GUIDELINES FOR THE TREATMENT OF GENERALISED ANXIETY DISORDER AND PANIC DISORDERS IN PRIMARY CARE

This guidance has been developed by South Yorkshire ICB Barnsley Medicines Optimisation Team in collaboration with colleagues from South West Yorkshire Partnership NHS Foundation Trust (SWYPFT).

The guidance has been subject to consultation and endorsement by the Barnsley Area Prescribing Committee on 10th July 2024.

Contact for advice: Medicines Management Team 01226 433798

Purpose

This guidance has been developed to support a consistent approach to the treatment of Generalised Anxiety Disorder (GAD) and Panic Disorder in primary care, utilising both non-pharmacological and pharmacological methods. It provides recommendations for adults in routine practice. It does not encompass the approach to patients with complex treatment-refractory GAD, patients with very marked functional impairment or those at high risk of self-harm. Treatment of such patients requires specialist input and often involvement of multi-agency teams.

GENERALIZED ANXIETY DISORDER (GAD)

NICE[1] recommends a stepped approach to treatment of GAD.

1. Identification - All known and suspected presentations of GAD:
    - Identify and communicate the diagnosis of GAD to the patient to help them understand the disorder and start effective treatment promptly.
    - Consider the diagnosis of GAD in people presenting with anxiety or significant worry, and in people who attend primary care frequently who have a chronic physical health problem; do not have a physical health problem but are seeking reassurance about somatic symptoms; are repeatedly worrying about a wide range of different issues.
2. Low-intensity psychological interventions for GAD - If GAD has not improved after education and active monitoring in step 1 interventions – offer one or more of the following as first line options (guided by patient preference):
    - Individual non-facilitated self-help (written or electronic self-help materials)
    - Individual guided self-help
    - Psychoeducational groups

In Barnsley patients can self-refer to Talking Therapies by calling 01226 644900 (Monday – Friday 9am – 5pm) or by visiting the Barnsley Talking Therapies website at https://barnsley-talkingtherapies.nhs.uk/

3. Treatment options - GAD with marked functional impairment or that has not improved with steps 1 and 2 above offer:

    Either individual high intensity psychological interventions (Cognitive behavioural therapy (CBT), applied relaxation)
    or drug treatment.

    There is no evidence that either mode of treatment is better.

    Provide written information on the benefits and disadvantages of each mode of treatment to allow the patient to make an informed choice based on their preferences. The availability of treatments should also be discussed (e.g. likely waiting times for non-pharmacological therapies).

4. Consider referral if the patient with GAD has severe anxiety with marked functional impairment in conjunction with:
    - a risk of self-harm or suicide or
    - significant comorbidity, such as substance misuse, personality disorder or complex physical health problems or
    - self-neglect or
    - an inadequate response to step 3 interventions

For further information on psychological treatments refer to NICE guidelines[1,2], the local Psychological Services Department or the local Talking Therapies services on 01226 644900.

PANIC DISORDER

NICE also recommends a stepped approach to treatment of panic disorder.

1. Recognition and diagnosis - be alert to the common clinical situation of comorbidity, in particular, panic disorder with depression and panic disorder with substance misuse.

2. Treatment in primary care - psychological therapy, medication and self-help have all been shown to be effective. Treatment choice will be guided by the assessment process and shared decision-making with the patient.

   The interventions that have evidence for the longest duration of effect, in descending order, are:
    - psychological therapy - Cognitive behavioural therapy (CBT)
    - pharmacological therapy (antidepressant medication).
    - self-help - Bibliotherapy based on CBT principles, information about support groups. Benefits of exercise as part of good general health should be discussed.

3. Review and consideration of an alternative intervention.

4. Review and referral to specialist mental health services. If there have been two interventions provided (any combination of psychological intervention, medication, or bibliotherapy) and the patient still has significant symptoms, then referral to specialist mental health services should be offered.

