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Evidence-Based Best Practices for the Treatment of Major Depressive Disorder in Primary Care in South Carolina

The SCORxE non-psychotic depressive disorder algorithm offers state providers with unbiased, evidence-based clinical information about drug therapy and best practices to assist with making best prescription decisions.

Adequate trial of an antidepressant consists of BOTH an adequate dose and duration.

- All classes of antidepressant medications are equally efficacious.
- An adequate acute antidepressant trial is a period of 6 to 12 weeks, including a minimum of 6 weeks at a maximum tolerated dose.

Rating scales such as the Patient Health Questionnaire (PHQ-9) are useful to assess symptom severity before initiating medication and at regular intervals to assess patient response.

- Remission is achieved with resolution of symptoms (e.g., PHQ-9 < 5).
- Results from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study show that the use of measurement-based care leads to improved remission rates for patients with chronic depression.

Treat to remission, not just response, and inform patients that remission is the goal of treatment.

- Patient education is critical to adherence and treatment success.

Total duration of treatment should last 9–12 months for first episode of depression, and potentially indefinitely for severe or recurrent episodes.

- Patients who received pharmacotherapy during the acute phase treatment (i.e., 6-12 weeks) should continue their medication at the same dose that produced therapeutic response for an additional 6 to 9 months after symptom remission.
- Patients experiencing 2 or more major depressive episodes may benefit from lifelong antidepressant medication depending on the clinical situation.

The information contained in this summary is intended to supplement the knowledge of clinicians regarding best practices and drug therapy to treat major depression in primary care patients ages ≥18 years. This information is advisory only and is not intended to replace sound clinical judgment, nor should it be regarded as a substitute for individualized diagnosis and treatment. Special considerations are needed when treating some populations such as the elderly, pregnant or breast-feeding women, and patients with certain medical conditions (e.g. cardiac disease, liver and renal impairment).

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Algorithm for the Treatment of Non-Psychotic Major Depressive Disorder in Primary Care

Patient assessment and discussion of treatment options

---> Discuss EBPT as option¹

STAGE 1

SSRIs, BUP, MRT, SNRIs

Partial Response

STAGE 1 AUGMENTATION

Choosing a different mechanism of action than the Stage 1 drug, augment with one of the following:² SSRI, SNRI, BUP, MRT, BUS, or T₃.³ Reconsider use of EBPT.

Non-response⁴: Re-evaluate Diagnosis.

STAGE 2

Switch to different SSRI or use alternate antidepressant monotherapy from different class.

Partial Response

STAGE 2 AUGMENTATION

Choosing a different mechanism of action than the Stage 2 drug, augment with one of the following:² SSRI, SNRI, BUP, MRT, BUS, or T₃.³ Reconsider use of EBPT. If an alternate SSRI is chosen in Stage 2, consider alternate monotherapy from a different drug class before augmenting.

Non-response⁴: Re-evaluate Diagnosis.

STAGE 3

Use alternate antidepressant monotherapy from a different class before combination therapy.

SSRI/SNRI + BUP or MRT

SSRI + TCA or SGA

For further management of a non-responsive patient, refer to a psychiatrist or see the complete treatment algorithm in the Best Practices Report available at <http://www.sccp.sc.edu/SCORxE>.

Adapted from personal communication with M. Lynn Crismon, Pharm.D., December 2007

Critical Decision Points for Each Stage

To Initiate New Medication

- At week 0:
 - Get baseline PHQ-9 score
 - Titrate to initial target dose within one week as tolerated

For Remission (PHQ-9 score < 5)

- At weeks 2, 4*, 6*, 9*, and 12*:
 - Continue current regimen (Continuation phase)

For Partial Response (> 20% decrease from baseline PHQ-9 score, or any clinically meaningful response short of remission)

- At weeks 2 and 4*:
 - Continue current dose or consider dose increase as tolerated
- At week 6*:
 - Increase/maximize dose or use augmentation
- At weeks 9* and 12*:
 - Increase/maximize dose, use augmentation, or go to next stage

