| Document name: | GUIDELINES FOR THE PHARMACOLOGICAL TREATMENT OF ANXIETY  
Version 5 |
<table>
<thead>
<tr>
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<tr>
<td>Portfolio</td>
<td>Medicines Management</td>
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<tr>
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<td>All prescribers, pharmacy and clinical staff within the Trust</td>
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Guidelines for the pharmacological treatment of anxiety

Abbreviations

NICE National Institute for Health and Care Excellence
GAD Generalised anxiety disorder
EPSEs Extra-pyramidal side effects
SSRI Selective serotonin re-uptake inhibitors
SNRIs Serotonin and noradrenaline re-uptake inhibitors
GP General Practitioner
TCAs Tricyclic antidepressants
CSM Committee on Safety of Medicines (Now Commission on Human Medicines)
MHRA Medicines and Healthcare Products Regulatory Authority
CBT Cognitive behavioural therapy
### Guidelines for the pharmacological treatment of anxiety

**Key messages and Formulary choices**

#### Formulary considerations GAD

<table>
<thead>
<tr>
<th><strong>SSRIs</strong></th>
<th>Sertraline, although unlicensed, is recommended as the first line SSRI in the NICE guidance on cost effectiveness basis. Citalopram, Fluoxetine not licensed, low acquisition costs Paroxetine licensed but not recommended due to increased reporting of discontinuation symptoms and movement disorders Ecitalopram licensed but has an increased cost without a clear benefit over other SSRIs in terms of efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SNRIs</strong></td>
<td>Venlafaxine – immediate release tablets are cheaper however are unlicensed for this indication.</td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td>Benzodiazepines for short term treatment during crises Buspirone Pregabalin, use where SSRI’s or SNRI’s are not tolerated or effective. Use twice daily dosing.</td>
</tr>
</tbody>
</table>

#### Formulary considerations for Panic Disorder

<table>
<thead>
<tr>
<th><strong>SSRIs</strong></th>
<th>NICE CG 113 does not differentiate between the SSRI’s for panic disorder Citalopram, licensed Paroxetine licensed but not recommended due to increased reporting of discontinuation symptoms and movement disorders Sertraline, Fluoxetine not licensed, low acquisition costs Ecitalopram licensed but has an increases cost without a clear benefit over other SSRIs in terms of efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
<td>Clomipramine Imipramine</td>
</tr>
</tbody>
</table>

### Key points and new recommendations from NICE CG113

- Sertraline, although unlicensed is recommended as the first line SSRI in the NICE guidance on cost effectiveness basis.
- If sertraline is ineffective in the treatment of GAD, offer an alternative SSRI or a SNRI, taking into account tendency to produce withdrawal syndrome, side effect profile, drug interactions, risk of suicide and likelihood of toxicity in overdose, previous experience.
- Benzodiazepines should not be prescribed for the treatment of panic disorder as in the longer term outcomes are less good.
- In GAD benzodiazepines should be used with caution in the short term and not normally longer than two to four weeks.
Guidelines for the pharmacological treatment of anxiety

- Do not offer an antipsychotic for GAD in primary care and prescribed after due consideration of the side effect burden in secondary care.
- Doses of SSRIs and SNRIs should be started low and increased gradually to reduce the risks of initial exacerbation of anxiety symptoms.
- 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.
- For people aged under 30 who are offered an SSRI or SNRI:
  - warn them that these drugs are associated with an increased risk of suicidal thinking and self-harm in a minority of people under 30 and
  - see them within 1 week of first prescribing and
  - 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.
- Prescribe pregabalin twice a day rather than three times, it is as effective but costs are cheaper due to the pricing structure.
- Venlafaxine, the Trust recommends that generic tablets of standard preparation (immediate release formulation) venlafaxine are prescribed. If an extended release preparation is required then ensure venlafaxine XL tablets are prescribed as these are cheaper than capsules.
- In older people, generally initiation and maintenance doses are lower than those used in younger adults and gradual and careful titration is required. Monitoring should be more frequent.
- MHRA – The MHRA has issued a letter dated 24th October 2011 warning of new lower dose recommendations for citalopram due to the risk of a dose-dependent QT prolongation.
1. TREATMENT ALGORITHMS