The choice of treatment for both GAD and panic disorder should be shared between the patient and clinician. This will improve concordance and clinical outcomes.

PHARMACOLOGICAL TREATMENT OF GAD AND PANIC DISORDER[1,3]

For further information please consult individual drug SPCs in the Medicines Compendium at www.medicines.org.uk or information in the British National Formulary at https://www.medicinescomplete.com/mc/bnf/current/

Before prescribing any medication, discuss the treatment options and any concerns the patient has about taking medication. Explain fully the reasons for prescribing and provide written and verbal information on:

- the likely benefits of different treatments
- the different propensities of each drug for side effects, withdrawal syndromes and drug interactions
- the risk of activation with SSRIs and SNRIs, with symptoms such as increased anxiety, agitation and problems sleeping
- the gradual development, over several weeks, of the full anxiolytic effect
- the importance of taking medication as prescribed and the need to continue treatment after remission to avoid relapse
- A useful resource for patients is the following website; www.choiceandmedication.org/swyp/

https://www.choiceandmedication.org/swyp/generate/handychartanxiety.pdf

https://www.choiceandmedication.org/swyp/generate/handychartpanic.pdf

https://www.choiceandmedication.org/swyp/condition/anxiety/

https://www.choiceandmedication.org/swyp/condition/panic-disorder/

PHARMACOLOGICAL TREATMENT OF GAD (see Algorithm Appendix 1)

Aims of treatment in GAD are to reduce symptoms of anxiety and to minimise disruption to day to day functioning, with minimal adverse effects.

- If a patient with GAD chooses drug treatment, offer a selective serotonin reuptake inhibitor. Sertraline, although unlicensed is recommended as the first line SSRI in NICE guidance. (Clinicians should bear in mind that recommendation was partly because at that time it was the most cost-effective option. However this is no longer the case, and it may be more pertinent to choose a SSRI based on patient preferences).
- If the initial SSRI is ineffective in the treatment of GAD, offer an alternative SSRI based on patient preference. Choice should take into account previous experience with the drug, tendency to produce withdrawal syndrome, side effect profile, drug interactions, risk of suicide and likelihood of toxicity in overdose. Paroxetine use is restricted and should not be prescribed for GAD.
- Escitalopram is licensed for GAD but NICE recommends use of more cost-effective SSRIs first.
- If SSRIs are ineffective or not tolerated offer a SNRI such as venlafaxine or duloxetine. These are licensed for GAD (MR venlafaxine licensed, immediate release is not).
- If the second line option is ineffective or the patient cannot tolerate SSRIs or SNRIs, consider referral to secondary care. Pregabalin is recommended by NICE where SSRIs and SNRIs are not tolerated, but in Barnsley this is an Amber-G indication and requires specialist recommendation or initiation.

Medication not to be prescribed for GAD:

- Combinations of antidepressants or augmentation of antidepressants with other drugs should be initiated by secondary care specialists.
- Benzodiazepines should not be used for long-term treatment. In GAD benzodiazepines should be used with caution in the short term and not normally for longer than two to four weeks. Patients should be advised about the risks of dependency. Benzodiazepines can impair driving performance and increase the risk of road traffic accidents. Patients who are taking benzodiazepines and drive should be advised in line with the Department of Transport guidance 2014[3]. A new offence of driving with certain specified controlled drugs (including certain benzodiazepines) in excess of specified levels in the body came into force in March 2015.
- Do not offer an antipsychotic for GAD in primary care.
- Propranolol is widely used, however, the evidence for use in anxiety is slim and the risks underestimated. Propranolol is toxic in overdose; deterioration can be rapid and occur before medical assistance is available. NICE does not recommend propranolol for generalised anxiety disorder and panic disorder in adults (CG113), there other safer and more effective options[4].

PHARMACOLOGICAL TREATMENT OF PANIC DISORDER (see Algorithm Appendix 2)

Aims of treatment in panic disorder are to reduce the severity and frequency of panic attacks, phobic avoidance and anticipatory anxiety and to improve social and occupational functioning, with minimal adverse effects.

