Lartil Injection 12.5mg/mL (1mL amp)

DESCRIPTION:
Lartil Injection 12.5mg/mL (1mL amp): Colourless or almost colourless solution.

COMPOSITION:
Each ml contains Prochlorperazine Mesylate 12.5mg.

PHARMACODYNAMICS:
Prochloperazine is a phenothiazine with a piperazine moiety in the side chain. It processes strong antiemetic and antipsychotic activity with less sedative action than chlorpromazine. As with other phenothiazines, prochloperazine has actions on several neurotransmitter systems:
1. Antidopamine action, which probably contributes to both the therapeutic effect and unwanted effects including extrapyramidal disorders and endocrine disturbances.
2. Alpha-adrenoceptors antagonism, which contributes to cardiovascular side effects such as orthostatic hypotension and reflex tachycardia.
3. Potentiation of noradrenaline by blocking its reuptake into nerve terminals.
4. Weak antiacetylcholinre action.
5. Weak antihistanminic action.
6. Weak serotonin antagonism.

Prochlorperazine also has an effect on temperature control and blocks conditioned avoidance responses.

PHARMACOKINETICS:
There are few published data on prochlorperazine pharmacokinetics in humans. Most studies have been done in rats and dose levels do not correspond to those used clinically and metabolic pathway may differ. Similar overall pharmacokinetic patterns however would occur in humans. Prochlorperazine is well absorbed from the gastrointestinal tract in rats but absorption is slowed in repeatedly treated animal. The drug is widely distributed to tissues including the brain, fat, kidney, heart and skin and is stored in reticuloendothelial tissues. Phenothiazines are metabolized primarily in the liver and are subject to enterohepatic circulation. Excretion is mainly in the faeces. Only a very small amount (approx. 0.1%) of prochlorperazine and its metabolites are excreted in the first 24 hours in the urine and the drug may continue to be excreted in the urine for up to 3 weeks after cessation of long term therapy. The elimination half-life is approximately 24 hours, presumably due to its enterohepatic circulation.

INDICATION:
Nausea and vomiting due to various causes including migraine; vertigo due to Meniere's syndrome, labyrinthitis and other causes; minor mental and emotional disturbances.

RECOMMENDED DOSAGE:
Usual Adult and Adolescent Dose:
Nausea and vomiting:
Intramuscular, 5 to 10mg (base), the dose being repeated every three to four hours if needed.
Nausea and vomiting in surgery:
Intramuscular, 5 to 10mg (base) one to two hours before induction of anesthesia, or to control acute symptoms during or after surgery, the dose being repeated once in thirty minutes if needed.
Intravenous, 5 to 10 mg (base), administered fifteen to thirty minutes before induction of anesthesia, or to control acute symptoms during or after surgery at a rate not to exceed 5mg per ml per minute, the dose being repeated once if needed.
Intravenous infusion, 20mg (base) in no less than 1 liter of isotonic solution, administered fifteen to thirty minutes before induction of anesthesia.
Psychotic disorders:
Initial (for immediate control of severely disturbed patients): Intramuscular, 10 to 20 mg (base) the dose being repeated every two to four hours as needed, usually up to three or four doses.
Maintenance: Intramuscular, 10 to 20mg (base) every four to six hours.
Anxiety:
Intramuscular, 5 to 10mg (base), the dose being repeated every three to four hours if needed.
Note: Geriatric, emaciated , or debilitated patients usually require a lower dose, the dosage being increased gradually as needed and tolerated.
Usual adult prescribing limits:
Nausea and vomiting – Up to 40 mg (base) a day.
Psychotic disorders – Up to 200mg (base) a day.
Usual pediatric dose:
Nausea and vomiting; or psychotic disorders or anxiety:
Children up to 2 years of age or 9kg of body weight: Dosage has not been established.
Children 2 to 12 years of age: Intramuscular, 132mcg (0.132mg) (base) per kg of body weight, not exceeding 10mg the first day, the dosage being increased, thereafter as needed and tolerated.
Children 12 years of age and over: see usual adult and adolescent dose.
Note: Usual pediatric prescribing limits are 20mg a day for children 2 to 5 years of age, and 25mg a day for children 6 to 12 years. Not recommended in pediatric surgery.
- The incidence extrapyramidal reactions associated with prochlorperazine is relatively high in children.
- Use of prochlorperazine should be avoided in children with suspected Reye's syndrome.

ROUTE OF ADMINISTRATION:
For deep i.m. & i.v. infusion

CONTRACINDICATIONS:
Circulatory collapse, central nervous system depression (coma or drug intoxication), previous history of a hypersensitivity reaction (eg. jaundice or blood dyscrasia) to phenothiazines especially to prochlorperazine, bone marrow depression).

WARNINGS & PRECAUTIONS:
WARNING

This preparation contains sulphite that may cause allergic type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible individuals. Sulphite sensitivity is seen more frequently in asthmatic patients.