1.1. Generalised Anxiety Disorder Algorithm

If, after consideration of the options, pharmacological treatment is the preferred option

Consider
• Age
• Previous treatments
• Risks of deliberate self harm or accidental overdose
• Tolerability
• Service user preference
• Cost (if all else equal)

*Discuss
• Potential side effects including transient anxiety
• Delay in onset of effect
• Length of treatment
• Licence implications, paroxetine and escitalopram are licensed for GAD
• Potential for interactions.
• Potential discontinuation or withdrawal symptoms
• Provide
• Written information
Prescribe low initial doses and gradually increase.

*Offer an SSRI, unless otherwise indicated. NICE CG113 2011 recommends sertraline as the most cost effective SSRI.

Review efficacy and tolerability within two weeks of starting treatment and then at 4, 6 and 12 weeks.

Has there been any improvement after 12 weeks?

Yes

Reassess and consider another option. If a second pharmacological option is appropriate, another SSRI or an SNRI should be offered.

Review efficacy and tolerability within two weeks of starting treatment and then every 2 to 4 weeks during the first three months and every 3 months thereafter.

Has there been any improvement after 12 weeks?

Yes

Continue for at least six months at a therapeutic dose. NICE recommend at least 1 year. Monitor every two to three months. If appropriate to discontinue at this time do so gradually over at least four weeks.

No

Reassess and consider another option. If another pharmacological option is appropriate, consider pregabalin.

Has there been any improvement after 12 weeks?

Yes

Reassess and consider another option. If another pharmacological option is appropriate, consider buspirone or beta-blockers or antipsychotics or combinations.

No

If immediate symptomatic relief is required pharmacological options to consider include
• Benzodiazepines on a ‘when required’ basis for 2 to 4 weeks only (Refer to the BNF)
• Sedative antihistamine e.g. hydroxyzine.

If immediate symptomatic relief is required

These options are not licensed for generalised anxiety disorder but have been shown to be effective in its management. Risks may outweigh benefits. Antipsychotics should not be prescribed in primary care for GAD.
1.2. Pharmacological Management of Panic Disorder Algorithm

If, after consideration of the options, pharmacological treatment is the preferred option

Consider
• Age
• Previous treatments
• Risks of deliberate self harm or accidental overdose
• Tolerability
• Service user preference
• Cost (if all else equal)

*Offer an SSRI licensed for panic disorder, unless otherwise indicated

Review efficacy and tolerability within two weeks of starting treatment and then at 4, 6 and 12 weeks.

Has there been any improvement after 12 weeks?

Yes

Continue for at least six months at a therapeutic dose. Monitor every two to three months. If appropriate to discontinue at this time do so gradually over at least four weeks.

No

Reassess and consider another option. If a second pharmacological option is required consider clomipramine or imipramine.*

*These options are not licensed for panic disorder but have been shown to be effective in its management.

*Discuss
• Potential side effects including transient anxiety
• Delay in onset of effect
• Length of treatment
• Potential discontinuation or withdrawal symptoms
Provide
• Written information

Prescribe low initial dose and gradually increase.
Guidelines for the pharmacological treatment of anxiety

2. INTRODUCTION

Anxiety is a normal physiological and behavioural reaction to major life events such as moving house, changing jobs or doing exams.

Generalised anxiety disorder (GAD) is excessive worry, tension and feelings of apprehension about everyday events, on most days for at least six months to the point where the person experiences distress or has problems performing day-to-day tasks.

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 occurs when there are recurrent unpredicted attacks and concern that further attacks will occur, worry about the consequences of these attacks or a significant change in behaviour related to the attacks.

