Appendix 2: Guide to medication for use in childhood mental disorders

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Table A1 Medications commonly used in childhood mental disorders

Disorder	Medication	How to use	Important side-effects	Points to remember
Attention-deficit hyperactivity disorder (ADHD)	***First line*** *Stimulants* 1. Methylphenidate i. short acting (3–4 h) ii. long acting (8–12 h) 2. Dexamphetamine (3–6 h duration of action) Stimulants are Schedule III drugs – availability varies between countries. Country-specific rules need to be followed when prescribing Individual responsiveness (which may be genetically determined) varies ***Second line*** *Non-stimulants* 1. Atomoxetine 2. Clonidine	***Stimulants*** *Short-acting methylphenidate* 0.3–0.5 mg/kg/dose Start at 5 mg OD/BD and increase by 5–10 mg weekly increments to a maximum dose of 1 mg/kg/day or 60 mg/day Can be given up to 2–3 doses per day – last dose should not be given after 16:00–17:00 h Start at 2.5–5.0 mg, increase weekly (up-titration) *Long-acting methylphenidate* 0.5–2.0 mg/kg OD dose Maximum 60 mg/day *Dexamphetamine* Start at 2.5 mg OD/BD and increase by 2.5–5 mg weekly increments to a maximum of 0.5 mg/kg/day or 40 mg/day ***Non-stimulants*** *Atomoxetine* Initiate at 0.5 mg/kg/day and increase every week to a target of 1.2 mg/kg Maximum daily dose: body weight <70 kg, 80 mg/day; body weight >70 kg, 100 mg/day OD/BD dosing; can be given in the evening *Clonidine* 3–7 μg/kg/day, maximum dose 0.3 mg Start with 25–50 μg and increase by 25 μg increments every 3–4 days Wait for 4 weeks for full therapeutic response OD at bedtime or BD dosing ***General*** Trial of discontinuation by tapering can be given after 1–2 years of adequate symptom control	***Stimulants*** Loss of appetite, ↓ sleep, irritability/instability/moodiness, alter pulse rate and blood pressure, may slow down growth (need to monitor weight, height, growth, blood pressure and pulse) Lowers seizure threshold – should be used with adequate precaution in children with seizures and only after the seizures are well controlled ***Non-stimulants*** *Atomoxetine* ↓ appetite, nausea, vomiting, ↓ sleep or tiredness, dry mouth *Clonidine* Sedation, dizziness, dry mouth At times, paradoxical worsening of symptoms and mood may be seen Monitor blood pressure as it is an antihypertensive and may lower blood pressure (rare)	***Stimulants*** Tics may be precipitated or worsened in some children Ask about personal or family history of tics, seizures or heart disease Not to give the medicine after 16:00–17:00 h, otherwise it may disturb sleep Supervised dosing in adolescents may also be needed in school to prevent inappropriate use and potential distribution to peers ***Non-stimulants*** *Atomoxetine* Avoid in case of jaundice/liver disease (pre-existing or emergent) Keep a watch for suicidal thinking that can emerge with this medication *Clonidine* Not to stop suddenly due to risk of rebound severe hypertension Useful in treating tics with or without ADHD as it is beneficial for both conditions, improves sleep
Depression	Psychotherapy should be considered before drugs ***First line (SSRIs)*** Fluoxetine ***Second line (SSRIs)*** Sertraline Citalopram Escitalopram	1. Start low (fluoxetine 5–10 mg, sertraline 12.5 mg, citalopram/escitalopram 2.5 mg, TCAs 10–25 mg) 2. Increase dose slowly to minimise the risk of treatment-emergent agitation 3. At least weekly follow up in the early stages of treatment 4. In early phase of treatment, monitor for suicidality or agitation	***SSRIs*** ↓ appetite, nausea, headache, insomnia, delayed ejaculation, ↓ sexual desire Stop in case of agitation or undue cheerfulness/excitement with sleep disturbance Monitor for suicidality that can occur with the use of SSRIs	Antidepressants need to be added if there is little or no response to 4–6 weeks of psychotherapy, or if depression is moderate to severe, or psychotherapy is simply not available SSRIs have mostly replaced TCAs for depression in children Adolescents can be expected to respond better to antidepressants than younger children

