

PRESCRIBING INFORMATION

LARGACTIL

**Chlorpromazine Hydrochloride Drops
40 mg/mL**

**Chlorpromazine Hydrochloride Suppositories
100 mg**

**Chlorpromazine Hydrochloride Liquid
25 mg/mL**

Neuroleptic

sanofi-aventis Canada Inc.
2150 St. Elzear Blvd. West
Laval, Quebec H7L 4A8

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NAME OF DRUG

LARGACTIL

**Chlorpromazine Hydrochloride Drops
Chlorpromazine Hydrochloride Suppositories
Chlorpromazine Hydrochloride Liquid**

THERAPEUTIC CLASSIFICATION

Neuroleptic

ACTION

Chlorpromazine is a phenothiazine of the aminopropyl group. It is a potent antipsychotic and sedative agent which can control various states of emotional tension, agitation, hyperactivity and confusion. In addition, it exerts an anti-emetic action and potentiates the effects of narcotics, barbiturates and analgesics.

INDICATIONS

In psychiatry - schizophrenia, manic depressive psychoses (manic phase), behavioural disorders, involuntal psychoses, senile psychoses and confusional states in the elderly.

In general medicine - nausea, vomiting; persistent hiccup and organic conditions associated with emotional stress: acute or chronic alcoholism and for the treatment of withdrawal symptoms of addicts and alcoholics.

In obstetrics and surgery - as a preoperative medication for the relief of apprehension; to reduce, by potentiation, narcotic and analgesic requirements; as an antiemetic; to prevent and treat traumatic or postoperative shock; for use in artificial hibernation and controlled hypotension.

CONTRAINDICATIONS

Severe CNS depression or comatose states due to alcohol, barbiturates, analgesics or other CNS depressants. In patients with blood dyscrasias, severe liver disease or a sensitivity to phenothiazines.

WARNINGS

As with other neuroleptics, very rare cases of QT interval prolongation have been reported with LARGACTIL. Neuroleptic phenothiazines may potentiate QT interval prolongation, which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalemia, and congenital or acquired (i.e., drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a neuroleptic agent and as deemed necessary during treatment (See PRECAUTIONS and ADVERSE REACTIONS).

Tardive Dyskinesia: As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or after drug discontinuation. The syndrome is mainly characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw. The manifestations may be permanent in some patients. The syndrome may be masked when treatment is reinstated, when the dosage is increased or when a switch is made to a different antipsychotic drug. LARGACTIL should be prescribed in a manner that is most likely to minimize the risk of tardive dyskinesia. The lowest effective dose and the shortest duration of treatment should be used, and treatment should be discontinued at the earliest opportunity, or if a satisfactory response cannot be obtained. If the signs and symptoms of tardive dyskinesia appear during treatment, discontinuation of LARGACTIL should be considered.

Neuroleptic Malignant Syndrome: Neuroleptic malignant syndrome (NMS) may occur in patients receiving antipsychotic drugs. NMS is characterized by hyperthermia, muscle rigidity, altered consciousness, and signs of autonomic instability including irregular blood pressure, tachycardia, cardiac arrhythmias and diaphoresis. Additional signs may include elevated serum creatine kinase, myoglobinuria (rhabdomyolysis), acute renal failure and leukocytosis.

Hyperthermia is often an early sign of this syndrome. Antipsychotic treatment should be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted.

PRECAUTIONS

LARGACTIL can potentiate the effects of other phenothiazines and CNS depressants. When treatment is initiated, the usual doses of barbiturates, analgesics, narcotics or antihistamines should be reduced by half. Patients should be warned against consuming alcoholic beverages while on LARGACTIL therapy.

Neuroleptic phenothiazines may potentiate QT interval prolongation. QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalemia, and congenital or acquired (i.e., drug induced) QT prolongation (See WARNINGS and ADVERSE REACTIONS).