Anxiety symptoms include

<table>
<thead>
<tr>
<th>Sensation of fear or dread</th>
<th>Irritability</th>
<th>Loss of concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Loss of appetite</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Memory loss</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tremor</th>
<th>Tensing of muscles</th>
<th>Perspiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpitations</td>
<td>Hypertension</td>
<td>Dyspnoea</td>
</tr>
<tr>
<td>Gastro-intestinal disturbances</td>
<td>Dizziness</td>
<td>Back pain</td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Amphetamines</th>
<th>Anticholinergics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensives (hydralazine, methyldopa)</td>
<td>Caffeine</td>
</tr>
<tr>
<td>Digoxin toxicity</td>
<td>Sympathomimetics (pseudoephedrine)</td>
</tr>
<tr>
<td>Levodopa</td>
<td>Antipsychotics, akathisia</td>
</tr>
<tr>
<td>Bronchodilators (salbutamol)</td>
<td>Thyroid hormones</td>
</tr>
<tr>
<td>SSRIs</td>
<td>Nicotine</td>
</tr>
</tbody>
</table>

NICE published clinical guidelines for the management of anxiety (panic disorder with or without agoraphobia, and generalised anxiety disorder) in adults in primary, secondary and community care in December 2004. These were amended in April 2007 in line with revised prescribing advice for venlafaxine from the MHRA. The publication of NICE CG113 in 2011 amended recommendations for the treatment of GAD. These included the recommendation of sertraline as the first line SSRI despite it being unlicensed as in their review they considered it the most cost effective SSR. The recommendations for panic disorder are unchanged.

This document will concentrate on the pharmacological treatment options. Other recommended options include psychological therapies such as cognitive behavioural therapy (CBT) and self help (such as support groups and bibliotherapy). Psychological therapies have the longest duration of effect.

For information on psychological treatments refer to the NICE guideline or the local Psychological Services Department.
3. GENERAL PRINCIPLES

NICE Key Messages

- Anxiety disorders are common, chronic, the cause of considerable distress and disability and often go untreated.
- If left untreated, they are costly to both the individual and society.
- A range of effective interventions is available to treat anxiety disorders, including medication, psychological therapies and self help.
- Individuals do get better and remain better.
- Involving individuals in an effective partnership with health care professionals, with all decision-making being shared, improves outcomes.
- Access to information, including support groups is a valuable part of any package of care.

- If low mood or loss of interest are present guidelines for the treatment of depression should be followed (NICE or Trust).
- These guidelines do not cover agoraphobia, social phobia or simple phobias (episodes triggered by external stimuli).
- Treatment of GAD and panic disorder should be offered in primary care in the first instance.
- The choice of treatment should be shared between the service user and the healthcare professionals. This improves concordance and clinical outcomes. Consider service user preference, experience and outcomes of previous treatments.
- Be alert to co-morbidity, which is common (particularly anxiety with depression and anxiety with substance misuse).
- Personal history, any self-medication, cultural and individual characteristics are important considerations in care.
- The rest of the document will assume service user preference is for pharmacological therapy, but at each review other options should be discussed. If the first intervention does not lead to an improvement another of the first line options should be considered.
- Aims of treatment in GAD are to reduce symptoms of anxiety and to minimise disruption to day to day functioning, with minimal adverse effects.
- 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.
- If medication is prescribed, review efficacy and side effects of treatment at regular intervals, more frequently in the early stages.
- The Hamilton Anxiety Scale can be used to measure efficacy in GAD.
- Benzodiazepines should not be prescribed for the treatment of panic disorder as in the longer term outcomes are less good.
- In GAD benzodiazepines should be used with caution in the short term and not normally longer than two to four weeks.
- Clinical judgement may suggest that continuing a course of benzodiazepines for longer than one month would be more beneficial for an individual than alternative treatments. The service user should be warned of the risks of tolerance and dependence, prescribing should be reviewed at regular intervals and periodic attempts to slowly reduce and stop should be made.
- Doses of SSRIs and SNRI should be started low and increased gradually to reduce the risks of initial exacerbation of anxiety symptoms.
- Monitor closely for suicidal ideation and behaviour during treatment with antidepressants and pregabalin.
- For people aged under 30 who are offered an SSRI or SNRI:
o warn them that these drugs are associated with an increased risk of suicidal thinking and self-harm in a minority of people under 30 and see them within 1 week of first prescribing and
  o 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.
• Prescribe pregabablin twice a day rather than three times, it is as effective but costs are cheaper due to the pricing structure.
• Referral to specialist mental health services should be considered if symptoms remain after two interventions. Pharmacological and psychological therapies should be further explored.
• For people who develop side effects soon after starting drug treatment, provide information and consider one of the following strategies:
  o monitoring the person’s symptoms closely (if the side effects are mild and acceptable to the person) or
  o reducing the dose of the drug or
  o stopping the drug and, according to the person’s preference, offering either an alternative drug or a high-intensity psychological intervention.

