

PRODUCT MONOGRAPH  
INCLUDING PATIENT MEDICATION INFORMATION

Pr **IMIPRAMINE**

Imipramine Hydrochloride Tablets

Tablets, 10 mg, 25 mg, 50 mg and 75 mg, Oral

USP

Antidepressant

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Date of Initial Authorization:  
DEC 31, 1975

Date of Revision:  
MAY 23, 2023

Submission Control Number: 270511

## RECENT MAJOR LABEL CHANGES

<a href="#">2 Contraindications</a>	05/2023
<a href="#">7 Warnings and Precautions, Neurologic</a>	05/2023
<a href="#">7 Warnings and Precautions, Ophthalmologic</a>	05/2023

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## PART I: HEALTH PROFESSIONAL INFORMATION

### 1 INDICATIONS

IMIPRAMINE (imipramine hydrochloride) is indicated for:

- The relief of symptoms of depressive illness.

#### 1.1 Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

#### 1.2 Geriatrics

Geriatrics (≥65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness. See [4.2 Recommended Dose and Dosage Adjustment](#) and [7.1.4 Geriatrics](#).

### 2 CONTRAINDICATIONS

IMIPRAMINE (imipramine hydrochloride) is contraindicated in:

- Patients who are hypersensitive to imipramine hydrochloride or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see [6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING](#).
- Patients with known or suspected hypersensitivity to tricyclic antidepressants (TCA) belonging to the dibenzazepine group.
- Conjunction with, or within 14 days before or after treatment with monoamine oxidase inhibitors (MAOIs), as it may result in hyperpyretic crises, severe convulsive seizures, and death. See [9.1 Serious Drug Interactions](#) and [9.4 Drug-Drug Interactions](#).
- During the acute recovery phase following a myocardial infarction and in the presence of acute congestive heart failure. See [7 WARNINGS AND PRECAUTIONS, Cardiovascular](#).
- Patients with narrow angle glaucoma, as the condition may be aggravated due to the atropine-like effects of the drug. See [7 WARNINGS AND PRECAUTIONS, Ophthalmologic, Angle-Closure Glaucoma](#).

### 3. SERIOUS WARNINGS AND PRECAUTIONS BOX

#### Serious Warnings and Precautions

Increased risk of self-harm, harm to others, suicidal thinking and behavior with antidepressant use. Closely monitor all antidepressant-treated patients for clinical worsening and for emergence of agitation-type and/or suicidal thoughts and behaviors (see [7 WARNINGS AND PRECAUTIONS, Psychiatric](#)).

## 4 DOSAGE AND ADMINISTRATION

### 4.1 Dosage Considerations

- **Cardiovascular**

Patients with circulatory liability or with cardiovascular disease should receive IMIPRAMINE in low dosage and under careful observation and only when a clear indication for the drug has been established. See [7 WARNINGS AND PRECAUTIONS, Cardiovascular](#).

- **Renal**

Exercise extreme caution when IMIPRAMINE is used in patients with urinary retention, particularly in the presence of prostatic enlargement. See [7 WARNINGS AND PRECAUTIONS, Renal](#).

- **Pregnant women**

IMIPRAMINE should not be used during the first trimester of pregnancy. See [7.1.1 Pregnant Women](#).

- **Breast-feeding**

The use of IMIPRAMINE should be avoided during breast-feeding. See [7.1.2 Breast-feeding](#).

- **Elderly Patients**

Elderly patients should receive IMIPRAMINE in low dosage and under careful observation and only when a clear indication for IMIPRAMINE has been established. See [7.1.4 Geriatrics](#).

- **Important interactions**

When IMIPRAMINE is substituted for a MAOI, at least 14 days should elapse between the treatments. Administration of IMIPRAMINE should then be started cautiously and increased gradually. See [9.1 Serious Drug Interactions](#), [9.4 Drug-Drug Interactions](#).

### 4.2 Recommended Dose and Dosage Adjustment

#### Initial dose

**Adult patients:** The recommended initial dosage is 25 mg three times/day. This should be increased gradually as required and tolerated, up to 150 mg/day. Dosage over 200 mg/day is not recommended for outpatients. Severely ill or hospitalized patients may require up to 300 mg/day.