For Non-response (≤ 20% decrease from baseline PHQ-9 score)

- At week 2:
 - Too early to consider non-response
- At week 4*:
 - Maximize dose or go to next stage
- At week 6*:
 - Use augmentation or go to next stage
- At weeks 9* and 12*:
 - Go to next stage

**Consider switching antidepressant if side effects are intolerable*

KEY

BUP: bupropion SR/XL

BUS: buspirone

EBPT: evidence-based psychotherapy

MRT: mirtazapine

SGA: second generation antipsychotic

SNRI: serotonin-norepinephrine reuptake inhibitor

SSRI: selective serotonin reuptake inhibitor

T₃: liothyronine

TCA: tricyclic antidepressant

¹ EBPT is an option before starting or in combination with pharmacotherapy at any stage in the algorithm.

² In general, SSRIs and SNRIs are not used together because of their similar mechanisms of action.

³ Use with extreme caution in patients with cardiovascular or coronary artery disease.

⁴ When reassessing diagnosis due to non-response, consider comorbid disease states and non-adherence. Reach target dose and duration of medication before documenting treatment failure.

Dosing Guidelines for Antidepressant Agents

Type/Class	Medication	Initial Starting Daily Dose	Initial Target Daily Dose (Serum Level)*	Maximum Daily Dose (Serum Level)	Recommended Administration
SSRI	Citalopram	10-20 mg	20 mg	60 mg	AM
	Escitalopram	5-10 mg	10 mg	20 mg	AM
	Fluoxetine	10-20 mg	20 mg	40-80 mg	AM
	Paroxetine (i)	10-20 mg	20-30 mg	40-60 mg (ii)	AM or HS
	Sertraline	25-50 mg	50-100 mg	150-200 mg	AM
SNRI	Duloxetine	20-30 mg	40-60 mg	120 mg (iii)	Daily or BID
	Venlafaxine	37.5-75 mg	150-225 mg	375 mg	BID
	Venlafaxine XR	37.5-75 mg	75-225 mg	225 mg	Daily
Other (iv)	Bupropion	75 mg	225-300 mg	450 mg	TID ≤150 mg/dose
	Bupropion SR	100-150 mg	200-300 mg	400 mg	BID ≤200 mg/dose
	Bupropion XL	150 mg	300 mg	450 mg	Daily
	Mirtazapine	7.5-15 mg	30 mg	60 mg (v)	HS
TCA	Amitriptyline	25-50 mg	150-200 mg	300 mg	HS
	Clomipramine	25 mg	100-150 mg	250 mg	HS
	Desipramine	25-50 mg	150 mg (>125 ng/ml)	300 mg	HS
	Imipramine	25-50 mg	150 mg (>200 ng/ml) (vi)	300 mg (200-400 ng/ml) (vi)	HS
	Nortriptyline	25-50 mg	75-100 mg (50-150 ng/ml)	150 mg (50-150 ng/ml)	HS

SSRI: selective serotonin reuptake inhibitor **SNRI:** serotonin-norepinephrine reuptake inhibitor **TCA:** tricyclic antidepressant

* Antidepressant dosage can be increased every 2 to 3 weeks as tolerated if remission has not occurred. (i) Paroxetine and paroxetine CR have similar side effect profiles, comparable half-lives, and reach steady state plasma concentrations at similar time intervals. (ii) Manufacturer recommended maximum dose for major depressive disorder (MDD) is 50 mg/day. (iii) Manufacturer recommended maximum dose for MDD is 60 mg/day. (iv) Trazodone is not included as a treatment option for MDD because therapeutic doses are hard to achieve due to excessive sedation (therapeutic dose 300-600 mg/day). Trazodone may be considered during the acute treatment phase as adjunctive therapy when sedation is desired. (v) Manufacturer recommended maximum dose is 45 mg/day. (vi) Serum level includes parent drug and active metabolite (imipramine and desipramine, respectively).

