NHS Oxfordshire Clinical Commissioning Group

NHS Oxford Health NHS Foundation Trust

Primary Care Generalised Anxiety Disorder Guideline for Adults and Older Adults

Generalised anxiety disorder is characterised by excessive and inappropriate worrying that is persistent (lasting more than a few months) and not restricted to particular circumstances. Patients have physical anxiety symptoms and key psychological symptoms (restlessness, fatigue, difficulty concentrating, irritability, muscle tension and disturbed sleep) causing clinically significant distress or impairment in social, occupational or other important areas of functioning.

NICE uses a stepped care approach to treating GAD. The recommendations for treating GAD with marked functional impairment or that has not improved after a low intensity psychological intervention (individual non-facilitated self-help, individual guided self-help, psychoeducational groups) [step 3] are:

- an individual high-intensity psychological intervention
  or
- drug treatment

Pharmacological and psychological approaches have broadly similar efficacy in acute treatment; however patients with severe anxiety may struggle to engage with psychological intervention; this guideline specifically addresses the drug treatment of GAD only.

FIRST LINE:

- Offer an SSRI – first choice = SERTRALINE
  - NICE recommends offering sertraline* because it is the most cost-effective.
  - There is also evidence of benefit with most other SSRIs: escitalopram[ψ], citalopram[ψ], and paroxetine.
  - Consider using half the initial starting dose to reduce the risk of exacerbating anxiety symptoms during the first 1 to 2 weeks, and titrate gradually.
  - Response begins gradually and continues with time. A period of up to 12 weeks may be necessary to fully assess efficacy. However absence of any clinical benefit within four weeks warns that a response to unchanged treatment is unlikely [BAP].

GOOD RESPONSE:

- Continue for at least 18 months following remission, as relapse risk is high

NON RESPONSE TO FIRST LINE TREATMENT:

2nd line -

- A different SSRI or
- An SNRI[φ] (duloxetine[♣] or venlafaxine XL)

POOR/NON RESPONSE TO SECOND LINE TREATMENT:

Consider either:

- **3rd line drug treatment** – Pregabalin[⊗] (monotherapy or augmentation[♦]) OR
- **Referral to secondary care psychiatrist.**

ALTERNATIVE FIRST LINE OPTIONS when an SSRI is CONTRAINDICATED:

- Consider 1st, if not similarly contraindicated: SNRI[φ] - duloxetine[♣] or venlafaxine XL tablets.
- If SNRI is similarly contraindicated , consider pregabalin[⊗]

SSRI POORLY TOLERATED:

- Consider first: A different SSRI or an SNRI (duloxetine[♣] or venlafaxine XL[φ] tablets).

If tolerability continues to be an issue:

- Consider offering pregabalin[⊗] (3rd line)

For information only:
Secondary care initiation - 4th line drug treatment options might include (alphabetical):
Agomelatine* (red secondary care prescribing only), buspirone*, hydroxyzine*, imipramine*, quetiapine*, trazodone.

* not licensed for GAD
ψ citalopram and escitalopram are contraindicated with any other drug that prolongs the QT interval
♣ Duloxetine is a cheaper SNRI option than venlafaxine XL.
φ Low doses may be sufficient (e.g. venlafaxine XL 75mg daily); immediate release preparations are not licensed for GAD but XL are.
⊗ Higher daily doses of pregabalin may be associated with greater response rates (≥200mg/day)
♦ The addition of pregabalin to SSRI or SNRI antidepressant drugs is superior to continued treatment with antidepressants alone. When there has been a partial/good response to an antidepressant but residual symptoms continue, it may be appropriate to add pregabalin. When there has been limited or no response to an antidepressant, a switch to pregabalin and a trial of monotherapy is indicated.
For other medicines mentioned, use standard BNF doses quoted for depression.

For information on the recommended dosing of pregabalin for GAD – click here

ADDITIONAL NOTES:

FORMULARY TRAFFIC LIGHT STATUS	Sertraline Citalopram Escitalopram Paroxetine Duloxetine Venlafaxine XL Pregabalin	Buspirone¥	Agomelatine

¥ amber initiation – specialist must prescribe for a minimum of a month. The patient must be reviewed again to assess response and once stabilised, a further 2 week supply will need to be provided before asking the GP to continue the prescribing.

- ✓ People with anxiety disorders are more prone to develop adverse effects.
- ✓ Adequate treatment of anxiety may prevent future development of depression.
- ✓ Discuss potential adverse effects early in treatment, including increased nervousness, worsened agitation, and review patient progress carefully over the first few weeks of treatment.
- ✓ Effective medication should be continued for at least 18 months after remission, as relapse risk is high.
- ✓ Medication should be discontinued over *at least* 3 months at the end of treatment

- ➢ Benzodiazepines can be useful for short term management (less than 2 weeks) in patients with mild to moderate anxiety or as an adjunct in more severe anxiety (preferably short term). Patients need to be made aware of risk of sedation, falls and addiction.
- ➢ Propranolol is only helpful for the physical symptoms of anxiety (e.g. sweating, tachycardia and tremor). In GAD with lots of worry, propranolol may not be indicated.
- ➢ Duloxetine – avoid in patients with known liver disease and patients considered to be at risk of hepatic dysfunction, severe renal impairment and uncontrolled hypertension.
- ➢ Pregabalin is efficacious in relieving depressive symptoms of mild to moderate intensity in generalised anxiety disorder.
- ➢ Pregabalin - there is evidence of benefit of in the elderly. It is licensed for use, but may require lower dose due to the possibility of deteriorating renal function in this age group.
- ➢ Antipsychotics – strongest evidence is with quetiapine (acute treatment and relapse prevention).
- ➢ Agomelatine – efficacy in acute treatment and in relapse prevention, but red in primary care; not licensed for GAD; requires regular LFT monitoring (contraindicated in hepatic impairment); less likely to cause sexual dysfunction than SSRIs and SNRIs.
- ➢ TCAs – greater burden of side effects; avoid in patients with cardiovascular disease; avoid if there is a high risk of suicide.
- ➢ Mirtazapine – evidence is limited and inconsistent.
- ➢ Buspirone and hydroxyzine – evidence in acute phase of treatment, but no published evidence in relapse prevention.

References:

- NICE Clinical Guideline [CG113] Generalised anxiety disorder and panic disorder in adults: management, 2011
- British Association for Psychopharmacology. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: A revision of the 2005 guidelines from the British Association for Psychopharmacology. Journal of Psychopharmacology 2014;1-37
- Baldwin D, Woods R, Lawson R and Taylor D. Efficacy of drug treatments for generalised anxiety disorder: systematic review and meta-analysis. BMJ 2011;342:d1199
- Taylor D, Paton C, and Kapur S. The Maudsley Prescribing Guidelines in Psychiatry 12th edition, Wiley Blackwell 2015
- Montgomery S, Chatamra K, Pauer L, Whalen E, and Baldinetti F. Efficacy and safety of pregabalin in elderly people with generalised anxiety disorder. British Journal of Psychiatry 2008;193:389-394

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