

**Anxiety Disorders Formulary Guidance [v2]**

**(adapted from NICE guideline CG113 (updated 2020) and CG159)**

1. **Introduction**

These Guidelines are intended for routine use. They are intended primarily in adults, there is a reference to under 18’s in section 2.3.1 in social anxiety However, there will be instances where they are not suitable for the patient you are managing, where more bespoke treatment will be necessary. In such instances the rationale for prescribing away from formulary must be recorded.

Treatment should be based on individualised person-centred care.

Where anxiety is the primary condition, this should be treated, and other co-morbid conditions as exist.

Frith Prescribing Guidelines may be of use when considering managing patients with intellectual disabilities.

When prescribing due consideration should be made as to the traffic light status of the medications involved. The Integrated Care Board (ICB) website can be consulted for further information.

See tables at the end of the document for a summary of individual medication.

The advice is split into Generalised Anxiety Disorder (GAD), Social Anxiety Disorder, Panic Disorder, Obsessive Compulsive Disorder and Post Traumatic Disorder (PTSD)

NICE guideline suggest a stepped care\* approach for managing of anxiety disorders

*(\*Adapted from NICE CG113  Anxiety)*

* **Step 1**: Identification and assessment; education about anxiety disorder and treatment options, active monitoring.
* **Step 2**: Use of low-intensity psychological interventions: individual non-facilitated self-help, individual guded slef help and psycho-educational groups.
* **Step 3**: For inadequate response to step 2 interventions or marked functional impairment. Choice of a high intensity psychological intervention (CBT/applied relaxation) or a drug treatment
* **Step 4**: Complex treatment-refractory anxiety disorder and very marked functional impairment or a high risk of self harm; requiring highly specialist treatment

1. **Prescribing in Anxiety States – Key Points**

2.1 Pharmacological Treatments

* Pharmacological treatment of anxiety disorders should be considered for severe and persistent symptoms which result in occupational and social disability.
* Psychological interventions should be offered to service users who prefer non-pharmacological treatment or have not benefited from or who are unable to engage with pharmacological interventions.
* The choice of initial treatment should be guided by preference, risks and benefits, side effects, prior treatment history, presence of other physical or psychiatric conditions, suicide risk, potential interaction and cost.
* Discuss the condition and treatment options fully and provide written information.
* Selective Serotonin Reuptake Inhibitors (SSRIs) are effective for a range of anxiety disorders and are suitable first line treatments.
* Inform service users prescribed antidepressants about a delayed onset of effect (at least 2 weeks) likely length of treatment and the need to take medication as prescribed.
* Decisions about off-label use of medications for anxiety disorders should be led by evidence-based guidelines and clinical experience. Informed consent for off label use should be gained and documented.

2.2 General Anxiety Disorder (GAD)

* NICE advises that pharmacological interventions are **only**indicated in people with inadequate response to psychological treatments.
* Use low initial doses of antidepressant and titrate up slowly. Initial worsening of anxiety may be evident.
* Antidepressants can take several weeks to have an effect (it usually takes four to six weeks or maximal response to SSRI’s), so initial augmentation with a benzodiazpine may be required, the risks of dependance on benzodiazepines should be clearly explained to the patient.
* For people with GAD, review the effectiveness and side effects of the drug every 2–4 weeks during the first three months of treatment and three monthly thereafter.
* If treatment is effective and tolerable, continue for at least 1 year as the likelihood of relapse is high.

2.3 Social Anxiety Disorder

* Pharmacological treatment is **only** indicated if social anxiety disorder (social phobia) inteferes significantly with social or occcupational activities.
* SSRIs are considered to be the drugs of choice for the treatment of social anxiety disorder. Standard antidepressant starting doses are indicated for social phobia
* Treatment should be continued for at least 1 year and possibly longer in some cases
* Co-morbidities e.g. depression, alcohol and substance misuse should be managed.
* Do not offer St John's wort or other over-the-counter medications and preparations for anxiety to treat social anxiety disorder. Explain the potential interactions with other prescribed and over-the-counter medications and the lack of evidence to support their safe use

