

ANTIPSYCHOTICS

thioridazine (Mellaril®)

INDICATIONS

- 1) Schizophrenia, refractory (failed other classes of antipsychotics)

PRECAUTIONS TO CONSIDER

Contraindications

Absolute:

- 1) History of anaphylactic reaction and similarly severe significant hypersensitivity to medication prescribed or structurally related medication
- 2) Severe CNS depression
- 3) QTc > 450 msec
- 4) Concomitant use of other drugs known to prolong QTc interval
- 5) Congenital long QT syndrome
- 6) Personal history of syncope
- 7) Family history of sudden death at an early age (under age of 40 years)
- 8) Known heart disease
- 9) Hypomagnesemia
- 10) Hypokalemia
- 11) Retinitis Pigmentosa
- 12) Known poor CYP2D6 metabolizer
- 13) Concomitant use with drugs that inhibit thioridazine metabolism (fluvoxamine, propranolol, pindolol)
- 14) Concomitant use with drugs that inhibit CYP2D6 (fluoxetine, paroxetine)

Relative:

- 1) Pregnancy/nursing mothers
- 2) History of drug induced agranulocytosis or leukopenia
- 3) Breast cancer
- 4) History of neuroleptic malignant syndrome
- 5) Narrow angle glaucoma
- 6) Impaired hepatic function
- 7) Prostatic hypertrophy
- 8) Parkinson's disease

Precautions

Alcoholism (active), recent or current blood dyscrasias, angina, hypotension, congestive heart failure, arrhythmias, glaucoma, poorly controlled seizure disorder, urinary retention, patients at risk for paralytic ileus, severe tardive dyskinesia, dementia-related psychosis.

Pregnancy and Breast-Feeding

See relative contraindications. Most antipsychotics are FDA Pregnancy Category C.

ANTIPSYCHOTICS - continued

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PRECAUTIONS TO CONSIDER (continued)

Drug Interactions of Major Significance

- 1) Concomitant use of CNS depressants
- 2) Antithyroid agents
- 3) Concomitant use of agents that cause EPS (including droperidol metoclopramide, amoxapine, metyrosine, pimozide, reserpine)
- 4) Concomitant use of hypotension producing agents
- 5) Levodopa
- 6) Concomitant anticholinergic drugs
- 7) Concomitant use with drugs that inhibit thioridazine metabolism (fluvoxamine, propranolol, pindolol)
- 8) Concomitant use with drugs that inhibit CYP2D6 (fluoxetine, paroxetine)
- 9) Concomitant use of CYP2D6 inducers

SEE TABLE A: Cytochrome P450 Drug Metabolism/Inhibition

Age-Specific Considerations

- 1) Conservative dosing and careful monitoring are advised in children and the elderly

Side Effects Which Require Medical Attention

- 1) Anticholinergic effects
- 2) Visual changes
- 3) Extrapyramidal side effects (akathisia, dystonia, pseudo-Parkinsonism)
- 4) Tardive dyskinesia
- 5) Hypotension
- 6) Rashes, photosensitivity and altered pigmentation
- 7) Early symptoms of agranulocytosis (fever, sore throat, weakness)
- 8) Galactorrhea
- 9) Amenorrhea
- 10) Gynecomastia
- 11) Fluctuating vital signs
- 12) Altered consciousness

PATIENT MONITORING

Patient Monitoring Parameters

- 1) Pregnancy test – as clinically indicated
- 2) BMI and waist circumference measurements – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated and quarterly when the antipsychotic dose is stable.

ANTIPSYCHOTICS - continued

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PATIENT MONITORING (continued)

- 3) Fasting plasma glucose level or hemoglobin A_{1c} – before initiating a new antipsychotic, then yearly.

If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly.

- 4) Lipid screening [total cholesterol, low- and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl

If no lipid screening has been done within the last 2 years, then a lipid profile should be obtained within 30 days of initiation of the drug.

- 5) Sexual function inquiry – inquire for evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbance yearly.

If a patient is receiving an antipsychotic known to be associated with prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly

- 6) Prolactin level – if there is evidence of galactorrhea/gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory yearly.
- 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase
- 8) Tardive dyskinesia evaluation – every 3 months and as clinically indicated.
- 9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly
- 10) Ocular evaluations – yearly for patients older than age 40 years; every 2 years for younger patients
- 11) Serum potassium level – baseline, every six months and as clinically indicated
- 12) Serum magnesium level – baseline and as clinically indicated (especially if potassium level is low)
- 13) EKG prior to initiating therapy; 7-14 days after dose change; 7-14 days after other medication changes that could significantly alter the cardiac effects of thioridazine; every six months; and as clinically indicated.

Dosing

See DSHS/DADS Drug Formulary for dosage guidelines.

Exceptions to maximum dosage must be justified as per medication rule.