**GRAVINATE**
(Dimenhydrinate B.P I. V/I.M)

**COMPOSITION**

Each ampoule of 1 ml contains: Dimenhydrinate BP 50mg

**THERAPEUTIC INDICATIONS**

Dimenhydrinate Injection, USP is indicated for the prevention and treatment of nausea, vomiting, or vertigo of motion sickness

**DOSAGE AND ADMINISTRATION**

Dimenhydrinate in the injectable form is indicated when the oral form is impractical.

**Adults**

Nausea or vomiting may be expected to be controlled for approximately 4 hours with 50 mg, and prevented by a similar dose every 4 hours. Its administration may be attended by some degree of drowsiness in some patients, and 100 mg every 4 hours may be given in conditions in which drowsiness is not objectionable or is even desirable.
For intramuscular administration, each milliliter (50 mg) of solution is injected as needed, but for intravenous administration, each milliliter (50 mg) of solution must be diluted in 10 mL of 0.9% Sodium Chloride Injection, USP and injected over a period of 2 minutes.

**Pediatric**

For intramuscular administration, 1.25 mg/kg of body weight or 37.5 mg/m 2 of body surface area is administered four times daily. The maximum dose should not exceed 300 mg daily.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit

**CONTRAINDICATIONS**

Neonates and patients with a history of hypersensitivity to dimenhydrinate or its components (diphenhydramine or 8-chlorotheophylline) should not be treated with dimenhydrinate.

**SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

**WARNINGS**

Caution should be used when dimenhydrinate is given in conjunction with certain antibiotics that may cause ototoxicity, since dimenhydrinate is capable of masking ototoxic symptoms, and an irreversible state may be reached.

This drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery. The concomitant use of alcohol or other central nervous system depressants may have an additive effect. Therefore, patients should be warned accordingly.

Dimenhydrinate should be used with caution in patients having conditions which might be aggravated by anticholinergic therapy (i.e., prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction, bladder neck obstruction, narrow-angle glaucoma, bronchial asthma, or cardiac arrhythmias).

The preparation should not be injected intra-arterially.

**Pediatric Patients**

For infants and children especially, antihistamines in overdosage may cause hallucinations, convulsions, or death.

As in adults, antihistamines may diminish mental alertness in pediatric patients. In the young child, particularly, they may produce excitation.

**PRECAUTIONS**

**General**

Drowsiness may be experienced by some patients, especially with high dosage. This effect frequently is not undesirable in conditions for which the drug is used.

**EFFECTS ON ABILITY TO DRIVE**

Because of the potential for drowsiness, patients taking dimenhydrinate should be cautioned against operating automobiles or dangerous machinery

**FERTILITY, PREGNANCY AND LACTATION**

**Pregnancy**

*Pregnancy Category B.*

Reproduction studies have been performed in rats at doses up to 20 times the human dose, and in rabbits at doses up to 25 times the human dose (on a mg/kg basis), and have revealed no evidence of impaired fertility or harm to the fetus due to dimenhydrinate. There are no adequate and well-controlled studies in pregnant women. However, clinical studies in pregnant women have not indicated that dimenhydrinate increases the risk of abnormalities when administered in any trimester of pregnancy. It would appear that the possibility of fetal harm is remote when the drug is used during pregnancy. Nevertheless, because the studies in humans cannot rule out the possibility of harm, dimenhydrinate should be used during pregnancy only if clearly needed.

**Labor and Delivery**

The safety of dimenhydrinate given during labor and delivery has not been established. Reports have indicated dimenhydrinate may have an oxytocic effect. Caution is advised when this effect is unwanted or in situations where it may prove detrimental.

**Nursing Mothers**

Small amounts of dimenhydrinate are excreted in breast milk. Because of the potential for adverse reactions in nursing infants from dimenhydrinate, 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.

**ADVERSE DRUG REACTIONS**

The most frequent adverse reaction to dimenhydrinate is drowsiness. Dizziness may also occur. Symptoms of dry mouth, nose and throat, blurred vision, difficult or painful urination, headache, anorexia, nervousness, restlessness or insomnia (especially in pediatric patients), skin rash, thickening of bronchial secretions, tachycardia, epigastric distress, lassitude, excitation, and nausea have been reported.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at pv@searlecompany.com

**OVERDOSE**

Drowsiness is the usual clinical side effect. Convulsions, coma, and respiratory depression may occur with massive overdosage. No specific antidote is known. If respiratory depression occurs, mechanically assisted respiration should be initiated and oxygen should be administered. Convulsions should be treated with appropriate doses of diazepam. Phenobarbital (5 to 6 mg/kg) may be given to control convulsions in pediatric patients.

The oral LD 50 in mice and rats is 203 mg/kg and 1320 mg/kg, respectively. The intraperitoneal LD 50 in mice is 149 mg/kg.

**PHARMACOLOGICAL PROPERTIES**

**Pharmacodynamic properties**

Dimenhydrinate is a theoclate salt of the ethanolamine derivative diphenhydramine. The content ratio varies from 53% - 55.5% for diphenhydramine, and 44% - 47% for 8- chlorotheophylline. The mechanism by which dimenhydrinate exerts its antiemetic, anti-motion sickness, and antivertigo effects is not precisely known, but may possibly be related to its central anticholinergic action. Other actions may involve an effect on the medullary chemoreceptor trigger zone or dose-related inhibition of vestibular stimulation (i.e., first acting on the otolith system and in larger doses on the semicircular canals).

**Pharmacokinetic properties**

Dimenhydrinate is well absorbed after oral administration. Antiemetic effects occur almost immediately after IV administration, within 20-30 minutes after IM administration and 15-30 minutes after oral administration.

Serum concentrations (ng/mL) 1 and 2 hours after administration of a 50 mg dimenhydrinate tablet were: 3.65 and 3.15. While not directly applicable to dimenhydrinate, it is suggested that when plasma concentration of diphenhydramine exceeds 70 ng/mL, sleep may occur. Dimenhydrinate, like diphenhydramine, is widely distributed into body tissues, and crosses the placenta. Small amounts of dimenhydrinate are distributed into milk. After oral administration of 4x50 mg dimenhydrinate tablets, a distribution volume of 3-4 L/kg, and protein binding of 70- 85% for dimenhydrinate and 98-99% for diphenhydramine were reported. The duration of effect and therapeutic plasma level were respectively 4-6 hours and 0.1µg/mL. The plasma elimination half-life was 5-8 hours. Dimenhydrinate is metabolized by the liver, and excreted in urine. There are three known metabolites: diphenyl-methoxy-ethylamine, diphenyl-methoxy-acetic acid, and diphenylmethoxy-N-methylamine

**PRECLINICAL SAFETY DATA**

Mutagenicity screening tests performed with dimenhydrinate, diphenhydramine, and 8-chlorotheophylline produced positive results in the bacterial systems and negative results in the mammalian systems. There are no human data that indicate dimenhydrinate is a carcinogen or mutagen or that it impairs fertility.

**PRESENTATION**

Ampoules Box of 25 ampoules

**STORAGE INSTRUCTIONS**

To be sold on prescription of a registered medical practitioner only

Protect from moisture, freezing, Excessive heat and sunlight

Keep out of the reach of children

**REGISTRATION NUMBER**

014408

Mfg. USP Specs.

**MANUFACTURED BY.**
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**DATE OF PUBLICATION**

**June 2021**

**SPL/SPC-GRA.I/621-000(001)**