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Depression (cont.)	***Third line (TCAs)*** Imipramine Amitriptyline ***Avoid*** Paroxetine and venlafaxine	5. Maximum daily dose: fluoxetine 20–40 mg, sertraline 100–200 mg, citalopram/escitalopram 10–20 mg, TCAs 150 mg 6. Should be continued for at least 1 year of symptom-free period	***TCAs*** Sedation, weight gain, dry mouth, constipation May also cause urinary retention, glaucoma, changes in heart rhythm (baseline and on-treatment ECG are needed)	
Obsessive–compulsive disorder	***First line (SSRIs)*** Sertraline Fluoxetine Fluvoxamine Citalopram Escitalopram ***Second line (TCA)*** Clomipramine	1. Start low (sertraline 12.5 mg, fluoxetine 5–10 mg, fluvoxamine 25 mg, citalopram/escitalopram 2.5–5 mg, clomipramine 10–25 mg) 2. Increase dose slowly to minimise the risk of treatment emergent agitation 3. At least weekly follow up in the early stages of treatment 4. In early phase of treatment, monitor for suicidality or agitation 5. Maximum daily dose: sertraline 150–250 mg, fluoxetine 40–60 mg, fluvoxamine 150–250 mg, clomipramine 150 mg 6. Should be continued for 6 months to 1 year of symptom-free period. If reduction of dose causes relapse, may need to continue indefinitely.	***SSRIs*** ↓ appetite, nausea, headache, insomnia, delayed ejaculation, ↓ sexual desire Stop in case of agitation or undue cheerfulness/excitement with sleep disturbance Monitor for suicidality that can occur with the use of SSRIs ***TCAs*** Sedation, weight gain, dry mouth, constipation May also cause urinary retention, glaucoma, changes in heart rhythm (baseline and on-treatment ECG are needed)	All children and adolescents with obsessive–compulsive disorder should be offered CBT, even if they are on medication
Anxiety disorders (generalised anxiety disorder, separation anxiety, specific phobias, social phobia, PTSD)	Psychotherapy should be considered before drugs ***Acute and short-term control (2–4 weeks)*** Benzodiazepines (lorazepam, clonazepam, alprazolam, diazepam) ***Long-term management*** *SSRIs* Fluoxetine (drug of choice) Fluvoxamine Sertraline *Anxiolytic* Buspirone (mainly as an add-on agent) ***Avoid*** TCAs	***Benzodiazepines*** Daily dose ranges: lorazepam 0.5–4 mg in up to 4 divided doses; clonazepam 0.25–2.0 mg in up to 3 divided doses; diazepam 2.5–20.0 mg in up to 3 divided doses; alprazolam 0.125–1.0 mg in up to 3 divided doses Use lowest possible effective dose for shortest possible time and then taper off ***SSRIs*** *Fluoxetine* Start with 2.5 mg in the morning and increase by 2.5 mg every week up to 10–20 mg/day (OD dose) *Fluvoxamine* Start with 25 mg and increase weekly by 25 mg up to 100–125 mg/day (night doses or BD doses with larger dose at night)	***Benzodiazepines*** Sedation, dizziness Forgetfulness, ataxia (less common at lower doses) Can cause dependence, paradoxical worsening or excitation ***SSRIs*** ↓ appetite, nausea, headache, insomnia, delayed ejaculation, ↓ sexual desire Stop in case of agitation or undue cheerfulness/excitement with sleep disturbance Monitor for suicidality that can occur with the use of SSRIs ***Anxiolytic (buspirone)*** Sedation, dizziness Can occasionally cause disinhibition and worsen aggression (less common than in benzodiazepines)	CBT is usually the recommended first-line treatment. If anxiety is severe or disabling and CBT is unavailable or has failed, use of medication should be considered Combination of CBT and SSRI is superior to both therapies alone Alprazolam and mouth-dissolving clonazepam are often used to curb a panic attack (immediate action) Children are more likely to develop excitation/disinhibition with benzodiazepines than adults. Need to monitor for the same Rapid reduction of benzodiazepines can precipitate seizures in vulnerable children (past/personal/family history of seizure disorder needs to be known) Buspirone does not cause dependence or withdrawal

