

Table 1. Key considerations for selecting a second-generation antidepressant in MDD. Antidepressants listed are locally-registered for MDD treatment. Information sourced from international literature^{10,16,36,46–55} and local drug information resources^{56,57} (including package inserts). The information in this table is not exhaustive of the subject matter. Refer to package inserts and drug information resources for further details — including contraindications, drug interactions, and medication doses.

Second-generation antidepressant for treating MDD**	Other labelled indications††	Key precautions††		Additional considerations
				<ul style="list-style-type: none"> ➢ Advantageous ➤ Disadvantageous ● May be advantageous or disadvantageous, depending on context of individual patient
Selective serotonin reuptake inhibitor				
Escitalopram	GAD, OCD, panic disorder	Risk of bleeding abnormalities with SSRIs; bleeding tendency may be increased if concurrently used with anticoagulants, or medications that affect platelet function (e.g. NSAIDs and aspirin).	Dose-dependent QTc prolongation (higher risk than other SSRIs).	<ul style="list-style-type: none"> ➢ Lower treatment drop-out due to side effects, compared to other antidepressants ● Greater propensity for weight gain compared to other antidepressants
<u>Fluoxetine</u>	Bulimia nervosa, OCD, pre-menstrual dysphoric disorder		Strong inhibitor of CYP2D6.	<ul style="list-style-type: none"> ➢ Lower treatment drop-out due to side effects, compared to other antidepressants ➢ Suitable for patients with poor medication adherence due to a long half-life ➢ Lower risk of discontinuation symptoms compared to other antidepressants ➤ Insomnia very commonly reported ➤ Greater difficulty in switching to another antidepressant due to long half-life ● Activating effect
<u>Fluvoxamine</u>	OCD		Strong inhibitor of CYP1A2, CYP2C19, and CYP3A4.	<ul style="list-style-type: none"> ● Sedating effect
Paroxetine	Pre-menstrual dysphoric disorder, social anxiety disorder		Strong inhibitor of CYP2D6; contraindicated for concurrent use with CYP2D6 substrates that can prolong QT interval.	<ul style="list-style-type: none"> ➤ Greater propensity for anticholinergic effects compared to other antidepressants ➤ Higher risk of discontinuation symptoms compared to other antidepressants ● Greater propensity for weight gain compared to other antidepressants ● Sedating effect
<u>Sertraline</u>	OCD, panic disorder, pre-menstrual dysphoric disorder, PTSD, social anxiety disorder		Risk of bleeding abnormalities with SSRIs; bleeding tendency may be increased if concurrently used with anticoagulants, or medications that affect platelet function (e.g. NSAIDs and aspirin).	<ul style="list-style-type: none"> ➢ Dose adjustment not routinely required in renal insufficiency ➤ Insomnia very commonly reported ● Activating effect
Serotonin–norepinephrine reuptake inhibitor				
Desvenlafaxine	Nil	Risk of bleeding abnormalities with SNRIs; bleeding tendency may be increased if concurrently used with anticoagulants, or medications that affect platelet function (e.g. NSAIDs and aspirin).	May cause increased blood pressure (therefore may not be suitable for patients with uncontrolled hypertension).	<ul style="list-style-type: none"> ➤ Insomnia very commonly reported ➤ Higher risk of discontinuation symptoms compared to other antidepressants
<u>Venlafaxine</u>	GAD, panic disorder, social anxiety disorder		May cause increased blood pressure and is contraindicated in patients with uncontrolled hypertension.	<ul style="list-style-type: none"> ➤ Higher risk of discontinuation symptoms compared to other antidepressants
Duloxetine	Diabetic peripheral neuropathic pain, GAD, pain associated with fibromyalgia		Contraindicated if substantial alcohol use is present, if severe renal impairment (creatinine clearance <30 mL/min) is present, or if liver disease is present. Contraindicated for concurrent use with strong CYP1A2 inhibitors (such as ciprofloxacin and fluvoxamine).	<ul style="list-style-type: none"> ➤ Higher risk of discontinuation symptoms compared to other antidepressants

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