LARGACTIL should be used cautiously in patients suffering from arteriosclerosis, cardiovascular disease or other conditions where it is necessary to avoid a sudden drop in blood pressure. If hypotension does occur and it is necessary to use a hypertensive agent, norepinephrine should be used, not epinephrine, as the latter agent can aggravate hypotension.

Because of its anticholinergic properties, LARGACTIL must be used with caution in patients with glaucoma or prostatic hypertrophy.

During protracted therapy and especially if high dosages are administered, it is recommended that blood counts and liver function tests be performed at regular intervals.

Drowsiness may occur at the beginning of treatment; patients should therefore be warned against operating motor vehicles or participating in activities requiring mental alertness until this effect has subsided.

Phenothiazines can provoke epileptic seizures by lowering the seizure threshold; therefore, during LARGACTIL therapy, the patient's usual anticonvulsant medication should be continued at the same dosage.

Because of its antiemetic effect, LARGACTIL can obscure symptoms of intracranial hypertension or intestinal obstruction.

False positive or negative pregnancy tests have occurred in patients receiving phenothiazine therapy.

ADVERSE REACTIONS

Drowsiness frequently occurs at the beginning of treatment but gradually disappears or subsides with a downward adjustment of the dosage - also at the beginning of treatment, there are rare cases of orthostatic hypotension, particularly when high doses are used - dystonic and extrapyramidal reactions may appear during prolonged treatment with elevated dosages, but can be eliminated by lowering the doses or administering an antiparkinsonian agent.

Other side effects which are observed less frequently include: nasal congestion, blurred vision, xerostomy, sedation, nausea, constipation, changes in libido, gynecomastia, weight gain, skin and corneal pigmentation, photosensitivity, blood dyscrasias, leukopenia, eosinophilia and EEG changes.

Very rare cases of QT interval prolongation have been reported. There have been isolated reports of sudden death, with possible causes of cardiac origin (see WARNINGS and PRECAUTIONS), as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.

Cholestatic jaundice and liver injury, mainly of cholestatic or mixed type, are rarely reported in patients treated with LARGACTIL.

Systemic lupus erythematosus has been very rarely reported in patients treated with LARGACTIL. In some cases, positive anti-nuclear antibodies may be seen without evidence of clinical disease.

Priapism has been very rarely reported in patients treated with LARGACTIL.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms – Agitation, hyperactivity, confusion, CNS depression followed by somnolence, coma and circulatory collapse.

Treatment - No specific antidote. Gastric lavage and symptomatic treatment.

For hypotension: glucose solutions in I.V. infusion and, if necessary norepinephrine added to the infusion liquid.

For respiratory depression: oxygen and artificial respiration

For extrapyramidal reactions: antiparkinsonian drugs

To prevent respiratory infections: wide spectrum antibiotics

Because of the antiemetic action of LARGACTIL, centrally acting emetics are ineffective. Dialysis does not assist in eliminating the drug from the blood.

DOSAGE AND ADMINISTRATION

ADULTS

In general medicine and psychiatry

Oral route: average daily dose of 30 to 75 mg (mild cases) or 75 to 100 mg (more severe cases) in divided doses. It is occasionally necessary to give a higher dosage which, when increased gradually, can reach 900 mg or more per day in some psychiatric patients.

Once the optimum dosage has been reached, it is maintained as long as necessary for the control of symptoms during the critical phase of the illness. Eventually, however, it should be gradually reduced so that the patient can be maintained on the lowest effective dosage.

Rectal route: 100 to 300 mg or 1 to 3 suppositories of 100 mg daily.

In surgery and anesthesia

To potentiate hypnotics, analgesics and anesthetics and as an antiemetic.

Oral route: doses of 25 to 50 mg are administered 2 to 3 hours before anesthesia and every 4 to 6 hours after surgery.

