# DSH PSYCHOTROPIC MEDICATION Operational Procedures

## FIRST GENERATION (CONVENTIONAL) ANTIPSYCHOTICS PROTOCOL:

### I. Indications:

A. At least 1 of the following clinical indications is present and documented in the chart:

1. DSM diagnosis of schizophrenia, schizoaffective disorder or other acute and/or chronic psychosis.

2. DSM diagnosis of bipolar disorder, current episode manic or mixed.

3. DSM diagnosis of a major depressive episode with current psychotic features.

4. Severe persistent agitation, aggressive, self-injurious, stereotypic, or impulsive behaviors with evidence that a behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective.

### II. Contraindications:

A. Hypersensitivity to the antipsychotic used or any of the components of its formulation.

B. Presence of neuroleptic malignant syndrome or an episode of neuroleptic malignant syndrome within the previous 2 weeks.

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

A. Tardive dyskinesia, tardive akathisia, or tardive dystonia.

B. Parkinson’s disease or Lewy-body dementia.

C. Hypertriglyceridemia or hypercholesterolemia (currently or by history).

D. Cerebrovascular disease and conditions that would predispose individuals to hypotension (e.g., dehydration, hypovolemia and treatment with antihypertensive medications). Low and mid potency first generation antipsychotics (e.g., chlorpromazine, loxapine, thiothixene, perphenazine, and trifluoperazine), are more likely than high-potency medications (e.g., fluphenazine or haloperidol) to cause hypotension.

E. Severe cardiovascular disease, especially history of torsade de pointes.

F. Liver disease, history of hepatitis or treatment with potentially hepatotoxic drugs.

G. History of active (poorly controlled) seizure disorder requiring anticonvulsant treatment or use of other drugs known to lower seizure threshold without neurological consultation.

H. Pregnancy or breast feeding. May cause neonatal dyskinesia.

I. History of prolactin sensitive or dependent tumors (e.g., breast cancer), or other conditions or drugs known to elevate prolactin (e.g., metoclopramide, pituitary adenoma).

J. Ultraviolet exposure. (Applies especially to chlorpromazine.)

K. Renal impairment.

L. Elderly neurocognitively disordered individuals. The U.S. Food & Drug Administration issued a black-box warning for this class.

**IV. The following initial workup should be completed:**

A. There is informed consent or alternate legal authorization.

B. There is chart documentation of:

1. Weight/BMI.

2. Waist circumference.

3. Personal or family history of Parkinson's disease.

4. Personal past history of high BMI.

C. Initial work up includes:

1. Electrolytes and LFTs within 30 days.

2. Serum prolactin within 30 days.

3. AIMS rating within 1 year.

4. Neurology consultation (for individuals with history of an active [poorly controlled] seizure disorder).

5. ECG within 1 year.

6. Vital signs within 30 days.

**V. Monitoring:**

A. Monthly monitoring includes weight.

B. Semi-annual monitoring includes ECG if concurrent use of medications which prolong QT interval is present, as indicated by boxed warning in the package insert.

C. Annual monitoring includes:

1. Serum prolactin level. Prolactin measurement should be obtained sooner if prolactin-related symptoms are present such as menstrual cycle changes, galactorrhea, gynecomastia and/or hirsutism occur. Medical consultation and consideration of brain imaging with focus on the pituitary/sella turcica if symptoms persist despite interventions such as changing to a less robust dopamine antagonist medication or partial dopamine agonist medication, lowering the dose of the medication, or treating with a dopamine agonist medication. Please see the appendix chapter of this policy regarding hyperprolactinemia. Prolactin-related adverse effects become increasingly likely at serum concentrations > 50 ng/ml.

2. Breast examination in men and women (including a note regarding presence or absence of galactorrhea or gynecomastia). Medical consultation and consideration of brain imaging with focus on the pituitary/sella turcica if galactorrhea or gynecomastia persist despite the interventions cited above.

3. Persisting prolactin level, despite the aforementioned interventions, above 100 ng/ml results in medical consultation and consideration of brain imaging with focus on the pituitary/sella turcica.

