

# **Medication Audit Criteria and Guidelines**

## **Benzodiazepines - Anxiolytics and Hypnotics**

- alprazolam (Xanax®, Xanax XR®)
- chlordiazepoxide (Librium®)
- clonazepam (Klonopin®)
- clorazepate (Tranxene®)
- diazepam (Valium®)
- lorazepam (Ativan®)
- oxazepam (Serax®)
- temazepam (Restoril®)
- triazolam (Halcion®)

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## Indications

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

## Label:

Note that some of these agents have other FDA labeled indications not listed, including treatment of seizures.

- Alcohol/substance withdrawal (chlordiazepoxide, diazepam, oxazepam, clorazepate [not in treatment guidelines])
- Anxiety disorders (alprazolam, chlordiazepoxide, clorazepate, diazepam, lorazepam, oxazepam; off label for clonazepam)
- Short term relief of anxiety symptoms (chlordiazepoxide, clorazepate diazepam, lorazepam, oxazepam; off label for clonazepam)
- Panic disorder with or without agoraphobia (alprazolam, clonazepam)
- Short term use for the treatment of insomnia (temazepam, triazolam)

Off Label:

- Acute intervention for anxiety, agitation, violent behavior (lorazepam, chlorpromazine)
- Akathisia (lorazepam)
- Catatonia (lorazepam)
- Neuroleptic malignant syndrome (diazepam, lorazepam)

- Sedative hypnotic withdrawal
- Serotonin syndrome (lorazepam)
- Tardive dyskinesia (clonazepam)
- Vertigo (alprazolam, clonazepam, diazepam, lorazepam)

#### **Black Box Warning**

Risks from Concomitant use with opioids: Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for patients with inadequate alternative treatment options. Limit dosages and durations to the minimum required and follow patients for signs and symptoms of respiratory depression and sedation.

Misuse and addiction: The use of benzodiazepines exposes users to the risk of misuse and addiction, which can lead to overdose or death. Misuse of benzodiazepines commonly involve concomitant use of other medications, alcohol, and or illicit substances, which is associated with an increased frequency of serious adverse outcomes.

Dependence and withdrawal reactions: The continued use of benzodiazepines may lead to clinically significant physical dependence. The risks of dependence and withdrawal increase with longer treatment duration and higher daily dose. Abrupt discontinuation or rapid dosage reduction after continued use may precipitate acute withdrawal reactions, which can be life threatening. To reduce the risk of withdrawal reactions, use an individualized gradual taper, taking into account dosage and length of treatment, to discontinue or reduce dosage.

#### Contraindications

- Concomitant use with strong CYP 3A inhibitors including itraconazole, ketoconazole, nefazodone, lopinavir, ritonavir (alprazolam, triazolam)
- History of anaphylactic reaction or similarly severe significant hypersensitivity to the medication prescribed or other benzodiazepines

#### **Warnings and Precautions**

- Acute narrow angle glaucoma (alprazolam, clonazepam, clorazepate, diazepam, lorazepam)
- Concomitant use with alcohol or CNS depressants
- Concomitant use of IM benzodiazepines with IM olanzapine
- Concomitant use with opioids
- Dementias/delirium
- Depression and/or suicidal ideation
- Discontinuation or rapid dose reduction with use over 1 month
- Fall risk and CNS depression

- History of alcohol or other substance misuse
- Myasthenia gravis (diazepam)
- Porphyria
- Pregnancy/nursing mothers
- Renal impairment
- Respiratory disease (i.e., sleep apnea, COPD)
- Severe hepatic impairment
- Severe respiratory insufficiency
- Untreated open angle glaucoma (diazepam)

## **Adverse Reactions**

Side Effects Which Require Medical Attention

- Antiretrograde amnesia
- Ataxia
- Delirium
- Falls
- Obtundation
- Psychomotor impairment
- Redness, swelling or pain at injection site
- Respiratory depression
- Significant sedation
- Withdrawal syndrome
- Worsening agitation, disinhibition, or aggression (paradoxical reaction) especially in pediatrics, older adults, or those with developmental disabilities

## **Drug Interactions of Major Significance**

See: Contraindications

See: Indiana Univ Drug Interaction Table

See: Lexicomp, Micromedex for more information

## **Special Populations**

- Pediatrics/Adolescents
  - Chlordiazepoxide, clorazepate, triazolam: Not considered in the Psychotropic Medication Utilization Parameters for Children and Youth in Texas Public Behavioral Health (6th Version).
  - Alprazolam, clonazepam, diazepam, lorazepam, oxazepam, temazepam: Reviewed for the "Psychotropic Medication Utilization Parameters for Children and Youth in Texas Public Behavioral Health (6th Version)" but not included/recommended due to evidence of possible harm/increased incidence of adverse effects and potential for misuse and/or addiction.

- If used, use lowest effective dose.
- Geriatric
  - Included in Beers Criteria, use with caution.
  - If used, use lower doses of short half-life agents.
- Renal
  - Lorazepam: no dosage adjustment necessary for mild to severe impairment but use repeated doses with caution.
- Hepatic
  - Alprazolam, lorazepam: Dosing adjustment needed, see the package insert, Lexicomp, or Micromedex for specific recommendations.
  - Lorazepam injection: use not recommended in severe impairment or failure.
  - Diazepam: in cirrhosis, reduce daily dose by 50%.
- Hemodialysis
  - Clonazepam, diazepam, lorazepam, oxazepam: no adjustments necessary.
- Pregnancy and Breastfeeding
  - See Warnings and Precautions.
  - Review product-specific labeling. Consider risks/benefits in reviewing medication-specific labeling.

#### **Patient Monitoring Parameters**

Baseline Tests:

• Pregnancy test (females)

Ongoing Tests:

- Pregnancy test (females) as clinically indicated
- Assess for signs of CNS depression and respiratory depression

#### Dosing

- See HHSC Psychiatric Drug Formulary for dosage guidelines.
- If a medication is prescribed at dosages in excess of the Psychotropic Dosage Guidelines found in the HHS Psychiatric Drug Formulary, documentation in the patient chart is recommended.