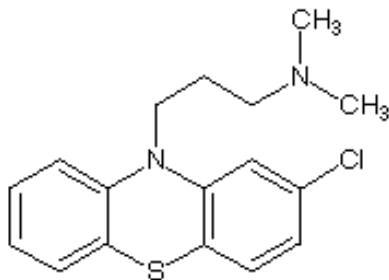
CHILDREN

Usual single dose: 1/4 mg per pound (1/2 mg/kg) by oral route. This dose can be repeated every 4 to 6 hours as necessary. The normal daily dose is 40 mg for a child of 5 years (40 pounds), 75 mg for children of 5 to 12 years (50 to 100 pounds) except in psychiatric patients where dosages can be progressively elevated above these levels.

In surgery and anesthesia, doses of 1/4 mg per pound, by the same method recommended for adults.

PHARMACEUTICAL INFORMATION

2-chloro-10 (3-dimethylaminopropyl) phenothiazine or chlorpromazine utilized primarily as the hydrochloride. Its structural formula may be represented as follows:



Molecular weight: 355.33

Chlorpromazine hydrochloride is a white or off-white crystalline powder which has a slightly pungent odor. It is very soluble in water, soluble in methanol, ethanol and chloroform, and insoluble in ether and benzene.

AVAILABILITY OF DOSAGE FORMS

Liquid of 25 mg/5 mL: Each 5 mL of colorless liquid contains: chlorpromazine base 25 mg (as the hydrochloride). Non-medicinal ingredients: alcohol, ascorbic acid, citric acid, ethyl vanillin, glycerin, peach flavor, purified water, sodium benzoate and sucrose. Alcohol: 0.5% v/v. Sucrose: 3.9 g/5 mL. Tartrazine-free. Bottles of 500 mL. Protect from light or discoloration may occur.

Liquid of 100 mg/5 mL: Each 5 mL of yellow liquid contains: chlorpromazine base 100 mg (as the hydrochloride). Non-medicinal ingredients: alcohol, artificial fruit flavor, citric acid, D&C Yellow No. 10, ethyl vanillin, glycerin, purified water, sodium benzoate and sucrose. Alcohol: 0.5% v/v. Sucrose: 3.6 g/5 mL. Tartrazine-free. Bottles of 500 mL. Protect from light or discoloration may occur.

Oral Drops: Each mL of brown solution contains: chlorpromazine base 40 mg (4%) (as the hydrochloride). Non-medicinal ingredients: alcohol, artificial and natural custard flavor, caramel, citric acid, glycerin, purified water, sucrose and terpeneless orange oil. Alcohol: 17.5% v/v. Sucrose: 200 mg. Bottles of 100 mL with calibrated dropper. Protect from light or discoloration may occur.

Suppositories: Each rectal suppository contains: chlorpromazine base 100 mg (as the hydrochloride). Non-medicinal ingredients: hydrogenated vegetable glycerides. Tartrazine-free. Boxes of 10 suppositories. Store in a cool place.

PHARMACOLOGY

Chlorpromazine possesses potent sedative and antiemetic effects and potentiates CNS depressants. It is also a moderately strong adrenolytic agent, but has only weak anticholinergic activity. The LD₅₀ in the mouse is 260 mg/kg P.O. and in the rat, 360 mg/kg P.O. The drug did not interfere with normal reproductive activity nor did it exert any teratogenic effect on the offspring of the animals studied.

CONSUMER INFORMATION

Pr LARGACTIL®
Chlorpromazine Hydrochloride Drops
Chlorpromazine Hydrochloride Suppositories
Chlorpromazine Hydrochloride Liquid

This leaflet is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Largactil®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Largactil® is used:

- To treat symptoms of schizophrenias, psychoses, behavioural disorders or confusion in the elderly
- To control nausea, vomiting or persistent hiccup

Largactil® is also used:

- In conditions associated with emotional stress
- In the treatment of withdrawal symptoms of addicts and alcoholics.
- Before a surgery to reduce anxiety, to reduce the need for drugs relieving pain, to control nausea and vomiting or to prevent and treat shock following the surgery.

