsiness, cognitive impairment and falls (in older people).[1, 3]

A benzodiazepine may be considered short term for select patients with GAD in certain clinical situations after consideration of the possible benefits and risks. For example, during the initiation of a SSRI/SNRI for patients experiencing a transient increase in anxiety (although data supporting this practice are limited).[2, 3]

Benzodiazepines should be avoided in patients with risk factors for misuse, e.g. substance use disorder, and it is important to make clear to the patient that the benzodiazepine is for short-term use only.[18, 24] Benzodiazepines with a longer half-life, e.g. diazepam, clonazepam, prevent the need for multiple daily dosing and are less likely to be associated with breakthrough anxiety, however, they are generally associated with more adverse effects.[3, 9, 24]

Other treatments: atypical antipsychotics, beta blockers, complementary and alternative medicines

Atypical antipsychotics, e.g. quetiapine (unapproved indication), are effective in the management of GAD, however, use is generally discouraged due to problematic adverse effects, e.g. weight gain, sedation, QT interval prolongation, misuse, and a high rate of discontinuation.[1, 19]

Beta blockers, e.g. propranolol (unapproved formulation), are sometimes prescribed to patients to control the physical

symptoms of anxiety, e.g. tremor, elevated heart rate, however, their use is generally discouraged in GAD due to a lack of efficacy.[1, 6]

Botanicals and supplements. There is some evidence that chamomile, ginkgo biloba capsules, ashwagandha, kava, lavender and magnesium may reduce anxiety, including in people with GAD, however, further studies are required.[10, 19, 20]

N.B. Medicinal cannabis is not recommended for the management of GAD due to insufficient evidence of efficacy.[10, 20]

Follow-up and ongoing monitoring

Patients should be monitored (either in person or via phone) regularly, e.g. every two to four weeks, and then with decreasing frequency as they stabilise, e.g. every three to six months.[1, 5] At each follow-up, assess and monitor adherence, symptoms/response and any adverse effects (including self-harm and suicidal ideation).[1, 5] The GAD-7 can be used to monitor severity and response to treatment (Table 2).[1, 5]

It usually takes four to six weeks of treatment before the patient will begin to notice an improvement in symptoms.[1] If there is an inadequate response to treatment after a sufficient time, re-enforce lifestyle changes and self-help strategies and modify the patient's treatment regimen after checking adherence, e.g. prescribe a SSRI if the patient has been trialling CBT, or if the patient is already taking a SSRI, either increase the dose/switch to another SSRI (or other medicine) or add in CBT.[1, 5] If there is still inadequate response after modifying treatment:[1, 5]

- Re-consider the diagnosis and patient co-morbidities
- Trial combination psychological and pharmacological treatment (if not already) or consider recommending that the frequency of CBT sessions be increased (if possible)
- Discuss with or refer the patient to a psychiatrist or other mental health specialist[20]

Preventing and managing anxiety relapse

Continue pharmacological treatment with antidepressants for 6 – 12 months after symptoms have resolved before attempting a gradual withdrawal to reduce the risk of relapse; some patients may require a longer treatment duration, e.g. those with severe anxiety.[5, 19] Discontinuation symptoms such as dizziness, nausea, fatigue and headache may occur after stopping pharmacological treatment.[2]

Many patients will experience a relapse of anxiety symptoms after treatment, particularly during stressful situations; up to 40% of patients experience a relapse of anxiety within 6 – 12 months of stopping pharmacological treatment.[5, 18] During a relapse, patients may benefit from engaging (or re-engaging) in CBT and self-help strategies.[5, 18] Pharmacological treatment can also be re-initiated for some patients if relapse occurs during or after the medicine has been discontinued, however, there is limited evidence to support this practice.[18]

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