# 122 - Psychological approaches

# Psychological approaches

Depression and anxiety disorders CHAPTER 3 OCD (where there is moderate or severe functional impairment) ■ ■Use an SSRI or intensive CBT. ■ ■Combine the SSRI and CBT if the response to a single strategy is suboptimal. ■ ■Use clomipramine if SSRIs fail. ■ ■If response is still suboptimal, add an antipsychotic or combine clomipramine and citalopram. Boxes 3.6–3.10 give details of specific drugs used in anxiety spectrum disorders. Box 3.6 Generalised anxiety disorder Drug Comment Crisis management Benzodiazepines Normally for short-term use only, maximum 2–4 weeks, although some are of the opinion that risks are overstated44 First-line treatment (in order of preference)30 SSRIs (up to maximum licensed dose) May initially exacerbate symptoms. A lower starting dose is recommended. Fluoxetine and sertraline are preferred options.12 Vortioxetine may not be effective.45 SNRIs14 (up to maximum licensed dose) May initially exacerbate symptoms. A lower starting dose is recommended. Pregabalin 150–600mg/day in divided doses Response may be seen in the first week of treatment.46 Increasingly misused. Significant withdrawal syndrome. Overdose risk with opiates. Second-line treatment (less well tolerated or weaker evidence base; no order of preference) Agomelatine47 10–50mg/day Agomelatine has been shown to prevent relapse over a 6-month period48,49 Betablockers Propranolol 40–120mg/day in divided doses Initiate at 40mg and titrate dose up to effect if needed. Useful for somatic symptoms, particularly tachycardia.50 Otherwise has limited efficacy. Highly toxic in overdose.51 Buspirone 15–60mg/day in divided doses Has a delayed onset of action; takes up to 6 weeks to show equal efficacy to benzodiazepines52 Hydroxyzine 50–100mg/day in divided doses Unclear that hydroxyzine is effective due to a direct anxiolytic effect or to a broader sedative effect53 Quetiapine (MR, 50–300mg) Recommended as monotherapy. Probably not effective as adjunctive therapy to SSRI/SNRI in treatment resistance.54 Tricyclic antidepressants Clomipramine 50–250mg/day55–57 Initiate at 10mg/day and increase the dose gradually Imipramine 75–200mg/day in divided doses58 Initiate at 25mg/day every 4 days and when at 100mg can increase in 50mg increments10 (Continued)

450 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Drug Comment Monoamine oxidase inhibitors Phenelzine 45–90mg/day in divided doses59 For mixed anxiety and depressive states. Patients need to avoid food high in tyramine. Mirtazapine 15–30mg at night60,61 Experimental Cannabidiol Large effect size62 Chamomile 220–1500mg/day Two RCTs, one positive, one negative using standardised doses of chamomile and placebo63 Gingko biloba 240–480mg/day

One positive RCT using standardised doses of Gingko biloba and placebo64 Ketamine Seemingly rapidly effective65 Lavender oil preparation 80–160mg/day Substantial supporting evidence66 Riluzole 50–100mg/day doses67 Liver function monitoring required Box 3.7 Panic disorder Drug Comment Crisis management Benzodiazepines Rapid effect although panic symptoms return quickly if the drug is withdrawn.68 NICE does not recommend.6 Cochrane lukewarm.69 Probably the most effective treatment.70 Alprazolam is not superior to other benzodiazepines71 and its effects may have been overestimated.72 First-line treatment (in order of preference)6,73 SSRIs (up to maximum licensed dose) Therapeutic effect can be delayed (this applies to all antidepressants)74 and patients can experience an initial exacerbation of panic symptoms.6 Use supported by Cochrane75 and a 2022 meta-analysis.76 Venlafaxine MR 75–225mg73 Initiate at 37.5mg for 7 days (Continued)

