

# ❖❖ TRICYCLIC ANTIDEPRESSANTS (TCAs)

## VISUAL COMPARISON CHART

### ❖❖ Complete Clinical Reference with Visual Guide

#### ❖❖ COMPREHENSIVE TCA CLINICAL REFERENCE

| ❖❖ Medication                                        | Brand Name        | ❖❖ Starting Dose    | ❖❖ Therapeutic Range | ❖❖ Max Dose | 🕒 Half Life              | ❖❖ Sedation  | ❖❖ Anticholinergic | ❖❖ Orthostatic |
|------------------------------------------------------|-------------------|---------------------|----------------------|-------------|--------------------------|--------------|--------------------|----------------|
| ❖❖ Amitriptyline<br>(Thour & Marwaha, 2023)          | Elavil, Endep     | 25mg<br>❖❖          | 50-150mg daily       | 300mg       | 10-50 Hrs<br>10-28 hours |              | ❖❖❖❖<br>❖❖❖❖       | ❖❖❖❖<br>❖❖❖    |
| ❖❖ Nortriptyline<br>(Merwar et al., 2020)            | Pamelor, Aventyl  | 25mg TID/75mg<br>❖❖ | 75-150mg daily       | 150mg       | 16-90 Hrs<br>38 hours    | ❖❖❖❖<br>❖❖   | ❖❖❖❖❖❖             | ❖❖❖❖           |
| ❖❖ Imipramine<br>(Fayez & Gupta, 2021)               | Tofranil          | 75mg daily          | 150-300 mg daily     | 300mg       | 11-25 Hrs                | ❖❖❖❖❖<br>❖❖❖ | ❖❖❖❖❖❖<br>❖❖       | ❖❖❖❖❖<br>❖❖❖   |
| ❖❖ Desipramine<br>(Maan & Abdolreza Saadabadi, 2019) | Norpramin         | 100mg daily         | 150-300 mg daily     | 300mg       | 15-24 Hrs<br>>60 hours   | ❖❖❖❖         | ❖❖❖❖               | ❖❖❖❖           |
| ❖❖ Doxepin<br>(Almasi & Meza, 2022)                  | Sinequan, Silenor | 75mg daily          | 150-300 mg daily     | 300mg       | 15 hrs<br>8 to 52 hours  | ❖❖❖❖<br>❖❖   |                    | ❖❖❖❖❖<br>❖     |
| ❖❖ Clomipramine<br>(Wilson & Tripp, 2020)            | Anafranil         | 25mg daily          | 100-250 mg daily     | 250mg       | 19-37 hrs                | ❖❖❖❖❖<br>❖❖❖ | ❖❖❖❖❖❖<br>❖❖       | ❖❖❖❖❖<br>❖     |
| ❖❖ Trimipramine                                      | Surmontil         | 75mg daily          | 150-300 mg daily     | 300mg       | 7-30 hrs                 | ❖❖❖❖❖<br>❖   |                    | ❖❖❖❖❖<br>❖     |

|                                                                                                                        |          |            |               |      |           |                                                                                    |                                                                                     |                                                                                     |
|------------------------------------------------------------------------------------------------------------------------|----------|------------|---------------|------|-----------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| <br>Protriptyline (Saef et al., 2021) | Vivactil | 15mg daily | 15-60mg daily | 60mg | 67-89 hrs |  |  |  |
|------------------------------------------------------------------------------------------------------------------------|----------|------------|---------------|------|-----------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|

**Visual Legend:**

-  = Minimal/Mild
-  = Mild
-  = Moderate
-  = High
-  = Very High
-  = Bedtime dosing

**PHARMACOKINETIC PROFILES**

**CYP450 METABOLISM VISUAL MAP:**

|  TCA            |  Primary CYP450 |  Inhibits |  Active Metabolite |
|---------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
|  Amitriptyline | CYP2D6, 1A2, 2C19                                                                                 |  CYP2D6   |  Nortriptyline    |
|  Nortriptyline | CYP2D6                                                                                            |  None     |  None             |
|  Imipramine    | CYP2D6, 1A2                                                                                       |  None     |  Desipramine      |
|  Desipramine   | CYP2D6                                                                                            |  None     |  None             |
|  Doxepin       | CYP2D6, 1A2                                                                                       |  None     |  Nordoxepin       |
|  Clomipramine  | CYP2D6, 1A2                                                                                       |  None     |  Norclomipramine  |
|  Trimipramine  | CYP2D6, 2C19                                                                                      |  None     |  None             |
|  Protriptyline | CYP2D6                                                                                            |  None     |  None             |

