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eTable 4 Specific side effects of medications considered for treating oppositional behaviour, conduct problems, and aggression in children and adolescents with ADHD, ODD, or CD

Medication	Side Effects			
	Very Common (≥10%)	Common (1% to <10%)	Uncommon (0.1% to <1%)	Rare (<0.1%)
Psychostimulants (methylphenidate and amphetamines)	Decreased appetite/weight loss Insomnia Headache Abdominal pain Small increases in heart rate and blood pressure	Irritability and other emotional changes Social withdrawal Nausea/vomiting Dry mouth Modest growth suppression*63	Manic/psychotic symptoms64	Priapism65 Serious cardiovascular events**63, 66, 67
Atomoxetine	Gastrointestinal symptoms Sedation Small increases in heart rate and blood pressure Decreased appetite/weight loss Headache Dry mouth	Insomnia Irritability and other emotional changes Dizziness	Manic/psychotic symptoms64 Possible increased risk of suicide-related events29–31 Seizures	Severe liver injury68 Priapism65 Serious cardiovascular events**63, 67
Guanfacine	Sedation Headache	Bradycardia Hypotension Rebound tachycardia and hypertension (with abrupt discontinuation of higher doses)34 Dizziness Irritability and other emotional changes Gastrointestinal symptoms Dry mouth Modest QTc prolongation49		ECG abnormalities69, 70
Clonidine	Sedation Dry mouth	Bradycardia Hypotension Rebound tachycardia and hypertension (with abrupt		ECG abnormalities71, 72

		discontinuation of higher doses)35 Dizziness Irritability and other emotional changes Gastrointestinal symptoms Headache		
Risperidone***	Sedation Extrapyramidal symptoms (including akathisia) Weight gain Increased prolactin	Orthostatic changes Elevated lipids Impaired glycemic tolerance/diabetes Modest QTc prolongation73	Seizures Neutropenia Tardive dyskinesia/dystonia Neuroleptic malignant syndrome	
Quetiapine***	Sedation Weight gain Orthostatic changes	Elevated lipids Impaired glycemic tolerance/diabetes Extrapyramidal symptoms (including akathisia) Anticholinergic symptoms (typically minimal)74 Modest QTc prolongation73 Thyroid abnormalities53	Seizures Neutropenia Tardive dyskinesia Neuroleptic malignant syndrome	
Haloperidol	Sedation Extrapyramidal symptoms (including akathisia) Increased prolactin	Orthostatic changes Anticholinergic symptoms Weight gain Elevated lipids75 Impaired glycemic tolerance/diabetes75, 76 Modest QTc prolongation73 Tardive dyskinesia/dystonia	Seizures Neutropenia Neuroleptic malignant syndrome	
Valproate	Sedation Insomnia Gastrointestinal symptoms Headache Dizziness Tremor	Weight gain Hair loss Ataxia Cognitive disturbances Mild increase in liver enzymes77 Thrombocytopenia78 Polycystic ovarian syndrome79 Decreased bone density80	Severe hepatotoxicity81 Pancreatitis82 Hyperammonemia83 Encephalopathy (with or without hyperammonemia)84 Parkinsonism85 Hypofibrinogenemia78 Renal toxicity (Fanconi syndrome)77	Severe hematological alterations78 Possible increased risk of suicide-related events87

			Severe skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis)86	
Lithium	Sedation Weight gain Gastrointestinal symptoms Polyuria/polydipsia	Tremor Acne/rash Hair loss Hypothyroidism Hyperparathyroidism ECG abnormalities Dose-related toxicity	End-stage renal failure88, 89	Nephrotic syndrome90
Carbamazepine	Gastrointestinal symptoms Dizziness Ataxia Cognitive disturbances	Sedation Weight gain Rash Visual disturbances Mild increase in liver enzymes91 Mild leukopenia91 Hyponatremia92 Decreased bone density80, 93	Severe skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis)86	ECG abnormalities94 Hypothyroidism95 Severe hematological alterations78, 91 Severe hepatotoxicity91 Pancreatitis91 Possible increased risk of suicide-related events87

Note: Categories for side effect rates (very common, common, uncommon, and rare) are based on international standards.96 Side effect rates for each medication were derived from the trials in the accompanying systematic review,14, 15 other reports as cited in the table, and the drug information resource Micromedex 2.0.97 When paediatric data were not available, side effect rates were estimated from adult data. When information was missing or inconsistent, we categorized side effects based on our clinical experience. Not all potential side effects are included.

*In the Multimodal Treatment Study of Children with ADHD, psychostimulant-naïve school-age children with ADHD who were treated with a psychostimulant for three years showed average growth of 2.0 cm and 2.7 kg less than children with ADHD who did not receive medication.98 The groups were not determined by random assignment, however, and the unmedicated children had a growth rate that was greater than expected. In addition, the clinical significance of the growth discrepancy between the medicated and unmedicated children is subject to debate, and the effect of prolonged psychostimulant treatment on final height is unclear.63

**Although very rare cases of serious cardiovascular events, including sudden death, have been reported in children and adolescents taking psychostimulants or atomoxetine, several large cohort studies have not found a significant association in children and adolescents without cardiac risk factors.99–102

***Evidence-based guidelines for monitoring the safety of second-generation antipsychotics, and managing their metabolic complications and extrapyramidal side effects, have been developed as part of the Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children (CAMESA) Guideline Project.53–55