**Elderly patients:** The recommended initial dosage is 30 to 40 mg/day. Increase the dose by 10 mg/day to a maximum of 100 mg/day. See [1.2 Geriatrics](#); [7.1.4 Geriatrics](#).

**Pediatric patients (<18 years of age):** Health Canada has not authorized an indication for pediatric use.

#### Maintenance

In suitable subjects, the maintenance dose may be administered in a single dose before bedtime. It does not have as much sedative effect as amitriptyline which may be used at bedtime for this effect.

#### 4.4 Administration

IMIPRAMINE tablets should be swallowed whole with water.

#### 4.5 Missed Dose

If the patient misses a dose, instruct the patient to take the dose as soon as they remember. If it is almost time for the next dose, inform the patient to skip the missed dose and continue the regular dosing schedule.

### 5 OVERDOSAGE

Deaths by deliberate or accidental overdose have occurred with this class of drugs. Children have been reported to be more sensitive than adults to an acute overdose of imipramine. An acute overdose in infants or young children must be considered serious and potentially fatal.

Since the propensity for suicide is high in depressed patients, a suicide attempt by other means may occur during the recovery phase. The possibility of simultaneous ingestion of other drugs should also be considered.

**Symptoms:** High doses may cause temporary confusion, disturbed concentration, transient visual hallucinations, agitation, hyperactive reflexes, muscle rigidity, vomiting, or hyperpyrexia, in addition to anything listed under Adverse Effects. Based on imipramine's known pharmacologic actions, overdose may cause drowsiness, hypothermia, tachycardia, and other arrhythmic abnormalities such as bundle branch block, ECG evidence of impaired conduction and congestive heart failure. Other manifestations may be dilated pupils, convulsions, severe hypotension, stupor, and coma. All patients suspected of an overdose should be admitted to a hospital as soon as possible.

**Treatment:** No specific antidote is available, and treatment is essentially symptomatic and supportive. Cardiac arrhythmias and CNS involvement pose the greatest threat with tricyclic antidepressant overdose and may occur suddenly even when initial symptoms appear to be mild. Therefore, patients who may have ingested an overdose of imipramine, particularly children, should be hospitalized and kept under close surveillance.

Activated charcoal may be administered to reduce absorption of the drug.

An adequate airway should be established in comatose patients and assisted ventilation instituted, if necessary, but respiratory stimulants should not be used. Hyperpyrexia should be controlled by external measures, such as ice packs and cooling sponge baths. Acidosis may be treated by cautious administration of sodium bicarbonate. Adequate renal function should be maintained.

External stimulation should be minimized to reduce the tendency to convulsions. If convulsions occur, anticonvulsants (preferably i.v. diazepam) should be administered. Barbiturates may intensify respiratory depression, particularly in children, and aggravate hypotension and coma. Paraldehyde may be used in some children to counteract muscular hypertonus and convulsions with less likelihood of causing respiratory depression. If the patient fails to respond rapidly to anticonvulsants, artificial ventilation should be instituted. Prompt control of convulsions is essential since they aggravate hypoxia and acidosis and may thereby precipitate cardiac arrhythmias and arrest.

ECG monitoring in an intensive care unit is recommended in all patients, particularly in the presence of ECG abnormalities, and should be maintained for several days after the cardiac rhythm has returned to normal. A patient who has ingested a toxic overdose of a tricyclic antidepressant may remain medically and psychiatrically unstable for several days due to sustained excessive drug levels. Unexpected cardiac deaths have occurred up to 6 days after overdosage with other antidepressants. The QRS interval of the electrocardiogram appears to be a reliable correlate of the severity of overdosage. If the QRS interval exceeds 100 milliseconds any time during the first 24 hours after dosage, cardiac function should be continuously monitored for 5 to 6 days.

