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| Brand Name : PROMETHAZINE HYDROCHLORIDE TABLETS | |
| Generic Name : Promethazine Hydrochloride Tablets BP 25 mg | 2021 |
| Module 1 | Administrative Information and Product Information |
| 1.5 | Product Information Confidential |

1.5 PRODUCT INFORMATION

1.5.1 Prescribing information (Summary of products characteristics)

SUMMARY PRODUCT CHARACTERISTICS

1. Name of drug product:
PROMETHAZINE HYDROCHLORIDE TABLETS (Promethazine Hydrochloride Tablets BP 25 mg)

2. Qualitative and Quantitative Composition:

Each Sugar Coated Tablets contains: Promethazine Hydrochloride Tablets BP 25 mg

3. Pharmaceutical form:

White Circular, Sugar Coated tablets.

4. Clinical particulars:

4.1 Therapeutic indications

Promethazine is a phenothiazine derivative which differs structurally from the antipsychotic phenothiazines by the presence of a branched side chain and no ring substitution. It is thought that this configuration is responsible for its relative lack (1/10 that of chlorpromazine) of dopamine antagonist properties.

Promethazine is an H1 receptor blocking agent. In addition to its antihistaminic action, it provides clinically useful sedative and antiemetic effects.

Promethazine is well absorbed from the gastrointestinal tract. Clinical effects are apparent within 20 minutes after oral administration and generally last four to six hours, although they may persist as long as 12 hours. Promethazine is metabolized by the liver to a variety of compounds; the sulfoxides of promethazine and N-demethylpromethazine are the predominant metabolites appearing in the urine.



AGOG Pharma Ltd.



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4.2 Posology and method of administration

Promethazine Hydrochloride, is useful orally for.

Perennial and seasonal allergic rhinitis.

Vasomotor rhinitis.

Allergic conjunctivitis due to inhalant allergens and foods.

Mild, uncomplicated allergic skin manifestations of urticaria and angioedema.

Amelioration of allergic reactions to blood or plasma.

Dermographism.

Anaphylactic reactions, as adjunctive therapy to epinephrine and other standard measures, after the acute manifestations have been controlled.

Preoperative, postoperative, or obstetric sedation.

Prevention and control of nausea and vomiting associated with certain types of anesthesia and surgery.

Therapy adjunctive to meperidine or other analgesics for control of post-operative pain.

Sedation in both children and adults, as well as relief of apprehension and production of light sleep from which the patient can be easily aroused.

Active and prophylactic treatment of motion sickness.

Antiemetic therapy in postoperative patients.

4.3 Contraindications

Promethazine hydrochloride tablets, USP are contraindicated for use in pediatric patients less than two years of age.

Promethazine hydrochloride tablets, USP are contraindicated in comatose states, and in individuals known to be hypersensitive or to have had an idiosyncratic reaction to promethazine or to other phenothiazines.

Antihistamines are contraindicated for use in the treatment of lower respiratory tract symptoms including asthma.

4.4 Dosage and Administration

Allergy

The average oral dose is 25 mg taken before retiring; however, 12.5 mg may be taken before meals and on retiring, if necessary. Single 25-mg doses at bedtime or 6.25 to 12.5 mg taken three times daily will usually suffice. After initiation of treatment in children or adults, dosage should be adjusted to the smallest amount adequate to relieve symptoms. The administration of promethazine hydrochloride in 25-mg doses will control minor transfusion reactions of an allergic nature.



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Motion Sickness

The average adult dose is 25 mg taken twice daily. The initial dose should be taken one-half to one hour before anticipated travel and be repeated 8 to 12 hours later, if necessary. On succeeding days of travel, it is recommended that 25 mg be given on arising and again before the evening meal. For children, promethazine hydrochloride tablets, USP, 12.5 to 25 mg, twice daily, may be administered.

Nausea and Vomiting

Antiemetics should not be used in vomiting of unknown etiology in children and adolescents (see [WARNINGS-Use in Pediatric Patients](#)).

The average effective dose of promethazine hydrochloride for the active therapy of nausea and vomiting in children or adults is 25 mg. When oral medication cannot be tolerated, the dose should be given parenterally (cf. Promethazine hydrochloride Injection). 12.5- to 25-mg doses may be repeated, as necessary, at 4- to 6-hour intervals.

