PRODUCT MONOGRAPH

DIMENHYDRINATE INJECTION USP

Dimenhydrinate

Solution for IM administration or IV administration if diluted

50 mg/mL

Antiemetic

Hikma Canada Limited
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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Product	Route of Administration	Dosage Form / Strength	Non-medicinal Ingredients
Dimenhydrinate Injection USP	Intramuscular injection (or IV administration if diluted)	Sterile solution / 50 mg/mL 1 mL single use ampoules	50% propylene glycol, water for injection, and hydrochloric acid for pH adjustment
Dimenhydrinate Injection USP	Intramuscular injection (or IV administration if diluted)	Sterile solution / 50 mg/mL (250 mg/5 mL) 5 mL multidose vials	50% propylene glycol, water for injection, hydrochloric acid for pH adjustment, and methylparaben (as sodium methylparaben) and propylparaben (as sodium propylparaben) as preservatives

INDICATIONS AND CLINICAL USE

Dimenhydrinate Injection USP is indicated for use in the prevention and relief of nausea, vomiting and/or vertigo. These symptoms may be associated with clinical situations such as motion sickness, radiation sickness, postoperative recovery, drug-induced nausea and vomiting, Menière's disease and other labyrinthine disturbances. Parenteral therapy is available when oral or rectal therapy is inappropriate.

Geriatrics (over 65 years of age)
See **WARNINGS AND PRECAUTIONS —*Special Populations*, Geriatrics**.

Pediatrics (under 2 years of age)
The safety and efficacy of Dimenhydrinate Injection USP in children under the age of 2 have not been established. Dimenhydrinate Injection USP should not be used in this population (see **CONTRAINDICATIONS** and **WARNINGS AND PRECAUTIONS —*Special Populations*, Pediatrics)**.

CONTRAINDICATIONS

- Patients who are hypersensitive to dimenhydrinate or its components (diphenhydramine or 8- chlorotheophylline) or to any ingredient in the formulations or component of the container. For a complete listing, see **DOSAGE FORMS, COMPOSITION AND PACKAGING**
- During or within two weeks following therapy with a monoamine oxidase inhibitor (see **DRUG INTERACTIONS, Drugs with Anticholinergic Effects**)
- Patients with glaucoma (narrow angle)
- Patients with chronic lung disease
- Patients with prostatic hypertrophy
- Patients under 2 years of age.

WARNINGS AND PRECAUTIONS

General

Dimenhydrinate Injection USP contains 50% (v/v) propylene glycol and is for intramuscular injection only. In exceptional circumstances, if the product is required for intravenous use, it must be diluted at least 1:10 with a compatible physiological solution such as sterile saline or 5% dextrose in water, to prevent propylene glycol-associated cardiogenic shock (see **DOSAGE AND ADMINISTRATION, Dosing Considerations**).

Dimenhydrinate Injection USP in 5 mL multidose vials contains the preservatives methylparaben and propylparaben. They are known to be associated with hypersensitivity in single or repeated uses.

The anticholinergic effects of the drug should be considered when administering dimenhydrinate to patients with conditions that might be aggravated by anticholinergic therapy (e.g. angle-closure glaucoma, enlargement of the prostate gland). These patients should be closely monitored during therapy with dimenhydrinate.

Avoid using dimenhydrinate within 14 days of MAO inhibitor use as this combination may prolong and intensify anti-cholinergic effects.

DIMENHYDRINATE INJECTION USP IS NOT INTENDED FOR PROLONGED USE EXCEPT ON THE ADVICE OF A PHYSICIAN.

Dimenhydrinate may impair the ability to perform hazardous activities requiring mental alertness or physical coordination such as operating machinery or driving a car. Patients receiving dimenhydrinate should be cautioned against operating automobiles or dangerous machinery because of the drowsiness associated with the drug. If drowsiness is excessive, dosage should be reduced.

The concomitant use of alcohol or other central nervous system depressants may have an additive effect and should be avoided.

Abuse/Dependence/Tolerance
Dimenhydrinate has substance abuse potential due to its hallucinogenic and euphoric effects. At higher doses, confusion, hallucinations, temporary amnesia and paranoia may occur. Chronic abuse of antihistamines can lead to drug interaction accidents, overdose, and in extreme cases to death (see **OVERDOSAGE**). Tolerance and psychological dependency may develop, which may lead to overdose and in some cases, even death (see **OVERDOSAGE**). Withdrawal symptoms may include lethargy, agitation, hostility, clumsiness, nausea, vomiting, hallucinations, confusion and aggression.