**PROTEIN BINDING CHART:**

-  Highest (95-97%):  Clomipramine,  Trimipramine,  Amitriptyline (Wilson & Tripp, 2024)
-  High (90-93%):  Nortriptyline,  Protriptyline,  Imipramine,  Desipramine
-  Moderate (76%):  Doxepin

**BIOAVAILABILITY RANKING:**

-  Protriptyline - 77% 

2. **Desipramine** - 60%
3. **Nortriptyline** - 51%
4. **Clomipramine** - 50%
5. **Amitriptyline** / **Imipramine** - 45%
6. **Trimipramine** - 44%
7. **Doxepin** - 13-45% (variable)

## **CLINICAL INDICATIONS & SPECIALTIES**

### **PRIMARY DEPRESSION:**

**First-line TCAs:** **Nortriptyline**, **Desipramine** (better tolerated) **Severe Depression:** **Amitriptyline**, **Imipramine** (more potent) **Elderly Patients:** **Nortriptyline** (therapeutic levels available)

### **SPECIALIZED INDICATIONS:**

#### **OCD:**

**Gold Standard:** **Clomipramine** (FDA-approved, most serotonergic)

#### **Chronic Pain/Fibromyalgia:**

**First-line:** **Amitriptyline** (most evidence)

**Alternative:** **Nortriptyline**

#### **Migraine Prevention:**

**First-line:** **Amitriptyline**

#### **Insomnia (low-dose):**

**Options:** **Doxepin** (Silenor 3-6mg), **Amitriptyline** (10-25mg)

#### **Enuresis (Pediatric):**

**Specific:** **Imipramine**

#### **Panic Disorder:**

**Well-studied:** **Imipramine**



## **CONTRAINDICATIONS & PRECAUTIONS**

## 💡💡 ABSOLUTE CONTRAINDICATIONS:

♥ **Recent MI** (within 6 months) - ALL TCAs

💡💡 **Concurrent MAOI use** - ALL TCAs

💡💡 **Known TCA allergy** - specific agent

## ⚠️ **RELATIVE CONTRAINDICATIONS:**

**Narrow-angle glaucoma** - especially 💡💡💡💡💡 (high anticholinergic) 💡💡 **Urinary retention** - especially 💡💡💡💡

♥ **Severe cardiac conduction defects** - ALL TCAs

💡💡 **Severe liver disease** - ALL TCAs

## 💡💡 SPECIAL POPULATIONS:

💡💡 **Pregnancy:** Category C (most), Category D (💡💡💡💡)

💡💡 **Elderly:** Start 25-50% adult dose, prefer 💡💡 Nortriptyline

💡💡 **Children:** Only 💡💡 Clomipramine (OCD, age 10+) and 💡💡 Imipramine (enuresis)

## 💡💡 THERAPEUTIC DRUG MONITORING

### 💡💡 MEDICATIONS WITH ESTABLISHED LEVELS:

| 💡💡 TCA                           | 💡💡 Therapeutic Range | 💡💡 Notes              |
|----------------------------------|----------------------|-----------------------|
| 💡💡 Nortriptyline                 | 50-150 ng/mL         | 💡💡 Therapeutic window |
| 💡💡 Imipramine + Desipramine      | 150-300 ng/mL        | 💡💡 Combined levels    |
| 💡💡 Desipramine                   | 115-300 ng/mL        | 💡💡 Individual levels  |
| 💡💡 Amitriptyline + Nortriptyline | 100-250 ng/mL        | 💡💡 Combined levels    |

### 💡💡 WHEN TO ORDER LEVELS:

💡💡 **Lack of response** at adequate doses

💡💡 **Suspected toxicity** or overdose

💡💡 **Drug interactions** affecting metabolism

💡💡 **Elderly patients** or medical comorbidities

💡💡 **Poor metabolizers** (genetic testing available)

### 🕒 **TIMING:**

💡💡 **Steady state:** 5-7 days after dose change

💡💡 **Sample timing:** 10-14 hours after last dose (trough)

## 💡💡 DOSING STRATEGIES

### 💡💡 STARTING PRINCIPLES:

💡💡 **"Start low, go slow"** - especially 💡💡 elderly

💡💡 **Single bedtime dosing** - most TCAs (sedation)

