

Memorandum

Date : October 26, 2010

To : Chiefs of Mental Health
Chief Psychiatrists
Senior Psychiatrists
Staff Psychiatrists

Subject: **MAJOR DEPRESSIVE DISORDER DISEASE MEDICATION MANAGEMENT
GUIDELINE - REVISED**

Please ensure that **ALL** psychiatrists are provided a copy of the attached REVISED Disease Medication Management Guideline (DMMG) on Major Depressive Disorder, with this cover memo, for review and implementation.

This algorithm is a product of concerted research and collaboration with Maxor's pharmacy staff and a dedicated workgroup of seasoned field and headquarters' psychiatrists, with final approval by the Statewide Pharmacy and Therapeutics Committee.

Highlighted in the DMMG is the medication selection for Major Depressive Disorder with and without psychotic features. Concomitant information such as monitoring and dosing adjustments, prescribing combination therapy, polypharmacy practices, management of adverse effects, switching strategies and drug interactions rounds out this pragmatic and useful tool for California Department of Corrections and Rehabilitation Mental Health prescribers.

As you study the updated depression guideline algorithm, you will note the following revisions:

1. We are now requiring clear documentation of the DSM diagnostic criteria supporting the diagnosis of depression.
2. When considering using second tier antidepressants, the documented diagnostic criteria as well as the rationale for choosing the second tier antidepressant, must be documented.
3. Monitoring for Serotonin Syndrome has also been added, especially when cross titrating antidepressants.
4. Treatment resistant depression has been operationally clarified.
5. Additional medical conditions and drugs that can cause or worsen depression have been included.
6. Updated therapeutic dose ranges and recommended laboratory monitoring frequency.

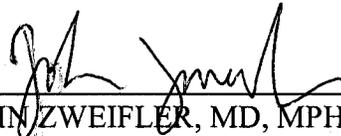
All the antidepressants listed were chosen by the psychiatrist workgroup based foremost on therapeutic benefits, community practices and clinical utility of these medications in this correctional environment. Available antidepressants have not changed from the 2008 DMMG.

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In this cost containment era, physicians should consider all effective economical medication options when available and clinically appropriate. For example, if clinically indicated, selection of lower cost agents should be ordered.

If you have any questions, please contact Dr. Karen Higgins at (916) 324-9452.


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Major Depressive Disorder (MDD)

Meets Criteria for MDD?

- Rule out secondary causes of depression including substance abuse, current medications or medical conditions and treat accordingly.
- Consider past/present comorbid psychiatric conditions and **rule out bipolar disorder**.
- Must document specific criteria for a DSM depressive disorder

This pathway does not replace sound clinical judgment or apply to all patients

Is pharmacotherapy appropriate?
Is patient willing to take medication (or court ordered)?

Yes

Discuss treatment options and attempt to obtain informed consent.

History of efficacy with antidepressant?

Yes

Consider initiating previously successful therapy or medication with similar MOA. Go to Monitoring & Dose Adjustment box, page 2.

No

Psychotic features present?

Yes

Initiate SGA antipsychotic along with antidepressant from next box. Taper and DC antipsychotic as clinically appropriate.

No

INITIATE MONOTHERAPY WITH SSRI
*SSRI's should be considered 1st line

SSRI	Usual Dose
Fluoxetine	20-80mg
Citalopram	20-60mg
Paroxetine	20-50mg
Sertraline	50-200mg

***Alternate 2nd Tier Formulary Antidepressants**

Mirtazapine	15-45mg
Venlafaxine	75-375mg
Venlafaxine ER	75-225mg

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Antidepressants should not routinely be used for the treatment of mild depression because the risk:benefit ratio is poor.

The availability & need for psychotherapy should be evaluated at each stage.

Abbreviations

- AD = antidepressant
- SGA = second generation antipsychotic
- SSRI = selective serotonin reuptake inhibitor
- MAOI = monoamine oxidase inhibitor
- TCA = tricyclic antidepressant
- MOA = mechanism of action

*If considering 2nd tier AD must document full criteria for depression and justify in progress note why you have skipped the use of the 1st tier SSRI AD.

Major Depressive Disorder (MDD)

This pathway does not replace sound clinical judgment or apply to all patients

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MONITORING & DOSE ADJUSTMENT

- Monitor acute treatment every 1-4 weeks.
- Monitor for Emergence of Serotonin syndrome or initial treatment-emergent adverse effects such as anxiety, restlessness, and jitteriness that may increase the risk of suicidal behavior.
- Monitor for activation due to a Bipolar condition.
- Evaluate initial response at 4-6 week intervals and titrate to maximum therapeutic dose according to response and tolerance.
- Assess compliance and side effects at each encounter and consider blood levels if indicated.
- Assess full response after at least 8 weeks at maximum therapeutic dose.

Treatment effective?

YES

REMISSION

Continue treatment dose for 6-12 months
THEN if

First Episode – taper off antidepressant.

OR

High Risk of Recurrence or ≥ 2 episodes – continue maintenance treatment and reassess compliance and continued need annually.

