Medication Audit Criteria and Guidelines

Trazodone (Desyrel®), Nefazodone (Serzone®)

PEFC Approved: January 2023

Indications

If a medication is prescribed for an off-label indication, documentation in the patient chart is recommended.

Label:

- Major Depressive Disorder

Off-label:

- Insomnia

Black Box Warning

- Increased risk of suicidal thinking and behavior in children, adolescents and young adults (≤ 24 years) taking antidepressants. Monitor for worsening and emergence of suicidal thoughts and behaviors.
- Nefazodone: Cases of life-threatening hepatic failure have been reported in patients treated with nefazodone. Ordinarily, treatment with nefazodone should not be initiated in individuals with active liver disease or with elevated baseline serum transaminases. Nefazodone should be discontinued if clinical signs or symptoms suggest liver failure. Patients who develop evidence of hepatocellular injury such as increased serum AST or serum ALT levels ≥ 3 times the upper limit of NORMAL, while on nefazodone should be withdrawn from the drug.

Contraindications

- Co-administration with an MAOI, including linezolid or IV methylene blue, or use within 14 days of discontinuing an MAOI
- History of anaphylactic reaction or similarly severe significant hypersensitivity to trazodone or nefazodone
- Trazodone: recovery phase of myocardial infarction
- Nefazodone: history of liver injury due to previous nefazodone treatment
- Nefazodone: concurrent therapy with carbamazepine, cisapride, terfenadine, astemizole, pimozide, or full doses of triazolam

Warnings and Precautions

- Cardiovascular disorders including arrhythmia, heart block and failure
- Diagnosis of a seizure disorder or history of seizures, head trauma, or concurrent therapy with medications that may lower the seizure threshold
- Discontinuation syndrome after abrupt discontinuation
- CNS depression and enhanced response to alcohol, barbiturates, other CNS depressants
- History of priapism
- Hypotension, including orthostatic hypotension and syncope
- Bipolar disorder in the absence of a mood stabilizer
- Prolonged QTc interval especially with concomitant use of CYP3A4 inhibitors or other drugs known to prolong the QTc interval and in patients with congenital long QT syndrome, hypokalemia, or hypomagnesemia
- Suicidal thoughts and behaviors in children, adolescents, and young adults (≤ 24 years)
- Hepatic function impairment or elevated baseline serum transaminases
- Renal function impairment
- Abnormal bleeding especially when used concomitantly with antiplatelets and/or anticoagulants or in patients with preexisting platelet dysfunction or coagulation disorders

Adverse Reactions

Side Effects Which Require Medical Attention

- Nausea and vomiting
- Constipation
- Headache
- Xerostomia
- Cardiac dysrhythmia, including bradycardia
- Hypotension, dizziness, lightheadedness, or fainting
- Priapism
- Seizure
- Serotonin syndrome
- Prolonged QT interval
- Torsades de pointes
- Nefazodone: signs and symptoms of liver failure such as elevated liver function tests, jaundice, anorexia, GI complaints, or malaise
- Nefazodone: tinnitus
- Nefazodone: visual disturbance

Drug Interactions of Major Significance

See: Indiana Univ Drug Interaction Table

See: Lexicomp, Micromedex for more information

Special Populations

- Pediatrics/Adolescents: Safety and efficacy have not been established in children younger than 18 years.
- Geriatric:
  - Trazodone: less likely to tolerate oral once daily dosing; consider divided doses for the treatment of depression.
  - Nefazodone: start at lower doses and titrate gradually based on response and tolerability.
- Renal: dosage adjustment not required.
- Hepatic:
  - Trazodone: has not been studied. Use with caution.
  - Nefazodone: no specific recommendations but use with caution and avoid initiation in patients with active liver disease/elevated baseline serum transaminases.
- Hemodialysis:
  - Trazodone: no dosage adjustment necessary, not significantly dialyzed. Titrate with caution.
  - Nefazodone: no specific recommendations provided.
- Pregnancy and Breastfeeding
  - Review product-specific labeling. Consider risks/benefits in reviewing medication-specific labeling.

Patient Monitoring Parameters

Baseline Tests:

- Pregnancy test (females)
- CBC
- ECG as clinically indicated
- Liver function

Ongoing Tests:

- Pregnancy test (females) as clinically indicated
- Trazodone: Liver function tests as clinically indicated
- Nefazodone: Liver function tests at 1, 2, 4, 6 and 12 months, then annually and as clinically indicated. Discontinue if AST or ALT levels are 3 times (or greater) the upper limit of normal.
- CBC as clinically indicated

- ECG as clinically indicated
- Monitor for emergence of suicidal ideation or behavior or worsening depression

Dosing

- See HHSC Psychiatric Drug Formulary for dosage guidelines.
- Exceptions to maximum dosage must be justified as per medication rule.