**Divided dosing** - if GI upset or orthostatic hypotension

💡💡 **Food administration** - with food to reduce GI upset

### 💡💡 TITRATION SCHEDULE:

💡💡 Week 1-2: Starting dose

💡💡 Week 3-4: ⬆ Increase by 25-50mg

💡💡 Week 5-6: ⬆ Increase by 25-50mg

💡💡 Week 7-8: 💡💡 Assess response, consider levels

### 💡💡 ELDERLY DOSING:

💡💡 **Start:** 10-25mg daily

💡💡 **Titrate:** 10-25mg weekly

💡💡 **Target:** 50-100mg daily (often adequate)

### 💡💡 PEDIATRIC DOSING (where approved):

💡💡 **Clomipramine (OCD):** Start 25mg daily, max 3mg/kg or 200mg

💡💡 **Imipramine (enuresis):** 1.5mg/kg daily, max 2.5mg/kg

## 💡💡 SIDE EFFECT PROFILES

### 💡💡 ANTICHOLINERGIC EFFECTS (High to Low):

1. 💡💡 **Amitriptyline** - 💡💡💡💡💡💡💡💡 (dry mouth, constipation, urinary retention, blurred vision)
2. 💡💡 **Clomipramine** - 💡💡💡💡💡💡💡💡 (similar to amitriptyline)
3. 💡💡 **Doxepin** - 💡💡💡💡💡💡💡 (moderate effects)
4. 💡💡 **Imipramine** - 💡💡💡💡💡💡💡 (moderate effects)
5. 💡💡 **Trimipramine** - 💡💡💡💡💡 (moderate effects)
6. 🟡 **Protriptyline** - 💡💡💡💡💡 (moderate effects)
7. 💡💡 **Nortriptyline** - 💡💡💡💡💡 (lower effects)
8. 💡💡 **Desipramine** - 💡💡💡💡 (lowest effects)

## 💎 SEDATION RANKING (High to Low):

1. 💎💎💎💎💎💎 Amitriptyline, Doxepin, Trimipramine -  
💎💎💎💎💎💎💎💎💎 (very high)
2. 💎💎💎💎 Clomipramine, Imipramine -  
💎💎💎💎💎💎💎 (high)
3. 💎💎 Nortriptyline - 💎💎💎💎💎 (moderate)
4. 💎💎 Desipramine - 💎💎💎💎 (mild)
5. 🟡 Protriptyline - 💎💎 (minimal, can be activating)

## ❤️ CARDIAC EFFECTS:

- ⚠️ All TCAs: Quinidine-like effects, conduction delays
- 💎💎 Most problematic: 💎💎 Amitriptyline, 💎💎 Imipramine
- 💎💎 Least problematic: 💎💎 Nortriptyline, 💎💎 Desipramine
- 💎💎 Monitoring: Baseline ECG, especially if cardiac risk factors

## ⚖️ WEIGHT GAIN (High to Low):

1. 💎💎 Amitriptyline - ⚖️⚖️⚖️⚖️⚖️⚖️⚖️ (significant)
2. 💎💎💎💎 Doxepin, Imipramine - ⚖️⚖️⚖️⚖️⚖️ (moderate)
3. 💎💎💎💎 Nortriptyline, Clomipramine - ⚖️⚖️⚖️⚖️ (mild-moderate)
4. 💎💎 Trimipramine - ⚖️⚖️⚖️ (mild)
5. 💎💎🟡 Desipramine, Protriptyline - ⚖️ (minimal)

## 💎💎 DRUG INTERACTIONS

### 💎💎 MAJOR CYP2D6 INTERACTIONS:

#### 💎💎 STRONG INHIBITORS (⬆️ increase TCA levels):

- 💎💎 Fluoxetine, Paroxetine, Bupropion, Quinidine
- Management: ⬇️ Reduce TCA dose by 25-50%

