PACKAGE LEAFLET: Information for the patient

KLORPROMAZINE

Sugar-coated tablets – 100 mg

Solution for injection – 50 mg / 2 ml

(Chlorpromazine hydrochloride)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

What is in this leaflet

1. WHAT KLORPROMAZINE IS AND WHAT IT IS USED FOR

Chlorpromazine is the first antipsychotic in practice that represents the aliphatic phenothiazines. It has a wide range of activity arising from its depressant actions on the CNS and its alpha-adrenergic blocking and some weak antimuscarinic activities.

Chlorpromazine is a dopamine inhibitor and stimulates the release of prolactine. There is some evidence that the antagonism of central dopaminergic function, especially at the D_2-dopaminergic receptor, is related to the therapeutic effect in psychotic conditions.

Chlorpromazine possesses sedative properties but patients usually develop tolerance rapidly to

sedation. It has antiemetic, serotonin-blocking, and weak antihistaminic properties and slight ganglion-blocking activity. Chlorpromazine inhibits the heat-regulating centre so that the patient tends to acquire the temperature of the surroundings. Chlorpromazine can relax skeletal muscles.

Chlorpromazine sugar-coated tablet and solution for injection is used:

- in acute and chronic schizophrenia in adults and children;
- to reduce acute mania, as in bipolar disorder;
- in the control of agitated, or violent behavior in adults and children and sometimes other psychiatric conditions;
- in autistic children;
- as an adjunct for the short-term treatment of severe anxiety, and to reduce pre-operative anxiety in adults and children;
- as an antiemetic in some forms of nausea and vomiting in adults and children; it is ineffective in motion sickness;
- in the alleviation of intractable hiccup;
- as an adjunct in the treatment of tetanus in adults and children and to control symptoms in acute intermittent porphyria;
- for induction of hypothermia;
- in surgery – preparation for anesthesia, prophylaxis and treatment of states of shock;
- in obstetrics – obstetric analgesia, eclampsia.

2. BEFORE YOU TAKE KLORPROMAZINE

Do not take Klorpromazine and tell your doctor if you:

- are hypersensitive to chlorpromazine hydrochloride or other phenothiazines;
- are allergic to any of the excipients of Klorpromazine mentioned in the end of this leaflet;
- suffer from any comatose states caused by central nervous system depressant such as: alcohol, narcotics, barbiturates;
- suffer from bone-marrow suppression;
- suffer from blood dyscrasia;
- suffer from severe impairment of hepatic function;
- suffer from cerebral arteriosclerosis;

- suffer from coronary artery disease;
- suffer from hypotension or severe tension;
- suffer from phaeochromocytoma;
- suffer from hypothyroidism.

Consult with your doctor or go directly to the hospital in these conditions.

You should seek help from your relatives or your close friends when you are depressed or have an anxious disorder, and tell them to read the leaflet. You should ask them if your depression or anxiety gets worse, or if they are worried about a change in your behavior.

Take special care with Klorpromazine

Talk to your doctor or pharmacist before taking Klorpromazine.

Klorpromazine should be used with caution in the elderly, in patients with cardiovascular, cerebrovascular and respiratory diseases, and in those with parkinsonism, acute infections, in pregnancy and breast-feeding, liver and renal function impairments (must be avoided in severe impairments), hyperthyroidism, in patients with a history of jaundice and leucopenia; myasthenia gravis, angle-closure glaucoma, prostatic hyperplasia or urinary retention, in patients with risk factors for ictus or thromboembolism.

It should be used with caution in the elderly when the temperature is too low or two high because body temperature regulation is impaired by phenothiazines.

Klorpromazine may potentiate the effect of alcohol and other depressants of central nervous system, anticholinergics, tricyclic antidepressants.

Care is required in patients with epilepsy as phenothiazines may lower the seizure threshold.

The effect of phenothiazines in the vomiting center may mask the symptoms of overdosage of other drugs, or of other disorders such as gastrointestinal obstruction, or central nervous system disorders such as cerebral tumors or Reye syndrome.