Ask your doctor if you have any questions about why Largactil® has been prescribed to you.

What it does:

Largactil® helps to:

- reduce and control psychotic symptoms and induce sleep which can control various states of emotional tension, agitation, hyperactivity and confusion.
- control nausea and vomiting.
- intensify the effects of drugs that relieve pain.

When it should not be used:

Do not use Largactil® if you:

- Are allergic to Largactil®, to phenothiazines (a type of antipsychotic) or to any of the ingredients in the product (see the section "What the non-medicinal ingredients are")
- Are in an altered state of consciousness or coma, especially if this is caused by alcohol or drugs
- Have a blood disorders
- Have liver disease

What the medicinal ingredient is:

chlorpromazine hydrochloride

What the non-medicinal ingredients are:

Liquid of 25 mg/5 mL: alcohol, ascorbic acid, citric acid, ethyl vanillin, glycerin, peach flavor, purified water, sodium benzoate and sucrose.

Liquid of 100 mg/5 mL: alcohol, artificial fruit flavor, citric acid, D&C Yellow No. 10, ethyl vanillin, glycerin, purified water, sodium benzoate and sucrose.

Oral drops: alcohol, artificial and natural custard flavor, caramel, citric acid, glycerin, purified water, sucrose and terpeneless orange oil.

Suppositories: hydrogenated vegetable glycerides.

What dosage forms it comes in:

- Liquid 25 mg/5 mL
- Liquid 100 mg/5 mL
- Oral drops 40 mg/mL
- Suppositories 100 mg

WARNINGS AND PRECAUTIONS

At the beginning of treatment, Largactil® may cause some people to become drowsy or less alert. You should not drive a car, operate machinery or participate in activities requiring total alertness until you are sure Largactil® does not affect you.

Tardive dyskinesia, neuroleptic malignant syndrome and cardiac disorders may occur in some patients taking Largactil® (See the section "**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**").

Before using Largactil®, tell your doctor if you:

- Have heart or blood vessel disease
- Have constipation or intestinal blockage
- Suffer from an enlarged prostate (Benign prostatic hypertrophy)
- Suffer from an increase pressure within the eyes (glaucoma)
- Have or have had seizure disorders (e.g. epilepsy)
- Plan to have surgery (or a procedure requiring anaesthetics)
- Are or are planning to become pregnant
- Are breast-feeding

If you experience severe constipation and you are elderly, please consult your doctor as soon as possible.

During long-term therapy, liver and blood tests should be done at regular intervals.

INTERACTIONS WITH THIS MEDICATION

Largactil® can add to the effects of alcohol. You should avoid consuming alcoholic beverages while on Largactil® therapy.

Before using any prescription, over-the-counter medicines or herbal products, check with your doctor or your pharmacist.

Largactil® can add to the effects of other drugs that cause drowsiness. Some examples of drugs that cause drowsiness are:

- Drugs for allergies
- Drugs for sleep
- Drugs for pain
- Drugs for seizure
- Drugs for depression
- Drugs for mental illness

Largactil® may cause a false pregnancy test result. Please check with your doctor if this happens.

PROPER USE OF THIS MEDICATION

Usual dose:

Your doctor has decided the best dose for you based on your individual situation and needs. It is important to take Largactil® the way your doctor told you. Your doctor may increase or decrease your dose depending on your response.

You may experience side effects if the drug is stopped suddenly. Contact your physician before stopping your drug.

Adults - In general medicine and psychiatry

Oral route: The average dose is 30 to 75 mg a day (mild cases) or 75 to 100 mg a day (more severe cases). The daily dose is divided into smaller doses during the day. Your doctor may decrease or increase your dose if needed.

Rectal route: 1 to 3 suppositories daily.

Adults - In surgery and anesthesia

Oral route: doses of 25 to 50 mg are administered 2 to 3 hours before anesthesia and every 4 to 6 hours after surgery.

Children

Oral route: Dose is based on body weight.