2.3.1 CAMHS Social Anxiety Disorder

* Do not routinely offer pharmacological interventions to treat social anxiety disorder in children and young people. (NICE CG159)

2.4 Panic Disorder with or without Agoraphobia

* Pharmacologic therapy may be considered if behavioural or cognitive therapy fails.
* Use low initial doses of antidepressant and titrate up slowly, Higher doses may be necessary if standard doses are ineffective.
* There may be an initial exacerbation of anxiety and panic symptoms.
* It can take several weeks before the effects of antidepressants are evident.
* When new medication is started, efficacy and side-effects should be reviewed within 2 weeks of initiation and again at 4, 6 and 12 weeks.
* If there is no improvement after 12 weeks, switch to an alternative antidepressant, if assured compliance has been good.
* Remission of symptoms may take up to 6 months or longer (including 4–6 weeks at the highest comfortably tolerated dose).
* Medication should be continued for 6 months to 1 year after acute response to reduce the risk of recurrence. Long-term treatment may be necessary for some people, and should be available if indicated.
* Antidepressants for panic disorder should be discontinued over at least 4 weeks

2.5 Obsessive Compulsive Disorder

* Offer drug treatment to those with poor response to psychological interventions.
* A combination of pharmacological, behavioural, and psychosocial methods appears to have the most successful long term outcome.
* Doses at the upper end of the indicated dose range may be necessary.
* Most people will not experience substantial improvement until 4-6 weeks after starting medication, and others may show little improvement in the intial 12 weeks.
* If successful, treatment should be continued for 1 – 2 years before considering a gradual withdrawal over 1-2 months, whilst monitoring for any recurrence or relapse. However most will require long term treatment.

2.6 Post-Traumatic Stress Disorder

* Pharmacological treatments should be offered to people who cannot start a psychological therapy or who have gained minimal benefit from it.
* Drug therapy is largely aimed at accompanying symptoms of anxiety or depression NICE recommends the use of paroxetine, mirtazapine, amitriptyline or phenelzine.
* Lower initial dose are recommended although higher target doses (within approved limits) may be necessary for full effect.
* Treatment periods of 8- 12 weeks are needed to assess efficacy, if a good response occurs treat for a period of 12 months, before considering a gradual withdrawal.
  1. Benzodiazepines
* Whilst benzodiazepines are recommended for short term use there will be situations where people may have been them for some time. The following guidance covers the prescribing, monitoring and discontinuation of these agents, due to the risks of dependance and withdrawal.
  + See [NICE NG215](https://www.nice.org.uk/guidance/ng215) for details.

1. **Side-effects and Interactions**

* **SSRIs** are better tolerated and safer in overdose than other antidepressants.Common side effects of SSRIs are headache, nausea, and anxiety/agitation, especially when starting treament usuuallly settle on continued treatment Other side effects are insomnia, tremor, akathisia, sweating, paraethesias, sexual dysfunction, including diminished libido and difficulty with erection and orgasm, muscle/joint pain, weight gain and manic or psychotic symptoms
* **Tricyclic antidepressants** have similar efficacy to SSRIs but are more likely to be discontinued because of side effects and and are toxic in overdose. Common side effects of include anxiety, drowsiness, dizziness, agitation, confusion, anticholinergic effects discontinued because of side-effects and are toxic in overdose. Common side effects (dry mouth, constipation, urinary retention and blurred vision); cardiovascular effects (hypotension, tachycardia, arrhythmias and other ECG changes - baseline ECG is advised, where appropriate); hepatic changes and changes in blood sugar, weight gain and sexual dysfunction.
* **Monoamine Oxidase Inhibitors (MAOIs)** can have dangerous interactions with some food and drugs, and should be reserved for initiation by consultants. Service users prescribed these drugs should be monitored carefully (blood pressure), and given written dietary advice and information of drug interactions, and what to do in the event of a crisis.
* **Benzodiazepines**,due to risk of dependence, tolerance, withdrawal and rebound symptoms, they should be reserved for short term (2- 4 weeks ideally) at the lowest effective dose, Benzodiazepines can cause sedation, fatigue, ataxia, slurred speech, and risk of falls and fractures. Long term use can cause memory impairments, dependence, impaired alertness and impaired ability to perform skilled tasks, such as driving.
* **Mirtazapine** has few antimuscarinic effects, but causes sedation during initial treatment and is associated with weight gain and rarely blood dyscrasias.
* **Venlafaxine/Duloxetine** Have similar side effects to SSRI’s, a cardiac history should be taken before prescribing, paying particular attention to hypertension.
* **Antipsychotics** may be used with caution in anxiety with agitation or psychotic symptoms, when other agents are either ineffective or contraindicated