Caution should be taken in patients with breast cancer, because continuous treatment with chlorpromazine hydrochloride may cause an increase of the level of prolactine, which may affect the targeted organs.

In case of hypotension, do not use adrenaline because it may cause further lowering of the blood pressure.

If you have diabetes mellitus or known risk factors for developing diabetes you must undergo glycemic monitoring or glucose intolerance monitoring.
Regular eye examinations are advisable for patients receiving long-therm phenothiazine therapy and avoidance of undue exposure to direct sunlight is recommended.
Blood counts are advised if the patient develops an unexplained infection or fever.
Abrupt withdrawal of phenothiazine therapy is best avoided.
If you have an intolerance to some sugars, you should contact your doctor before taking the tablets.

Interactions with laboratory tests
Products resulting from the metabolism of phenothiazines can impart a dark color to urine and give false positive responses to amylase, urobilinogen, uroporphyrins, porphobilinogens and 5-hydroxy indolacetic acid tests.
In women on treatment with phenothiazines, false positive pregnancy tests were reported.

Taking other medicines
Concomitant use with other drugs may affect or be affected by Klorpromazine.
Please tell your doctor or pharmacist if you are taking or have taken recently other drugs, including those taken without prescription. Remember to tell your doctor about the treatment with Klorpromazine if you are given another drug during treatment because:

- chlorpromazine can potentiate the suppression of CNS caused by other drugs such as: benzodiazepines, barbiturates, ethanol, general anaesthetics, opiod agonists and anxiolytics and other hypnotics;
- the interaction with antihypertensives may cause further lowering of the blood pressure; because of its alpha-blocking effect, chlorpromazine may potentiate the hypotensive effect or the other central effects of clonidine, when they are used concomitantly;
- chlorpromazine may reduce the hypotensive effect of peripheral sympatholytics such as guanethidine after reducing the reuptake of these drugs from the nerve endings;
- propranolol reduces the hepatic metabolism of phenothiazines, whereas phenothiazines reduce the hepatic metabolism of propranolol. Hepatic metabolism of chlorpromazine is reduced also from fluoxetine and antimalarials;

- when combined with antiepileptics, phenothiazines may increase the suppression of CNS and decrease the seizure threshold;
- chlorpromazine use should be avoided with drugs that block dopaminergic receptors in CNS, such as droperidol, haloperidol, metoclopramide, metyrosine, olanzapine and risperidon, becuase the risk of side effects in CNS is increased; for this reason concomitant use should be avoided;
- rifampicin increases the hepatic clearance of chlorpromazine;
- combination with lithium may result in decrease of chlorpromazine efficacy and in increased incidence of extrapyramidal side effects, delirium, convulsions and encephalopathy in maniacal patients;
- antimuscarinic effects may be potentiated in case of combination of chlorpromazine with other anticholinergic drugs such as: atropine and other antimuscarinics, some H_1 antihistaminics, tricyclic antideppressants, and other drugs with antimuscarinic action such as: amantadine, benztropine, clozapine, cyclobenzaprine, diphenoxylate, disopyramide, maprotiline, orphenadrine, propantheline, trihexyphenidyl;
- alpha-adrenergic effects of adrenaline and other adrenergic agonists may be blocked by the concomitant use with phenothiazines;
- phenothiazines reduce the efficacy of antiparkinsonian drugs such as: lisuride, levodopa, pergolide, bromcriptine, cabergoline, piribedil, pramipexole or ropirinol;
- combination of chlorpromazine with drugs that cause QT interval prolongation increase the risk for arrythmia such as torsade de pointes. These drugs are: amiodarone, astemizole, bepridil, cisapride, flecainide, grepafloxacin, sparfloxacin, pimozide, procainamide, probucol, quinidine, sotalol, terfenadine, tocainide and some antideppressants;
- cimetidine reduces the oral absorption of chlorpromazine; antiacids reduce the biodisponibility of chlorpromazine (it is recomended that they should be taken in an interval of 2 hours);
- amphetamine worsens the psychotic symptoms, whereas chlorpromazine reduces the efficacy of amphetamine because of neuronal reuptake blocking of dopamine and noradrenaline. The use of chlorpromazine with amphetamine should be avoided;
- combination with tramadol increases the risk for convulsions;

- simultaneous use of phenothiazines with oral contraceptives, quinolones, sulphonamides, sulphonylurea, tetracyclines, thiazide diuretics and vitamin A analogues, increase the photosensitivity caused by these drugs.