Life-threatening cardiac arrhythmias may respond to lidocaine. Quinidine, procainamide and disopyramide generally should be avoided in the management of conduction abnormalities and cardiac arrhythmias since these agents may further depress myocardial conduction and contractility. Because of its effect on cardiac conduction, digitalis should be used only with caution. If rapid digitalization is required for the treatment of congestive heart failure, special care should be exercised in using the drug.

Shock should be treated with supportive measures such as intravenous fluids, plasma expanders and oxygen. The use of corticosteroids in treating shock is controversial and may be contraindicated in tricyclic antidepressant overdose. Hypotension usually responds to elevation of the foot of the bed. Pressor agents, such as norepinephrine (but not epinephrine), are rarely indicated and should be given only after careful consideration and under continuous monitoring.

Since it has been reported that physostigmine may cause severe bradycardia, asystole and seizures, its use is not recommended in cases of overdosage with IMIPRAMINE.

Peritoneal and hemodialysis are of no value because of low plasma concentrations of the drug. Most of the administered dose is distributed in tissue and not in plasma. When aggressive medical management is inadequate, hemoperfusion, but not hemodialysis, has shown some good results.

For management of a suspected drug overdose, contact your regional poison control centre.

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

**Table 1 – Dosage Forms, Strengths, Composition and Packaging**

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Tablet 10 mg ,25 mg, 50 mg and 75 mg of imipramine hydrochloride	Carnauba wax, hydroxypropyl methylcellulose, lactose monohydrate (in 25 mg, 50 mg, and 75 mg tablets only), magnesium stearate, microcrystalline cellulose, polyethylene glycol, red ferric oxide, sunset yellow aluminum lake 40%, titanium dioxide, and yellow ferric oxide.

IMIPRAMINE (imipramine hydrochloride) 10 mg tablets: Each light brown, round, biconvex, film-coated tablet, engraved “10” on one side, other side is plain, contains imipramine hydrochloride 10 mg.

IMIPRAMINE (imipramine hydrochloride) 25 mg tablets: Each light brown, round, biconvex, film-coated tablet, engraved “25” on one side, other side is plain, contains imipramine hydrochloride 25 mg.

IMIPRAMINE (imipramine hydrochloride) 50 mg tablets: Each light brown, round, biconvex, film-coated tablet, engraved “50” on one side, other side is plain, contains imipramine hydrochloride 50 mg.

IMIPRAMINE (imipramine hydrochloride) 75 mg tablets: Each light brown, round, biconvex, film-coated tablet, engraved score over “75” on one side, other side plain, contains imipramine hydrochloride 75 mg.

Available in bottles of 100 or 1000 tablets.

## 7 WARNINGS AND PRECAUTIONS

Please see [3 SERIOUS WARNINGS AND PRECAUTIONS BOX](#).

### Cardiovascular

IMIPRAMINE is contraindicated in the acute recovery period following myocardial infarction and in the presence of acute congestive heart failure. See [2 CONTRAINDICATIONS](#).

Exercise extreme caution when IMIPRAMINE is given to patients with coronary thrombosis, angina pectoris, disorders of cardiac rate or rhythm or conduction.

Patients with circulatory liability or with cardiovascular disease should receive IMIPRAMINE in low dosage and under careful observation and only when a clear indication for IMIPRAMINE has been established. A few instances of unexpected death have occurred in patients with cardiovascular disorders.



## Hematologic

Leukocyte and differential counts should be performed in any patient who develops fever and sore throat during therapy; the drug should be discontinued if there is evidence of pathologic neutrophil depression.

## Neurologic

### Serotonin toxicity / Serotonin syndrome

Serotonin toxicity, also known as serotonin syndrome, is a potentially life-threatening condition and has been reported with tricyclic antidepressants, including IMIPRAMINE.