4. Waist circumference.

5. ECG.

6. AIMS rating. Done quarterly if positive until twice negative.

7. Fasting serum glucose is 100 mg/dl or higher or elevated Hgb A1c results in glucose tolerance test or 2-hour postprandial glucose measurement and medical consultation.

8. Nutritional consultation and appropriate dietary and exercise interventions if any of the following weight gain indicators occur:

    a. Weight increase of 5% in 1 month, 7.5% in three months, or 10% in six months;

    b. Waist circumference increase from below 35in. to > 35in. for females and from below 40in. to > 40in. for males

    c. BMI increase from normal to overweight (less than 25 to higher than 25) or from overweight to obese (25 – 29.9 to 30 or higher).

9. Abnormal or rising triglyceride and cholesterol levels result in medical consultation and appropriate interventions.

**VI. Dose initiation and titration:**

A. Please see the package insert for individual medications regarding typical initial dosing.

B. If treatment is well tolerated and symptoms persist, dose can be increased slowly.

In general, oral antipsychotics should be titrated upward every two weeks until one of four endpoints is reached, i.e., the desired clinical result is achieved, intolerable unmanageable adverse effects are encountered, the point of futility for the antipsychotic is reached, or an upper dose limit established by law or regulation is reached.

C. Typical dose is 600 to 1000 chlorpromazine equivalents per day. Haloperidol has an identified optimal plasma concentration range of 5 to 20 ng/ml of the parent compound. Please see the chapter of this policy regarding Depot Antipsychotics for dosing of fluphenazine decanoate and haloperidol decanoate.

D. Lower doses are typically started in the elderly and in those with renal or hepatic impairment. Dose is titrated slowly with careful monitoring for EPS, orthostatic blood pressure abnormality, and sedation.

E. There is documented explanation if doses exceed those listed in the Dose Maximum Tables of this policy for more than 15 days. (MRC or TRC consultation or review is required for doses exceeding listed maximums for more than 15 days. Haloperidol Decanoate may exceed the dose listed in the Dose Maximum Tables for up to 6 weeks in the context of initial loading.)

F. Dosage accounts for drug-drug interactions:

1. Approximately twofold increase in dose may be needed if used with carbamazepine, a metabolic inducer. Similar changes may be needed for other metabolic inducers (e.g., phenytoin, phenobarbital, rifampin, and possibly oxcarbazepine).

2. Lower doses may be needed if used with CYP2D6 and/or CYP3A4 inhibitors (e.g., fluoxetine, paroxetine, bupropion, sertraline, fluvoxamine, ketoconazole, erythromycin, clarithromycin, and diltiazem.). Avoid combining first-generation antipsychotic medications with cimetidine, grapefruit juice and protease inhibitors.

G. Pulse and blood pressure are monitored prior to dose administration as clinically indicated (for 1 week after starting or increasing dose). Signs of orthostatic hypotension are documented if the individual can verbalize. Pulse and blood pressure are recorded first in the seated position after 3 minutes and then in the standing position after 2 minutes. If the individual cannot stand up, he/she is monitored closely until the dose is stable if he/she is known to try to get up and not follow recommendations.

If any recorded item lies outside the following parameters, the measure is repeated after 15 minutes. If the item is then within the parameter, the antipsychotic may be given. If still outside the parameter, the physician is called to assess before dose administration. The parameters are:

1. Systolic blood pressure below 90 mm or above 150 mm.

2. Diastolic blood pressure below 60 mm or above 100 mm.

3. Drop greater than 20 mm in systolic or diastolic pressure between sitting and standing.

4. Pulse greater than 120 beats/min or less than 60 beats/min.

**VII. Rare severe adverse reactions include:**

A. Transient ischemic attack and stroke especially in elderly patients with dementia.

B. Neuroleptic Malignant Syndrome.

C. QT interval prolongation and torsade de pointes.

**VIII. Additional Considerations:**

Risk is increased if the individual has cardiac arrhythmias; history of sudden death in the family; significant risk of electrolyte imbalances (e.g., diarrhea, diuretic treatment) or concomitant use of drugs that have demonstrated QT prolongation as one of their pharmacological effects and have this effect described in the full prescribing information as a contraindication or a boxed or bolded warning (e.g., mefloquine, pimozide).

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