APPROVED
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Instruction for medical use

VERTINEX®

Composition:
active substance: Prochlorperazine Maleate;
1 tablet contains 5 mg of Prochlorperazine Maleate;
excipients: Lactose monohydrate, Microcrystalline Cellulose, Maize Starch, Croscarmellose sodium, Sodium lauryl Sulphate, Magnesium Stearate, Colloidal anhydrous Silica.

Pharmaceutical form. Tablets.
Main physical and chemical properties: white to off-white, round shaped, biconvex tablets, smooth on both sides.

Pharmacotherapeutic group.
Antipsychotics. Phenothiazines with piperazine structure. ATC code: N05AB04.

Pharmacological properties.
Pharmacodynamics.
Prochlorperazine maleate is a phenothiazine derivative.
Prochlorperazine has a wide range of activity arising from its depressant actions on the CNS and its alpha-adrenergic blocking and weaker anti-muscarinic properties. It inhibits dopamine- and prolactin-release-inhibitory factor, thus stimulating the release of prolactin and increasing the metabolism of dopamine in the brain. There is evidence that the therapeutic effect in psychotic conditions is due to the antagonism of prochlorperazine to dopamine receptors in CNS.
Prochlorperazine has sedative properties but tolerance to the sedation usually develops rapidly. Prochlorperazine has anti-emetic, anti-pruritic, serotonin-blocking properties. Besides, prochlorperazine has weak antihistamine effect and slight ganglion-blocking activity. Also, prochlorperazine inhibits the heat regulating centre, has relaxing effect on smooth muscles, and membrane stabilizing and local anaesthetic properties. The effect of prochlorperazine on the autonomic nervous system produces vasodilatation, arterial hypotension tachycardia, hyposalivation and reduction of gastric secretions.

Pharmacokinetic properties.
Prochlorperazine is well absorbed from the gastrointestinal tract but is subject to considerable first pass metabolism from the gut wall. It is also extensively metabolised in the liver and is excreted in the urine and bile. Plasma concentrations following oral administration are much lower than those following intramuscular injection. There is no direct correlation between plasma concentrations of prochlorperazine and its metabolites, and therapeutic effect.
Prochlorperazine may be metabolized by hydroxylation and conjugation with glucuronic acid, N-oxidation, oxidation of the sulphur atom and dealkylation. Plasma half-life is reported to be only a few hours but elimination of the metabolites may be very prolonged. Prochlorperazine is extensively bound to plasma proteins and widely distributed in the body, its metabolites cross the placental barrier and are excreted in milk. The rate of metabolism and excretion of prochlorperazine decreases in elderly patients.

Clinical characteristics.

Indications.

Vertigo due to Meniere's syndrome, arising from Menier's syndrome, inflammation of the inner ear and other causes.

Nausea and vomiting from whatever cause including that associated with migraine.

It may also be used as an adjunct to the short-term management of anxiety.

Contraindications.

Known hypersensitivity to prochlorperazine or other components of the drug.

Interaction with other medicinal products and other forms of interaction.

Adrenaline must not be used in patients overdosed with prochlorperazine (see "Overdose" section).

The CNS depressant effect of prochlorperazine may be intensified (additively) by alcohol, barbiturates and other sedatives. Respiratory depression may occur.

Anticholinergic agents may reduce the antipsychotic effect of prochlorperazine.

The mild anticholinergic effect of prochlorperazine may be enhanced by other anticholinergic drugs, possibly leading to constipation, heat stroke, etc.

Antacids, antiparkinsonian drugs and lithium may interfere with absorption of prochlorperazine.

Where treatment for neuroleptic-induced extrapyramidal symptoms is required, anticholinergic antiparkinsonian agents should be used in preference to levodopa, since neuroleptics antagonise the antiparkinsonian action of dopaminergics.

High doses of neuroleptics reduce the hypoglycaemic effect of sugar-lowering medicines, the dosage of which might have to be adjusted.

The hypotensive effect of most antihypertensive drugs especially alpha adrenoceptor blocking agents may be exaggerated by neuroleptics.

Prochlorperazine as well as other phenothiazine neuroleptics may suppress the action of some drugs: amphetamine, levodopa, clonidine, guanethidine and adrenaline.

There is data on changes in plasma concentrations of a number of drugs (e.g. propranolol, phenobarbital) which have no clinical significance.

Simultaneous administration of prochlorperazine and desferrioxamine has been observed to induce transient metabolic encephalopathy characterized by loss of consciousness for 48–72 hours.

There is an increased risk of arrhythmias when prochlorperazine is concomitantly used with QT prolonging drugs (including certain antiarrhythmics, antidepressants and other antipsychotics) and drugs causing electrolyte imbalance.

There is an increased risk of agranulocytosis when prochlorperazine is used concurrently with drugs with myelosuppressive potential (carbamazepine or certain antibiotics and cytotoxics).

In patients treated concurrently with neuroleptics and lithium preparations, there have been rare reports of neurotoxicity.

Special warnings and precautions for use.

