DSH PSYCHOTROPIC MEDICATION Operational Procedures

QUETIAPINE 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 (e.g., major depression with psychotic features). Quetiapine is effective for adjunctive treatment of major depression.

2. DSM diagnosis of bipolar disorder, current episode manic, mixed, or depressed. Data suggest efficacy in treating bipolar depression. May provide adjunctive prophylactic benefit, probably via effects of norquetiapine (a norepinephrine reuptake inhibitor).

3. Severe persistent aggression or self-injurious behavior 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 quetiapine or any of the components of its formulation;

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

1. Diabetes mellitus, glucose intolerance, hyperglycemia, personal history of high BMI, family history of diabetes, drug exposure to alpha or beta blockers, hypertension, obesity (especially abdominal);

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

3. Hypertriglyceridemia or hypercholesterolemia (currently or by history);

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

5. Severe cardiovascular disease, history of myocardial infarction or ischemia, or heart failure;

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

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

8. Signs (or, history) of tardive dyskinesia. Least provocative of the dopamine antagonist antipsychotics, with the exception of clozapine;

9. Elderly neurocognitively disordered individuals with psychosis;

10. Pregnancy or breast feeding. May cause neonatal dyskinesia;

11. 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.

III. 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 diabetes mellitus;

4. Personal past history of high BMI;

5. Personal history of elevated triglycerides or hypercholesterolemia.

C. Initial workup includes:

1. Fasting serum 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 or poorly controlled seizure disorder);

6. Vital signs within 30 days;

7. ECG within one year.

IV. Monitoring:

A. Monthly monitoring includes weight;

B. Semi-annual monitoring includes:

1. Fasting blood glucose and/or Hgb A1c (optional);

2. Lipid panel or triglycerides and cholesterol;

3. Semi-annual monitoring includes ECG, if medications known to prolong QT

interval are concurrently 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, 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.]

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 above cited interventions;

3. Waist circumference;

4. Fasting blood glucose levels of 100 mg/dL or higher or elevated Hgb A1c result in glucose tolerance test or 2-hour postprandial glucose measurement and medical consultation;

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

6. ECG;

7. Discussion of risks of cataracts and benefits of eye examination. Examination only performed if desired by the treated individual or indicated by visual change;

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

   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).

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

V. Dose initiation and titration:

A. Typical initial dose is 25 – 50 mg BID daily, or as clinically indicated. The extended release formulation is typically initiated at 200 mg QHS and titrated at a rate of 200 – 400 mg per week.

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. For acute mania, initial dose may be 50 mg BID, or as clinically indicated.

C. If treatment is well tolerated and symptoms persist, dose can be increased by 25 – 50 mg BID or TID per day or as clinically indicated.

D. Typical dose is 400 – 800 mg (e.g., 400 mg by day #4 and up to 800 mg by day #6). Maximum dose is 1200 mg/day. Higher doses for > 15 days require MRC or TRC consultation or review.

E. Dose is typically started lower and titrated more slowly in individuals with renal or hepatic impairment, with careful monitoring of orthostatic blood pressure and sedation.

1. Dosage accounts for drug-drug interactions:

a Higher doses (up to 5-fold increase) may be needed if used with CYP P450 3A4 inducers (e.g., carbamazepine, phenytoin, barbiturates, glucocorticoids, or rifampin).

b Lower doses may be needed if used with CYP P450 3A4 inhibitors (e.g., ketoconazole, itraconazole, fluconazole, erythromycin, fluoxetine, fluvoxamine, clarithromycin or diltiazem).

2. 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, quetiapine may be given. If still outside the parameter, the physician is called to assess before dose administration.

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.

VI. Possible adverse reactions:

A. Sedation and incoordination;

B. Hypotension and rare pulmonary edema;

C. Dizziness related to orthostasis;

D. Weight gain;

E. Hyperglycemia;

F. Diabetes mellitus;

G. Hyperlipidemia;

H. Hyperprolactinemia (least provocative dopamine antagonist, except clozapine);

I. Cataract formation (doubtful in humans);

J. Renal impairment;

K. Rare severe adverse effects include:

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

2. Neuroleptic malignant syndrome (very rare);

3. QT interval prolongation (very rare).

VII. Additional Considerations:

Consider and document discussion with treated individual or conservator regarding benefits of ophthalmic examination (by methods adequate to detect cataract formation) and risks of no examination.

References:

American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists & North American Association for the Study of Obesity 2004. Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care,* 27**,** 596-601.

AstraZeneca Pharmaceuticals LP 2020a. Seroquel Package Insert. Wilmington, Delaware.

AstraZeneca Pharmaceuticals LP 2020b. Seroquel XR Package Insert. Wilmington, Delaware.

Citrome, L. 2017. Activating and Sedating Adverse Effects of Second-Generation Antipsychotics in the Treatment of Schizophrenia and Major Depressive Disorder: Absolute Risk Increase and Number Needed to Harm. *J Clin Psychopharmacol,* 37**,** 138-147.

Devane, C. L. & Nemeroff, C. B. 2001. Clinical pharmacokinetics of quetiapine: an atypical antipsychotic. *Clin Pharmacokinet,* 40**,** 509-22.

Meyer, J. M. 2001. Effects of atypical antipsychotics on weight and serum lipid levels. *J Clin Psychiatry,* 62 Suppl 27**,** 27-34; discussion 40-1.