Serotonin toxicity is characterized by neuromuscular excitation, autonomic stimulation (e.g., tachycardia, flushing) and altered mental state (e.g., anxiety, agitation, hypomania). In accordance with the Hunter Criteria, serotonin toxicity diagnosis is likely when, in the presence of at least one serotonergic agent, one of the following is observed:

- Spontaneous clonus
- Inducible clonus or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypertonia and body temperature  $>38^{\circ}\text{C}$  and ocular clonus or inducible clonus

If concomitant treatment with IMIPRAMINE and other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. See [2 CONTRAINDICATIONS](#), [4 DOSAGE AND ADMINISTRATION](#), and [9 DRUG INTERACTIONS](#). If serotonin toxicity is suspected, discontinuation of the serotonergic agents should be considered.

## Ophthalmologic

### Angle-Closure Glaucoma

As with other antidepressants, IMIPRAMINE can cause mydriasis, which may trigger an angle-closure attack in a patient with anatomically narrow ocular angles. Health professionals should inform patients to seek immediate medical assistance if they experience eye pain, changes in vision or swelling or redness in or around the eye.

Exercise extreme caution when imipramine is used in patients with glaucoma.

## Psychiatric

IMIPRAMINE should be used cautiously in hyperactive or agitated patients, in epileptic patients, or ambulatory, seriously depressed patients with suicidal tendencies.

The possibility of suicide in depressed patients remains during treatment and until significant remission occurs, this type of patient should not have access to large quantities of the drug.

## Renal

Exercise extreme caution when imipramine is used in patients with urinary retention, particularly in the presence of prostatic enlargement.

## 7.1 Special Populations

### 7.1.1 Pregnant Women

IMIPRAMINE should not be used during the first trimester of pregnancy.

### 7.1.2 Breast-feeding

The use of IMIPRAMINE should be avoided during breast-feeding.

### 7.1.3 Pediatrics

**Pediatrics (<18 years of age):** Health Canada has not authorized an indication for pediatric use.

### 7.1.4 Geriatrics

**Geriatrics (≥65 years of age):** Elderly patients should receive IMIPRAMINE in low dosage and under careful observation and only when a clear indication for IMIPRAMINE has been established. See [4.2 Recommended Dose and Dosage Adjustment](#).

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

Although the listing which follows includes a few adverse reactions which have not been reported with this specific drug, the pharmacological similarities among the tricyclic antidepressant drugs require that each of the reactions be considered when IMIPRAMINE is administered.

**Blood and lymphatic system disorders:** bone marrow depression including agranulocytosis; eosinophilia; purpura; thrombocytopenia.

**Cardiac disorders:** tachycardia, palpitation, myocardial infarction, arrhythmias, heart block.

**Endocrine disorders:** gynecomastia in the male.

**Eye disorders:** blurred vision, disturbances of accommodation, mydriasis.

**Gastrointestinal disorders:** dry mouth, and rarely, associated sublingual adenitis, constipation, paralytic ileus, nausea and vomiting, epigastric distress, diarrhea, peculiar taste, stomatitis, abdominal cramps, black tongue, parotid swelling.

**General disorders and administration site conditions:** edema (general or of face and tongue), drug fever, weakness, fatigue, headache.

**Hepatobiliary disorders:** jaundice (simulating obstructive), altered liver function.

**Immune system disorders:** cross-sensitivity with desipramine.

**Injury, poisoning and procedural complications:** falls.

**Investigations:** alterations in EEG patterns, elevation or depression of blood sugar levels, weight gain or loss.

**Metabolism and nutrition disorders:** anorexia.

**Nervous system disorders:** numbness, tingling, paresthesia of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures, drowsiness, dizziness, tinnitus.

**Psychiatric disorders:** confusional states (especially in the elderly) with hallucinations, disorientation, delusions, anxiety, restlessness, agitation; insomnia and nightmares; hypomania; exacerbation of psychosis.

**Renal and urinary disorders:** urinary retention, delayed micturition, dilation of the urinary tract, urinary frequency.

**Reproductive system and breast disorders:** breast enlargement and galactorrhea in the female; increased or decreased libido, impotence; testicular swelling.

**Skin and subcutaneous tissue disorders:** skin rash, petechiae, urticaria, itching, photosensitivity (avoid excessive exposure to sunlight), perspiration, flushing.

