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Prescribing for anxiety disorders in children and adolescents

582 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 5 Anxiety disorders in children and adolescents Diagnostic issues Fear and worry are common in children and they are part of normal development. At the same time, anxiety disorders often begin in childhood and adolescence1 and they are the most common psychiatric disorders in this age group, with overall prevalence between 8% and 30% depending on the impairment cut-offs used.2 Anxiety disorders may be even more common in children with neurodevelopmental disorders.3 In children, the more obvious clinical presentation with distress and avoidance may be masked by prominent behavioural symptoms (e.g. irritability and angry outbursts linked to avoidance). Therefore, the assessment and treatment of anxiety disorders in children need to be undertaken by clinicians who can discriminate normal, developmentally appropriate worries, fears and shyness from anxiety disorders that significantly impair a child's functioning, and who can appreciate developmental variations in the presentation of symptoms. Clinical guidance Anxiety symptoms in children and adolescents often improve with age, presumably in parallel to the development of the prefrontal cortex and, in particular, executive function. However, anxiety disorders are distressing and impairing conditions that need to be treated promptly. Chronic stress mediators may have significant impact on brain development4 and functional impairment linked to anxiety symptoms may prevent young people from accessing normative experiences that are critical for social, emotional and cognitive development. Finally, early and effective treatment may prevent continuity of psychopathology into adulthood: for example, young people with anxiety disorders are three times more likely to have anxiety and depression in adult life compared with non-anxious youth.5 Guidelines for the treatment of anxiety disorders in children and adolescents have been made available in the UK and the USA. NICE guidelines focus on the treatment of social anxiety disorder in children and adolescents, suggesting the use of cognitive behavioural therapy and cautioning against the routine use of pharmacological treatment for social anxiety in this age

group.6 Guidelines from AACAP cover the treatment of all anxiety disorders except post-traumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) (which are classified separately according to DSM).7 AACAP guidelines suggest multimodal treatment including psychoeducation, psychotherapy (e.g. a 12-session course of exposure-based CBT) and pharmacotherapy. Drug treatment is endorsed for moderate-to-severe anxiety symptoms, when impairment makes participation in psychotherapy difficult, or when psychotherapy leads to only partial response. Prescribing for anxiety disorders in children and adolescents Before prescribing ■ ■Exclude other diagnoses: Anxiety symptoms can be mimicked by a range of psychiatric disorders including depression (inattention, sleep problems), bipolar disorder (irritability, sleep problems, restlessness), oppositional-defiant disorder (irritability,

Prescribing in children and adolescents CHAPTER 5 oppositional behaviour), psychotic disorders (social withdrawal, restlessness), ADHD (inattention, restlessness), autism spectrum disorder (social withdrawal, poor social skills, repetitive behaviours and routines) and learning disabilities. They may also be mimicked by a range of endocrine (hyperthyroidism, hypoglycaemia, phaeo-chromocytoma), neurological (migraine, seizures, delirium, brain tumours), cardiovascular (cardiac arrhythmias) and respiratory (asthma) conditions and lead intoxication. Anxiety-like symptoms can be observed in response to several drugs and substances including anti-asthma medications, sympathomimetics, steroids, SSRIs, antipsychotics (akathisia), diet pills, cold medicines, caffeine and energy drinks. ■ ■Beware contraindications to SSRIs and potential interactions. ■ ■Measure baseline severity: Use structured interviews including the Anxiety Disorders Interview Schedule (ADIS) and the Kiddie-Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS); questionnaires including the Revised Children's Anxiety and Depression Scale (RCADS), Screen for Child Anxiety and Related Emotional Disorders (SCARED) or the Multidimensional Anxiety Scale for Children (MASC); and measures of functional impairment including the Children's Global Assessment Scale (CGAS). ■ ■Obtain consent: Discuss treatment with the young person and the family (e.g. name of medication, starting/estimated ending dose, titration timeline, possible side effects and strategies to monitor/minimise them, strategies to monitor progress, interventions for treatment-resistant cases). Document consent in writing. What to prescribe ■ ■SSRIs: These are the medications of choice for the treatment of anxiety disorders in children and adolescents. SSRI treatment is at least as effective as non-drug treatments.8 A 2019 meta-analysis identified seven short-term RCTs (<16 weeks; n treatment = 446, n control = 386) testing the efficacy of SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline) on changes in severity of anxiety in young people (Clinical Global Impression I [CGI-I] scale). The odds ratio (vs placebo) of overall treatment response was 4.6 (95%CI = 3.1–7.5) and, in anxiety symptoms specifically, 5.2 (95%CI = 2.8–8.8).9 The Childhood Anxiety Multimodal Study (CAMS) showed that monotherapy with sertraline (55% response) is as effective as CBT for anxiety (60% response) and better than placebo (24% response), and that combined therapy with sertraline and CBT is most likely to be successful (81% response).10 A 2017 network meta-analysis found that SSRIs significantly reduce clinician-reported and parent-reported (but not child-reported) anxiety symptoms and increased rates of remission.11 Another network meta-analysis found that the likelihood of treatment response was higher for SSRI compared with the following other medications;9 a standard meta-analysis showed that clinically significant treatment effects typically emerge by week 6 of treatment, and that SSRIs are associated with more rapid and greater improvement than these other medications.12 The most recent meta-analysis (11 studies, 2122 participants [2023])13 suggests broadly similar efficacy for SSRIs/ serotonin–noradrenaline reuptake inhibitors (SNRIs). With regard to tolerability, SSRIs are

the best tolerated class of medications, particularly escitalopram and fluoxetine.14