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Anxiety (cont.)		*Sertraline* Start with 12.5 mg morning and increase every week by 12.5–25 mg up to 100–125 mg/day (OD dose) Continue for at least 1 year of symptom-free period ***Anxiolytic (buspirone)*** Start with 2.5 mg 2–3 times a day Maximum dose 15–20 mg/day		
Psychosis (early-onset schizophrenia, acute psychosis)	***SGAs*** Risperidone Olanzapine Quetiapine Aripiprazole Amisulpride Clozapine (most effective in treatment-resistant cases) *Avoid* Ziprasidone (can cause cardiac arrhythmia) ***FGAs*** Haloperidol Chlorpromazine Sulpiride	Use the lowest effective dose For acute psychosis, mania with psychotic symptoms and psychotic depression, antipsychotics can be tapered off after at least 6 months of symptom-free period For schizophrenia, a trial of discontinuation can be given by gradually tapering after 6 months of symptom-free period High rates of relapse are known and may require to continue indefinitely ***SGAs*** *Risperidone* Start with 0.25–0.5mg BD, maximum dose 4–6 mg/day *Olanzapine* Start with 2.5 mg night or BD dose, maximum dose 15–20 mg/day *Quetiapine* Start with 25 mg BD, maximum dose 400–800 mg/day *Aripiprazole* Start with 2 mg OD, maximum dose 10 mg/day *Sulpiride/amisulpiride* Start with 25–50 mg BD, maximum dose 400–800 mg/day *Clozapine* Start with 12.5 mg BD, weekly increase 25 mg/day, maximum dose 300–350 mg/day *Haloperidol* Start with 0.5 mg, maximum dose 15–20 mg/day BD/TID *Chlorpromazine* Start with 25 mg BD, maximum dose 400 mg/day	***SGAs*** May cause weight gain, sedation, and metabolic abnormalities including obesity, insulin resistance, type 2 diabetes and metabolic syndrome Seizures, agranulocytosis, myocarditis (rare), hypersalivation with clozapine ***FGAs*** Sedation, constipation, extrapyramidal or Parkinsonism-like symptoms with tremor and rigidity, acute muscle spasms or dystonia, akathesia, and tardive dyskinesia in long-term use Weight gain in some children on chlorpromazine	Mostly, FGAs have been replaced by SGAs ***Other uses of antipsychotics*** Mania in bipolar disorder, psychotic depression, impulsive/aggressive behaviours Haloperidol (0.5–3 mg/day) and risperidone (0.25–2.0 mg/day) in tics and Tourette syndrome Risperidone is particularly useful in autism for disruptive behaviours and aggression Patients on SGAs need monitoring for BMI and metabolic parameters Patients on olanzapine will need monitoring for liver function tests in addition to weight gain and type 2 diabetes Patients on clozapine will need monitoring for blood count and baseline ECG and EEG

