THIS IS WHY with Dr. Busti

ANTIDEPRESSANTS: ATYPICAL ANTIDEPRESSANTS

BASIC DRUG CLASS SUMMARY

Drugs	Targeted Neurotransmitter(s)	Other Receptor Targets	Mechanism of Action	Common Side Effects	Clinical Pearls
Bupropion (Wellbutrin) (Zyban) Others	NE (Norepinephrine) & DA (Dopamine)	n/a	Blocks NE and DA reuptake pumps, increasing neurotransmission of NE and DA	▪ Agitation ▪ Anxiety ▪ Excitement ▪ Headache ▪ Insomnia ▪ Nausea	▪ Unique indications: Seasonal Affective Disorder & Smoking Cessation ▪ Good alternative for SSRI-associated sexual dysfunction ▪ Avoid in patients with epilepsy and with anorexia or bulimia (↑seizure risk)
Mirtazapine (Remeron)	NE (Norepinephrine) & 5-HT (Serotonin)	Antagonism of presynaptic α-2 receptor. Also, antagonisms of 5-HT_3, 5-HT_{2A}, 5-HT_{2C}, & histaminic (H_1) receptors.	Antagonized the presynaptic alpha-2 receptor, which enhances the release of monoamines (does not block the monoamine transporter) and causes increased 5-HT and NE neurotransmission	▪ Weight gain ▪ Increased appetite ▪ Dry mouth & constipation (*higher doses 45 to 60 mg) ▪ Sedation (*lower doses ~7.5 mg) ▪ Overall, a favorable GI profile compared to others	▪ Unique indications: Headache prophylaxis, Insomnia, Panic Disorder, SSRI Associated Sexual Dysfunction ▪ Assists patients with poor appetite to gain weight ▪ Can help treat insomnia ▪ Well-tolerated for most
Trazodone (Desyrel)	5-HT (Serotonin) Dose-Influenced	Antagonism of 5-HT_{2a}, alpha-1, H_1 receptors	5-HT reuptake inhibition (SRI), alpha-adrenergic antagonist properties and weak antihistaminic effects	▪ Orthostatic hypotension (at higher doses), sedation, headache, nausea, blurred vision, constipation, dry mouth	▪ Used primarily as an adjunct for insomnia or sexual dysfunction caused by SSRIs (higher doses needed for depression) ▪ Rarely can cause priapism
Vilazodone (Viibryd)	5-HT (Serotonin)	5-HT_{1A} partial agonist	Serotonin 1A partial agonist and reuptake inhibitors (SPARI)	▪ GI distress with initiation ▪ Insomnia in some patients	▪ Generally, well-tolerated except for GI side effects ▪ Less sexual dysfunction
Vortioxetine (Trintellix)	5-HT (Serotonin)	5-HT_{1A} agonist; 5-HT_{1B} partial agonist; 5-HT_3, 5-HT_{1D} & 5-HT_7 antagonist	5-HT_{1A} agonist, 5-HT_3 antagonist, 5-HT reuptake inhibition, weak antagonism at 5-HT_7 and 5-HT_{1D}, & partial agonist at 5-HT_{1B}	▪ Gastrointestinal (GI) distress with initiation	▪ Generally, well-tolerated except for GI side effects ▪ May improve cognitive function in geriatric patients ▪ Less sexual dysfunction

Note: All agents are indicated or used for Major Depressive Disorder, but some agents have unique uses listed above. Nefazodone is not included because of its limited use worldwide and in the U.S. 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.

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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.

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ATYPICAL ANTIDEPRESSANTS
OVERVIEW OF SIDE EFFECTS

Medications	Anticholinergic Effects	GI Effects	Hypotension	Insomnia & Agitation	Sedation	Sexual Dysfunction	Weight Gain	Other
Bupropion (Wellbutrin)	-	+	-	+/++	-	-	-	▪ More insomnia/agitation with IR versus SR dosage forms. ▪ Able to lower the seizure threshold (especially with intentional overdose). ▪ Little to no QTc prolongation (at normal doses).
Mirtazapine (Remeron)	+	-	-	-	+++	+	+++	▪ More anticholinergic effects and GI disturbances at higher doses (45 to 60 mg). ▪ More sedation and weight gain at lower doses (~ 7.5 mg)
Trazodone (Desyrel)	-	+/++	+/++	-	+++	+	-/+	▪ Hypotension and weight gain are more prominent with higher doses
Vilazodone (Viibryd)	-	+++	-	+/++	-	+	-	▪ GI effects commonly include nausea, vomiting, and diarrhea.
Vortioxetine (Brintellix)	-	++	-	-	-	+	-	▪ Relatively benign side effect profile

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.

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