NO

CONSIDER THE FOLLOWING OPTIONS:

(always optimize the dose and ensure compliance before changing therapy, monotherapy is preferred)

- 1) Monotherapy with **alternate SSRI**.
- 2) Monotherapy with **alternate AD class**.
- 3) **Venlafaxine** may be considered after failure of two formulary ADs.
- 4) SGA's and/or a trial with lithium as clinical indicated may be considered as adjuncts to AD therapy for **treatment resistant depression** (i.e. after failure of 2 formulary ADs and trial of lithium augmentation) or when psychotic features are present. (Aripiprazole has FDA approval as an augmenting agent.)
- 5) **Augmentation** with thyroid, or buspirone may be considered for patients who have failed at least 2 trials of formulary ADs or for those with only a partial response to standard monotherapy.
- 6) **Combination AD therapy** may be considered for treatment resistant patients with careful monitoring of adverse effects and compliance.

Major Depressive Disorder (MDD)

MEDICAL CONDITIONS

that can cause or worsen

Depression:

Cancer
 Coronary Artery Disease
 Diabetes
 Cerebral Vascular Accident
 Hypothyroidism or Hyperthyroidism
 Degenerative Brain Conditions
 Chronic Pain Syndrome

DRUGS that can cause or worsen Depression:

Clonidine, Methyldopa, Reserpine
 Lipophilic beta blockers (propranolol)
 Corticosteroids
 Sedatives/Hypnotics
 Benzodiazepines
 Estrogens/Progesterones
 Opiates
 Anticonvulsants
 Indomethacin
 Interferons (Hep C, MS)

Switching Antidepressants

Three methods:

- 1) Stopping the first drug with a washout period before beginning the new drug.
 - a. For drugs that can potentially interact (MAOIs), a wash-out period between antidepressants is necessary.
- 2) Cross-tapering
 - a. Often used when switching to an antidepressant with a different mechanism of action (SSRI to bupropion or mirtazapine).
 - b. Cross-tapering may be considered when switching from paroxetine or immediate release venlafaxine to avoid discontinuation syndrome. In general, taper antidepressants over 4 weeks.
 - c. Important Note: new symptoms can be due to THREE different causes.
 1. Discontinuation symptoms from stopping the first drug.
 2. Side effects from the new drug.
 3. Depression or anxiety symptoms because neither drug is working.
- 3) Direct switching
 - a. SSRI to SSRI can be done by direct switch. Some may consider waiting 4-7 days when switching from fluoxetine (long half life) then starting a low dose of another SSRI.

Symptoms of Discontinuation Syndrome:

- Include dizziness, lethargy, headache, and nausea
- Rare with treatment less than 5 weeks
- Usually occur 1-3 days after dose reduction
- Usually resolves in ~ 10 days
- Can be treated by increasing the dose of the discontinued agent and tapering more slowly
- Important when switching antidepressants to inform patients that symptoms are not due to starting the new drug

Major Depressive Disorder (MDD)

DRUG INTERACTIONS

DRUG	Dosage Range per Day	Monitoring / Side Effects	Drug Interactions / Enzyme Inhibition
SSRI			
Citalopram	20 – 60mg		Weak / Moderate 2D6
Fluoxetine	20-80mg	Avoid in hepatic impairment (long t _{1/2})	Potent 2D6
Paroxetine	20-50mg	Avoid abrupt discontinuation due to withdrawal.	Potent 2D6
Sertraline	50-200mg		Weak / Moderate 2D6
SNRI			
Venlafaxine	75-375mg IR 75-225mg ER	Monitor blood pressure (See FDA recommendations) . Doses above 225mg increase risk of hypertension. Avoid abrupt discontinuation due to withdrawal.	Weak 2D6, 3A4
Novel MOA			
Mirtazepine	15-45mg	Give HS. Causes sedation, weight gain. Monitor weight.	

Drug	Contraindicated	Avoid if Possible	Monitoring / Dose Adjustment
Fluoxetine	MAOI	TCAs, phenytoin, codeine, flecainide mexiletine, propafenone	warfarin, haloperidol, clozapine, alprazolam, triazolam, aripiprazole, risperidone, carbamazepine, beta blockers, cyclobenzaprine, lithium , phenothiazines, serotonergic drugs (eg, tramadol, triptans, dextromethorphan)
Sertraline	MAOI	codeine	TCAs, haloperidol, warfarin, aripiprazole, cimetidine, diazepam, lithium , serotonergic drugs
Paroxetine	MAOI	TCAs, codeine, flecainide, mexiletine, propafenone	Haloperidol, warfarin, aripiprazole, risperidone, lithium , digoxin, phenobarbital, cimetidine, theophylline, phenytoin, phenothiazines, serotonergic drugs
Citalopram	MAOI	None identified	TCAs, metoprolol, cimetidine, lithium , serotonergic drugs
Venlafaxine	MAOI	Norepinephrine agonists (when high doses of venlafaxine are prescribed)	serotonergic agents
Mirtazepine	MAOI	Diazepam	Serotonergic drugs, antihistamines, alpha1-adrenergic antagonists (eg, doxazosin), alcohol

*Table lists common clinically significant drug interactions but is not all inclusive. Always check current drug information reference for specific drug interactions.

For I/P at higher risk for underlying medical illness, consideration should be given to assessing the following: CBC with diff, electrolytes, glucose, BUN/ Cr, LFT's TSH, RPR, B12/folate and UA.