#### 💎💎 MODERATE INHIBITORS:

- 💎💎 Sertraline, Duloxetine, Terbinafine

#### 💎💎 WEAK INHIBITORS:

- 💎💎 Citalopram, Escitalopram

### 💎💎 CONTRAINDICATED COMBINATIONS:

💡💡 **MAOIs:** ⌚ Wait 14 days between TCA and MAOI

💡💡 **Linezolid:** 💡💡 Serotonin syndrome risk (especially 💡💡

clomipramine) 💡💡 **Tramadol:** 💡💡 Seizure risk, serotonin syndrome

### ⚠️ **SIGNIFICANT INTERACTIONS:**

💡💡 **Warfarin:** TCAs may ⬆️ increase anticoagulant effect

💡💡 **Thyroid hormones:** May ⬆️ increase TCA toxicity

💡💡 **Sympathomimetics:** ⬆️ Increased pressor response

💡💡 **Alcohol:** ⬆️ Enhanced CNS depression

### 💡💡 **MONITORING PARAMETERS**

#### 💡💡 **BASELINE ASSESSMENT:**

❤️ **ECG** - especially if >40 years or cardiac risk factors

💡💡 **Blood pressure** - orthostatic measurements

⚖️ **Weight/BMI** - baseline for monitoring

💡💡 **Liver function tests** - baseline

⚡ **Electrolytes** - especially in elderly

#### 💡💡 **ONGOING MONITORING:**

💡💡 **Weekly (first month):** Blood pressure, weight, side effects

💡💡 **Monthly:** Clinical response, side effects, adherence

💡💡 **Every 3-6 months:** Weight, blood pressure, ECG if indicated

💡💡 **As needed:** Drug levels, liver function tests

#### 💡💡 **RED FLAGS - IMMEDIATE ATTENTION:**

❤️ **Cardiac:** Chest pain, palpitations, syncope, new arrhythmias

💡💡 **Neurological:** Seizures, severe confusion, movement disorders

💡💡 **Psychiatric:** Suicidal ideation, mania/hypomania, psychosis

💡💡 **Anticholinergic toxicity:** Hyperthermia, delirium, coma

### 💡💡 **CLINICAL PEARLS**

#### 💡💡 **CHOOSING THE RIGHT TCA:**

💡💡💡💡 **Depression + Insomnia:** 💡💡 Amitriptyline, 💡💡 Doxepin

💡💡💡💡 **Depression + Fatigue:** 💡💡 Desipramine, ⚪ Protriptyline

💎💎 **Elderly patients:** 💎💎 Nortriptyline (therapeutic levels available)

❤️ **Cardiac patients:** 💎💎 Nortriptyline, 💎💎 Desipramine (least cardiotoxic) 💎💎 **Pain syndromes:** 💎💎 Amitriptyline (most evidence)

💎💎 **OCD:** 💎💎 Clomipramine (only FDA-approved TCA)

## OPTIMIZATION STRATEGIES:

💎💎 **Poor response:** ✅ Check adherence, 💎💎 drug levels, 💎💎

interactions 💎💎 **Side effects:** ⬇️ Lower dose, 💎💎 switch to better-tolerated TCA

💎💎 **Partial response:** 💎💎 Optimize dose, 💎💎 check levels, + consider

augmentation 💎💎 **Breakthrough symptoms:** ✅ Assess adherence, stressors, interactions

## ⬇️ DISCONTINUATION:

💎💎 **Taper gradually:** 25mg every 3-7 days

💎💎 **Withdrawal symptoms:** Flu-like symptoms, dizziness,

nausea 🕒 **Protriptyline:** Longest taper due to very long half-life

## ⚠️ SPECIAL CONSIDERATIONS:

💀 **Overdose potential:** Very dangerous - 💎💎 refer to emergency care 💎💎 **Pregnancy:** Avoid if possible, especially first trimester

💎💎 **Breastfeeding:** 💎💎 Nortriptyline, 💎💎 Imipramine preferred if needed

💎💎 **Switching antidepressants:** Cross-taper carefully, watch for interactions

## 💎💎 VISUAL LEGEND SUMMARY

### 💎💎 TCA Color Coding:

💎💎 = Amitriptyline (High sedation/anticholinergic)

💎💎 = Nortriptyline (Balanced profile, elderly-friendly)

💎💎 = Imipramine (Classic TCA, panic disorder)

💎💎 = Desipramine (Low sedation/anticholinergic)

💎💎 = Doxepin (Very sedating, insomnia)

💎💎 = Clomipramine (OCD specialist)

💎💎 = Trimipramine (Very sedating)

🕒 = Protriptyline (Activating, long half-life)

## ◆◆ Severity Indicators:

◆◆ = Minimal

◆◆◆◆ = Mild

◆◆◆◆◆◆ = Moderate

◆◆◆◆◆◆◆◆ = High

◆◆◆◆◆◆◆◆◆◆ = Very High

## ◆◆ Clinical Symbols:

◆◆ = Bedtime dosing

◆◆ = Elderly considerations

◆◆ = Pediatric use

♥ = Cardiac monitoring

◆◆ = CNS effects

◆◆ = Drug interactions

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