Service user information

Before prescribing any medication, discuss the treatment options and any concerns the person with GAD or panic disorder 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 1 week or more, of the full anxiolytic effect
  • the importance of taking medication as prescribed and the need to continue treatment after remission to avoid relapse.
  • Refer to www.choiceandmedication.org/swyt

Committee on Safety of Medicines (CSM) and Medicines and Healthcare Regulatory Authority (MHRA) Advice

• Hyponatraemia (usually in the elderly and possibly due to inappropriate secretion of antidiuretic hormone) has been associated with all types of antidepressants, however it has been reported more frequently with SSRIs than with other antidepressants. The CSM has advised that hyponatraemia should be considered in all patients who develop drowsiness, confusion or convulsions while taking an antidepressant.

• CSM advice (SSRIs for major depressive disorder in children and adolescents): following a review of the safety and efficacy of SSRIs for the treatment of depression in children and adolescents the CSM has advised (December 2003) that the SSRIs citalopram, escitalopram, paroxetine and sertraline and the related antidepressant venlafaxine are contra-indicated in those under 18 years; fluvoxamine should also not be used to treat depression in these individuals because there is insufficient information on safety and efficacy.

• CSM advice (paroxetine dosage): the recommended dose for the treatment of depression, social anxiety disorder, generalised anxiety disorder, and post-traumatic stress disorder is
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20mg and for obsessive-compulsive disorder and panic disorder it is 40mg daily. There is no
evidence that higher doses are more effective.

- CSM advice (venlafaxine): treatment with venlafaxine for those with severe depression or
those needing doses of 300mg daily or above should be initiated by specialist mental health
practitioners and there should be arrangements in place for continuing supervision of the
patient. The CSM also advised that 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.

- MHRA – The MHRA has issued a letter dated 24th October 2011 warning of new lower dose
recommendations for citalopram due to the risk of a dose-dependent QT prolongation. These
followed the FDA lead from August and are as follows:
  - Citalopram should not be used above 40mg/d in adults (is unlicensed in under 18s)
  - Citalopram should not be used above 20mg/d in the elderly and people with reduced hepatic
    function
  - Citalopram is contraindicated in people:
    o with a known QT prolongation or congenital long QT syndrome
    o taking other medicines known to prolong QT interval*
  - Citalopram should only be used with caution in people with higher risk of developing
    Torsades de Pointes e.g. CHF, recent MI, bradyarrhythmias, or hypokalaemia or
    hypomagnesaemia

