THIS IS WHY with Dr. Busti

ANTIDEPRESSANTS: TRICYCLIC ANTIDEPRESSANTS (TCAs)

BASIC DRUG CLASS SUMMARY

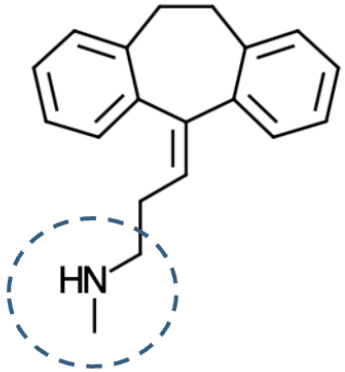
Drugs	Indications & Common Uses	Other Receptor Targets	Mechanism of Action	Common Side Effects	Clinical Pearls
Tertiary Amines					
Amitriptyline (Elavil) **Clomipramine** (Anafranil) **Doxepin** (Silenor) **Imipramine** (Tofranil) **Imipramine** (Surmontil)	▪ Cyclic vomiting (amitriptyline) ▪ Fibromyalgia (amitriptyline) ▪ Irritable bowel pain (amitriptyline) ▪ Major depressive disorder ▪ Migraine prophylaxis ▪ Neuropathic pain ▪ Obsessive-compulsive disorder (clomipramine) ▪ Panic disorder (clomipramine)	5-HT >> NE, & DA **Other Receptor Targets** Inhibition of: ▪ Muscarinic ▪ Histaminic ▪ Alpha 1 ▪ Cardiac hNav1.5 (VGSC)	Inhibit presynaptic reuptake of 5-HT >> NE, increasing their concentration at CNS receptors.	▪ Anticholinergic effects, drowsiness, orthostatic hypotension, relevant weight gain, and sexual dysfunction ▪ Risks of QRS widening leading to QT prolongation & seizures are dose-dependent (risks greatest in overdose; can be fatal in doses as low as 10x daily dose)	▪ Obtain baseline ECG in ≥ 40 years old, with cardiac symptoms, cardiac history, receiving medication with QT-prolonging capacity if using higher doses for depression. ▪ Little to no insomnia, agitation, or GI toxicity ▪ May help improve sleep (dose at bedtime due to sedation) ▪ Also used for neuropathic pain, fibromyalgia, & migraine prevention ▪ If using for major depressive disorder, will need larger doses and drug level monitoring.
Secondary Amines					
Amoxapine (Asendin) **Desipramine** (Norpramin) **Nortriptyline** (Pamelor) **Protriptyline** (Vivactil)	▪ As above ▪ Bipolar depression adjunct (doxepin) ▪ Insomnia (doxepin) ▪ Neuralgia ▪ Irritable bowel syndrome (desipramine)	NE >> 5-HT,& DA **Other Receptor Targets** Same as tertiary	Inhibit presynaptic reuptake of NE >> 5-HT, increasing their concentration at CNS receptors.	▪ Same side effects above, but less pronounced	▪ Helpful for use throughout the day, while providing less sedation for pain. ▪ Nortriptyline is the active metabolite of amitriptyline ▪ Desipramine is the active metabolite of imipramine

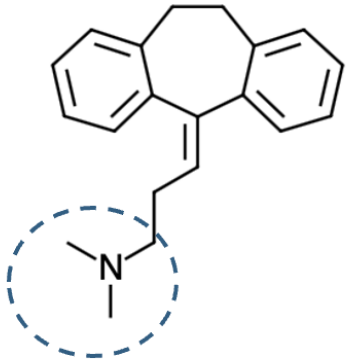
Note: Brand names are listed for historical context since most are not available. The summary represents the editor's best effort to compile information from reputable sources of information and reported clinical trial data. It is also meant to be for educational purposes only and is not intended to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

Anthony J. Busti, MD, PharmD, MSc, FNLA, FAHA

TRICYCLIC ANTIDEPRESSANTS
CLASSIFICATIONS

SECONDARY AMINES	TERTIARY AMINES
Amoxapine Desipramine Nortriptyline* Protriptyline	Amitriptyline* Clomipramine Doxepin Imipramine Trimipramine





Anthony J. Busti, MD, PharmD, MSc, FNLA, FAHA

THISISWHY.HEALTH

THIS IS WHY with Dr. Busti

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.

Anthony J. Busti, MD, PharmD, MSc, FNLA, FAHA

THIS IS WHY with Dr. Busti

TRICYCLIC ANTIDEPRESSANTS (TCA)

OVERVIEW OF SIDE EFFECTS

Medication	Anticholinergic Effects	GI Effects	Hypotension	Insomnia & Agitation	Sedation	Sexual Dysfunction	Weight gain	Other Considerations
Secondary Amine TCAs								
Amoxapine	+/++	-/+	+/++	+/++	+/++	+	+/++	▪ Do not confuse with atomoxetine (used for ADHD) ▪ One of the more expensive TCAs
Desipramine	+	-/+	+/++	+	+/++	++	+	▪ Active metabolite of imipramine ▪ Most overdose potential
Nortriptyline	+/++	-/+	+	-/+	+/++	+	+	▪ Least orthostatic hypotension ▪ Active metabolite of amitriptyline
Protriptyline	+/++	+	+/++	+	+	++/+++	+	▪ Least sedation ▪ May be activating
Tertiary Amine TCAs								
Amitriptyline	+++	+	++	-/+	+++	++/+++	++/+++	▪ Most anticholinergic ▪ Most affordable and commonly used
Clomipramine	++/+++	-/+	+/++	+	+++	+++	++/+++	▪ Most serotonergic ▪ Most tolerable GI profile ▪ QT prolongation more likely
Doxepin	++	-/+	+/++	-/+	++	+	++/+++	▪ Use Silenor (3mg, 6mg) for insomnia ▪ Sinequan for MDD, anxiety, and bipolar depression. ▪ QT prolongation is more likely
Imipramine	++	+	++/+++	+	++	++	++/+++	▪ QT prolongation more likely ▪ One of the more expensive TCAs
Trimipramine	++/+++	-/+	++	+	+++	+	+++	▪ CYP2D6 substrate (major)

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. Mann JJ. N Engl J Med 2005.

Anthony J. Busti, MD, PharmD, MSc, FNLA, FAHA