DSH PSYCHOTROPIC MEDICATION Operational Procedures

ANTIDEPRESSANT PROTOCOL:

NOTE: Please see the section of the DSH Psychotropic Medication Policy regarding a specific protocol for selective serotonin reuptake inhibitor (SSRI) antidepressants (Chapter 31).

I. Indications:

A. The treated individual cooperates with treatment and monitoring.

B. At least one of the following clinical indications is present and documented in the chart. Note that some indications are limited to specific antidepressants.

1. DSM major depressive disorder.

2. DSM dysthymic disorder.

3. DSM bipolar mood disorder, depressed phase.

   [NOTE: Tricyclic antidepressants should be avoided due to risk of rapid cycling. SSRI antidepressants and bupropion appear the least likely to induce switches into mania. Also, recent data indicates that antidepressants may offer limited efficacy in the context of treating the depressed phase of bipolar or schizoaffective disorder while increasing overall instability and the rate of mood cycling.]

4. DSM complicated bereavement.

5. Depressive signs and symptoms occurring comorbidly with another psychiatric or medical disorder, including postpartum depression. (Note that if a treatable cause of secondary depression is known, then treatment of the primary disorder should be the focus of clinical efforts.)

6. DSM seasonal affective disorder in which phototherapy is not available or not preferred.

7. DSM panic disorder

   [NOTE: Tricyclic antidepressants, monoamine oxidase inhibitors (MAOIs), and SSRI antidepressants have the best established efficacy.]

8. DSM obsessive-compulsive disorder (OCD).

   [NOTE: SSRI antidepressants and the tricyclic, clomipramine have demonstrated efficacy. In general; however, clomipramine should rarely be used due to its greater risk of adverse effect profile.]

9. DSM post-traumatic stress disorder (PTSD).

[NOTE: SSRI antidepressants have the best established data regarding efficacy, however, almost all of the antidepressants have anecdotal support for associated depressive and anxiety symptoms.]

10. DSM acute stress disorder (ASD). [Efficacy is less well established than for PTSD. The SSRI antidepressants have been most studied.]

11. DSM social phobia. [Studies have been limited primarily to the SSRI antidepressants.]

12. DSM generalized anxiety disorder (GAD). [The SSRI antidepressants have been the most studied, with most studies showing moderate efficacy.]

13. Chronic pain syndromes.

    a. Amitriptyline, nortriptyline, desipramine, and duloxetine have demonstrated efficacy.

    b. Several antidepressants also have demonstrated prophylactic efficacy for migraine headaches.

    c. Although milnacipran is indicated for treatment of fibromyalgia, levomilnacipran SR has not been indicated by the U.S. Food and Drug Administration for treatment of fibromyalgia but would likely be effective.

14. Smoking cessation. [Bupropion under the trade name Zyban has been the best studied.]

15. Eating disorders. [SSRI antidepressants have shown efficacy in bulimia nervosa and in binge eating disorder.]

16. DSM impulse control disorders and paraphilic disorders. [SSRI antidepressants have shown modest efficacy in some studies.]

17. Premature ejaculation. [SSRI antidepressants have shown efficacy in delaying orgasm.]

II. Contraindications:

A. Hypersensitivity to the medication or any of the components of the formulation.

B. Present hypomania or mania.

C. For tricyclic antidepressants, current heart block or narrow angle glaucoma.

D. For bupropion, current seizures due to unstable seizure disorder or unstable electrolyte status. Bupropion also carries a risk of diversion and abuse in forensic populations, as when insufflated or injected it acts as an amphetamine-like drug.

E. For venlafaxine, desvenlafaxine, duloxetine, or levomilnacipran SR, current unstable hypertension.

F. For MAOIs, pregnancy. [MAOIs cause severe retardation of fetal growth across pregnancy, often causing fetal death.]

III. Precautions (documented risk/benefit analysis supports use):

A. Hepatic disease (e.g., liver impairment may increase plasma concentrations)

1. Nefazodone (no longer actively marketed in the U.S.) may cause acute necrosis.

B. Renal disease (e.g., may cause accumulation of more toxic hydroxy metabolites.

C. Cardiac disease (e.g., tricyclic antidepressants delay cardiac conduction)

1. Desipramine may cause arrhythmia and sudden death in children.

D. Hypertension (e.g., venlafaxine, desvenlafaxine, duloxetine, and levomilnacipran SR may increase diastolic pressures).

E. Poorly controlled seizure disorder or unstable electrolyte status.

F. Pregnancy or breast-feeding

1. SSRI antidepressants cause decreased growth in the third trimester and may cause post-partum irritability, insomnia, and poor feeding.

2. Paroxetine may cause cardiovascular defects in 1 per 25 live births with exposure in the first trimester. Half of the malformations are ventricular septal defects. Teratogenic risks were not supported by some later meta-analyses. Paroxetine also has caused post-partum seizures in the neonate.