**Vascular disorders:** hypotension, hypertension, stroke.

**Withdrawal symptoms:** though not indicative of addiction, abrupt cessation of treatment after prolonged therapy may produce nausea, headache and malaise.

## 8.5 Post-Market Adverse Reactions

Information is not available.

## 9 DRUG INTERACTIONS

### 9.1 Serious Drug Interactions

#### Serious Drug Interactions

- Co-Administration with Monoamine Oxidase inhibitors (MAOIs). See [2 CONTRAINDICATIONS](#), [9.4 Drug-Drug Interactions](#).

### 9.3 Drug-Behavioural Interactions

Patients should be warned that, while taking IMIPRAMINE their responses to alcoholic beverages may be exaggerated.

### 9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

**Table 2 - Established or Potential Drug-Drug Interactions**

Proper/Common name	Source of Evidence	Effect	Clinical comment
Antihypertensives	T	↓ anti-hypertensives effect	Since imipramine may diminish or abolish the antihypertensive effect of adrenergic neuron inhibitors, such as guanethidine, patients requiring concomitant treatment for hypertension should be given antihypertensives of a different type.
Cimetidine	T	↑ imipramine	Caution should be exercised if imipramine is administered together with cimetidine since cimetidine has been shown to inhibit the metabolism of several tricyclic antidepressants and clinically significant increases in plasma levels of imipramine may occur.
CNS depressants or anticholinergic agents	T	↑ CNS depressants or anticholinergic agents	Patients should be warned that, while taking imipramine their responses to other CNS depressants or anticholinergic agents may be exaggerated.
Methylphenidate	T	↑ activity and plasma concentrations of tricyclic antidepressants	

Proper/Common name	Source of Evidence	Effect	Clinical comment
Monoamine Oxidase inhibitors (MAOIs)	T	Hyperpyretic crises, severe convulsive seizures and death may occur.  The potentiation of adverse effects can be serious, or even fatal.	The concomitant use of IMIPRAMINE with MAOI is contraindicated. See <a href="#">2 CONTRAINDICATIONS</a> and <a href="#">7 WARNINGS AND PRECAUTIONS, Neurologic</a> .  When IMIPRAMINE is substituted for a MAOI, at least 14 days should elapse between the treatments. Administration of IMIPRAMINE should then be started cautiously and increased gradually.
Norepinephrine or epinephrine	T	↑ cardiovascular effects of norepinephrine or epinephrine	

Legend: T = Theoretical

## 9.5 Drug-Food Interactions

Interactions with food have not been established.

## 9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

## 9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

# 10 CLINICAL PHARMACOLOGY

## 10.1 Mechanism of Action

The mechanism of antidepressant action of imipramine is not clear although it has been shown to block the reuptake of various neurotransmitters at the neuronal membrane. As a result, the actions of norepinephrine and serotonin may be potentiated. Imipramine has strong anticholinergic actions as well. Imipramine is not an MAO inhibitor.

### 10.3 Pharmacokinetics

#### **Absorption:**

Imipramine is absorbed after oral administration with peak plasma levels occurring within 1 hour to 2 hours.

#### **Distribution:**

The half-life of imipramine ranges from 8 hours to 16 hours.

#### **Metabolism:**

Imipramine is extensively metabolised by the liver. One metabolite, desipramine, is active.

Imipramine undergoes first-pass metabolism in the liver when administered orally. Enterohepatic circulation and secretion of the drugs and their metabolites into gastric juice may occur.

#### **Elimination**

The metabolites are excreted primarily by the kidney.

#### **Special Populations and Conditions**

- **Pediatrics:** The data on which the indication was originally authorized is not available.
- **Geriatrics:** The data on which the indication was originally authorized is not available.
- **Sex:** The data on which the indication was originally authorized is not available.
- **Pregnancy and Breast-feeding:** The data on which the indication was originally authorized is not available.
- **Genetic Polymorphism:** The data on which the indication was originally authorized is not available.
- **Ethnic Origin:** The data on which the indication was originally authorized is not available.
- **Hepatic Insufficiency:** The data on which the indication was originally authorized is not available.
- **Renal Insufficiency:** The data on which the indication was originally authorized is not available.
- **Obesity:** The data on which the indication was originally authorized is not available.