For nausea and vomiting in children, the usual dose is 0.5 mg per pound of body weight, and the dose should be adjusted to the age and weight of the patient and the severity of the condition being treated.

For prophylaxis of nausea and vomiting, as during surgery and the postoperative period, the average dose is 25 mg repeated at 4- to 6-hour intervals, as necessary.

Sedation

This product relieves apprehension and induces a quiet sleep from which the patient can be easily aroused. Administration of 12.5 to 25 mg promethazine hydrochloride by the oral route or by rectal suppository at bedtime will provide sedation in children. Adults usually require 25 to 50 mg for nighttime, presurgical, or obstetrical sedation.

Pre- and Postoperative Use

Promethazine hydrochloride in 12.5- to 25-mg doses for children and 50-mg doses for adults the night before surgery relieves apprehension and produces a quiet sleep.

For preoperative medication, children require doses of 0.5 mg per pound of body weight in combination with an appropriately reduced dose of narcotic or barbiturate and the appropriate dose of an atropine-like drug. Usual adult dosage is 50 mg promethazine hydrochloride with an appropriately reduced dose of narcotic or barbiturate and the required amount of a belladonna alkaloid.

Postoperative sedation and adjunctive use with analgesics may be obtained by the administration of 12.5 to 25 mg in children and 25- to 50-mg doses in adults.

Promethazine hydrochloride tablets, USP are contraindicated for children under 2 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

CNS Depressants - Promethazine hydrochloride tablets, USP may increase, prolong, or intensify the sedative action of other central-nervous-system depressants, such as alcohol, sedatives/hypnotics (including barbiturates), narcotics, narcotic analgesics, general



anesthetics, tricyclic antidepressants, and tranquilizers; therefore, such agents should be avoided or administered in reduced dosage to patients receiving promethazine hydrochloride. When given concomitantly with promethazine hydrochloride tablets, USP the dose of barbiturates should be reduced by at least one-half, and the dose of narcotics should be reduced by one-quarter to one-half. Dosage must be individualized. Excessive amounts of promethazine hydrochloride relative to a narcotic may lead to restlessness and motor hyperactivity in the patient with pain; these symptoms usually disappear with adequate control of the pain.

Epinephrine - Because of the potential for promethazine hydrochloride to reverse epinephrine's vasopressor effect, epinephrine should NOT be used to treat hypotension associated with promethazine hydrochloride tablets, USP overdose.

Anticholinergics - Concomitant use of other agents with anticholinergic properties should be undertaken with caution.

Monoamine Oxidase Inhibitors (MAOI) - Drug interactions, including an increased incidence of extrapyramidal effects, have been reported when some MAOI and phenothiazines are used concomitantly. This possibility should be considered with promethazine hydrochloride tablets, USP.

Drug/Laboratory Test Interactions

The following laboratory tests may be affected in patients who are receiving therapy with promethazine hydrochloride:

Pregnancy Tests

Diagnostic pregnancy tests based on immunological reactions between HCG and anti-HCG may result in false-negative or false-positive interpretations.

Glucose Tolerance Test

An increase in blood glucose has been reported in patients receiving promethazine hydrochloride.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to assess the carcinogenic potential of promethazine, nor are there other animal or human data concerning carcinogenicity, mutagenicity, or impairment of fertility with this drug. Promethazine was nonmutagenic in the *Salmonella* test system of Ames.

4.6 Fertility, pregnancy and lactation

Pregnancy

Teratogenic Effects - Pregnancy Category C

Teratogenic effects have not been demonstrated in rat-feeding studies at doses of 6.25 and 12.5 mg/kg of promethazine hydrochloride. These doses are from approximately 2.1 to 4.2 times the maximum recommended total daily dose of promethazine for a 50-kg subject,



depending upon the indication for which the drug is prescribed. Daily doses of 25 mg/kg intraperitoneally have been found to produce fetal mortality in rats.

Specific studies to test the action of the drug on parturition, lactation, and development of the animal neonate were not done, but a general preliminary study in rats indicated no effect on these parameters. Although antihistamines have been found to produce fetal mortality in rodents, the pharmacological effects of histamine in the rodent do not parallel those in man. There are no adequate and well-controlled studies of promethazine hydrochloride tablets, USP in pregnant women.