This interaction list is not complete. There are also other drugs that may interact with Klorpromazine.

Taking Klorpromazine with food and drinks

Alcohol consumption should be avoided during treatment with Klorpromazine, because it can be dangerous as it stimulates the onset of side effects.

Pregnancy and breastfeeding

Ask your doctor or pharmacist before taking this drug.

Pregnancy

Risk in pregnancy: category C – when the benefits for the mother outweigh the risk of the fetus.
The use of Klorpromazine in late pregnancy is not recommended; such use may be associated with intoxication of the neonate. Chlorpromazine may prolong labour and should be withheld until the cervix is dilated 3 to 4 cm.
It is concluded that the benefits of continuing antipsychotic treatment at the minimum effective dose would usually outweigh any risks to the fetus, so the balance benefit-risk tends to be to the benefit side.

So, during pregnancy Klorpromazine may be taken only with medical prescription when the specialist considers it very important for the life of the mother.

Breastfeeding

It is considered that the use of chlorpromazine by mothers during breast-feeding may be of concern, since there have been reports of galactorrhoea in the mother and of drowsiness, lethargy, and declines in developmental scores in the infant.
So, chlorpromazine may be used only when the benefits outweigh the risks and only with medical advice.

Fertility

Chlorpromazine may reduce the chances to get pregnant, being that it decreases the fertility in women.

Driving and using machines

The sedative effects of phenothiazines are noticed more in the first few days of treatment. For this reason, the affected patients should not drive or operate machines.

Important information about some of the excipients of Klorpromazine

Klorpromazine sugar-coated tablets contain sucrose and lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

The sugar-coated tablets contain sodium benzoate.

The solution for injection Klorpromazine contains sodium metabisulphite and sodium sulphite which may rarely cause severe hypersensitivity reactions and bronchospasm.

3. HOW TO TAKE KLORPROMAZINE

Always take Klorpromazine exactly as your doctor has told you. If you are not sure, ask your doctor or pharmacist. If you feel that the effect of Klorpromazine is too strong or too weak, talk to your doctor or pharmacist.

The tablets should be taken orally with at least one glass of water (250 ml water).

You should not take alcoholic drinks during this treatment.

Dosage varies individually and depends on the purpose for which the drug is being used.

Sugar-coated tablet: In most patients with psychiatric conditions, oral treatment may be used from the start, typically commencing with a dosage of 25 mg of chlorpromazine hydrochloride, three times daily and increasing as necessary. Daily doses of 75 mg may be given as a single dose at night. In some patients doses of 10 mg three times daily may be adequate. Maintenance doses, when required, usually range from 25 to 100 mg three times daily, although psychotic patients may require daily doses of up to 1 g or more.

Doses of 10 to 25 mg every 4 to 6 hours orally are recommended for control of nausea and vomiting.
In intractable hiccup the recommended dose is 25 to 50 mg three or four times daily.
Children: oral Klorpromazine may be given to children aged 1 to 12 years in a dose of 500 micrograms/kg every 4 to 6 hours.
Elderly or debilitated patients: one-half the usual adult dose has been recommended.

Solution for injection: For parenteral use, intramuscular injection is preferable, but diluted solutions have sometimes been given by slow intravenous infusion for indications such as tetanus, severe intractable hiccup, or nausea and vomiting associated with surgery.
Subcutaneous injection is contraindicated.
After injection of chlorpromazine, patients should remain in the supine position for at least 30 minutes; blood pressure should be monitored. The usual dose by intramuscular injection is 25 to 50 mg repeated every 6 to 8 hours if required, although oral therapy should be started as soon as possible.
Intramuscular doses *in the elderly* may need to be reduced to up to one-quarter of the usual dose.
Children: Chlorpromazine hydrochloride may be given to *children* aged 1 to 12 years in a dose of 500 micrograms/kg every 6 to 8 hours by intramuscular injection.
Daily doses (of sugar-coated tablets and solution for injection) should not normally exceed 40 mg of chlorpromazine hydrochloride for children aged 1 to 5 years or 75 mg for children over 5 years of age. Chlorpromazine may be given to infants under 1 year of age if considered life-saving.