### 11 STORAGE, STABILITY AND DISPOSAL

Store at controlled room temperature (15°C-30°C).

Keep out of reach and sight of children.

IMIPRAMINE should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended.

## 12 SPECIAL HANDLING INSTRUCTIONS

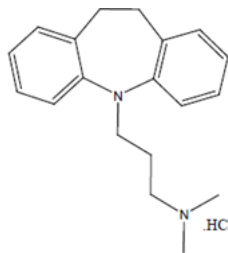
None.

## PART II: SCIENTIFIC INFORMATION

### 13 PHARMACEUTICAL INFORMATION

#### Drug Substance

Proper name:	imipramine hydrochloride.
Chemical name:	a) 10,11-Dihydro-N,N-dimethyl-5H-dibenz[b,f]azepine-5-propanamine Hydrochloride b) 5-(3-dimethylaminopropyl)-10,11-dihydro-5H-dibenz[b,f]azepine Hydrochloride c) N-(γ-dimethylaminopropyl)iminodibenzyl Hydrochloride
Molecular formula and molecular mass:	C <sub>19</sub> H <sub>24</sub> ClN <sub>2</sub> and 316.88 g/mol
Structural formula:	



#### Physicochemical properties:

Description	White crystalline powder, slightly hygroscopic
Solubility	Soluble in water, Soluble in DMF and DMSO.
Stability	Stable, air sensitive, hygroscopic material.

### 14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

### 15 MICROBIOLOGY

No microbiological information is required for this drug product.

### 16 NON-CLINICAL TOXICOLOGY

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether imipramine hydrochloride affects fertility in males or females.



## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

#### Pr **IMIPRAMINE**

#### **Imipramine Hydrochloride Tablets**

Read this carefully before you start taking **IMIPRAMINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **IMIPRAMINE**.

#### **Serious Warnings and Precautions**

##### **Self-harm or suicide:**

- Antidepressants, such as IMIPRAMINE, may increase the risk of suicidal thoughts and actions.
- **If you have thoughts of harming or killing yourself at any time, tell your healthcare professional or go to a hospital right away.** Close observation by a healthcare professional is necessary in this situation.

#### **What is IMIPRAMINE used for?**

IMIPRAMINE is used to relieve the symptoms of depression (feeling sad, a change in appetite or weight, difficulty concentrating or sleeping, feeling tired, headaches, unexplained aches and pain).

#### **How does IMIPRAMINE work?**

IMIPRAMINE is an antidepressant drug that belongs to a group of medicines called tricyclic antidepressant drugs. It is not known exactly how IMIPRAMINE works. It is thought to increase the concentration of certain chemicals in the brain which can help with the symptoms of depression.

#### **What are the ingredients in IMIPRAMINE?**

Medicinal ingredients: imipramine hydrochloride.

Non-medicinal ingredients: carnauba wax, hydroxypropyl methylcellulose, lactose monohydrate (in only the 25 mg, 50 mg, and 75 mg tablets), magnesium stearate, microcrystalline cellulose, polyethylene glycol, red ferric oxide, sunset yellow aluminum lake 40%, titanium dioxide, and yellow ferric oxide.

#### **IMIPRAMINE comes in the following dosage forms:**

Tablets: 10 mg, 25 mg, 50 mg, and 75 mg.

**Do not use IMIPRAMINE if:**

- you are allergic to imipramine hydrochloride, or any of the ingredients in IMIPRAMINE.
- you are allergic to tricyclic antidepressants that belong to the dibenzazepine group. Talk to your healthcare professional if you are not sure.
- you are taking or have taken monoamine oxidase inhibitors (MAOIs) within the last 14 days.
- you have recently had a heart attack.
- you are in heart failure.
- you have glaucoma (increased eye pressure).