- Antidepressants should be the only pharmacological intervention used in the longer-term management of panic disorder.
- The classes of antidepressants that have an evidence base for effectiveness in the treatment of panic disorder are:
    - selective serotonin reuptake inhibitors (SSRIs).
    - serotonin noradrenaline reuptake inhibitors (SNRIs).
    - tricyclic antidepressants (TCAs) – clomipramine or imipramine initiated under specialist supervision.
- Unless otherwise indicated, an SSRI licensed for panic disorder should be offered.
    - Citalopram licensed.
    - Sertraline licensed.
    - Escitalopram licensed
    - Paroxetine licensed but not recommended and restricted use in Barnsley formulary due to increased reporting of discontinuation symptoms and movement disorders.
- If antidepressants are not suitable or there is no improvement after a 12-week course consider referral to secondary care.

Medication not to be prescribed for Panic Disorder

- Benzodiazepines should not be prescribed for the treatment of panic disorder as in the longer-term outcomes are poorer.
- Sedating antihistamines or antipsychotics should not be prescribed for the treatment of panic disorder.

General Advice when Prescribing Antidepressants for Anxiety Disorders[1,3]

- Doses of SSRIs and SNRIs should be started low (half the usual starting dose for depression) and increased gradually to reduce the risks of initial exacerbation of anxiety symptoms.
- SSRIs and SNRIs may take up to 3 months to produce a therapeutic effect.
- Take into account the increased risk of bleeding associated with SSRIs, particularly for older people or people taking other drugs that can damage the gastrointestinal mucosa or interfere with clotting (for example, NSAIDS or aspirin). Consider prescribing a gastroprotective drug in these circumstances.
- Monitor closely for suicidal ideation and behaviour during treatment with antidepressants and pregabalin. NICE recommends every 2-4 weeks for the first 3 months, then 3 monthly thereafter.
- For people aged under 30 who are offered an SSRI or SNRI:[1]
    - warn them that these drugs are associated with an increased risk of suicidal thinking and self-harm in a minority of people under 30
    - see them within 1 week of first prescribing
    - monitor the risk of suicidal thinking and self-harm weekly for the first month.
- If there is a risk of suicide consider the likelihood of toxicity in overdose, especially with venlafaxine.
- TCAs are also more dangerous in overdose than SSRIs.
- In older people, initiation and maintenance doses are usually lower (half the usual starting dose) than those used in younger adults and gradual and careful titration is required. Monitoring of side effects and efficacy should be more frequent.
- For people who develop side effects soon after starting drug treatment, provide information and consider one of the following strategies:
    - monitoring the patient's symptoms closely (if the side effects are mild and acceptable to the patient) or
    - reducing the dose of the drug or
    - stopping the drug and, according to the patient's preference, offering either an alternative drug or a high-intensity psychological intervention.
- Patients should also be made aware sexual dysfunction can be a common side effect of treatment and how to seek help if this occurs rather than stopping treatment prematurely.
- Stopping antidepressants abruptly can cause discontinuation/withdrawal symptoms. To minimise this risk when stopping antidepressants, the dose should be reduced gradually over an extended period of time.
- The MHRA has issued guidance regarding lower dose recommendations for citalopram and escitalopram due to the risk of dose-dependent QT interval prolongation[6].
- Consider MHRA updated prescribing advice for venlafaxine[7]. Treatment with venlafaxine for severe depression or patients needing doses of 300mg daily or above should be initiated by specialist mental health practitioners; venlafaxine is contra-indicated in those with an identified high risk of a serious cardiac ventricular arrhythmia and uncontrolled hypertension. Regular blood pressure monitoring is recommended for all patients taking venlafaxine.
- In 2014 the MHRA published guidance on the prescribing of SSRIs and SNRIs and associated risks[8] including information on:
    - risk of suicidal behaviour with SSRIs and SNRIs
    - withdrawal reactions with SSRIs and SNRIs
    - safety concerns of SSRIs and SNRIs in pregnancy
    - effects of SSRIs on tamoxifen effectiveness
    - small increased risk of bone fractures with SSRIs
    - venlafaxine and risks associated with overdose
    - interaction with SSRIs and SNRIs with methylthioninium chloride