Overdose:

If you have taken too much Largactil®, immediately see your doctor or go to your nearest hospital emergency department. Show the doctor your bottle or box of Largactil®. Do this even if there are

no signs of discomfort or poisoning. The signs if you have taken too much Largactil® may include agitation, hyperactivity, confusion, drowsiness and coma.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Largactil®, like any medication, may cause some side effects. Discuss with your doctor if you do experience side effects.

Side effect include:

- Drowsiness frequently occurs at the beginning of treatment but gradually disappear with time or with a reduction of the dose. If this effect persists, discuss this with your doctor.
- Blurred vision, changes in libido, coloration of the skin or the cornea (transparent portion of the outer covering of the eyes), constipation, dryness of the mouth, enlargement of the breast in male, nasal congestion, nausea, sleepiness, weight gain.
- Your skin may be more sensitive to sunlight

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
<u>See text below for more details</u>				
Common	Hypotension ^{a)}		√	
Uncommon	Allergic Reactions			√
	Blood disorders ^{b)}		√	
	Cardiac disorders ^{a)}		√	
	Extrapyramidal reactions ^{c)}		√	
	Liver disorders ^{b)}		√	
	Lung disorders ^{b)}		√	
	Neuroleptic malignant syndrome ^{d)}		√	
Tardive dyskinesia ^{e)}		√		

a) Cardiac disorders: At the start of treatment, some people may have low blood pressure and feel dizzy, especially when getting up from a lying or sitting position, particularly when high doses are used. Uncommonly, Largactil® may cause the heartbeat to

become faster or irregular. Check with your doctor immediately if you experience any of these side effects.

b) Blood, liver and lung disorders have been associated with this class of drug. It is important that you tell your doctor at once about any unexplained symptom you might experience. Examples of this are soreness of the mouth, gums or throat or any symptoms of upper respiratory infection, unexplained fever, itching, flu-like symptoms, coughing, abdominal pain or jaundice.

c) Extrapyramidal reactions are rare and usually appear only after long-term therapy at high doses. The signs and symptoms of extrapyramidal reactions include tremor, muscle stiffness, body spasm, impairment of voluntary movement, upward eye rolling, exaggeration of reflexes or drooling. Tell your doctor immediately if you experience any of these side effects. Your medication might have to be reduced.

d) Neuroleptic malignant syndrome. Another possible serious unwanted effect is the neuroleptic malignant syndrome. Signs and symptoms of the neuroleptic malignant syndrome include severe muscle stiffness, increased sweating, fever, fast or irregular heartbeat, high or low blood pressure, difficult or fast breathing and confusion. If any of the above side effects occur, consult your doctor immediately.

e) Tardive dyskinesia may occur in some patients on long-term therapy or after they stop using Largactil®. Signs of tardive dyskinesia include muscle twitching or uncontrolled movements of the mouth, tongue, face or jaw. In some patients, this side effect may not go away after they stop using Largactil®. Tell your doctor immediately if you experience any muscle twitching or abnormal body movements.

Other very rare side effects include:

- painful erection or systemic lupus erythematosus (an autoimmune disease: the immune system turns against parts of the body it is designed to protect. This leads to inflammation and damage to various body tissues).

This is not a complete list of side effects. For any unexpected effects while taking Largactil®, contact your doctor or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345

toll-free fax 866-678-6789

By email: cadrmpp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness
Information Division
Marketed Health Products Directorate
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

Your physician, nurse and pharmacist are always your best source of information about your condition and treatment. If you have additional questions or concerns, be sure to ask them.

This document plus the full product monograph is available upon request to the sponsor, sanofi-aventis Canada Inc., 2150 St Elzear Blvd. West, Laval, Quebec H7L 4A8, at: 1-800-265-7927

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HOW TO STORE IT

Largactil® oral drops, liquid and suppositories should be protected from exposure to light.

Largactil® suppositories should be stored in a cool place.

Keep out of reach of children.