1. **Warnings**

(see Depression Formulary Guidance for more detail)

* Antidepressants are associated with an initial worsening of anxiety/agitation and an increased risk of suicidal behaviour and thinking. Monitor closely particularly at the start of treatment, and dosage changes.
* Discontinue antidepressants gradually. Abrupt discontinuation (sometimes reduced or missed doses) of antidepressants can lead to withdrawal symptoms (see depression guidelines)
* Use antidepressants with care in glaucoma, bipolar disorders, prostate hypertrophy, bleeding disorders and seizures.
* Hyponatraemia has been associated with all antidepressants; Mirtazapine may be a suitable choice if this occurs.
* SSRIs can increase risk of bleeding. Caution is required in older adults and when used in combination with NSAID’s, aspirin or anticoagulants
* SSRIs can increase risk of falls and osteoporotic fractures in people over 50 years.
* Serotonin syndrome can occur with serotonergic drugs and requires emergency management.

1. **Further information**
2. NICE Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113 (updated 2020). [www.nice.org.uk/guidance/CG113](http://www.nice.org.uk/guidance/CG113)
3. NICE Obsessive – Compulsive Disorder - NICE: clinical Guideline 31 [www.nice.org.uk/CG31](http://www.nice.org.uk/CG31)
4. NICE Social anxiety disorder: recognition, assessment and treatment [NICE Guidance CG159](https://www.nice.org.uk/guidance/cg159)
5. NICE. Post-Traumatic Stress disorder [www.nice.org.uk/CG26](http://WWW.nice.org.uk/CG26)
6. Evidence- based Guidelines for the pharmacological treatment of anxiety disorders BAP: <http://www.bap.org.uk/pdfs/Anxiety_Disorder_Guidelines.pdf>
7. BNF online [www.bnf.org](http://www.bnf.org)
8. SPC for all the drugs [www.medicines.org.uk](http://www.medicines.org.uk)
9. Psychotropic Drug Directory Bazire 2010
10. [Frith Prescribing Guidelines for people with intellectual disability 3rd Edition](https://www.wiley.com/en-gb/The+Frith+Prescribing+Guidelines+for+People+with+Intellectual+Disability%2C+3rd+Edition-p-9781118897201)

**Table 1: GENERALISED ANXIETY DISORDER**

**1a:**

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| **First Line** | **Relative costs** | **Notes** |
| Sertraline | £ | Not currently licensed for the treatment of GAD; Recommended first-line by NICE  If successfully treated previously with another antidepressants, re-initiate prior therapy  Offer high-intensity psychological intervention and anxiety management techniques |
| **Second Line** | **Relative costs** | **Notes** |
| Alternative SSRI |  | Offer another SSRI not tried first-line  Switch if unable to tolerate treatment or no response after 12 weeks at effective dose - after  checking adherence and confirming diagnosis; if partial response consider dose increase. |
| Paroxetine | £ | Use lower initial doses; high likelihood of discontinuation reactions |
| Citalopram | £ | Off-label use; consider preference, side effects - including QT effects and previous response |
| Venlafaxine (XL) | £ (££) | More toxic in overdose than SSRIs; High risk of discontinuation reactions |
| **Third Line** | **Relative costs** | **Notes – SECONDARY CARE INITIATION ONLY** |
| Escitalopram | ££ | Branded product and costs are greater than those for generic SSRI |
| Duloxetine | ££ | Branded product and costs are greater than those for generic SSRI/SNRI; Monitor blood pressure |
| Pregabalin | £££ | Branded product and costs are greater than those for generic SSRI; NICE recommends  pregabalin only if SSRIs or SNRIs not tolerated; somnolence and dizziness are common |
| **Other Agents** | **Relative Costs** | **Notes** |
| Benzodiazepines  Diazepam/Lorazepam | £ | Not  recommended except as a short-term measure during crisis because of risk of side  effects, dependence and misuse. Useful adjuncts in agitated patients. |
| Buspirone | ££ | For short-term use only – delayed onset of action; greater risk of discontinuation due to side  effects; Efficacy is reduced in previous extensive use of benzodiazepines; may be useful where  benzodiazepines not used before |
| Propranolol | £ | May be useful for somatic symptoms particularly tachycardia; check contraindications |
| Hydroxyzine | £ | Limited effectiveness; use for sedative effect inappropriate |