Prochlorperazine should be avoided in patients with liver or renal dysfunction, Parkinson's disease, hypothyroidism, cardiac failure, phaeochromocytoma, myasthenia gravis and prostate hypertrophy. Prochlorperazine should not be given to patients with known hypersensitivity to prochlorperazine, patients with a history of narrow angle glaucoma or agranulocytosis.

Close monitoring is required in patients with a history of epilepsy or seizures, as prochlorperazine may lower the seizure threshold.

Since agranulocytosis has been reported in association with prochlorperazine therapy, regular monitoring of complete blood count is recommended. Appearance of infection of unknown origin or fever in patient may indicate blood dyscrasia; therefore immediate haematological investigation is necessary.

It is imperative that prochlorperazine treatment be discontinued in the event of fever of unknown origin, as this may be a sign of neuroleptic malignant syndrome (pallor, hyperthermia, autonomic dysfunction, altered consciousness, muscle rigidity). Signs of autonomic dysfunction, such as hyperhidrosis and arterial blood pressure instability, may precede the onset of hyperthermia and serve as precursory symptoms of neuroleptic malignant syndrome. Although this syndrome may be idiosyncratic in origin, dehydration and organic brain disease are predisposing factors.
Since there is data on acute withdrawal symptoms (including nausea, vomiting and insomnia, extrapyramidal reactions) following the abrupt cessation of high doses of neuroleptics, gradual withdrawal of prochlorperazine is appropriate.
Prochlorperazine, as well as other neuroleptic phenothiazines, may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmia of the torsade de pointes type, which is potentially fatal (sudden death). The risk of QT prolongation is increased in the presence of bradycardia, hypokalaemia, and congenital or acquired (i.e. drug induced) QT prolongation. Therefore, the risk-benefit should be fully assessed before prochlorperazine is prescribed. Before prochlorperazine therapy and during the initial phase of treatment, and as deemed necessary during the treatment, it is recommended to perform appropriate clinical and laboratory investigations (e.g. biochemical status and ECG) to rule out possible risk factors (e.g. cardiac disease; family history of QT prolongation; metabolic abnormalities such as hypokalaemia, hypocalcaemia or hypomagnesaemia; anamnestic data on fasting, alcohol abuse; concomitant therapy with other drugs known to prolong the QT interval) (see also "Interaction with other medicinal products and other forms of interaction" and "Adverse reactions" sections).
Concomitant treatment with other neuroleptics should be avoided (see "Interaction with other medicinal products and other forms of interaction" section).
Stroke: in randomized clinical trials conducted in a group of elderly patients with dementia who received treatment with some atypical antipsychotics, there was a threefold increase in the risk of cerebrovascular events compared to patients receiving placebo. Since the mechanism of this risk is not known, it can not be excluded in the use of other antipsychotics or when used in other groups of patients. Prochlorperazine should be used with caution in patients with risk factors for stroke.
Like other antipsychotics, prochlorperazine should not be taken as monotherapy if the patient is dominated by depression. However, it can be added to antidepressant therapy to treat conditions when depression and psychosis are combined.
Because of the risk of photosensitisation, patients treated with prochlorperazine should avoid exposure to direct sunlight.
To prevent skin sensitization in people who often have contact with phenothiazine derivatives, they should avoid skin contact (see "Adverse reactions" section).
Elderly patients.
The drug should be used with caution in elderly patients, particularly during very hot or very cold weather due to the possible risk of hyper-, hypothermia. Besides, elderly patients are prone to postural hypotension. Also, patients in this age group have increased risk of drug-induced Parkinsonism, especially after prolonged use of prochlorperazine. Since elderly patients are more susceptible to the action of drugs that affect the CNS, they are advised to prescribe a lower daily dose of prochlorperazine, especially at the beginning of treatment.
Increased mortality in elderly patients with dementia.
There is data on the increased risk of mortality in elderly patients with dementia treated with antipsychotic drugs. Since there is not enough data to assess the magnitude and causes of this risk, prochlorperazine should not be prescribed for the treatment of dementia-related behavioral disorders.
Increased risk of venous thromboembolism (VTE).
VTE cases have been documented in the use of antipsychotic drugs. Since patients with antipsychotic drugs often have risk factors for developing VTE, they need to be identified with further appropriate preventive measures before and during prochloroperazine therapy.
Hyperglycaemia and intolerance to glucose.

Hyperglycemia or glucose intolerance have been reported in patients treated with antipsychotics from the phenothiazine group. Patients with diagnosed diabetes or individuals with risk factors for diabetes need adequate glycemic control before and during treatment with prochlorperazine.
Excipients.
The drug contains lactose. If you have intolerance to some sugars, consult your doctor before taking this medicine.

Pregnancy and lactation.
Pregnancy.
There is no adequate evidence of prochlorperazine safety during pregnancy in humans. Prochlorperazine should be avoided during pregnancy, unless the physician considers it vital. Since neuroleptics can prolong labor, at birth, this drug should be withheld until the cervix is dilated 3 to 4 cm. There is a risk of adverse effects of prochlorperazine on the neonate which may be manifested by low Apgar score, lethargy or, on the contrary, by paradoxical hyperexcitability and tremor.
Since neonates whose mothers used antipsychotics, including prochlorperazine, during the third trimester of pregnancy are at risk of serious adverse effects including extrapyramidal and/or withdrawal symptoms (agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder) such babies should be carefully monitored.
Lactation.
Since prochlorperazine can penetrate into breast milk, breastfeeding should be discontinued during treatment.