Carcinogenesis and Mutagenesis
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.

Cardiovascular
Use with caution in patients with cardiac arrhythmias or cardiovascular disease (including hypertension and ischemic heart disease).

Ear/Nose/Throat
Dimenhydrinate may mask the presence of underlying organic abnormalities or the toxic effects of certain antibiotics and other drugs, particularly those drugs causing ototoxicity.

Endocrine and Metabolism
Use with caution in patients who are poor CYP2D6 metabolizers and in patients with thyroid dysfunction.

Gastrointestinal
Use with caution in patients with pyloroduodenal obstruction (including stenotic peptic ulcer).

Genitourinary
Dimenhydrinate Injection USP is contraindicated in patients with prostatic hyperplasia (see **CONTRAINDICATIONS**). Use with caution in patients with other genitourinary obstruction.

Hematologic
Rarely, prolonged therapy with antihistaminic drugs can produce blood dyscrasia. Use with caution in patients with porphyria.

Hepatic/Biliary/Pancreatic
Use with caution in patients with hepatic impairment.

Neurologic
Dimenhydrinate should be used with caution in patients with seizure disorders.

Ophthalmologic
Dimenhydrinate is contraindicated in patients with increased intraocular pressure or narrow angle glaucoma (see **CONTRAINDICATIONS**).

Psychiatric
Dimenhydrinate may cause euphoria, hallucinations, confusion and paranoia at higher doses (see **WARNINGS AND PRECAUTIONS; Abuse/Dependence/Tolerance)**

Respiratory
Dimenhydrinate Injection USP is contraindicated in patients with chronic lung disease such as chronic obstructive pulmonary disease (see **CONTRAINDICATIONS**). Use with caution in patients with a history of asthma or lower respiratory tract symptoms.

Skin
In rare cases, serious skin reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiform have been associated with the use of dimenhydrinate. Because the rate of these reactions is low, they have usually been noted during post-marketing surveillance in patients taking other medications also associated with the potential development of these serious skin reactions. Thus, causality is NOT clear. These reactions are potentially life threatening but may be reversible if the causative agent is discontinued and appropriate treatment instituted. Patients should be advised that if they experience a skin rash they should discontinue dimenhydrinate and contact their physician for assessment and advice, including which additional therapies to discontinue.

Special Populations
Pregnant Women: The use of dimenhydrinate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential hazards. There are no adequate and well-controlled studies with dimenhydrinate in pregnant women. Reproduction studies in rats and rabbits using dimenhydrinate doses up to 20 and 25 times the human dose (mg/kg), respectively, have not revealed evidence of harm to the fetus or impaired fertility.

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.

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

Geriatrics: Older adults may be more sensitive to the side effects of this drug, especially drowsiness, confusion, constipation, or trouble urinating. Drowsiness and confusion can increase the risk of falling. Dimenhydrinate may be inappropriate in older adults depending on comorbidities (e.g. dementia, delirium, etc.) due to its potent anticholinergic effects.

Pediatrics (< 12 years of age): For infants and children especially, antihistamines in overdosage

may cause hallucinations, convulsions, or death (see **CONTRAINDICATIONS**). As in adults, antihistamines may diminish mental alertness in pediatric patients. Antihistamines may also produce excitation in younger children, therefore caution is advised in patients under 6 years of age (see **INDICATIONS**, **Pediatrics (under 2 years of age)** and **CONTRAINDICATIONS)**.

Dimenhydrinate Injection USP is not recommended for children under 2 years of age. Discontinue use and contact the physician if symptoms of paradoxical excitation (restlessness, nervousness, hallucinations, delirium, or seizures), especially in small children, occur.

ADVERSE REACTIONS

Drowsiness and dizziness are reported most frequently, particularly on high dosage. Pain may occur at the site of IM injection. Since dimenhydrinate contains 50% diphenhydramine, the possibility of diphenhydramine side effects must also be considered.

The following adverse reactions have also been reported:

Blood and lymphatic system disorders: anemia, thrombocytopenia, agranulocytosis, leukopenia, pancytopenia.