**1b: TREATMENT REFRACTORY GENARALISED ANXIETY DISORDER**

**Initiated and stabilised in Secondary Care**

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|  | **Relative costs** | **Notes - Discuss benefits and side effects and consider previous response** |
| General principles |  | Review current and past treatments and adherence  Increase the dose of the current treatment to the maximum dose;  Switch to an alternative evidence-based treatment not previously tried  Use a combination of psychological interventions and drug treatments. |
| Antidepressant  combinations | £-£££ | Seek consultant advice. Limited evidence and side effects and interactions more likely, including the risk of serotonin syndrome |
| Antidepressant +  Antipsychotic | £-£££ | Consultant initiation only. Do not use routinely due to limited evidence of effect; Side effects and  interactions more likely. Long-term use of antipsychotic should be avoided. |
| Antidepressants +  other agents, e.g.  buspirone, diazepam,  pregabalin etc | £-£££ | Seek consultant advice. No clear evidence of benefit. Check for contraindications |
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**Table 2: PANIC DISORDER**

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| **First Line** | **Relative costs** | **Notes** |
| SSRI eg  Sertraline  Citalopram  Paroxetine | £  £  £ | Offer psychological therapies and encourage self help  Consider preference, previous response, side effects and potential interactions  Start with low doses then gradually increase to a full dose, as tolerated  Citalopram is more cardiotoxic than other SSRIs and can cause QT prolongation at higher doses  Paroxetine has a short half life and a high risk of withdrawal symptoms  Fluoxetine and fluvoxamine are not licenced for panic disorder; may be tried if previous good  response shown. Consider long half life when switching or stopping fluoxetine. GI side effects are  common with fluvoxamine; bradycardia and ECG changes have been noted |
| **Second Line** | **Relative costs** | **Notes** |
| Mirtazapine | £ | Not licenced for panic disorder but has shown some benefit; sedating; risk of weight gain |
| Venlafaxine | £-££ | Monitor blood pressure; cardiotoxic in overdose |
| Escitalopram | ££ | Branded product and costs greater than generic SSRIs; Consider for those who have failed to  respond to initial treatments with generic SSRI; Cause dose-dependent QT prolongation |
| Benzodiazepines | £ | Benzodiazepines should not be prescribed except for short term use in severe, distressing and  disabling panic symptoms |

**Table 3: SOCIAL ANXIETY DISORDER**

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| **First Line:** | **Relative Cost** | **Notes** |
| **SSRI e.g.**  Paroxetine  Sertraline  Fluoxetine | **£**  **£**  **£** | Offer psychological interventions - CBT is known to be efficacious for long-term treatment  SSRIs considered to be the drugs of choice for the treatment of social anxiety disorder  Consider combining SSRI + CBT in those with high risk of relapse |
| **Second Line:** | **Relative Cost** | **Notes** |
| **Alternative SSRI** |  | Offer another SSRI not tried first-line |
| Fluvoxamine | **£** | Risk of nausea and vomiting higher with fluvoxamine than other SSRIs; Risk of interactions |
| Escitalopram | **££** | Usually 2-4 weeks are necessary to obtain symptom relief with escitalopram |
| **SNRIs** |  |  |
| Venlafaxine | **£ - ££** | Monitor blood pressure; High risk of discontinuation reactions; cardiotoxic in overdose |