Promethazine hydrochloride tablets, USP should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects-

Promethazine hydrochloride tablets, USP administered to a pregnant woman within two weeks of delivery may inhibit platelet aggregation in the newborn.

Labor and Delivery

Promethazine hydrochloride may be used alone or as an adjunct to narcotic analgesics during labor (**DOSAGE AND ADMINISTRATION**). Limited data suggest that use of promethazine hydrochloride during labor and delivery does not have an appreciable effect on the duration of labor or delivery and does not increase the risk of need for intervention in the newborn. The effect on later growth and development of the newborn is unknown (see also **Nonteratogenic Effects**).

Nursing Mothers

It is not known whether promethazine hydrochloride is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from promethazine hydrochloride tablets, USP a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Because the duration of action may be up to 12 hours, patients should be advised that if they feel drowsy they should not drive or operate heavy machinery.

4.8 Undesirable effects

The following CIOMS frequency rating is used: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1000$ to $< 1/100$); rare ($\geq 1/10000$ to $< 1/1000$); very rare ($< 1/10000$), not known (cannot be estimated from the available data).

Side effects may be seen in a few patients: drowsiness, dizziness, restlessness, headaches, nightmares, tiredness, and disorientation. Anticholinergic side effects such as blurred vision, dry mouth and urinary retention occur occasionally. Infants are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability. The elderly are particularly susceptible to the anticholinergic effects and



confusion due to promethazine. Other side-effects include urticaria, rash, pruritus, anorexia, gastric irritation, palpitations, hypotension, arrhythmias, extrapyramidal effects, restless legs syndrome, muscle spasms and tic-like movements of the head and face. Anaphylaxis, jaundice and blood dyscrasias including haemolytic anaemia rarely occur. Photosensitive skin reactions have been reported. Strong sunlight should be avoided during treatment.

4.9 Overdose

Signs and symptoms of overdosage with promethazine hydrochloride range from mild depression of the central nervous system and cardiovascular system to profound hypotension, respiratory depression, unconsciousness, and sudden death. Other reported reactions include hyperreflexia, hypertonia, ataxia, athetosis, and extensor-plantar reflexes (Babinski reflex).

Stimulation may be evident, especially in children and geriatric patients. Convulsions may rarely occur. A paradoxical-type reaction has been reported in children receiving single doses of 75 mg to 125 mg orally, characterized by hyperexcitability and nightmares.

Atropine-like signs and symptoms-dry mouth, fixed, dilated pupils, flushing, as well as gastrointestinal symptoms-may occur.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Antihistamines for systemic use; Phenothiazine derivatives, ATC code: R06AD02

Potent, long acting, antihistamine with additional anti-emetic central sedative and anti-cholinergic properties.

5.2 Pharmacokinetic properties

Promethazine is distributed widely in the body. It enters the brain and crosses the placenta. Promethazine is slowly excreted via urine and bile. Phenothiazines pass into the milk at low concentrations.

5.3 Preclinical safety data

No additional preclinical data of relevance to the prescriber.

6. Pharmaceutical particulars:

6.1 List of Excipients:

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|------------------------------------|----|
| Di Basic Calcium Phosphate | BP |
| Lactose | BP |
| Micro Crystalline Cellulose Powder | BP |
| Maize Starch | BP |
| Methyl Paraben Sodium | BP |
| Propyl Paraben Sodium | BP |
| Sodium Metabisulphite | BP |
| Talcum | BP |
| Magnesium Stearate | BP |



| | |
|-----------------------------|-----|
| Sodium Starch Glycolate | BP |
| Calcium Carbonate | BP |
| Sucrose | BP |
| Gelatin | BP |
| Gum Accacia | BP |
| Titanium Dioxide | BP |
| Colour Brilliant Blue Supra | INH |
| Carnauba Wax | BP |
| Bees Wax | BP |
| Carbon Tetra Chloride | INH |

6.2 Incompatibilities:

None Reported

6.3 Shelf-Life:

36 months from the date of manufacture.

6.4 Special Precautions for Storage:

Store under normal storage conditions (15°C-30°C) Protect from light.

6.5 Nature and Contents of Container:

10 tablets packed in one Blister. 10 Blister packed in unit of carton along with its package insert. Such carton packed in export worthy shipper.

6.6 Special precautions for disposal:

None reported.

7. Registrant:

AGOG PHARMA LTD.

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9. Date of revision of the text :