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take IMIPRAMINE. Talk about any health conditions or problems you may have, including if you:**

- have heart problems including:
  - blood clots that form in the blood vessels or arteries of the heart,
  - angina,
  - heart failure,
  - disorders affecting heart rate, rhythm or conduction and
  - heart or blood vessel disease.
- have trouble urinating.
- have an enlarged prostate.
- have thoughts of harming or killing yourself.
- suffer from epilepsy or seizures.
- are pregnant, think you might be pregnant or planning to become pregnant. IMIPRAMINE should not be used during the first trimester of pregnancy.
- are breastfeeding or are planning to breastfeed.
- are 65 years of age or older.
- you have one of the following rare hereditary diseases:
  - Galactose intolerance
  - Lapp lactase deficiency
  - Glucose-galactose malabsorptionBecause lactose is a non-medicinal ingredient in IMIPRAMINE.

**Other warnings you should know about:**

**Angle-closure Glaucoma:** IMIPRAMINE can cause an acute attack of glaucoma. Having your eyes examined before you take IMIPRAMINE could help identify if you are at risk of having angle-closure glaucoma. Seek immediate medical attention if you experience:

- eye pain.
- changes in vision.
- swelling or redness in or around the eye.

**Laboratory Tests:** Tell your healthcare professional if you develop a fever and sore throat while taking IMIPRAMINE. Your healthcare professional will do blood tests. These tests will monitor your white blood cell count.

**Serotonin toxicity** (also known as Serotonin syndrome): IMIPRAMINE can cause Serotonin toxicity, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop Serotonin toxicity if you take IMIPRAMINE with certain anti-depressants or migraine medications.

Serotonin toxicity symptoms include:

- fever, sweating, shivering, diarrhea, nausea, vomiting;
- muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.**

**Serious Drug Interactions**

**Do not** take IMIPRAMINE if you are taking a monoamine oxidase inhibitor (MAOI), or if you have taken one in the last 14 days as this can cause serious side effects.

**The following may interact with IMIPRAMINE:**

- alcohol beverages.
- other medicines used to treat depression.
- anticholinergic agents, used to relieve stomach cramps, spasms and travel sickness.
- cimetidine used to treat stomach ulcers.
- medicines used to treat high blood pressure such as guanethidine.
- norepinephrine used to treat low blood pressure.
- epinephrine used to treat anaphylaxis, cardiac arrest, and severe asthma attacks.
- methylphenidate used to treat attention-deficit/hyperactivity disorder (ADHD).

**How to take IMIPRAMINE:**

- Take IMIPRAMINE exactly as your healthcare professional tells you to. Talk to your healthcare professional if you are not sure.
- Swallow the tablets whole with a glass of water.

**Usual dose:**

Your healthcare professional will determine the dose that is right for you and how often you should take it. Your dose will depend on your age and if you have any heart problems. Based on how you respond to IMIPRAMINE and your tolerability, your healthcare professional may change your dose.

**Overdose:**

Signs of an overdose may include:

- confusion
- disturbed concentration
- visual hallucinations
- restlessness
- overactive reflexes
- muscle rigidity
- vomiting
- high fever
- drowsiness
- hypothermia
- heart rhythm problems

If you think you, or a person you are caring for, have taken too much IMIPRAMINE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

**Missed Dose:**

If you miss a dose of IMIPRAMINE, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Do not take two doses at the same time to make up for the missed dose.

### **What are possible side effects from using IMIPRAMINE?**

These are not all the possible side effects you may have when taking IMIPRAMINE. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- dry mouth
- swelling of salivary glands
- constipation
- diarrhea
- nausea, vomiting
- stomach pain, stomach cramps
- unpleasant taste in the mouth
- sore mouth
- black tongue
- change in appetite
- weight gain or loss
- fever
- weakness
- tiredness
- headache
- falls
- impaired coordination
- shaking
- drowsiness
- dizziness
- dilated pupils
- change in libido
- inability to have or maintain an erection
- swelling of testicles
- problem emptying your bladder
- frequent urination
- itching
- sweating more than usual
- flushing