Depression and anxiety disorders CHAPTER 3 Drug Comment Second-line treatment (less well tolerated or weak evidence base; no order of preference) Mirtazapine 15–60mg/day77 A meta--analysis suggests that mirtazapine does not help with panic symptoms but with the anxiety associated with this disorder.73 Rather limited data overall.78 Moclobemide 300–600mg/day79 One fixed dose study of 450mg/day and one flexible dose study suggest efficacy.79,80 Brofaromine (a similar drug) is also effective.70 Monoamine oxidase inhibitors Phenelzine 10–60mg/day74 No long-term studies; reserve for treatment-resistant cases due to poor tolerability74 Tricyclic antidepressants Clomipramine 25–250mg/day74 Start with a low dose and increase dose according to response and tolerability. Good evidence of effectiveness.70 Imipramine 25–300mg/day74 Lofepramine 70–210mg/day in divided doses81 Experimental Gabapentin 600–3600mg/day One RCT showed no difference between gabapentin and placebo. However, significant improvement was demonstrated in the more severely ill.82 Inositol 12g/day83 One positive RCT in 21 patients. Equivalent to fluvoxamine in one study.84 Well tolerated. Levetiracetam 250mg twice daily78 Usually well tolerated Pindolol 7.5mg/day Efficacy suggested in a small 21 patient RCT where 2.5mg tds was used to augment fluoxetine in treatment-resistant panic disorder85 Valproate 500–2250mg/day Two very small positive open studies86,87 Hydrocortisone Only acute treatment shown to prevent development of post-traumatic stress disorder88

Box 3.8 Post-traumatic stress disorder Drug Comments First-line treatment (in order of preference) (Psychological approaches should be used before drug treatments)89,90 SSRIs (up to maximum licensed doses) Paroxetine, sertraline or fluoxetine are the preferred SSRIs.91,92 Recommended by NICE.89 Good support but small effective size.93,94 Venlafaxine modified release 37.5–300mg95 Recommended by NICE89 Supported by meta-analyses93,96 Second-line treatment (less well tolerated or weak evidence base; no order of preference) Antipsychotics May be effective for the intrusion symptoms (flashbacks and nightmares) but not the avoidance and hyperarousal symptoms of post-traumatic stress disorder. Studies done as monotherapy or as adjunctive treatment.97 Olanzapine 5–20mg May be the most effective treatment96 Risperidone 0.5–6mg Specifically mentioned by NICE89 Quetiapine 50–800mg98 More robust support than for risperidone93,96 Mirtazapine 15–45mg/day99 Recommended by NICE89 Second most effective drug in a network meta-analysis100 Monoamine oxidase inhibitors Phenelzine 15–75mg/day101 Recommended by NICE89 Most effective drug in a network meta-analysis100 Prazosin 2–15mg at night102 For nightmares and sleep disturbances. Initiate at 1mg at night and titrate dose gradually to reduce the risk of hypotension. Supported by a systematic review103 and meta-analysis.93

Tricyclic antidepressants Start at a low dose and increase dose according to tolerability Amitriptyline 50–300mg/day104 Recommended by NICE89 For all TCAs start at a low dose and increase dose according to tolerability Imipramine 50–300mg/day Best supporting evidence is for desipramine but this drug is not widely available100 Ketamine IV105,106 Rapid reduction in symptom severity suggested. Developing evidence showing acute and chronic efficacy.107–109 Experimental Duloxetine 60–120mg Two small open studies suggest efficacy. Start at 30mg for 1 week110,111 Lamotrigine up to 500mg/day Small double-blind study in 15 patients112 MDMA--assisted therapy Developing database113 Phenytoin plasma concentration 10–20ng/ml114 Open-label study in 12 patients Valproate up to 2.5g115 Probably not effective100 MAOI, monoamine oxidase inhibitor; MDMA, 3,4-methylenedioxymethamphetamine.

