Tofranil 
(Tofranil) imipramine hydrochloride tablets USP

10 mg, 25 mg, and 50 mg

DESCRIPTION

Tofranil is supplied in tablet form for oral administration. Tofranil, imipramine hydrochloride USP, the original tricyclic antidepressant, is a member of the phenothiazine group of compounds. It is designated 3-dimethylaminomethyl-5-diethylaminomethyl-10 H-phenothiazine hydrochloride. Its structural formula is:

\[
\text{C}_{21}\text{H}_{29}\text{ClN}_{2} + \text{H}_2\text{O} \rightarrow \text{C}_{21}\text{H}_{27}\text{N}_{2} \text{Cl} + \text{H}_3\text{O}
\]

Imipramine hydrochloride USP is a white or off-white, odorless, or practically odorless, free-flowing, hygroscopic, odorless powder, soluble in alcohol, water, and benzol.

CLINICAL PHARMACOLOGY

The mechanism of action of Tofranil is not definitely known. It is not clear whether it acts primarily in the brain or in various extraneuronal systems. The clinical effect is hypothesized to be due to a balance of sympathomimetic and sympatholytic effects. The possibility of multiple mechanisms is thought to be important in its antidepressant effect.

INDICATIONS AND USAGE

Depression - For the treatment of endogenous depression. Endogenous depression is likely to be distinguished from other depressions. On the other hand, the patient may be correctly diagnosed with depression and the lack of response to treatment may be thought to be a sign of the antidepressant effect.

INDUCED OPIOID AND OPIOID USE DISORDERS

The use of opioids in the treatment of depression is a complex and multifaceted issue. The potential for opioid dependence and misuse is a concern, and the appropriate management of opioid use requires careful consideration.

CONTRAINDICATIONS

The concurrent use of monoamine oxidase inhibitors with tricyclic antidepressants is contraindicated. The use of these two classes of compounds may result in serious or sometimes fatal cardiovascular toxicity. Patients should be advised not to take any medications containing monoamine oxidase inhibitors with tricyclic antidepressants.

WARNINGs

Promen Vorsicht bei Patienten mit Herzkranckheiten

WARNINGS

Clinical Worsening and Suicidal Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and may have the onset of new symptoms and/or exacerbation of existing symptoms, especially at the start of treatment and/or at times of dose changes, including during the period of clinical trials. Such symptoms may include (but are not limited to) manic or hypomanic symptoms, increased polemical or grandiose symptoms, impulsive or risky behavior, new or worsening physical symptoms, or agitation. These exacerbations may be serious and, in some cases, may lead to suicidal behavior and thoughts.

SUITABILITY AND ANTIDEPRESSANT DRUGS

Antidepressants can increase suicidal thoughts and behaviors in children, adolescents, and young adults. Suicidal thoughts or behaviors may occur relatively early during treatment with antidepressants, including tricyclic antidepressants (such as Tofranil). Therefore, it is important to monitor patients closely for any increase in suicidal thoughts or behaviors during treatment with tricyclic antidepressants.

Families and caregivers should be advised to be alert for any change in behavior, especially sudden changes, in the patient. Behavioral changes such as mood changes or actions different from usual should be reported immediately to the prescribing healthcare professional. Patients should be advised to report any change in behavior, especially sudden changes, to their healthcare provider immediately.

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SPECS

A dose of 2.5 mg/kg/day should not be exceed in childhood. EOG changes of unknown significance have been reported in pediatric patients with doses more than twice the amount.

**Geriatric Use**
In the literature, there were four well-controlled randomized, double-blind, placebo-controlled clinical trials with Tofranil in elderly patients. There was a total of 131 elderly patients (67 to 87 years old) in these studies. The following adverse experiences were reported in patients: somnolence, lethargy, weakness, and/or dizziness; confusion; constipation; depression; dyspepsia; and/or palpitations. However, in elderly patients, 2.5 mg/kg/day should be reduced to 1.0 mg/kg/day in the elderly or those who are at risk of hypotension, orthostatic hypotension, or other adverse reactions. Elderly patients may also have diabetes mellitus, chronic obstructive pulmonary disease, and/or chronic renal failure. The elderly may be at risk for adverse reactions due to the decreased plasma clearance of Tofranil. Therefore, elderly patients should be used with caution.
Read the Medication Guide that comes with you or your family member’s antidepressant medicine. This Medication Guide is only about the risk of suicidal thoughts and actions with antidepressant medicines. Talk to your, or your family member’s, healthcare provider about:

- all risks and benefits of treatment with antidepressant medicines
- all treatment choices for depression or other serious mental illness

What is the most important information I should know about antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions?

1. Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.
2. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a particularly high risk of having suicidal thoughts or actions. These include people who have (or have a family history of) bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions.
3. How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?
   - Pay close attention to any changes, especially sudden changes, in mood, behavior, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.
   - Call the healthcare provider right away to report new or sudden changes in mood, behavior, thoughts, or feelings.
   - Keep all follow-up visits with the healthcare provider as scheduled. Call the healthcare provider between visits as needed, especially if you have concerns about symptoms.

Call a healthcare provider right away if you or your family member has any of the following symptoms, especially if they are new, worse, or worry you:
- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood
• Visual problems: eye pain, changes in vision, swelling or redness in or around the eye

Who should not take Tofranil?
Do not take Tofranil if you:
• take a monoamine oxidase inhibitor (MAOI).
  Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid.
  » Do not take an MAOI within 2 weeks of stopping Tofranil unless directed to do so by your physician.
  » Do not start Tofranil if you stopped taking an MAOI in the last 2 weeks unless directed to do so by your physician.

What else do I need to know about antidepressant medicines?
• Never stop an antidepressant medicine without first talking to a healthcare provider. Stopping an antidepressant medicine suddenly can cause other symptoms.
• Visual problems: Only some people are at risk for these problems. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are.
• Antidepressants are medicines used to treat depression and other illnesses. It is important to discuss all the risks of treating depression and also the risks of not treating it. Patients and their families or other caregivers should discuss all treatment choices with the healthcare provider, not just the use of antidepressants.
• Antidepressant medicines have other side effects. Talk to the healthcare provider about the side effects of the medicine prescribed for you or your family member.
• Antidepressant medicines can interact with other medicines. Know all of the medicines that you or your family member takes. Keep a list of all medicines to show the healthcare provider. Do not start new medicines without first checking with your healthcare provider.
• Not all antidepressant medicines prescribed for children are FDA approved for use in children. Talk to your child’s healthcare provider for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Tofranil is a trademark of Mallinckrodt Inc.

Manufactured by Patheon Inc.
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Manufactured for Mallinckrodt Inc.
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