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
RARE			
Angle-closure Glaucoma: eye pain, changes in vision, and swelling or redness in or around the eye			√
Serotonin toxicity: a reaction which may cause feelings of agitation or restlessness, flushing, muscle twitching, involuntary eye movements, heavy sweating, high body temperature (> 38°C), or rigid muscles			√
UNKNOWN			
Agranulocytosis (decrease in white blood cells): frequent infection with fever, chills, sore throat			√
Bone marrow depression: easy bruising, bleeding, nose bleeds, bleeding gums, red spots on the skin, fever and chills, rash, extreme fatigue, pale skin and lips			√
Changes in feelings and behaviors:confusion, hallucinations (seeing or hearing things that are not really there), problems with attention, delusions, anxiety, restlessness, excitement, trouble sleeping, nightmares, extremely elevated and excitable mood memory problems		√	
Edema: unusual swelling of the arms, hands, legs, feet, ankles, face or airway passages		√	
Eosinophilia (increased numbers of certain white blood cells): abdominal pain, rash, weight loss, wheezing		√	
Extrapyramidal reactions: muscle stiffness, body spasms, upward eye rolling, exaggeration of reflexes, drooling, difficulty moving how and when you want, masklike face (appears to lack emotion), tremors, drooling, or dragging feet as you walk, difficulty swallowing, a feeling of restlessness, or inability to remain motionless			√
Heart rhythm problems: irregular heartbeat, fast heartbeat, shortness of breath, fainting, loss of consciousness		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>Hormonal changes:</b> breast enlargement in men, breast enlargement and abnormal milk production in women		√	
<b>Hypertension</b> (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		√	
<b>Hypotension</b> (low blood pressure): dizziness, fainting, lightheadedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)	√		
<b>Increased or decreased blood sugar:</b> frequent urination, thirst, hunger, shakiness, sweating and chills, irritability, confusion, dizziness	√		
<b>Jaundice</b> (buildup of bilirubin in the blood): yellowing of the skin and eyes, dark urine, light colored stool, or itching all over your body		√	
<b>Mania:</b> elevated or irritated mood, decreased need for sleep, racing thoughts, uneasiness		√	
<b>Myocardial infarction</b> (heart attack): pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint and possible irregular heartbeat			√
<b>Palpitations</b> (fast-beating, fluttering or pounding heart): skipping beats, beating too fast, pounding, fluttering rapidly			√
<b>Paralytic ileus</b> (muscles that move food through the intestines are paralyzed): new or worsening constipation, nausea, vomiting, dehydration, gas, or abdominal pain		√	
<b>Paresthesia</b> (pins and needles): numbness, weakness, tingling, burning; occurs in the arms, hands, legs or feet.		√	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>Peripheral neuropathy</b> (damage to the nerves outside the spinal cord and the brain): numbness or tingling sensation in the hands or feet		√	
<b>Seizures</b> (fits): uncontrollable shaking with or without loss of consciousness			√
<b>Skin disorders</b> <b>Photosensitivity</b> (sensitivity to sunlight): itchy, dry, red skin when exposed to sunlight <b>Petechiae</b> : pinpoint, red or purple round spots that appear on the skin <b>Urticaria</b> : skin with red spots which burn, itch or sting		√	
<b>Stroke</b> : sudden numbness or weakness of your arm, leg or face, especially if only on one side of the body; sudden confusion, difficulty speaking or understanding others; sudden difficulty in walking or loss of balance or coordination; suddenly feeling dizzy or sudden severe headache with no known cause			√
<b>Thrombocytopenia</b> (low blood platelets): bruising or bleeding for longer than usual if you hurt yourself, fatigue and weakness			√
<b>Tinnitus</b> : ringing, buzzing, clicking or hissing in the ears		√	
<b>Withdrawal symptoms</b> : feeling or being sick, stomach discomfort, diarrhea, vomiting, difficulty sleeping, nervousness, anxiety, headache, irritability	√		

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.



### Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### Storage:

Store at room temperature (15°C-30°C).

Keep out of reach and sight of children.

### If you want more information about IMIPRAMINE

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<https://www.aapharma.ca/en/>), or by calling 1-877-998-9097

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Last Revised: MAY 23, 2023