Prochlorperazine should be avoided in patients with renal dysfunction, Parkinson's disease, hypothyroidism, phaeochromocytoma, myasthenia gravis, prostate hypertrophy
Hypotension: The autonomic side effects of the piperazine derivatives are less troublesome than those of other phenothiazines, however care should be taken if prochloperazine injection is used in the elderly or in patients undergoing surgery with spinal anaesthesia.
Epileptics: Piperazine derivatives are also less epileptogenic than other phenothiazines, but care should still be exercised in epileptic patients.
Anticholinergic effects: Prochlorperazine can cause problems due to anticholinergic effects, especially in the elderly (urinary difficulties, constipation and precipitation of acute narrow angle glaucoma), but to a lesser extent than with other phenothiazines.
Hypocalcaemia: It appears from a study of 5 hypocalcaemic patients with hypoparathyroidism that such patients are particularly prone to acute severe dystonic reactions with prochlorperazine.
Sedative effect: Prochlorperazine may impair mental and physical activity especially during the first few days of therapy. Patients should be warned about activities requiring alertness.
Antiemetic effects: The antiemetic effects of prochloperazine may mask signs of overdosage of toxic drugs or obscure the diagnosis of conditions such as intestinal obstruction and brain tumour.
Hypothermia: Severe hypothermia may occur during swimming in cold water or in patients receiving antipyretic therapy.
Liver disease: caution should be used in patients with existing liver disease due to the extensive hepatic metabolism of prochlorperazine. A past history of jaundice resulting from phenothiazine therapy indicates a hypersensitivity reaction and there is a likelihood of cross sensitivity to other phenothiazines.
Tardive dyskinesia: Tardive dyskinesia may develop in patients on antipsychotic drugs. The disorder consist repetitive involuntary movements of the tongue, face, mouth or jaw (eg. protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). The trunk and limbs are less frequently involved. It has been reported that form vermicular movement of the tongue may be an early sign of the syndrome. Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of the drug increases. Less commonly, the syndrome can develop after relatively brief treatment periods at low doses. The risk seems to greater in elderly patients, especially females. The syndrome may become clinically recognizable either drug treatment, or upon dosage reduction, or upon withdrawal of treatment. The dosage of antipsychotic drug should be reduced periodically (if clinically possible) and the patient observed for the sign of the disorder, since the syndrome may be masked by a higher dose.
In patients requiring long-term treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. There is no known effective treatment for tardive dyskinesia. Antiparkinson agents usually do not alleviate the symptoms of this syndrome, if these symptoms appear, it is suggested that the antipsychotic be discontinued if symptoms of tardive dyskinesia appear.

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Neuroleptic Malignant Syndrome: A potentially fatal syndrome called neuroleptic malignant syndrome has been reported in association with antipsychotic drugs. The syndrome is characterized by muscular rigidity, fever, hyperthermia, altered consciousness and automatic instability (eg. tachycardia, labile blood pressure, profuse sweating, dyspnoea). The management of neuroleptic malignant syndrome should include immediate discontinuation of antipsychotic drugs, intensive monitoring and treatment of symptoms and treatment of any associated problems.
Use in children: Prochlorperazine injection is not recommended for use in children under 10kg in weight or under 2 years of age as acute extrapyramidal reactions are more likely to occur.

INTERACTION WITH OTHER MEDICAMENTS:

Prochloperazine may enhance the CNS depressant effects of alcohol and other depressant drugs, and potentiate the anticholinergic effects of atropinic agents and tricyclic antidepressants. Simultaneous administration of desferrioxamine and prochlorperazine has been observed to induce a transient metabolic encephalopathy characterised by loss of conciousness for 48 – 72 hours. Procarbazine has been reported to potentiate the extrapyramidal side effects encountered with the use of prochloperazine. Phenothiazines have been reported both to impair and increase metabolism of phenytoin with uncertain clinical significance. Patients on levodopa should not be given phenothiazines because the two drugs are physiologically antagonistic.
Phenothiazines can diminish the effect of oral anticoagulants.
Thiazide diuretics may accentuate the orthostatic hypotension that may occur with phenothiazines.
Antihypertensive effects of guanethidine and related compounds may be counteracted when phenothiazines are used concomitantly.
Concomitant administration of propranolol with phenothiazines results in increased plasma levels of both drugs.
Phenothiazines may lower the convulsive threshold; dosage adjustments of anticonvulsants may be necessary.

USE IN PREGNANCY & LACTATION:

Use in pregnancy:
When given in high doses during late pregnancy, phenothiazines have caused extrapyramidal disturbances in the child. There is inadequate evidence of safety of prochlorperazine injection in human pregnancy but it has been widely use for many years without apparent ill consequences. There is evidence of harmful effects in animals. Like other drug it should be avoided in pregnancy unless the physician considers it essential. Neuroleptics may occasionally prolong labour and at such a time should be withheld until the cervix is dilated 3 to 4cm. Possible adverse effects on the foetus include lethargy or paradoxical hyperexcitability, tremor and low Apgar score.
Use in lactation:
Trace amounts of another phenothiazine, chlorpromazine, have been detected in breast milk, but there is no information available for prochlorperazine. Consequently, it is not known whether it is excreted in breast milk, nor whether it has a harmful effect on the newborn. Therefore, prochlorperazine injection is not recommended for nursing mothers unless the expected benefits outweigh any potential risk.

