TIANEPTINE

THERAPEUTICS

Brands • Coaxil
• Stablon
• Tatinol
see index for additional brand names

Generic? Yes

Class

- Neuroscience-based Nomenclature: glutamate; yet to be determined (Glu)
- Glutamatergic modulator
- Often classified as a tricyclic antidepressant, but pharmacologically distinct

Commonly Prescribed for

(bold for FDA approved)
- Major depressive disorder
- Dysthymia
- Anxiety associated with depression

How the Drug Works

✻ Modulates glutamatergic neurotransmission, perhaps through potentiation of AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropioninc acid) receptor function

How Long Until It Works

- Onset of therapeutic actions usually not immediate, but often delayed 2–4 weeks
- If it is not working within 6–8 weeks for depression, it may require a dosage increase or it may not work at all
- May continue to work for many years to prevent relapse of symptoms

If It Works

- The goal of treatment is complete remission of current symptoms as well as prevention of future relapses
- Treatment most often reduces or even eliminates symptoms, but not a cure since symptoms can recur after medicine stopped
- Continue treatment until all symptoms are gone (remission)
- Once symptoms gone, continue treating for 1 year for the first episode of depression
- For second and subsequent episodes of depression, treatment may need to be indefinite

If It Doesn't Work

- Many patients have only a partial response where some symptoms are improved but others persist (especially insomnia, fatigue, and problems concentrating)
- Other patients may be nonresponders, sometimes called treatment-resistant or treatment-refractory
- Consider increasing dose, switching to another agent, or adding an appropriate augmenting agent
- Consider psychotherapy
- Consider evaluation for another diagnosis or for a comorbid condition (e.g., medical illness, substance abuse, etc.)

Best Augmenting Combos for Partial Response or Treatment Resistance

- Augmentation has not been systematically studied with tianeptine

Tests

- None recommended for healthy individuals

SIDE EFFECTS

How Drug Causes Side Effects

✻ Mild anticholinergic activity (less than some TCAs) could possibly lead to sedative effects, dry mouth, constipation, and blurred vision
- Most side effects are immediate but often go away with time

✻ Pharmacologic studies do not indicate tianeptine to be a potent alpha 1 antagonist or H1 antihistamine

Notable Side Effects

- Headache, dizziness, insomnia, sedation
- Nausea, constipation, abdominal pain, dry mouth
- Abnormal dreams
- Increased transaminases
- Tachycardia

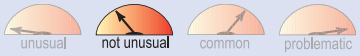
Life-Threatening or Dangerous Side Effects

- Theoretically, rare induction of mania and activation of suicidal ideation or behavior
- Cases of activation of suicidal ideation and behavior (suicidality) (short-term did not show an increase in the risk of suicidality with antidepressants compared to placebo beyond age 24)
- Hepatitis that can, in exceptional cases, be severe
- Dermatitis bulbous in exceptional cases

Weight Gain

- Not well studied

Sedation



- Occurs in significant minority

What to Do About Side Effects

- Wait
- Wait
- Wait
- Lower the dose
- In a few weeks, switch or add other drugs
- For skin reactions, stop treatment

Best Augmenting Agents for Side Effects

- Augmentation for side effects of tianeptine has not been systematically studied

DOSING AND USE

Usual Dosage Range

- 37.5 mg/day

Dosage Forms

- Tablet 12.5 mg

How to Dose

- 12.5 mg 3 times/day

Dosing Tips

- Tianeptine's rapid elimination necessitates strict adherence to the dosing schedule

✻ Short half-life means multiple daily doses

Overdose

- Effects are generally mild and nonfatal; unlikely to cause cardiovascular effects

Long-Term Use

- Safe

Habit Forming

- Abuse and dependence may occur, in particular in patients under 50 years of age with a history of drug or alcohol dependence

How to Stop

- Many patients tolerate 50% dose reduction for 3 days, then another 50% reduction for 3 days, then discontinuation
- If withdrawal symptoms emerge during discontinuation, raise dose to stop symptoms and then restart withdrawal much more slowly

