DSH PSYCHOTROPIC MEDICATION Operational Procedures

SSRI ANTIDEPRESSANT PROTOCOL:

I. Indications:

A. At least one of the following clinical indications is present and documented in the chart:

1. Depressive disorder
2. Generalized anxiety disorder
3. Obsessive-compulsive disorder
4. Panic disorder
5. Social phobia
6. Acute stress disorder or Post-traumatic stress disorder
7. Premenstrual dysphoric disorder
8. Severe persistent self-injurious behavior with evidence that a behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective

   [NOTE: SSRI antidepressants may worsen irritability and impulsiveness in some individuals with a history of brain injury or an autism spectrum disorder.]

9. Intermittent explosive disorder

II. Contraindications:

A. Hypersensitivity to the drug or components of the formulation

B. Current prescription of monoamine oxidase inhibitor (MAOI) or use of MAOI within the previous 2 weeks

C. Current prescription of pimozide (Orap®)

D. Please see also Section V.D.1. – V.D.14.

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

A. Already receiving medication which raises serotonin levels (e.g., meperidine or tramadol)

B. Prior history of serotonin syndrome

C. Pregnancy or breast feeding. In women during their fertile age taking paroxetine, document in the chart that the individual and/or guardian have been informed that studies have suggested that first trimester exposure had an increased risk of cardiovascular malformations, primarily ventricular (50%) and atrial septal defects in one of 25 live births

D. Seizure disorder

E. Liver disease or impairment

F. Current active hypomanic or manic phase

G. Presence of suicidal ideation

1. If suicidal ideation is present as a component of depressive illness, ensure thorough documentation is present in the record which addresses the risk- benefit determination in favor of the use of medication.

H. Hypersensitivity reactions to other medication(s) in the SSRI class

I. Dosage adjustment or increased monitoring may be necessary when any of the following medications or classes of medication are co-prescribed. [Please see also Section V.D.1. – V.D.14.]

1. Benzodiazepines

2. Tricyclic antidepressants and Bupropion (Wellbutrin®)

3. Phenothiazines and many of the atypical antipsychotics (see their specific protocols)

4. Lithium

5. Carbamazepine (Tegretol®), Phenytoin (Dilantin®) and valproic acid.

6. Warfarin (Coumadin®)

7. Digoxin (Lanoxin®)

8. Cimetidine (Tagamet®)

9. Triptans including Sumatriptan (Imitrex®), Naratriptan (Amerge®), Rizatriptan (Maxalt®), Zolmitriptan (Zomig®), Almotriptan (Axert®) and Frovatriptan (Frova®)

IV. The following initial workup should be completed:

A. There is informed consent or alternate legal authorization.

B. Initial work up includes basic metabolic panel and liver function tests within 30 days.

V. Dose initiation, titration and discontinuation:

A. Please see Table 1 (on p. 5) for usual recommended starting doses, titration rates, and maintenance doses.

B. NOTE: Titration schedules may need to be faster for typical hospitalized patients, so clinical indications should be documented.

C. Typical dosing schedule may need to be modified if patients have idiosyncratic sedation or activation from an agent that typically has the opposite effect; this should be documented.

D. Dose or choice of agent is adjusted to account for drug-drug interactions, considering the following information:

1. SSRI medications are extensively metabolized in the liver by cytochrome (CYP) P450 enzymes and are therefore susceptible to metabolically based drug interactions. *Care must be exercised when adding an SSRI to a multi- drug regimen.*

2. Sertraline in high doses may cause clinically significant interactions, particularly by inhibiting CYP2D6.

3. Paroxetine and fluoxetine are powerful inhibitors of CYP2D6.

4. Caution should be exercised with fluvoxamine and fluoxetine which have the potential to inhibit several CYP enzyme systems.

    a. Fluvoxamine powerfully inhibits CYP1A2 and may increase clozapine and olanzapine plasma concentrations several fold.

5. Escitalopram and citalopram are the least likely SSRIs to cause clinically significant drug-drug interactions.

6. Caution should be exercised when combining a SSRI with lithium.

    a. Lithium may enhance the serotonergic effect of SSRIs and increase the risk of serotonin syndrome.

    b. Lithium levels should be monitored closely when used in combination with a SSRI.

7. Medications which have the potential to prolong the QT interval (e.g., pimozide or thioridazine) are contraindicated in combination with SSRI antidepressants. Please consult the current manufacturer's product literature regarding these combinations.

8. Triptans including Sumatriptan (Imitrex®), Naratriptan (Amerge®), Rizatriptan (Maxalt®), Zolmitriptan (Zomig®), Almotriptan (Axert®) and

9. Frovatriptan (Frova) in combination with SSRIs have the potential to induce serotonin syndrome and should be used with caution.

10. St. John's wort (Hypericum perforatum) is a widely available over the counter herbal preparation that is contraindicated in combination with SSRIs due to the potential to cause serotonin syndrome.

11. Tramadol (Ultram®) has an increased potential to induce seizures as well as serotonin syndrome in combination with SSRIs.

12. SSRIs may increase plasma warfarin levels through displacement from plasma proteins and careful monitoring of clotting times is recommended.

13. MAOIs are contraindicated in combination with all SSRIs.

14. Combination of SSRIs with tricyclic antidepressants has the potential to cause anticholinergic excess as well as serotonin syndrome.

15. Tricyclic levels may increase to cardiotoxic concentrations with CYP2D6 inhibitors (e.g., paroxetine and fluoxetine).

