DSH PSYCHOTROPIC MEDICATION Operational Procedures

ASENAPINE 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 psychotic disorder.

2. DSM diagnosis of bipolar disorder. For acute treatment during a current episode (manic or mixed). For maintenance after achieving responder status for two weeks. The long-term usefulness of asenapine for the individual should be reassessed.

3. Severe persistent self-injurious or assaultive behavior, with evidence that a behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective.

B. Contraindications:

1. History of hypersensitivity to asenapine or any of the components of its formulation. May cause serious (type I) allergic responses.

2. CNS depression (coma).

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

A. Diabetes mellitus, glucose intolerance, hyperglycemia, personal history of high BMI, family history of diabetes, drug exposure to alpha or beta-blockers, hypertension and obesity (especially abdominal). Asenapine is less provocative of weight gain than related medications (i.e., clozapine and olanzapine).

B. Concomitant use of medications known to cause elevated blood glucose (e.g., steroids, niacin, thiazide diuretics, atypical antipsychotics).

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

D. Cerebrovascular disease or other conditions that would predispose individuals to hypotension (e.g., dehydration, hypovolemia and treatment with antihypertensive medications). Asenapine appears to pose less cardiovascular risk than related compounds (i.e., clozapine and olanzapine),

E. Severe cardiovascular disease. Asenapine appears to pose less risk than related medications (i.e., clozapine and olanzapine).

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

G. History of active (or, poorly controlled) seizure disorder requiring anticonvulsant treatment, without neurological consultation.

H. Use of drugs known to lower seizure threshold.

I. CNS depression or use of other drugs known to induce CNS depression.

J. Prostatic hypertrophy or paralytic ileus.

K. History of neuroleptic malignant syndrome.

L. Elderly individuals with neurocognitive disorder-related psychosis.

M. Signs (or, history) of tardive dyskinesia.

N. History of prolactin sensitive breast cancer. Pregnancy or breast feeding. May cause neonatal dyskinesia.

O. Leukopenia or history of severe neutropenia. The risk is low; however, the U.S. Food and Drug Administration has mandated a class warning for the second-generation antipsychotics.

III. The following initial workup should be completed:

A. There is informed consent or alternate legal authorization.

B. There is chart documentation of:

1. Waist circumference.
2. BMI.
3. Personal or family history of diabetes.
4. Personal history of high BMI.
5. Personal history of elevated triglycerides or hypercholesterolemia.

C. Initial work up includes:

1. Fasting blood glucose and/or Hgb A1c (optional) within 30 days.
2. Lipid panel or cholesterol and triglycerides within 30 days.
3. Electrolytes and liver function tests within 30 days.
4. AIMS rating within one year.
5. Neurology consultation (for individuals with history of an active (poorly controlled) seizure disorder).

6. ECG within one year.

7. Vital signs within 30 days.

IV. Monitoring:

A. Monthly monitoring includes:

1. Weight / BMI.

B. Semi-annual monitoring includes:

1. Lipid panel or triglycerides and cholesterol).

2. Fasting glucose and or optional Hgb A1c.

3. Semi-annual monitoring includes ECG (if concomitant medication that prolongs QT interval is present, as indicated by a boxed warning in the package insert).

C. Annual monitoring includes:

1. Serum prolactin level. Prolactin measurement obtained sooner if prolactin-related symptoms such as menstrual cycle changes, galactorrhea, gynecomastia and/or hirsutism occur. Prolactin-related adverse effects become increasingly likely at serum concentrations exceeding 50 ng/mL. Medical consultation and consideration of brain imaging with focus on the pituitary/sella turcica if symptoms persist or concentration persists at > 100 ng/mL, despite interventions such as lowering the dose of the medication, changing to a less robust dopamine antagonist medication, or treating with a dopamine agonist medication. Please see the appendix chapter of this policy regarding hyperprolactinemia.

2. Breast examination in men and women, including documentation 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 above cited interventions.

3. Waist circumference.

4. AIMS (unless positive, then quarterly) until negative twice.

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

6. 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 35in. to > 35in. for females and from below 40in. to > 40in. for males.

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

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

8. ECG.

V. Dose initiation and titration:

A. Asenapine is available only as sublingual dissolving wafers. Crushing, swallowing, or drinking within 10 minutes of administration substantially reduces plasma concentrations. Typical oral initial dose is 5 – 10 mg BID and is titrated as clinically indicated and tolerated. Steady-state occurs at about three days. In acute manic states, an initial dose of 10 mg BID is recommended, with possible taper to 5 mg BID as mania abates.

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. Doses greater than 20 mg per day for more than 15 days require MRC or TRC consultation.

C. There is documented explanation if dose higher than 20 mg/day is used.

D. Dosage accounts for drug-drug interactions:

1. An increase in dose may be required if used with carbamazepine, a metabolic inducer. Similar changes may be needed for other metabolic inducers (e.g., phenytoin, omeprazole, phenobarbital, or rifampin). Higher doses may be required in heavy smokers.

2. Lower doses may be needed if used with CYP1A2, 2D6, or 3A4 inhibitors (e.g., fluvoxamine, high dose caffeine, ciprofloxacin, cimetidine, paroxetine, or fluoxetine). Lower doses may be required if an individual stops smoking. Asenapine should not be used in moderate to severe liver impairment (Child-Pugh categories B or C).

E. Asenapine is circa 95% protein bound and may displace other protein-bound drugs (e.g., warfarin).

F. An effort is made to monitor pulse and blood pressure before giving asenapine doses and after 30 minutes during the first few days of administration. If the individual refuses them due to agitation, orthostatic changes are measured when calmer as clinically indicated (e.g., during titration or at doses above maximum. Signs of orthostatic changes are documented if the 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.

G. If any recorded item lies outside following parameters, the measure is repeated after 15 minutes. If the item is then within the parameter, asenapine 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/min or less than 60/min.

VI. Possible adverse reactions:

A. Weight gain. (less provocative than clozapine or olanzapine)
B. Hyperglycemia, ranging from mild glucose intolerance to diabetes mellitus.
C. Hyperlipidemia.
D. Peripheral edema.
E. Akathisia.
F. Somnolence.
G. Obtundation &/or confusion.
H. Extrapyramidal side effects.
I. Neuroleptic malignant syndrome.
J. Seizure.
K. Lightheadedness or syncope.
L. Nausea.
M. Dyspepsia.
N. Constipation.
O. Dry mouth.

P. Postural hypotension.

Q. Tachycardia.

R. Prolonged QTc interval (rare).

S. Cerebrovascular events in demented elderly.

T. Elevated liver enzymes.

U. Hyperprolactinemia.

References:

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