Supplement 1: A guide to SSRI and SNRI selection for GAD

The choice between individual SSRIs and SNRIs can be guided by factors like the patient's medical history, concomitant medications, risk of serious adverse effects, and hepatic or renal impairment.

Information is referenced from local product inserts and literature available at the time of guideline development or consolidated product monographs; refer to product inserts for full details on prescribing. Clinical judgement should be exercised at all times when making decisions for an individual patient.

Patient characteristic	Considerations	
GAD with insomnia as a symptom	Paroxetine* and fluvoxamine† are the more sedating SSRIs.[52,53]	
Hepatic disease	• SSRI: For most SSRIs, adjust dose. • SNRI: Adjust dose for venlafaxine. Duloxetine is contraindicated in pre-existing liver disease.	
Renal impairment‡	• SSRI: For most SSRIs, adjust dose. Sertraline* does not require dose adjustment. • SNRI: No dose adjustment needed for duloxetine in mild to moderate renal impairment, but it is contraindicated in severe renal impairment (creatinine clearance <30 mL/min). Adjust dose for venlafaxine.	
Elderly	• Adjust doses for the elderly, where applicable. • Consider choosing a medication with less anticholinergic activity (e.g. most SSRIs except paroxetine) and less sedation (escitalopram, sertraline, duloxetine, venlafaxine). • Fluoxetine* has a long elimination half-life and may require dose adjustment to reduce the risk of accumulation. Both SSRIs and SNRIs increase the risk of hyponatraemia and are associated with bone loss and fractures.	
Patients with hypertension	• SSRIs may be preferred as they do not affect blood pressure. • In uncontrolled hypertension, SNRIs should be avoided.	
Patients with cardiovascular disease	Sertraline* has been used safely after myocardial infarction and in heart failure.[53,54]	
Patient with neuropathic pain	Duloxetine is also indicated for neuropathic pain.	
Patients with risk factors for QTc interval prolongation (e.g. use of antiarrhythmic drugs, hypokalaemia)[55]	Escitalopram has been associated with clinically significant QTc interval prolongation.[56] Cases have also been reported for other SSRIs and venlafaxine, though it is recognised that these medications do not result in clinically significant QTc prolongation on their own.	
Patients on other medication(s) Check clinical significance of drug interactions using the patient's complete medication list. The examples shown are not exhaustive.	Medications metabolised extensively by CYP450 enzymes 1A2, 2C19, 2D6, and 3A4	Sertraline*, escitalopram, and venlafaxine, are less likely to cause CYP450-related drug interactions, as weak inhibitors.
	Diuretic medications	Monitor due to increased risk of hyponatraemia (class effect) – no preferred SSRI or SNRI
	Monoamine oxidase inhibitor (MAOI, e.g. selegiline, moclobemide, linezolid)	MAOIs should not be used concurrently with SSRIs or SNRIs due to increased risk of serotonin syndrome[57] (class effect). SSRI or SNRI treatment should only be started 2 weeks after discontinuing MAOI.
	Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs), oral anticoagulants	Monitor due to increased risk of bleeding, especially upper gastrointestinal bleeding (class effect) – no preferred SSRI or SNRI

* Off-label use for GAD; efficacy based on published meta-analysis of randomised clinical trials.[28]

† Off-label use for GAD; limited RCT evidence for fluvoxamine in GAD

‡ For the purpose of dosing, renal impairment is staged using creatine clearance for most SSRI and SNRI medications. Some may use glomerular filtration rates instead.

Refer to MDD ACE Cinical Guideline, Table 1, for further information on precautions and additional considerations for selecting among SSRIs and SNRIs (except desvenlafaxine). Information on agomelatine and mirtazapine is also available.