Pharmacokinetics

- Not primarily metabolized by CYP 450 enzyme system
- Tianeptine is rapidly eliminated
- Half-life approximately 2.5 hours

Drug Interactions

- Activation and agitation, especially following switching or adding antidepressants, may represent the induction of a bipolar state, especially a mixed dysphoric bipolar II condition sometimes associated with suicidal ideation, and require the addition of lithium, a mood stabilizer or an atypical antipsychotic, and/or discontinuation of tianeptine
- Other drug interactions not well studied

Other Warnings/ Precautions

- For elective surgery, tianeptine should be stopped 24–48 hours before general anesthesia is administered
- Generally, use only with extreme caution with MAOIs; do not use until 14 days after MAOIs are stopped; do not start an MAOI for at least 5 half-lives (5 to 7 days for most drugs) after discontinuing tianeptine

- Warn patients and their caregivers about the possibility of activating side effects and advise them to report such symptoms immediately
- Monitor patients for activation of suicidal ideation, especially children and adolescents
- Warn doctors to pay attention to patients with history of drug dependencies

Do Not Use

- If patient is taking an MAOI
- If patient is pregnant or nursing
- If there is a proven allergy to tianeptine

SPECIAL POPULATIONS

Renal Impairment

- Dose should be reduced for severe impairment to 25 mg/day

Hepatic Impairment

- In patients with severe cirrhosis (class C, Child Plugh's Scale), the dosage should be restricted to 25 mg/day

Cardiac Impairment

- Baseline ECG is recommended

Elderly

- Baseline ECG is recommended for patients over age 50
- Dose should be reduced to 25 mg/day
- Reduction in the risk of suicidality with antidepressants compared to placebo in adults age 65 and older

Children and Adolescents

- Tianeptine is not recommended for use in children or adolescents under 18
- Carefully weigh the risks and benefits of pharmacological treatment against the risks and benefits of nontreatment with antidepressants and make sure to document this in the patient's chart
- Monitor patients face-to-face regularly, particularly during the first several weeks of treatment
- Use with caution, observing for activation of known or unknown bipolar disorder and/or suicidal ideation, and inform parents or guardians of this risk so they can help observe child or adolescent patients

Pregnancy

- Not recommended for use during pregnancy

Breast Feeding

- Some drug is found in mother's breast milk
- ✻ Not recommended for use during pregnancy
- Immediate postpartum period is a high-risk time for depression, especially in women who have had prior depressive episodes, so drug may need to be reinstituted late in the third trimester or shortly after childbirth to prevent a recurrence during the postpartum period
- Must weigh benefits of breast feeding with risks and benefits of antidepressant treatment versus nontreatment to both the infant and the mother
- For many patients, this may mean continuing treatment during breast feeding

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages

- Elderly patients

Potential Disadvantages

- Patients who have difficulty being compliant with multiple daily dosing

Primary Target Symptoms

- Depressed mood
- Symptoms of anxiety

Pearls

- ✻ Possibly a unique mechanism of action as a glutamatergic antidepressant
- It is not metabolized by CYP450; therefore, the risk of pharmacokinetic drug–drug interactions is minimized

Suggested Reading

Kasper S, McEwen BS. Neurobiological and clinical effects of the antidepressant tianeptine. CNS Drugs 2008;22(1):15–26.

Kasper S, Olie JP. A meta-analysis of randomized controlled trials of tianeptine versus SSRI in the short-term treatment of depression. Eur Psychiatry 2002;17(suppl 3):331–40.

McEwen BS, Chattarji S, Diamond DM, et al. The neurobiological properties of tianeptine (Stablon): from monoamine hypothesis to glutamatergic modulation. Mol Psychiatry 2010;15:237–49.

Svenningsson P, Bateup H, Qi H, et al. Involvement of AMPA receptor phosphorylation in antidepressant actions with special reference to tianeptine. Eur J Neuorsci 2007;26:3509–17.

Wagstaff AJ, Ormrod D, Spencer CM. Tianeptine: a review of its use in depressive disorders. CNS Drugs 2001;15(3):231–59.