APPENDIX 1 Generalised Anxiety Disorder Treatment Algorithm[3]

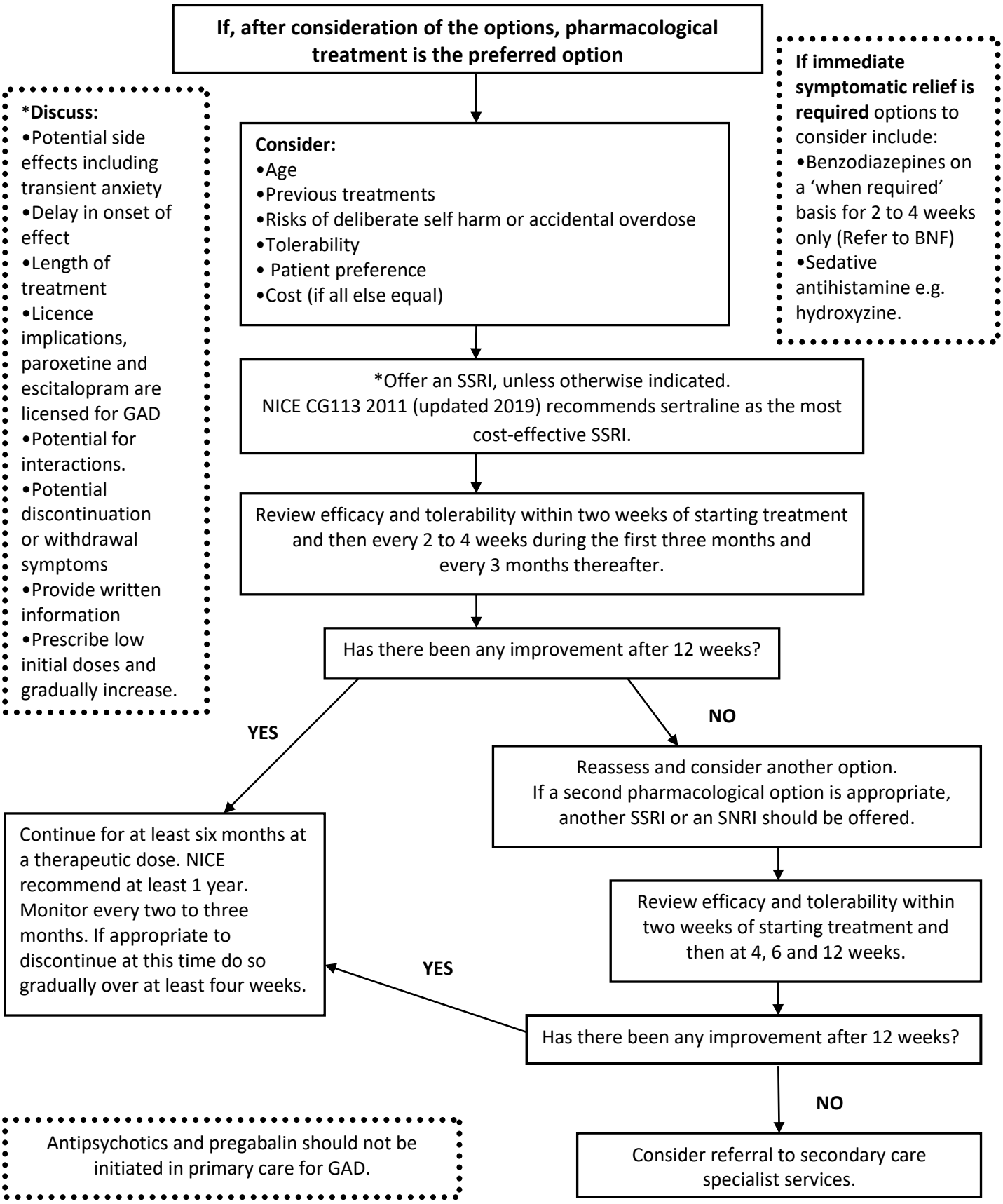
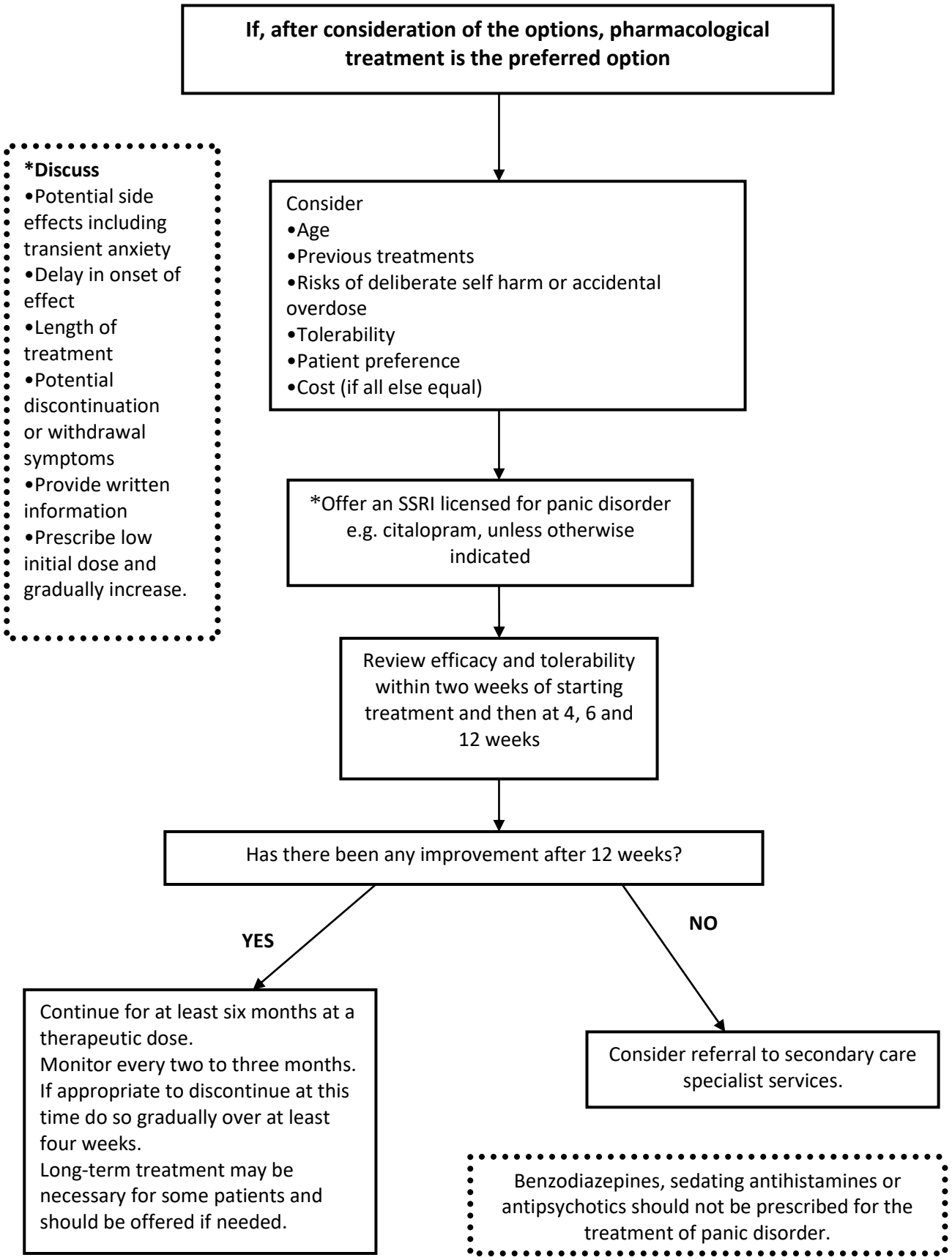