584 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 5 Sertraline, fluoxetine and fluvoxamine have been approved by the US FDA for treatment of paediatric OCD, and fluoxetine and escitalopram have been approved for treatment of paediatric depression. The FDA issued in 2004 a black box warning for concerns related to worsening of depression, agitation and suicidal ideation linked to SSRIs. These concerns were based on a review of studies of adolescents with depression rather than young people with anxiety. ■ ■SNRIs: Venlafaxine was tested in two short--term RCTs (n treatment = 294, n control = 311), duloxetine was tested in one short-term RCT (n treatment = 135, n control = 137) and atomoxetine was tested in one short-term RCT. The overall odds ratio of treatment response for SNRIs was 2.4 (95%CI = 1.7–3.6) over placebo.9 However, SNRIs did not show statistically significant effects on improvement in anxiety symptoms over placebo.9 The network meta-analysis mentioned earlier found that SNRIs significantly reduce clinician-reported (but not parent-reported or child-reported) anxiety symptoms.11 SSRIs are more effective and better tolerated9 so SNRIs could be considered a third-line treatment for anxiety disorders when two trials with different SSRIs prove ineffective. ■ ■Others: The 5HT1A agonist buspirone has been examined in one short-term RCT (n treatment = 334, n control = 225) and found not to be effective.15 The alpha2 agonist guanfacine was evaluated in one short-term RCT (n treatment = 62, n control = 21) and found to be associated with an increased odds ratio for treatment response (5.6 [95%CI = 1.4–26.8]) but not for improvement in anxiety symptoms.16 ■ ■Neither benzodiazepine nor tricyclic antidepressant use is supported by controlled trials in children.9 Benzodiazepine may also lead to paradoxical disinhibition in some children. Nevertheless, use of longer-acting benzodiazepines is at times considered in clinical practice either to alleviate disabling anxiety during initial titration of SSRIs or for rapid tranquillisation. Table 5.7 lists the doses for treating anxiety disorders in children and adolescents. After prescribing Acute phase ■ ■Start at the lowest available dose. ■ ■Monitor side effects. SSRIs are generally well tolerated during treatment for anxiety disorders in young people. Psychological side effects include worsening of anxiety symptoms, agitation and disinhibition. Physical side effects including gastrointestinal symptoms (e.g. nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, constipation), headache, increased motor activity and insomnia may occur, often in mild and transient form. ■ ■After 1 week of treatment with SSRIs (2 weeks for SNRIs) when the child is compliant with medications and does not manifest more than minimal side effects, titrate incrementally with weekly intervals to the minimal therapeutic dose. ■ ■Monitor side effects and response (e.g. RCADS, SCARED, MASC, CGAS, CGI-I) frequently and systematically. ■ ■Dosage for treatment with SSRIs is often similar to dosage in adults because of faster metabolism in children. ■ ■Therapeutic effect should appear by 6–8 weeks of treatment. It is important to communicate this to families. ■ ■If partial or non-response, consider accuracy of diagnosis, adequacy of medication trial and compliance of patient.

Prescribing in children and adolescents CHAPTER 5 ■ ■To improve response, consider adding CBT, changing medication (e.g. switch SSRIs, other classes) or combining medications (e.g. for comorbidities, to treat side effects, to potentiate action). Augmentation strategies with buspirone, benzodiazepines, atypical antipsychotics and stimulant medications have been proposed but lack empirical support.7 Maintenance phase ■ ■Continue maintenance treatment for at least 1 year of stable improvement. ■ ■Monitor response and side effects regularly. Discontinuation phase ■ ■Because of lack of information on long-term safety and possible improvement in symptoms with age and learning, consider discontinuing treatment after a period of stable improvement. A trial of

medication withdrawal should be started at a period of low stress/demands. Discontinuation should also be considered if the medication is no longer working or the side effects are too severe. Taper SSRIs slowly (e.g. 25% of previous dose weekly) to minimise the risk of discontinuation symptoms. Monitor closely for recurrence of symptoms/relapse and, if deterioration is noted, consider restarting medication. Table 5.7 Typical dosage of medications for treatment of anxiety disorders in children and adolescents. Medication Starting dose (mg) Dose range (mg/day) SSRI Sertraline 12.-5–25 25–200 Fluoxetine 5–10 10–60 Fluvoxamine 12.5–25 50–200 (bd if >50) Paroxetine 5–10 10–-40 Citalopram* 5–10 10–40 SNRI Venlafaxine XR 37.5 37.5–225 Duloxetine 30–120 Alpha2 agonist Guanfacine 1–6 5HT1A partial agonist Buspirone* 5 tds 15–60 Benzodiazepine (prn) Clonazepam* 0.25–0.5 – Lorazepam* 0.5–1 – Note: always check dose with latest formal guidance, e.g. British National Formulary for Children (in the UK). *Treatments not supported by randomised controlled trial evidence. bd, twice daily; prn, as required; tds, three times daily.

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