*****Please see next page for table delineating SSRI starting doses, titration rates, and maintenance doses.*****

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Table 1: SSRI starting doses, titration rate, and maintenance doses

MEDICATION	USUAL STARTING DOSE	USUAL DOSE RANGE (TITRATION RATE)	USUAL DAILY MAINTENANCE DOSE	DOSE FORMS
Citalopram (Celexa®)	20 mg QAM/QPM	20-40 mg (20 mg at intervals of ≥1 week)	40 mg 20 mg for elderly or hepatic impairment	10 mg tablets 20 mg tablets 40 mg tablets Oral Solution 10 mg/5 mL
Sertraline (Zoloft®)	25-50 mg QAM	50-200 mg QAM (25 mg at intervals of ≥1 week)	100-150 mg	25 mg tablets 50 mg tablets 100 mg tablets Oral Solution^^ 20 mg/mL (contains alcohol)
Paroxetine (Paxil®)	10-20 mg QAM	10-60 mg in AM (10 mg at intervals of ≥1 week)	20 mg	10 mg tablets 20 mg tablets 30 mg tablets 40 mg tablets Oral Solution 10mg/5mL
Fluvoxamine (Luvox®)	25-50 mg QHS	50-300 mg [in divided doses if total daily dose is >100 mg] (50mg at intervals of ≥1 week)	150-200 mg	50 mg tablets 100 mg tablets
Escitalopram (Lexapro®)	10 mg QAM/QPM	10-20mg (10mg at intervals of ≥1 week)	10-20mg	10mg tablets 20mg tablets Oral Solution 5mg/5mL
Fluoxetine (Prozac®)	5-20 mg QAM	10-80 mg in AM (10 mg at intervals of ≥1 week)*	20 mg	10 mg tab, capsule 20 mg capsules 40 mg capsule Elixir 20 mg/5 mL Prozac® Weekly™ 90 mg capsules
Vilazodone (Viibryd ®)	10 mg QAM	20-40 mg (10 mg in Wk. 1 and 20 mg in Wk. 2)	20-40 mg**	10 mg tablets 20 mg tablets 40 mg tablets
Vortioxetine (Trintellix®)	10 mg QD	Gradually titrate to 20 mg per day	20 mg/day^	5 mg tablets 10 mg tablets 15 mg tablets 20 mg tablets

***** Due to the long elimination half-lives of Prozac and its major active metabolite, changes in dose will not be fully reflected in plasma concentration for several weeks

****** Vilazodone 40 mg typically results in 50% receptor occupancy, suggesting higher doses may be beneficial in some cases.

^ Poor 2D6 metabolizers may not tolerate higher doses.

^^ Antabuse® contraindicated

VI. Dose is adjusted for special populations:

A. Hepatic impairment: A lower or less frequent dose should be used

B. Elderly: A lower or less frequent dose should be considered. (Table 2)

Table 2: Dosing adjustments recommended for elderly patients according to manufacturer's information

MEDICATION	DOSE ADJUSTMENT
Citalopram (Celexa®)	Initial dose ≤20 mg/day (max dose 40 mg/day)
Escitalopram (Lexapro®)	Maximum dose 10 mg/day
Sertraline (Zoloft®)	None recommended
Paroxetine (Paxil®)	Lower initial dose (10 mg/day) with slower upward dose adjustment
Fluvoxamine (Luvox®)	Avoid use in elderly
Fluoxetine (Prozac®)	None recommended

C. Pregnant women during the third trimester (consider tapering SSRI in third trimester)

D. Drug half-life and discontinuation issues are considered

1. Discontinuation symptoms (withdrawal) are recognized with SSRIs, particularly with paroxetine.

   a. The symptoms start within 1 week of treatment cessation, and should resolve by the end of 3 weeks

   b. The most common symptoms associated with discontinuation of SSRIs include dizziness, nausea, lethargy, and headache.

   c. Other symptoms can include flu-like feelings, panic attacks, numbness, agitation, and insomnia.

   d. Strategies to prevent antidepressant discontinuation syndrome include a gradual reduction in dose and avoiding sudden cessation of the medication.

   e. Reinstatement of the medication will usually reverse severe symptoms within 24 hours.

2. Fluoxetine and its major active metabolite norfluoxetine have long elimination half-lives.

   a. Changes in dose will not be fully reflected in plasma for several weeks.

   b. This affects strategies for both titration to final dose and withdrawal from treatment.

c. Side effects and drug-drug interactions may take weeks to disappear completely.

VII. Possible adverse reactions:

A. Serotonin Syndrome:

1. A potentially life-threatening adverse drug reaction associated with an excess of serotonin that results from therapeutic drug use, intentional self- poisoning or inadvertent interactions between drugs.

2. It is a triad of: mental-status changes, autonomic hyperactivity, and neuromuscular abnormalities.

3. An individual with a mild case may be afebrile but have tachycardia, shivering, diaphoresis or mydriasis, intermittent tremor or myoclonus as well as hyperreflexia.

4. An individual with a moderate case may have tachycardia, hypertension, hyperthermia, mydriasis, hyperactive bowel sounds, diaphoresis, clonus in the lower extremities, and/or a change in mental status (mild agitation, hypervigilance, or pressure of speech).

5. Practitioners who prescribe SSRIs should be familiar with the causes, presentation, and management of serotonin syndrome. Nursing assessments should consider that fever, confusion, autonomic and neuromuscular abnormalities may be signs of serotonin syndrome and should notify physicians.

B. Sexual dysfunction

C. Nausea

D. Lower birth weight and premature delivery with third trimester fetal exposure

1. Rare pulmonary hypertension in exposed neonates

2. Rare hypertension and eclampsia during the third trimester

E. Insomnia

F. Agitation and nervousness

G. Weight Loss or weight gain

H. Long-term treatment has been associated with increased risk of osteoporosis and hip fracture in later life.

1. In this context, vitamin D and calcium supplementation should be considered.

I. Citalopram carries a warning for QT interval prolongation at doses >40 mg/day.

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