**Table 4: OBSESSIVE COMPULSIVE DISORDER (OCD)**

**4a:**

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| **First Line:** | **Relative Cost** | **Notes** |
| **SSRI’s**  Citalopram  Fluoxetine  Paroxetine  Sertraline | **£**  **£**  **£**  **£** | If CBT is not accessible or available, offer drug treatment  Also offer CBT if medication not preferred and service users able to engage with CBT  Paroxetine can cause more weight gain and anticholinergic side effects than are other SSRIs and  greater risk of withdrawal symptoms.  Fluoxetine has a long half life. Citalopram causes dose dependant QT interval prolongation. |
| **Second Line:** | **Relative Cost** | **Notes** |
| **Alternative SSRI** | **£ - £££** | Offer SSRI not tried first line (escitalopram costs greater than for generic SSRIs) |
| **Clomipramine** | **£** | Consider clomipramine when SSRI ineffective or poorly tolerated or when it is the preferred option or where previous good response has been shown. Clomipramine is more likely to induce anticholinergic effects and can cause hypotension and postural dizziness. It can increase levels of liver transaminases and has a potential for seizures and cardiac arrhythmias, particularly at higher doses Consider ECG and blood pressure monitoring in cardiovascular disease |
| **Imipramine** | **£** | Recommended as an option by the British Association of Psychopharmacology but not by NICE |

**4b: TREATMENT RESISTANT OBSESSIVE COMPULSIVE DISORDER**

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| **Third Line:** | **Relative Cost** | **Notes – Secondary care initiation and stabilisation** |
| MAOIs  Phenelzine | £ | Consider MAOIs in severe OCD where all first-line treatments and most second-line treatments  have failed. |
| Combinations e.g.  SSRI + clomipramine  SSRI + mirtazapine | £-££  £-££ | Consultant initiation only Monitor carefully – risk of additive side effects and toxicity;  Off-label use- mirtazapine can also be considered  Increased risk of serotonin syndrome |
| Augmentation e.g.  SSRI + antipsychotic  SSRI + trazodone | £-£££  £-££ | Antipsychotics (risperidone, quetiapine, haloperidol) can be considered as augmentation strategy  where response to SSRI treatment is poor or incomplete  May be helpful in alleviating OCD and anxiety as well as sleep disturbances |
| Benzodiazepines e.g.  clonazepam; diazepam | £ | Benzodiazepines are not routinely recommended due to limited evidence for efficacy. Only  consider for short periods for severe anxiety |

**Table 5: POST TRAUMATIC STRESS DISORDER**

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| **First Line:** | **Relative Cost** | **Notes** |
| **SSRI** e.g.  Paroxetine  Sertraline | **£**  **£** | Offer trauma-focused psychological therapies before drug treatment;  Continue drug treatment for 12 months if response is evident at 12 weeks  Paroxetine and sertraline have current licences for PTSD |
| Mirtazapine | **£** | Off-label use; sedation and weight gain likely; blood dyscrasias - monitor |
| **Second Line:** | **Relative Cost** | **Notes** |
| **Alternative SSRI**  Citalopram  Fluoxetine | **£**  **£** | If first line SSRI unsuccessful or not tolerated, a suitable alternative SSRI e.g. citalopram or fluoxetine (off-label  use), can be tried |
| **Venlafaxine** | **£-££** | Venlafaxine may be considered as an alternative to SSRIs following non-response - preferred  over tricyclics or MAOIs as less adverse effects |
| **MAOIs i.e.**  phenelzine | **£** | Consultant only; Can reduce traumatic recollections and nightmares, and repress flashbacks;  MAOI treatment requires careful BP monitoring and advice on drug and food interactions |
| **Other Treatments** | **Relative Cost** | **Notes** |
| Hypnotics  liquids | **£**  **£££** | May be appropriate for short-term use only where lack of sleep is a major problem; risk of  dependence |
| Benzodiazepines | **£** | May be helpful for short-term management of severe anxiety; risk of dependence and misuse |
| Antiepileptics | **£-£££** | Carbamazepine, valproate, topiramate – limited benefits in some benefits; off-label for specific  symptom clusters; e.g. hyper-reactivity, violent behaviour, angry outbursts, avoidance (social  withdrawal) and intrusion |