G. Prostatic hypertrophy

1. Tricyclic antidepressants have substantial anticholinergic properties, especially the tertiary tricyclics.

2. Levomilnacipran SR also may cause urinary retention.

H. Like the SSRI antidepressants, other antidepressants may induce transient suicidal ideation.

I. Those with serotonergic activity may decrease platelet aggregation and increase the risk of bleeding.

IV. Pre-treatment workup:

A. Informed consent or alternative legal authorization is present.

B. Baseline workup includes:

1. ECG within 1 year.

2. Hepatic function tests within 30 days.

C. BUN and creatinine within 30 days.

D. EEG within 30 days if positive active seizure history is present.

V. Monitoring:

A. Semi-annually:

1. ECG with tricyclics for first 6 months.

2. LFTs for first year for nefazodone, venlafaxine, and duloxetine only.

3. BUN and creatinine for first year.

B. Annually:

1. LFTs.

2. BUN and creatinine.

3. ECG.

VI. Dosing:

A. Typical initial doses for the more commonly used heterocyclic antidepressants, excluding the SSRI antidepressants, are as follows:

MEDICATION	INITIAL DOSE	TITRATION	MAXIMUM DOSE
Amitriptyline	25 - 50 mg/day	25 - 50 mg Q-2 to 4 days	300 mg/day
Amoxapine	25 - 50 mg/day	25 - 50 mg Q-2 to 4 days	300 mg/day
Bupropion	37.5 mg BID or TID	37.5 - 75 mgQ-3 to 7 days	150 mg TID
Bupropion SR	75 mg BID	75 to 100 mg Q-1 week	200 mg BID
Bupropion XL	150 mg QAM	150 mg Q-1 week	450 mg QAM
Clomipramine	25 - 50 mg QHS	25 - 50 mg Q-2 to 4 days	300 mg/day
Desipramine	25 mg QAM	25 - 50 mg Q-2 to 4 days	300 mg/day
Desvenlafaxine	50 mg QD	50 mg QD after 2 – 4 weeks	100 mg/day
Doxepine	25 - 50 mg QHS	25 - 50 mg Q-2 to 4 days	300 mg/day

Duloxetine	30 mg/day	30 mg Q-1 week	120 mg/day
Imipramine	25 - 50 mg QHS	25 - 50 mg Q-2 to 4 days	300 mg/day
MEDICATION	INITIAL DOSE	TITRATION	MAXIMUM DOSE
Levomilnacipran SR	20 mg/day	Increase to 40 mg QD after 2 days, then titrate by 40 mg Q-2 days	120 mg/day
Maprotiline	25 mg QAM	25 mg Q-2 to 4 days	225 mg/day
Mirtazapine	7.5 - 15 mg QHS	7.5 - 15 mg Q-1 week	45 mg/day
Nortriptyline	25 - 50 mg/day	25 - 50 mg Q-2 to 4 days	150 mg/day
Protriptyline	10 mg QAM	10 mg Q-2 to 4 days	60 mg/day
Trazodone	25 - 50 mg QHS	25 - 50 mg Q-2 to 4 days	600 mg/day
Venlafaxine	37.5 mg BID	75 mg Q-1 week	375 mg/day
Venlafaxine XR	75 mg QAM	75 mg Q-1 week	225 mg/day

***** Doses greater than the cited maximum maintained for more than 15 days require Therapeutic Review Committee (TRC) or Medication Review Committee (MRC) consultation.

***** Please see the DSH Psychotropic Medication Policy regarding a specific protocol for the SSRI antidepressants.

B. Typical dosing for the monoamine oxidase inhibitors (MAOIs) is as follows:

MEDICATION	INITIAL DOSE	TITRATION	MAXIMUM DOSE
Isocarboxazid	10 mg/day	10 mg Q-1 week	30 mg/day
Phenylzine	30 mg/day	30 mg Q-1 week	90 mg/day
Transdermal Selegiline	6 mg/day	3 mg Q-1 week	12 mg/day
Tranylcypromine	15 mg/day	15 mg Q-1 week	60 mg/day

* Use of transcutaneous selegiline at doses of 6 mg per day does not typically require dietary restriction, but may prohibit use of sympathomimetic medications. Higher doses require the same dietary and medication restrictions as the other MAOIs, i.e. ingestion of tyramine rich foods or use of sympathomimetic medications may cause hypertensive crisis. Doses greater than the maximums cited above used for more than 15 days require MRC or TRC consultation.

C. Among elderly and medically fragile individuals, the initial dosing of antidepressants should generally be decreased by 30 to 50%. Also, the rate of titration should be slowed, such that the dose increase interval is increased by a factor of 2 to 3.

D. For the tricyclic antidepressants, it is worth noting that nortriptyline has an established therapeutic range of 75 – 150 ng/mL.

1. Although the therapeutic range is not as clearly defined for the other tricyclic antidepressants, it is worth noting that antidepressant efficacy is unlikely at plasma concentrations of <150 ng/mL, while increasing side-effects without further benefit becomes likely at plasma concentrations above 450 ng/mL.

2. Importantly, recent data suggest that unlike previously thought, tricyclic antidepressants are not superior to other antidepressants for treatment-resistant depression. Thus, they should rarely, if ever, be used at antidepressant doses due to their narrow therapeutic index and consequent lethal risk.

E. Because the tricyclic antidepressants may have a therapeutic index as low as 6 - 8. It should be noted that all of the tricyclic antidepressants are metabolized by cytochrome P450 2D6. Thus, drugs or substances which potently inhibit 2D6 (e.g., paroxetine and fluoxetine) may increase tricyclic concentrations to toxic or lethal levels.

F. Tricyclic antidepressants should never be added to an existing treatment with monoamine oxidase inhibitors, as the acute reuptake blockade of norepinephrine and/or serotonin may result in lethal hypertensive crisis or serotonin syndrome. In rare refractory cases, tricyclic antidepressants and MAOIs can be initiated together or MAOIs can be cautiously added to a tricyclic antidepressant treatment, however, these combinations still carry significant risks.

G. Medications which induce hepatic enzymes (e.g, carbamazepine) may cause loss of antidepressant efficacy due to declines in plasma concentrations. Adjustment of dose based on measurement of plasma concentrations may be required in such cases.

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