Effects on ability to drive and use machines.
Patients should be warned about drowsiness during the early days of treatment. It is not recommended to drive or operate machinery.

Posology and method of administration.
The drug is prescribed to adults. It should be used orally.
Prevention of nausea and vomiting.
1–2 tablets (5–10 mg) should be taken two or three times per day.
Treatment of nausea and vomiting.
4 tablets (20 mg) should be taken immediately after the onset of symptoms followed if necessary by 2 more tablets (10 mg) two hours later.
Vertigo.
1 tablet (5 mg) should be taken tree times per day. If necessary, the daily dose of drug may be increased to 6 tablets (30 mg). After several weeks the daily dose may be gradually reduced to 1–2 tablets (5–10 mg).
As an adjunct to the short-term management of anxiety.
1 tablet (5 mg) should be taken 3–4 times per day at the beginning of treatment. If necessary, the daily dose of drug may be increased to 8 tablets (40 mg) taken in divided doses 3–4 times per day.
Elderly patients.
Lower daily dosage of prochlorperazine is recommended for elderly patients.
Children.
There is no sufficient data on the use of prochlorperazine in children; therefore Vertinex® should not be given to this age group of patients.

Overdose.
Symptoms of overdose: drowsiness or loss of consciousness, arterial hypotension, tachycardia, ECG changes, ventricular arrhythmia, hypothermia, extrapyramidal dyskinesia.
Treatment.
First aid. If no more than 6 hours passed from the moment of taking the toxic dose of the medicinal product, gastric lavage should be performed. It is not recommended to cause vomiting with

medicines. Activated charcoal should be given. There is no specific antidote. Supportive and symptomatic treatment is recommended.
Arterial hypotension. In mild cases, lifting up the patient's upper extremities is a sufficient measure. In severe cases, infusion therapy may be necessary to correct the total volume of liquid. Pre-heated infusion solutions should be introduced (to prevent hypothermia). If fluid replacement is insufficient for correction of arterial hypotension, agents with positive isotropic effect may be used, such as dopamine.
Peripheral vasoconstrictor agents and adrenaline are not recommended.
Ventricular and supraventricular tachyarrhythmia. Usually restoration of normal body temperature, correction of total volume of circulating blood and/or metabolic disorders is an effective measure. If the above measures are ineffective or tachycardia is life-threatening, appropriate anti-arrhythmic therapy may be considered. Avoid lidocaine and long-acting anti-arrhythmic drugs.
CNS depression. Use of agents aimed at support of respiration is necessary, including artificial ventilation if required.
Dystonia. In severe cases, manifestations of dystonia may be improved with intravenous or intramuscular use of procyclidine (5–10 mg) or orphenadrine (20–40 mg).
Convulsive syndrome. Intravenous diazepam is necessary.
Malignant neuroleptic syndrome. It is necessary to use physical cooling methods. Dantrolene sodium may also be used.

Undesirable effects.
Immune system disorders: type I hypersensitivity reactions, including angioneurotic edema and urticaria.
Blood and lymphatic system disorders: leukopenia, agranulocytosis.
Endocrine system disorders: hyperprolactinaemia which may result in galactorrhea; gynaecomastia, amenorrhoea; impotence; glucose intolerance, hyperglycemia.
Metabolic disorders: syndrome of inappropriate antidiuretic hormone secretion, hyponatremia.
Nervous system disorders: acute dystonia or dyskinesia, including oculogyric crisis; akathisia; symptoms of Parkinsonism (tremor, rigidity, akinesia or others); tardive dyskinesia, insomnia, anxiety, convulsions.
Eye disorders: ocular changes.
Cardiac disorders: ECG changes (QT prolongation, ST depression, U-Wave and T-Wave changes), cardiac arrhythmia (ventricular arrhythmia and atrial arrhythmia, atrioventricular block, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest), sudden death.
Vascular disorders: hypotension, venous thromboembolism (including cases of pulmonary embolism), deep vein thrombosis.
Gastrointestinal disorders: dry mouth.
Respiratory disorders: respiratory depression, nasal stuffiness.
Hepatobiliary disorders: jaundice.
Skin and subcutaneous tissue disorders: metallic blue-purple coloration of the skin; skin rash; photosensitivity.
General disorders: malignant neuroleptic syndrome (hyperthermia, rigidity, autonomic dysfunction and altered consciousness).

Shelf life. 2 years.

Storage conditions.
Store below 25°C.
Keep out of reach of children.

Package.

10 tablets in a blister; 1 blister in a carton pack.
10 tablets in a blister; 1 blister in a carton pack; 10 carton packs in a carton box.

Conditions of supply. On prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of business activity.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

Date of last revision.