If you take more Klorpromazine than you should

If you take more Klorpromazine than you should, or if the children have taken this medicine by accident, please contact your doctor, the hospital or call the emergency to get an opinion of the risk and advice on the action to be taken.
The main symptoms of an acute intoxication are tonic-clonic seizures, central nervous system depression that may lead to coma and severe hypotension.

Treatment: begins with gastric lavage (do not administer emetics) and continues with perfusions of plasma derivatives in case of severe decrease of arterial pressure. Antiarrhythmics and diazepam should be administered to control the seizures.

If you forget to take Klorpromazine

If you forget a dose, take the next dose when it is the normal time to take it.
Do not take a double dose to make up for the forgotten dose.

If you stop taking Klorpromazine

Do not stop the treatment without consulting a doctor.
Treatment with Klorpromazine should not be stopped abruptly. The abrupt interruption may produce withdrawal symptoms. Ask your doctor how to interrupt gradually the treatment.
If you have any further questions on the use of this medicinal product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, chlorpromazine also can cause side effects, although not everybody may get them. Sometimes they may be serious, sometimes not. Do not panic from this list of possible side effects. You may not get any of them.
Some of the side effects appear in the beginning of the treatment and disappear spontaneously during treatment.

Stop taking Klorpromazine and contact your doctor if you get:

- extrapyramidal dysfunction (which can be avoided with reducing dose or from antimuscarinic drugs);
- during long-term treatment may appear: tardive dyskinesia, akathisia, hypothermia (sometimes pyrexia), drowsiness, apathy, jaundice, anxiety, insomnia, depression and rarely agitation, EEG changes, convulsions;
- antimuscarinic symptoms have been reported, such as: dry mouth, nasal congestion, constipation, difficulty with micturition, and blurred vision;
- cardiovascular symptoms, such as: hypotension, tachyarrhythmia, ECG changes;

- endocrine dysfunctions, such as: menstrual disorders, galactorrhoea, gynaecomastia, impotence, weight gain, hyperglycemia;
- haematological disorders such as: agranulocytosis, leucopenia, leucocytosis, haemolytic anaemia;
- photosensitivity reactions, changes in liver function, neuroleptic malignant syndrome;
- opacity of cornea, conjunctiva and retina have been reported after long-term treatment.

Other side effects (with unknown frequency) may appear:

- cardiovascular disorders (atrio-ventricular block, cardiac arrest, immediate death);
- respiratory disorders;
- hypersensitivity reaction, eczema, erythema, exfoliative and allergic dermatitis or angioedema;
- systemic erythematosus lupus;
- hypertriglyceridemia, hyponatremia.

Intramuscular injection may produce pain and cause hypotension and tachycardia.

If any of the side effects becomes worse or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE KLORPROMAZINE

Keep out of the reach and sight of children.

Do not use Klorpromazine after the expiry date which is stated on the package.

Do not store above 25°C.

Store in the original package to protect it from light and humidity!

6. FURTHER INFORMATION

What Klorpromazine contains

The active substance is chlorpromazine hydrochloride.

Each sugar-coated tablet contains 100 mg chlorpromazine hydrochloride.

The excipients are: starch, lactose, povidone, magnesium stearate, sodium starch glycolate, gelatin, calcium carbonate, titanium dioxide, sucrose, talc, quinoline yellow, indigo carmine, sodium benzoate, shellac, carnauba wax, beeswax white.

Each ampoule 2 ml contains 50 mg chlorpromazine hydrochloride.

The excipients are: sodium metabisulphite, sodium sulphite anhydrous, ascorbic acid, sodium chloride, hydrochloric acid may be added for pH adjustment, water for injections.

Contents of the pack

Tablets: box with 60 sugar-coated tablets.

Solution for injection: box with 10 ampoules.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

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