SIDE EFFECTS:

The following reactions have been reported for prochloperazine or phenothiazines in general.
More common reactions:
Gastrointestinal: constipation, dry mouth.
Nervous System: Drowsiness, akathisia, parkinsonism (with dyskinesia, tremor and rigidity).
Ocular: Blurred vision.
Less common reaction:
Biochemical abnormalities: elevated serum level of bilirubin and hepatic enzymes may occur if the patient develops cholestatic jaundice.
Cardiovascular: hypotension, peripheral oedema, cardiac arrhytmias, ECG changes.
Dermatological: dermatitis, maculopopular eruption, erythema, multiform, urticaria, photosensitivity, abnormal pigmentation.
Gastrointestinal: paralytic ileus.
Genito-urinary: urinary retention, inhibition of ejaculation.
Haematological: agranulocytosis, atypical lymphocytes, thrombocytopenia, leucopenia, aplastic anaemia.
Hepatic: cholestatic jaundice, liver damage.
Nervous System: acute dystonic reactions, seizures, EEG changes, headache, insomnia, catatonia.
Psychiatric: Activation of psychotic symptoms.
Serious or life threatening reactions:
Prochloperazine can cause very serious acute dystonic reactions in children leading cyanosis from laryngospasm, apnoea requiring artificial ventilation, life threatening tetanus like syndromes, coma and even death. These reaction can occur with a single therapeutic dose. For treatment, see Overdosage. Also, long term phenothiazine therapy has been associated with ECG changes and life threatening cardiac arrhythmias.

SYMPTOMS AND TREATMENT OF OVERDOSE:

Symptoms:
Overdosage with phenothiazines may cause CNS depression progressing from drowsiness to coma with areflexia. Patients with early or mild intoxication may experience restlessness, confusion and excitement. Other symptoms include hypotension, tachycardia convulsions, hypothermia, pupillary constriction, restlessness, tremor, muscle twitching, spasm or rigidity, convulsions, muscular hypotonia, difficulty in swallowing or breathing, cyanosis, and respiratory and / or vasomotor collapse, possible with sudden apnoea. There is no information available regarding lethal dose in man.
Treatment:
Acute dystonic reactions. Intramuscular benztropine (or another antiparkisonian agent) should be given immediately (adults: 1 to 2mg IM; children 0.2 to 0.25mg IM initially with increments, if necessary).
Overdosage:
Emesis should not be induced, not only because the antiemetic action of prochlorperazine prevents the effect of the emetic agent, but also because the sedative and extrapyramidal side effects increase the risk of pulmonary aspiration should vomiting occur. Gastric lavage may be useful even several hours after the drug has been ingested since prochlorperazine reduces gastric motility. Management is generally supportive with particular attention to the possibility of obstructed ventilation, severe hypotension, hypothermia, cardiac arrhythmias, convulsions and prolonged deep sedation. Acute dystonic reactions usually occur early (if at all): treatment is with anticholinergic agents as above.

INCOMPATIBILITIES:

An immediate precipitate was reported to have occurred when prochlorperazine mesylate 100mg per litre was mixed with aminophylline 1g per litre or with ampicillin sodium 2g per litre in glucose injection and sodium chloride injection, or with ethamivan 2g per litre in sodium chloride injection. An immediate precipitate also occurred with phenobarbitone sodium 800mg per litre, sulphadiazine sodium 4g per litre, or sulphadimide sodium 4g per litre in sodium chloride injection, but when they were mixed in glucose injection, a haze developed over 3 hours. A haze developed over 3 hours when prochlorperazine mesylate was mixed with amphotericin 200mg per litre or methohexitone sodium 2g per litre in glucose injection, or with benzylpenicillin 6g per litre, chloramphenicol 4g per litre, or chlorothiazide 2g per litre in sodium chloride injection.
Loss of clarity was reported to have occurred when solutions of prochlorperazine were mixed with those of calcium gluconate, chlorothiazide sodium, heparin, hydrocortisone sodium succinate, nitrofurantoin sodium, pentobarbitone sodium, and thiopentone sodium.

STORAGE CONDITIONS:

Store below 30°C. Protect from light. KEEP OUT OF REACH OF CHILDREN. JAUHKAN DARIPADA KANAK-KANAK.

Special Precautions for Storage:
1. Keep ampoules in unit carton until use.
2. Use immediately after solution syringed out from ampoule. Discard remaining unused portion.
3. Discard product if solution turns to yellow or darker.

SHELF LIFE:

Please refer to outer package.

PACK SIZE:

Packs of 10 x 1ml, 30 x 1ml, 50 x 1ml and 100 x 1ml ampoules per box.

PRODUCT REGISTRATION HOLDER & MANUFACTURER:

DUOPHARMA (M) SDN BHD
Lot 2599, Jalan Seruling 59 Kawasan 3,
Taman Klang Jaya, 41200 Klang, Selangor, MALAYSIA.

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