DSH PSYCHOTROPIC MEDICATION Operational Procedures

LURASIDONE PROTOCOL:

I. Indications:

A. At least one 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 psychoses.

2. DSM diagnosis of bipolar disorder, current episode manic, depressed, or mixed. Lurasidone may be especially effective in treating bipolar depression.

3. DSM diagnosis of a major depressive episode with current psychotic features. Adjunctive treatment also may benefit depressive 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 lurasidone or any of the components of its formulation.

B. Severe hepatic or renal disease/impairment.

C. Concurrent treatment with strong cytochrome P450 3A4 inducers (e.g., carbamazepine, phenobarbital, or rifampin) or inhibitors (e.g., ketoconazole).

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

A. Cerebrovascular disease and conditions that would predispose individuals to hypotension (e.g., dehydration, hypovolemia and treatment with antihypertensive medications).

B. Severe cardiovascular disease.

C. Liver disease, history of hepatitis or treatment with potentially hepatotoxic drugs. The initial dose should be limited to 20 mg per day, with a maximum dose of 80 mg per day.

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

E. Signs (or, history) of tardive dyskinesia or known proneness to acute neurological symptoms. Risk of akathisia may be reduced by evening dosing, such that peak plasma concentrations occur during sleep.

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

G. 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).

H. Parkinson's Disease.

I. Renal impairment. The initial dose should be limited to 20 mg per day, with a maximum dose of 80 mg per day.

J. Elderly neurocognitively disordered individuals with psychosis.

K. History of leukopenia or severe neutropenia. Risk is low; however, the U.S. Food and Drug Administration has mandated a class warning for the second-generation antipsychotics.

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.

C. Initial work up includes:

1. Electrolytes and liver function tests within 30 days.

2. Serum prolactin within 30 days.

3. AIMS rating within one year.

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

5. ECG within one year.

6. Vital signs within 30 days.

V. Monitoring:

A. Monthly monitoring includes weight.

B. Semi-annual monitoring includes:

1. Hepatic functions, if known liver disease

2. Basic metabolic panel, if known renal disease.

C. Annual monitoring includes:

1. Serum prolactin level. Prolactin measurement should be obtained sooner if prolactin-related symptoms, 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 should be considered 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. Prolactin-related adverse effects become increasingly likely at serum concentrations exceeding 50 ng/mL. [Please see the appendix chapter of this policy regarding hyperprolactinemia.]

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

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. Waist circumference.

4. ECG.

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

6. 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.

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

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

   b. Waist circumference increase from below 35 to higher than 35 in females and below 40 to higher than 40 in 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).

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

VI. Dose initiation and titration:

A. Initial dose is 40 – 160 mg per day. Dose titration is not typically required. Higher doses have been demonstrated to be substantially less likely to induce akathisia if lurasidone is given in the evening, such that peak plasma concentrations occur during sleep.

Typical dose is 40 – 160 mg/day. Adequate absorption requires that a meal of at least 350 Kcal be consumed proximately to lurasidone dosing (i.e., within less than two hours of eating). Doses should be initiated at 20 mg per day in the presence of mild to moderate hepatic or renal disease/impairment with a maximum dose of 80 mg per day.

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.

B. The lower dose of 20 mg is typically started in the elderly and in those with renal or hepatic impairment. In such cases, the maximum daily dose is 80 mg.

C. There is documented explanation if dose higher than 160 mg/day is used (see next section). Doses >160 mg/day for >15 days require MRC or TRC consultation or review.

D. Dosage accounts for drug-drug interactions:

1. A dose increase may be required for weak to moderate cytochrome P450 3A4 inducers (e.g., oxcarbazepine). Use is contraindicated with strong cytochrome P450 3A4 inducers (e.g., carbamazepine, phenobarbital, or rifampin).

2. Lower doses may be needed if used with weak or moderate cytochrome P450 3A4 inhibitors (e.g., diltiazem). Lurasidone is contraindicated with strong cytochrome P450 3A4 inhibitors (e.g., ketoconazole).

F. Pulse and blood pressure are monitored prior to dose administration as clinically indicated (e.g., during titration or at doses above maximum) for one week after starting or increasing dose. Signs of orthostatic hypotension are documented if individual can verbalize. Pulse and blood pressure are recorded first in the seated position after three minutes and then in the standing position after two minutes. If 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 following parameters, the measure is repeated after 15 minutes. If the item is then within the parameter, lurasidone may be given. If still outside the parameter, the physician is called to assess before dose administration.

1. The parameters are:

    a. Systolic blood pressure <90 mm or >150 mm.

    b. Diastolic blood pressure <60 mm or >100 mm.

    c. Drop >20 mm in systolic or diastolic pressure between sitting and standing.

    d. Pulse >120/min or <60/min.

VII. Possible adverse reactions:

A. Headache.

B. Sedation or fatigue.

C. Insomnia.

D. Agitation and anxiety.

E. Reversible extrapyramidal symptoms (parkinsonian side effects, akathisia and acute dystonic reactions).

F. Tardive Dyskinesia especially with the demented elderly.

G. Orthostatic Hypotension.

H. Hyperprolactinemia with associated decreased libido, galactorrhea, menstrual disturbances (including amenorrhea) infertility, decreased bone density (long term), gynecomastia, and erectile and ejaculatory dysfunction.

I. Dyspepsia and other upper gastrointestinal symptoms.

J. Rare severe adverse reactions include:

1. Transient ischemic attack and stroke especially with the demented elderly.

2. Neuroleptic Malignant Syndrome.

References:

American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists & North American Association for the Study of Obesity

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