Depression and anxiety disorders CHAPTER 3 Box 3.9 Obsessive–compulsive disorder Drug Comments First-line treatment (in order of preference) Any SSRI41 (up to maximum licensed dose) If the first SSRI is not tolerated or has a poor response an alternative SSRI may be tried30 Clomipramine (up to 250mg) Owing to poorer tolerability, recommended trying at least one SSRI first30 Second-line treatment (unlicensed or weaker evidence base; in no order of preference) Add antipsychotic to SSRI (low to moderate doses)116,117 Most evidence supports the use of aripiprazole or risperidone.116 Some evidence for haloperidol.117 Citalopram 40mg with clomipramine 150mg Based on small randomised open-label study.118 Recommended by NICE.30 ECG monitoring required. Acetylcysteine119 (up to 2400mg/day added to SSRI or clomipramine) GI adverse effects may be problematic. Two of five controlled studies negative. Pooled effect shows benefit.120 Lamotrigine 100mg+ added to SSRI121 Dose must be titrated gradually as indicated in the summary of product characteristics. May worsen OCD in some.122 Topiramate up to 400mg added to SSRI123,124 Not well tolerated; suggested benefits for compulsion but not obsessions.123 Two trials found it ineffective125,126 Experimental High-dose SSRIs Dose titrated gradually according to tolerability. ECG monitoring recommended. Higher doses have been safely used29 (e.g. sertraline 650mg, fluoxetine 120mg/day) Escitalopram 25–50mg127 Sertraline 250–400mg128 Memantine Good evidence for 20mg/day added to SSRIs.129 Most effective add-on treatment in a 2023 meta-analysis.130 NSAIDs (e.g. celecoxib 400mg/day) Some supporting evidence126 Amantadine 200mg/day One positive RCT131 SNRIs Venlafaxine up to 375mg132 Duloxetine 60mg133 Mirtazapine 30–60mg134 Small trial in 30 patients 5HT3 antagonists Granisetron 1mg with fluvoxamine 200mg135 Some evidence for each drug but ondansetron may be the more effective130,137,138 Ondansetron 4mg with fluoxetine 20mg136 (Continued)

 Drug Comments Pregabalin 75–225mg/day added to sertraline One small positive RCT139 Riluzole 50mg bd added to existing drug treatment140 Variable results in early trials126 Anti-androgen – triptorelin 3.75mg IM every 4 weeks added to existing drug treatment141 Open-label study done in six men Psilocybin Emerging evidence for effect142,143 IV treatment Quicker onset of action suggested compared with oral treatments Clomipramine IV144 IV may be more effective than oral clomipramine Ketamine IV145,146 Developing evidence base126 Once-weekly morphine 15–45mg added to existing drug treatment147 Small study involving 23 treatment-resistant patients. Positive effects were transient. Box 3.10 Social phobia (social anxiety disorder) Drug Comments First line drug treatment148 (in order of preference) SSRIs (up to maximum licensed dose) If no response to the first SSRI, try an alternative SSRI. Supporting meta-analyses for fluvoxamine149 and citalopram.150 Emerging data for vilazodone.151 Venlafaxine modified release 75–225mg/day Supporting meta-analysis152 Second line drug treatment (less well tolerated or weaker evidence

base, no order of preference) Olanzapine 5–20mg153 Few studies with antipsychotics. Most evidence with olanzapine. Atenolol 25–100mg/day Reduces autonomic symptoms in performance situations.153 Probably not effective in social phobia.154 Benzodiazepines: Helpful on prn basis. Most evidence for treatment with clonazepam and bromazepam. Switching an SSRI to venlafaxine no more effective than adding clonazepam to SSRI.155 Clonazepam 0.3–6mg/day153 Sertraline plus clonazepam up to 3mg/day155 Gabapentin 900–3600mg/day153 (Continued)

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Revision #1
Created 2026-01-04 20:15:07 UTC by Omar Ayman
Updated 2026-01-04 20:15:07 UTC by Omar Ayman