- 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.
### 4. MEDICATION

#### 4.1. Generalised Anxiety Disorder

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
<th>Costs per 28 days supply</th>
<th>Licensed / Unlicensed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRI antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine, citalopram, fluoxetine, fluvoxamine, sertraline</td>
<td>Low toxicity in overdose. Less sedative than other antidepressants. Less anticholinergic side effects than TCAs. Evidence of long term benefit. <strong>Sertraline, although unlicensed is recommended as the first line SSRI in the NICE guidance on cost effectiveness basis</strong></td>
<td>Delayed onset of effects. Exacerbation of symptoms in early stages. Withdrawal/discontinuation symptoms (more reports for paroxetine than other SSRIs).</td>
<td>Paroxetine 20mg once a day £1.79</td>
<td>Licensed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Escitalopram has an increased cost without a clear benefit over other SSRIs in terms of efficacy</td>
<td>Citalopram 20mg once a day £0.96</td>
<td>Not licensed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fluoxetine 20mg once a day £0.89</td>
<td>Not licensed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sertraline 50mg once a day £1.38</td>
<td></td>
</tr>
<tr>
<td>Escitalopram,</td>
<td></td>
<td></td>
<td>Escitalopram 10mg once a day £14.91</td>
<td>Licensed</td>
</tr>
<tr>
<td><strong>SNRI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Less sedative than other antidepressants. Less anticholinergic side effects than TCAs. Generic preparation of venlafaxine available Use immediate release preferentially, although these products do not have a license for GAD</td>
<td>Delayed onset of effects Exacerbation of symptoms in early stages. Withdrawal/discontinuation symptoms Blood pressure monitoring recommended.</td>
<td>Venlafaxine I/R tablets 37.5mg bd £2.53</td>
<td>Licensed for generalized anxiety disorder (only the modified release prep of venlafaxine is licensed)</td>
</tr>
<tr>
<td>Duloxetine</td>
<td></td>
<td></td>
<td>Venlafaxine M/R tablets 75mg once a day £10.45 (NB M/R capsules 75mg once a day £22.08)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Duloxetine 60mg once a day £27.72</td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
<td>Licensed for short term use in anxiety</td>
</tr>
<tr>
<td></td>
<td>Appropriate for immediate symptom management.</td>
<td>Sedative, long term efficacy not established. May lead to worse outcome than other treatment options. Tolerance and dependence if used long term.</td>
<td>Diazepam 5mg three times a day £2.58</td>
<td></td>
</tr>
<tr>
<td><strong>Sedating antihistamines</strong></td>
<td></td>
<td>Sedating. Benefit on long term outcomes unclear.</td>
<td>Hydroxyzine 50mg four times a day £9.76</td>
<td>Licensed for anxiety</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Appropriate for immediate symptom management.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pregabalin</strong></td>
<td>Evidence of benefit in short and long term May be used after an SSRI or SNRI</td>
<td>Sedation and dizziness, especially initially. Withdrawal / discontinuation may occur. Weight gain. Twice daily use is more cost effective. Some reports of misuse and diversion</td>
<td>Pregabalin 150mg mg twice daily £64.40 (100mg three times a day £96.60)</td>
<td>Licensed for generalized anxiety disorder</td>
</tr>
</tbody>
</table>
### Guidelines for the pharmacological treatment of anxiety

<table>
<thead>
<tr>
<th>Antipsychotics</th>
<th>Low proven efficacy. Any symptom control is probably due to sedative action. Risks of side effects outweigh benefits. Reserve for refractory anxiety disorders or infrequent sustained agitation</th>
<th>Costly in many cases see schizophrenia guidelines</th>
<th>Some licensed as adjunct in severe anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Buspirone</strong></td>
<td>Non-sedative. Lower incidence of abuse or dependence compared with benzodiazepines. Slow onset of action, requires at least four weeks at 10mg three times a day. Short term use only. Prescribing should not be transferred to primary care unless agreed with GP.</td>
<td>Buspirone 10mg three times a day £30.91</td>
<td>Licensed for anxiety</td>
</tr>
<tr>
<td><strong>Beta-blockers</strong></td>
<td>Non-sedative. No dependence or abuse. Do not help psychological symptoms. High doses may lead to cardiac side effects.</td>
<td>Propranolol 40mg three times a day £2.76</td>
<td>Licensed for anxiety with somatic symptoms</td>
</tr>
<tr>
<td><strong>Other antidepressants</strong></td>
<td>Adverse effects may outweigh benefits. Some evidence for efficacy for imipramine</td>
<td></td>
<td>Not licensed</td>
</tr>
</tbody>
</table>