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Bipolar disorder	***First-line mood stabilisers*** Lithium Valproic acid (sodium valproate, divalproex) ***Second-line mood stabilisers*** Carbamazepine Lamotrigine ***Third-line/add-on mood stabilisers*** Oxcarbazepine Topiramate ***Antipsychotics with mood-stabilising/anti-manic effects*** Risperidone Olanzapine Aripiprazole	Mood stabilisers are mostly needed to continue indefinitely. In first episode of mania, a mood stabiliser can be started if euphoria/irritability is not settling within 1–2 weeks of antipsychotic (SGA) treatment or the risk of another episode is high (severe symptoms, family history of bipolar disorder) ***Lithium*** Start with 300–450 mg/day in 2–3 divided doses and titrate upwards according to blood levels (desired blood level 0.8–1.2 mEq/l) ***Valproic acid*** 20–30 mg/kg/day in 2–3 divided doses ***Carbamazepine*** 10–20 mg/kg/day in 2–3 divided doses ***Lamotrigine*** Start with 12.5 mg/day. Weekly increase by 12.5 mg. Administer BD dose. Maximum dose 100–200 mg/day ***Oxcarbazepine*** Start with 8–10 mg/kg in two divided doses ***Topiramate*** Maximum dose 75–100 mg/day ***Risperidone*** Start with 0.25–0.5 mg BD, maximum dose 4–6 mg/day ***Olanzapine*** Start with 2.5 mg night or BD dose, maximum dose 15–20 mg/day ***Aripiprazole*** Start with 2 mg OD, maximum dose of 10 mg/day	***Lithium*** Excessive thirst, frequent urination, acne, weight gain, tremors ***Valproic acid*** Sedation, tremor, weight gain, gastrointestinal symptoms, hair loss, can cause liver function abnormality and polycystic ovarian disease ***Carbamazepine*** Dizziness, incoordination, skin rash (at times severe, e.g. Stevens–Johnson syndrome), can cause ↓ white blood cells ***Lamotrigine*** Skin rash needs to be monitored for the first 8 weeks. May cause Stevens–Johnson syndrome. ***Topiramate*** Dizziness, renal stones, metabolic acidosis, reduced appetite, recent memory difficulties, word retrieving difficulties	Except lithium, the other mood stabilisers are also used as anticonvulsants Monotherapy and starting doses at the lower end of the therapeutic range should be by default Lithium: monitoring needed for blood level, thyroid and renal function; monitor for signs of toxicity, especially in dry weather, dehydration Lithium and lamotrigine are useful in the depressive phase of bipolar disorder Valproic acid, carbamazepine and lithium can be used in episodic aggression/rage attacks/aggression with severe mood dysregulation episodes Topiramate can be added on when weight control or seizure control is needed. Can cause behavioural problems.
Insomnia	***First line*** Melatonin ***Second line*** *Benzodiazepines* Lorazepam Clonazepam *Non-benzodiazepine hypnotic* Zolpidem	***Melatonin*** 1.5–3.0 mg/night for sleep onset delay; 3–6 mg/night as a hypnotic ***Lorazepam*** Start with 0.05 mg/kg (maximum 2 mg/dose) and can be repeated every 4–8 h ***Clonazepam*** Start with 0.01 and 0.03 mg/kg/day but do not exceed 0.05 mg/kg/day given in 2–3 divided doses ***Zolpidem*** 6.25–12.5 mg/night; short-term use only (2–4 weeks)	***Melatonin*** Can cause headache, irritability, nausea, palpitation, itching May worsen seizures/asthma ***Zolpidem*** Can cause dizziness, headache and, rarely, excitation/disinhibition	Melatonin is used in autism, ADHD and depression when children have sleep difficulties Zolpidem is more expensive than benzodiazepines. It helps in reducing night-time awakenings, has fewer side-effects and causes less dependence than benzodiazepines.

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Extrapyramidal side-effects caused by antipsychotic drugs	***Anticholinergic drugs*** Benztropine Trihexyphenidyl (as anti-Parkinsonian agent in adolescents)	***Benztropine*** 0.02–0.05 mg/kg/dose OD/BD to a maximum dose of 0.1 mg/kg or 2–4 mg (If oral dose is not possible, the intramuscular or intravenous dose is 0.02 mg/kg stat; may repeat in 15 minutes) ***Trihexyphenidyl*** 1-2mg/dose based on need Maximum dose of 4–6 mg/day in divided doses	***Benztropine*** Can cause dry mouth, blurred vision, constipation, urinary retention, tachycardia, anorexia, drowsiness, disorientation ***Trihexyphenidyl*** Same side-effects as above	Benztropine should not be used in children under 3 years. It may decrease sweating and the body's ability to cool itself. The child will need to take care when outside in hot weather and will need to drink extra fluids.

BD, twice daily; BMI, body mass index; CBT, cognitive–behavioural therapy; ECG, electrocardiogram; EEG electroencephalogram; FGA, first-generation antipsychotic; OD, once daily; PTSD, post-traumatic stress disorder; SGA, second-generation antipsychotic; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; TID, three times daily.