Medication Audit Criteria and Guidelines

Tricyclic Antidepressants: amitriptyline (Elavil®), desipramine (Norpramin®, Pertofrane®), doxepin (Sinequan®), imipramine (Tofranil®), maprotiline (Ludiomil®), nortriptyline (Pamelor®, Aventyl®), protriptyline (Vivactil®), trimipramine (Surmontil®)

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Indications

- Anxiety disorders (doxepin)
- Attention deficit hyperactivity disorder (desipramine, imipramine, nortriptyline)
- Bipolar disorder – depressed phase (maprotiline)
- Bulimia nervosa (desipramine, imipramine)
- Chronic pain (amitriptyline, maprotiline)
- Depressive disorders
- Dysthymia (Maprotiline)
- Fibromyalgia (amitriptyline)
- Insomnia (doxepin)
- Irritable bowel syndrome (amitriptyline)
- Migraine prophylaxis (amitriptyline)
- Mixed anxiety and depressive disorder (Maprotiline)

- Neuropathic pain (desipramine, imipramine)
- Nocturnal enuresis (imipramine, nortriptyline)
- Panic disorder (imipramine)
- Smoking cessation (nortriptyline)
- Urinary incontinence (imipramine)

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.

Contraindications

Absolute

- History of anaphylactic reaction or similarly severe significant hypersensitivity to the medication prescribed
- History of seizure disorder or those at risk for seizure disorder (maprotiline)
- Recovery phase of myocardial infarction
- Use of a monoamine oxidase inhibitor within 14 days (including linezolid or IV methylene blue)

Relative

- Pheochromocytoma
- Pregnancy/nursing mothers

Precautions

- Alcohol intoxication
- Bipolar disorder in the absence of a mood stabilizer
- Cardiovascular disorders including arrhythmia
- Concomitant use with agents that impair metabolism of serotonin (e.g., MAO inhibitors including phenelzine, tranylcypromine, linezolid, methylene blue)

- Concomitant use with other serotonergic agents (e.g., SSRIs, SNRIs, triptans, TCAs, fentanyl, lithium, tramadol, buspirone, St John's wort, tryptophan)
- Diagnosis of a seizure disorder or history of seizures
- Discontinuation syndrome
- Disease states where increased anticholinergic activity may complicate disease course (narrow-angle glaucoma, benign prostatic hypertrophy, urinary retention)
- Falls
- Heart block and failure
- Hepatic function impairment
- Hyperthyroidism or hypothyroidism (e.g., patients receiving thyroid supplementation)
- Lower respiratory tract symptoms (asthma)
- Recent or current blood dyscrasias
- Renal failure
- Suicidal thoughts and behaviors in children, adolescents, and young adults (≤ 24 years)

Adverse Reactions

Side Effects Which Require Medical Attention

- Anticholinergic effects
- Dizziness, lightheadedness or fainting (orthostatic hypotension)
- Jaundice
- QTc>500 msec
- Seizures
- Sexual function impairment
- Tachycardia greater than 100 beats/min

Pregnancy and Breastfeeding

- See relative contraindications
- Review product-specific labeling. Consider risks/benefits in reviewing medication-specific labeling

Drug Interactions of Major Significance

- Cimetidine
- Concomitant monoamine oxidase inhibitors (furazolidone, procarbazine, selegiline, tranylcypromine, phenelzine, isoniazid)
- Concomitant use of CNS depressants
- Concomitant use of medications with anticholinergic effects
- Noradrenergic anti-hypertensive agents (clonidine, guanabenz guanethidine)
- SSRI

See Table A: Cytochrome P450 Drug Metabolism/Inhibition

Amitriptyline:

Substrate of 1A2, 2C9, 2C19, 2D6 (1A2 and 2C9 are not clinically relevant)

Desipramine:

Substrate of 2D6

Doxepin:

Substrate of 2D6

Inhibitor of 2D6

Imipramine:

Substrate of 1A2, 2C19, 2D6

Maprotiline:

Substrate of 2D6

Nortriptyline:

Substrate of 2D6 (not clinically relevant)

Special Populations

Age-Specific Considerations

- Most agents are not recommended for use in children; if used, conservative dosing, EKG prior to dosage increase and plasma concentration monitoring are advised.
- Geriatrics: Consider conservative initial dosage to minimize adverse effects
- Hepatic disease: begin with lower initial doses and increase dose as needed and tolerated (maprotiline, trimipramine)

Patient Monitoring Parameters

- Blood levels as clinically indicated
- Blood pressure during dosage titration and as clinically indicated
- EKG – baseline and as clinically indicated
- Monitor for emergence of suicidal ideation or behavior
- Pregnancy test—baseline and as clinically indicated
- Sodium level in high-risk patients (e.g., older than 65 years, previous history of antidepressant-induced hyponatremia, low body weight, concomitant use of thiazides or other hyponatremia-inducing agents, experiencing symptoms of hyponatremia), baseline, 4 weeks and as clinically indicated

Dosing

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