*Many of these products are in Category M of the drug tariff and are subject to significant price changes from month to month.*
### 4.2. Panic Disorder

<table>
<thead>
<tr>
<th>Drug</th>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
<th>Costs per 28 days supply</th>
<th>Licensed / Unlicensed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRIs</strong>&lt;br&gt;Paroxetine&lt;br&gt;Citalopram&lt;br&gt;Escitalopram, approved for the treatment of GAD in SWYMH&lt;br&gt;Fluoxetine, Sertraline and fluvoxamine</td>
<td>Low toxicity in overdose&lt;br&gt;Less sedative than other antidepressants.&lt;br&gt;Less anticholinergic side effects than TCAs.&lt;br&gt;Evidence of long term benefit.</td>
<td>Delayed onset of effects&lt;br&gt;Exacerbation of symptoms in early stages.&lt;br&gt;Withdrawal/discontinuation symptoms (more reports for paroxetine than other SSRIs).&lt;br&gt;Escitalopram has an increased cost without a clear benefit over other SSRIs in terms of efficacy</td>
<td><strong>Paroxetine 20mg once a day £1.79</strong>&lt;br&gt;<strong>Citalopram 20mg once a day £0.96</strong>&lt;br&gt;<strong>Escitalopram 10mg once a day £14.91</strong>&lt;br&gt;<strong>Fluoxetine 20mg once a day £0.89</strong>&lt;br&gt;<strong>Sertraline 50mg once a day £1.38</strong></td>
<td>Licensed&lt;br&gt;Licensed&lt;br&gt;Licensed&lt;br&gt;Not licensed&lt;br&gt;Not licensed</td>
</tr>
<tr>
<td><strong>Tricyclic antidepressants</strong>&lt;br&gt;Clomipramine&lt;br&gt;Imipramine</td>
<td>Good supporting evidence for efficacy.</td>
<td>Anticholinergic side effects including constipation dry mouth and blurred vision.&lt;br&gt;Sedative.&lt;br&gt;Cardiotoxic in overdose.</td>
<td><strong>Clomipramine 150mg a day £6.69</strong>&lt;br&gt;<strong>Imipramine 150mg a day £7.74</strong></td>
<td>Not licensed</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong>&lt;br&gt;E.g. Diazepam</td>
<td>Rapid anxiolytic effect.</td>
<td>Sedative, long term efficacy not established. May lead to worse outcome than other treatment options.&lt;br&gt;Tolerance and dependence if used long term.</td>
<td><strong>Diazepam 5mg three times a day £2.58</strong></td>
<td>Licensed for anxiety but not specific panic disorder</td>
</tr>
<tr>
<td><strong>Antihistamines</strong></td>
<td>No evidence of efficacy, sedative.</td>
<td></td>
<td></td>
<td>Not licensed</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td>No evidence of efficacy, sedative and high risk of side effects.</td>
<td></td>
<td></td>
<td>Not licensed</td>
</tr>
</tbody>
</table>
5. SPECIAL CONSIDERATIONS

5.1. Elderly Patients

Treatment for anxiety in older people should follow the same principles as for other patient groups. Many treatment regimens have not been studied directly in the elderly.

Pharmacodynamic and pharmacokinetic age related changes alter response to medication. This makes older people more prone to side effects due to increased end organ sensitivity, reduced circulation and reduced renal clearance. This is particularly important with tricyclic antidepressants and benzodiazepines.