Table 1: Pharmacological Treatment of GAD[1]

First-line Drug Treatment of GAD in Primary Care	
SSRIs	
Second-line Drug Treatment	
SNRIs	
Third-line Drug Treatment	
Pregabalin	Amber-G indication

APPENDIX 2 Panic Disorder Treatment Algorithm[1,3]



APPENDIX 3 Anxiety - Further Information

Generalised anxiety disorder (GAD) is a common disorder, of which the central feature is excessive worry, tension and feelings of apprehension about everyday events. Symptoms should be present on most days for at least 6 months for a diagnosis to be made and should cause clinically significant distress or impairment in social, occupational or other important areas of functioning[2].

A panic attack is a period in which there is a sudden onset of intense fear or apprehension with associated feelings of impending doom. Panic disorder is the presence of recurring, unforeseen panic attacks followed by at least 1 month of persistent worry about having another panic attack and concern about the consequences of a panic attack or a significant change in behaviour related to the attacks. At least two unexpected panic attacks are necessary for diagnosis[1]. Panic disorder can be diagnosed with or without agoraphobia.

GAD and panic disorder vary in severity and complexity. It is important to consider symptom severity, duration, degree of distress, functional impairment, personal history and co-morbidities when undertaking a diagnostic assessment[2].

Anxiety symptoms include[3]:

Sensation of fear or dread	Irritability	Loss of concentration
Fatigue	Loss of appetite	Insomnia
Memory loss	Dizziness	Back pain
Tremor	Tensing of muscles	Perspiration
Palpitations	Hypertension	Dyspnoea
Gastro-intestinal disturbances	Chest pain	

Anxiety symptoms can be seen in depression with anxiety, psychotic illness and dementias; drug and alcohol withdrawal; some personality disorders; arrhythmias, thyrotoxicosis, hypoglycaemia and phaeochromocytoma.

Medication which can cause side effects that mimic symptoms of anxiety:

Amphetamines	Anticholinergics
Antihypertensives (hydralazine, methyldopa)	Caffeine
Digoxin toxicity	Sympathomimetics (pseudoephedrine)
Levodopa	Antipsychotics (akathisia)
Bronchodilators (salbutamol)	Thyroid hormones
SSRIs	Nicotine

References

1. NICE CG 113 Generalized Anxiety Disorder and Panic Disorder in Adults: Management. January 2011 http://guidance.nice.org.uk/CG113

2. NICE CG 123 Common Mental Health Disorders (Identification and Pathways to Care). May 2011 http://guidance.nice.org.uk/CG123

3. Guidance for healthcare professionals on drug driving. July 2014 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/325275/healthcare-profs-drug-driving.pdf

4. South West Yorkshire Partnership Foundation Trust. Greenlight Alert – Propranolol. August 2023.

5. 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. 2014 https://www.bap.org.uk/pdfs/BAP_Guidelines-Anxiety.pdf

6. MHRA Drug Safety Update Citalopram and escitalopram: QT interval prolongation—new maximum daily dose restrictions (including in elderly patients), contraindications, and warnings. December 2011 https://www.gov.uk/drug-safety-update/citalopram-and-escitalopram-qt-interval-prolongation

7. MHRA Updated prescribing advice for venlafaxine (Efexor/Efexor XL): Information for healthcare professionals. May 2006 http://webarchive.nationalarchives.gov.uk/20141205150130/http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/CON2023846

8. MHRA Dec 2014 Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs): Use and safety https://www.gov.uk/government/publications/ssris-and-snris-use-and-safety

9. The Maudsley Prescribing Guidelines in Psychiatry 2018.