

ANTIDEPRESSANTS: SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs)

BASIC DRUG CLASS SUMMARY

Drugs	General Indications & Uses	Targeted Neurotransmitters	Mechanism of Action	Common Side Effects	Clinical Pearls
Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Levomilnacipran (Fetzima) Milnacipran (Savella) Venlafaxine (Effexor)	- Fibromyalgia - Generalized Anxiety Disorder - Major Depressive Disorder - Musculoskeletal pain - Neuropathic pain (secondary to DM) - Panic Disorder - Social Anxiety Disorder - Stress Urinary Incontinence	5-HT (Serotonin) NE (Norepinephrine) Other Targets DA (indirectly) (Dopamine)	Inhibits the reuptake of both norepinephrine (NE) and 5-HT, prolonging NE and 5-HT neurotransmission with additional downstream regulation of dopamine (DA) Note: Venlafaxine is classified as an SNRI and acts as an SNRI at high doses and an SSRI at low doses	- Insomnia and agitation - Dose-dependent sweating (hyperhidrosis) & dose-dependent HTN possible - Duloxetine is associated with N/V if used in patients with gastroparesis - Venlafaxine and desvenlafaxine are associated with a higher SIADH risk than other SNRIs and SSRIs, which increases the risk of hyponatremia (especially in the elderly).	- SNRIs share a tricyclic structure with TCAs but exhibit selective NE and 5-HT effects without the cholinergic, histaminic, and alpha-1 drawbacks of TCAs. - Avoid MAOIs as well as linezolid and tedizolid due to DDI - Little weight gain, sexual dysfunction, hypotension, & anticholinergic effects - Agents may assist with pain control, including fibromyalgia - Levomilnacipran is the active enantiomer of milnacipran - Venlafaxine is classified as an SNRI and acts as an SNRI at high doses and an SSRI at low doses. It “may” also have a faster onset of antidepressant effect due to its ability to cause rapid downregulation of beta-adrenergic receptors in the brain.

Note: The summary represents the editor's best effort to compile information from reputable sources of information and reported clinical trial data. It is also meant to be for educational purposes only and is not intended to replace medical decision-making or clinical judgment.

ANTIDEPRESSANTS GENERAL CLINICAL KNOWLEDGE

Medication Class	Efficacy (OR)*	Side effects	Cost	Notes
Selective Serotonin Reuptake Inhibitors (SSRIs)	1.52-1.75	Mild	\$	Considered most tolerable class & safest (except in overdoses with citalopram/escitalopram)
Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)	1.49-1.85	Moderate	\$\$	Additional treatment effects for pain, & energy
Atypical Antidepressants				
Mirtazapine	1.89	Mild	\$	Helps with sleep and appetite
Bupropion	-	Moderate	\$\$	Helps with fatigue and is an alternative to SSRI-induced sexual dysfunction. Higher risk of seizures in overdose.
Vortioxetine	1.66	Moderate	\$\$\$	May help with neuropsychological performance
Vilazodone	-	Mild	\$\$\$	Less sexual side effects
Tricyclic Antidepressants (TCAs)	1.49-2.13	High	\$	Helps with pain (including migraine prevention), insomnia
Monoamine Oxidase Inhibitors (MAOIs)	-	High	\$-\$	Reserved/last line; high efficacy but side effects and drug-food interactions limit use

*Efficacy based on Cipriani A et al. Lancet 2018;391:1357-66. The summary represents the editor's best effort to compile information from reputable sources of information and reported clinical trial data. It is also meant to be for educational purposes only and is not intended to replace medical decision-making or clinical judgment.

SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITOR (SNRI) OVERVIEW OF SIDE EFFECTS

Medications	Anticholinergic Effects	GI Effects	Hypotension	Insomnia & Agitation	Sedation	Sexual Dysfunction	Weight Gain	Other Considerations
Desvenlafaxine (Pristiq)	-	+/++	-	+	-	+	-/+	▪ Dosed at 50 mg daily and only titrated to 100 mg if insufficient response
Duloxetine (Cymbalta)	-	+/++	-	+	-	+	-/+	▪ Contraindicated with hepatotoxicity or active liver disease ▪ May cause biliary obstruction
Levomilnacipran (Fetzima)	-	+/++	-/+	-/+	-	+	-	▪ Per CANMAT guidelines may be used first-line for MDD ▪ May cause urinary hesitancy
Milnacipran (Savella)	-	+/++	-	-	+	+	-	▪ Per CANMAT guidelines may be used first-line for MDD
Venlafaxine (Effexor)	-	+/++	-	+	+	++	-/+	▪ Has SSRI activity at lower doses

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