Generally initiation and maintenance doses are lower than those used in younger adults and gradual and careful titration is required. Monitoring should be more frequent.

5.2. Pregnancy

- The risks of medication should be balanced against the risks of symptom relapse. Uncontrolled symptoms may affect the mother/child relationship directly or via an increase in risk taking, such as co-morbid alcohol, drug and nicotine use.
- Risks associated with use of medication to treat GAD and panic disorder in pregnancy include teratogenicity and neonatal side effects. The latter may be toxicity or withdrawal effects.
- A possible small increased risk of congenital cardiac defects may be seen in association with fluoxetine, similar to that seen with paroxetine.
- SSRIs and SNRIs given in the later stages of pregnancy may increase the risk of persistent pulmonary hypertension in the newborn.
- Some of the benzodiazepines are associated with an increased risk of teratogenicity. Taken close to birth the benzodiazepines may lead to withdrawal symptoms, floppy baby syndrome and respiratory depression in the neonate.
- Most of the danger for organ damage is in weeks 3 to 8 post conception. This may be before a woman is actually aware she is pregnant. All women of childbearing age should be advised about the importance of effective contraception. The woman should be encouraged to plan her pregnancy in conjunction with the psychiatrist or other clinician.
- Treatment options will depend on the patient’s previous history and the patient’s and clinician’s preferences. These may include switching treatment, a treatment break during the first trimester, continuing current effective treatment with monitoring or reducing or stopping treatment before delivery.
- NICE Guidance for Antenatal and Postnatal Mental Health recommend that benzodiazepines are not routinely prescribed to pregnant women except for the short term treatment of extreme anxiety and agitation. Gradual discontinuation should be considered in pregnant women already prescribed benzodiazepines.
- CBT or other non-pharmacological intervention is preferred. Do not use paroxetine.
- It is important to ensure all healthcare professional involved in the pregnancy and delivery are aware of any medication being prescribed.
6. REFERENCES AND FURTHER READING

1. NICE Clinical Guideline 113. Generalized anxiety disorder and panic disorder, with or without agoraphobia, in adults; Management in primary, secondary and community care. January 2011
5. Medicines and Healthcare Regulatory Authority/Committee on Safety of Medicines www.mhra.gov.uk
13. Hypnotics in clinical practice: Guidance on the use of hypnotics for the management of insomnia. SWYMHT, July 2010
14. Drug Tariff
15. Drug Safety Update, March 2010
APPENDIX 1 - Discontinuation /Withdrawal Symptoms Associated with Antidepressants

Stopping antidepressants abruptly can cause discontinuation/withdrawal symptoms. To minimize the risk, the dose should be reduced gradually over an extended period of time.

Symptoms are usually mild and self-limiting but can occasionally be severe especially if the antidepressant is stopped abruptly.

Some commonly experienced withdrawal symptoms

<table>
<thead>
<tr>
<th>Flu-like symptoms (chills, aches, sweating)</th>
<th>Nausea and vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>Numbness and tingling (electric shock sensations)</td>
</tr>
<tr>
<td>Irritability</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Excessive (vivid) dreams</td>
</tr>
</tbody>
</table>

Not all symptoms are associated with every antidepressant and may not all be experienced by one individual. The perception of symptoms may be made worse if no prior warning is given.

Symptoms of discontinuation may be misinterpreted as relapse of the original illness or a new physical illness. Onset is usually within 5 days of stopping, depending on the half-life of the antidepressant.

If symptoms are mild, discussion of the reason for the symptoms and reassurance of the self-limiting nature are required. The service user should be monitored for resolution of the symptoms.

If symptoms are severe the re-introduction of the antidepressant should be considered followed by a more gradual reduction. The use of another antidepressant from the same class with a longer half-life may make reduction easier. Fluoxetine, having a longer plasma half-life, seems to be associated with a lower incidence of discontinuation symptoms than other similar antidepressants (but is not licensed for the indications in this document).