Common Side Effects (SEs) of Antidepressant Medication

0 = Absent or rare to 4+ = common

Class	Antidepressant	Anticholinergic	Conduction Abnormalities	Drowsiness	Gastrointestinal Distress	Headache	Insomnia	Orthostatic Hypotension	Sexual Disturbances	Weight Gain	Comments
SSRI	Citalopram	0	0	0	3+	2+	2+	0	4+	1+	Activation, agitation and restlessness reported with all SSRIs
	Escitalopram	0	0	0	3+	0	2+	0	2+	1+	
	Fluoxetine	0	0	0	3+	2+	2+	0	4+	1+	
	Paroxetine	1+	0	1+	3+	2+	2+	0	4+	2+	
	Sertraline	0	0	0	3+	2+	2+	0	4+	1+	
SNRI	Duloxetine	1+	1+	1+	3+	2+	2+	0	4+	0	Higher rate of hypertension with doses > 225 mg/day
	Venlafaxine	1+	1+	1+	3+	2+	2+	0	4+	0	
Other	Bupropion	0	0/1+	0	1+	2+	2+	0	0	0	Increased risk of seizures with doses > 450 mg/day
	Mirtazapine	1+	1+	3+	0	1+	1+	1+	2+	3+	Less sedation with doses > 15 mg/day
TCA	Amitriptyline	4+	3+	4+	1+	1+	1+	3+	1+	4+	
	Clomipramine	4+	3+	4+	1+	1+	2+	2+	4+	4+	
	Desipramine	1+	2+	2+	0	0	1+	2+	1+	1+	
	Imipramine	3+	3+	3+	1+	2+	2+	4+	4+	4+	
	Nortriptyline	2+	2+	2+	0	0	0	1+	0	1+	

SSRI: selective serotonin reuptake inhibitor **SNRI:** serotonin-norepinephrine reuptake inhibitor **TCA:** tricyclic antidepressant

References: *Drug Information Handbook for Psychiatry*. Fuller MA, Sajatovic M, editors. Hudson, OH, Lexi-Comp, 2007; *Clinical Handbook of Psychotropic Drugs*. Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Toronto, ON, Hogrefe & Huber, 2006.

Patient Health Questionnaire (PHQ-9) and Scoring Instructions

This questionnaire is an important part of providing you with the best health care possible. Your answers will help in understanding problems that you may have.

Over the last 2 weeks, how often have you been bothered by:

	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
1. Little interest or pleasure in doing things				
2. Feeling down, depressed, or hopeless				
3. Trouble falling or staying asleep, or sleeping too much				
4. Feeling tired or having little energy				
5. Poor appetite or overeating				
6. Feeling bad about yourself-or that you are a failure or have let yourself or your family down				
7. Trouble concentrating on things, such as reading the newspaper or watching television				
8. Moving or speaking so slowly that other people could have noticed? Or the opposite-being so fidgety or restless that you have been moving around a lot more than usual				
9. Thought that you would have been better off dead or of hurting yourself in some way				

Subtotals

Total Score

If you checked off any problems on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all
 Somewhat difficult
 Very difficult
 Extremely difficult

Instructions for Use (for doctor or healthcare professional only)

Assessment for initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the two right columns (including Questions #1 or #2), consider a depressive disorder. Add score to determine severity.
3. **Consider Major Depressive Disorder**
 - If there are at least 5 ✓s in the two right columns (one of which corresponds to Question #1 or #2).
- Consider Other Depressive Disorder**
 - If there are 2 to 4 ✓s in the two right columns (one of which corresponds to Question #1 or #2).

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds, taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient. Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (e.g., every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Not at all = 0; Several days = 1; More than half the days = 2; and Nearly every day = 3.
3. Add together column scores to get a TOTAL score.
4. Interpretation of TOTAL score:
5. Results may be included in patients' files to assist you in setting up treatment goal, determining degree of response, as well as guiding treatment intervention.

Total Score	Depression Severity
0-4	None
5-9	Mild
10-14	Moderate
15-19	Moderately severe
20-27	Severe