Pharmacy Pearls

Antidepressant Management Algorithm for PCPs for Adults

Step 1: Assess Depression Severity

Mild Depressive Symptoms
PHQ-9 score of 5-9

Treatment options:
- Psychotherapy alone
- Pharmacotherapy *usually* ***not*** indicated

Moderate Depressive Symptoms
PHQ-9 score of 10-19

Treatment options:
- Pharmacotherapy alone **or**
- Pharmacotherapy and psychotherapy

Severe Depressive Symptoms
PHQ-9 score of ≥20

Treatment options:
- Immediate pharmacotherapy
- If severe impairment/poor response, expedite referral to mental health

Step 2: Initiate an Antidepressant

SSRIs are considered first-line treatment.

- Choice may be based on presenting symptoms, safety and tolerability, history of response, patient preference, cost, potential drug interactions, and comorbidities
- Sertraline, citalopram and escitalopram have fewer drug-drug interactions than fluoxetine and paroxetine
- Citalopram has a higher risk of QTc prolongation than other SSRIs
- Paroxetine has a higher incidence of adverse effects compared to other SSRIs, avoid in pregnancy
- All SSRIs are available generically and many are on $4 drug lists at pharmacies
- Fluoxetine capsules are **much** less expensive than tablets
- Set expectations with patients about time to effect as well as side effects and that they diminish over time

Refer to medication management tables

Step 3: Follow-up Assessment at 4 week intervals

Assess response (PHQ-9), side effects, adherence, and suicide risk at each visit. Treatment goal is Remission (PHQ-9 of <5).

Good Response
Reduction in PHQ-9 of ≥50%

Treatment options:
- Continue therapy(s)
- Reassess Q4 weeks until remission

Remission and Maintenance:
- Follow every 3 months
- First episode, taper to off after 9-12 months of remission
- If recurrent, consider long-term maintenance, especially if ≥3 lifetime episodes
- If symptoms recur, reenter treatment algorithm

Partial Response
PHQ-9 Improves, but <50%

Treatment options:
- Assess adherence
- Consider concurrent psychotherapy
- If no significant side effects and dose is not optimized : Increase dose by at least 50%
- If significant side effects: Switch to medication in the same or another drug class
- If failed 2 adequate dose and duration antidepressant trials: Consider combination therapy or specialty referral

No Response *No or minimal improvement in PHQ-9*

Treatment options:
- Assess adherence and reassess diagnosis (e.g. bereavement, bipolar)
- Engage behavioral health resources
- If no significant side effects and dose is not optimized : Increase dose at least 50%
- If significant side effects or dose is therapeutic: Switch to medication in the same or another drug class
- If failed 2 adequate dose and duration antidepressant trials: Consider combination therapy or specialty referral

Antidepressant Management Tables for PCPs for Adults

1. Antidepressant Doses and Side Effect Comparison

	Adult Dosing		Adverse Effect Potential							
	Starting Dose (mg)	Therapeutic dose range (mg)	Sedation	Anti-cholinergic	Insomnia/ Agitation	Orthostatic Hypotension	Sexual dysfunction	Wt. gain	GI	QTc
SSRIs										
Citalopram	20	20-40	0	0	1+	1+	3+	1+	1+	2+
Escitalopram	10	10-20	0	0	1+	1+	3+	1+	1+	1+
Fluoxetine	20[1]	20-80	0	0	2+	1+	3+	1+	1+	1+
Paroxetine	20[1]	20-50	1+	1+	1+	2+	4+	2+	1+	1+
Sertraline	50	25-200	0	0	2+	1+	3+	1+	2+	1+
SNRIs										
Duloxetine	20 BID[2]	40-60	0	0	2+	0	3+	0		0
Venlafaxine ER	75	75-225	0	0	2+	0	3+	0	2+	1+
MISC.										
Bupropion XL[3]	150[1]	300-450	0	0	2+	0	0	0	2+	1+
Mirtazapine	15 QHS	15-45	4+	1+	0	0	1+	4+		1+

[1]use lower doses in elderly and preferably dose in the morning; [2]dose BID initially, then can change to daily; [3]**contraindicated if significant anxiety, seizure disorder, active alcohol use or history of an eating disorder**

2. Options for Combination Therapy in Adults

Combination Medication	Typical Dose*	Symptoms this agent can be used to target:
Buproprion XL (Wellbutrin®)	150-300 mg daily	Reduced motivation or lack of energy
Mirtazepine (Remeron®)	7.5-30 mg QHS	Weight loss, nausea, insomnia or anxiety
Buspirone (Buspar®)	10-30 mg BID	Anxiety
Aripiprazole (Abilify®)	5-15 mg QAM	Irritability or obsessive thinking
Quetiapine (Seroquel®)	50-200 mg QHS	Anxiety, insomnia or agitation

*medications should be dosed at a scheduled frequency, not dosed prn

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3. Antidepressant Switch Strategies in Adults

Direct switches (abruptly stopping the current agent and starting the new on the next day) may be considered when drugs have similar pharmacologic properties. In situations where discontinuation syndrome or symptom recurrence may be of concern, **cross tapering** (gradually decreasing one agent while simultaneously increasing the other) should be considered.

	Direct Switch	Cross Taper
When to Consider	Agents in same drug class	Agents in a different drug class, high doses
Benefits	Simple for the patient	Minimizes discontinuation syndrome* and symptom relapse
Risks	Discontinuation syndrome*, drug interactions	Drug interactions, adverse effects
Notes	• If concerned about emergence of new side effects, start new agent at slightly lower dose • **Fluoxetine** has a long half-life – start new agent 4-7 days after last fluoxetine dose	Typically accomplished over 1-4 weeks. Longer durations may be warranted if doses are high, return of depressive symptoms, symptoms of withdrawal or side effects

*Discontinuation syndrome is of more concern with **paroxetine, duloxetine and venlafaxine**. Other factors that increase risk: shorter drug elimination half-life (<24 hours), higher antidepressant doses, prior history of discontinuation syndrome, etc.

Switching Scenarios:

Between SSRIs (except fluoxetine): Direct switch at approximate equivalent dose (Table 1) (potential for discontinuation syndrome most likely with paroxetine)
SSRI to SNRI (except fluoxetine): If coming from low dose SSRI, direct switch at approximate equivalent dose (Table 1) is generally appropriate. If high dose SSRI, cross taper
SSRIs to other antidepressant (except fluoxetine): Cross taper
Between SNRIs: At low doses (<60 mg duloxetine or <150 mg venlafaxine), direct switches at approximate equivalent dose (Table 1) may be trialed, otherwise cross taper
SNRIs to other antidepressant: Cross taper
Bupropion to other antidepressant: Cross taper generally recommended (bupropion does not exhibit discontinuation syndrome because it is not strongly serotonergic, but cross-tapering reduces periods of therapeutic gaps)
Mirtazapine to other antidepressant: Cross taper

Table 1. Approximate dose conversions:

	Approximate Equivalent Dose* (mg)
SSRIs	
Citalopram	20
Escitalopram	10
Fluoxetine	20
Paroxetine	20
Sertraline	100
SNRIs	
Duloxetine	30
Venlafaxine	75

*Equivalent doses are approximated and may vary based on patient-specific factors, Including tolerability.