Body as a whole - general disorders: lassitude, fatigue, drug withdrawal syndrome, injection site inflammation.

Cardiac disorders: tachycardia, palpitations, hypotension, arrhythmia.

Ear and labyrinth disorders: tinnitus, labyrinthitis, vertigo.

Eye disorders: mydriasis, vision blurred, diplopia.

Gastrointestinal disorders: epigastric distress, nausea, dry mouth, constipation, diarrhea, vomiting.

General disorders and administration site conditions: oedema.

Immune system disorders: hypersensitivity, anaphylactic reaction.

Metabolism and nutrition disorders: anorexia, decreased appetite.

Nervous system disorders: dizziness, headache, impaired coordination, somnolence, tremor, paraesthesia, ataxia, athetosis, convulsions, seizures, memory impairment, loss of consciousness.

Psychiatric disorders: depression, insomnia, hallucination, anxiety, confusional state, excitation, euphoric mood, nightmares, delirium, irritability, nervousness, restlessness, agitation.

Respiratory, thoracic, and mediastinal disorders: thickening of bronchial secretions,

respiratory depression, dyspnoea.

Renal and urinary disorders: dysuria, urinary retention.

Skin and subcutaneous tissue disorders: angioedema, hyperhidrosis, rash, rash erythematous, rash maculopapular, pruritus, urticaria, fixed drug eruption, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiform, photosensitivity.

Vascular disorders: hypotension, hypertension, flushing.

DRUG INTERACTIONS

Drug-Drug Interactions
CNS Depressants: Dimenhydrinate may enhance the effects of alcohol, barbiturates, tranquilizers, sedatives, or hypnotics. Caution must therefore be used to avoid overdose.

Drugs with Anticholinergic Effects: Because dimenhydrinate also has anticholinergic activity, it may potentiate the effects of other drugs with anticholinergic activity including tricyclic antidepressants, MAO inhibitors, and antihistamines. Solid potassium dose forms should be avoided as anticholinergics may slow gastrointestinal transit resulting in local exposure to high potassium concentrations.

Ototoxic Drugs: When given concurrently with aminoglycoside antibiotics or other ototoxic drugs, dimenhydrinate may mask the early symptoms of ototoxicity (see **WARNINGS AND PRECAUTIONS**).

Incompatibility: the incompatible substance with injectable preparations of dimenhydrinate include: phenothiazine derivatives, aminophylline, ammonium chloride, sodium amobarbital, diphenylhydantoin, sodium heparin, hydrocortisone sodium succinate, pentobarbital, phenobarbital, thiopental and certain types of antibiotics (tetracycline HCl).

Drug-Laboratory Interactions
As for other antihistamines, dimenhydrinate may inhibit the cutaneous histamine response in skin tests using allergen extracts, thus producing false- negative results. It is recommended that dimenhydrinate be discontinued at least 72 hours before testing.

DOSAGE AND ADMINISTRATION

Dosing Considerations
This preparation is designed for intramuscular (IM) use only and must not be used intravenously (IV) unless it has been diluted (see DOSAGE AND ADMINISTRATION, Intravenous Dilution Instructions below). Always inspect the solution visually for particulate

matter and discolouration prior to administration. Not to be injected intra-arterially. Substances which are physically incompatible with injectable solutions of dimenhydrinate include: phenothiazine derivatives, aminophylline, ammonium chloride, sodium amobarbital, diphenylhydantoin, heparin, hydrocortisone sodium succinate, pentobarbital, phenobarbital, thiopental and certain antibiotics.

Recommended Dose and Dosage Adjustment

Adults:
Intramuscular (IM) administration: 0.5 - 1 mL (25 - 50 mg) every 4 to 6 hours. 2 mL (100 mg) may be given every 4 – 6 hours when drowsiness is not objectionable or is even desirable. Dosage should not exceed 400 mg/day.

Intravenous (IV) administration: the usual dose is 1 mL (50 mg) diluted in 9 mL of 0.9% sodium chloride solution and injected over 2 minutes. Doses of 25 – 100 mg may be diluted in a 1:10 ratio and given every 4 – 6 hours. Diluted solutions can be stored for 24 hours at room temperature. Dosage should not exceed 400 mg/day.

Children:
Intramuscular (IM) administration:
0-2 Years of age: dimenhydrinate should not be used in children under 2 (see **CONTRAINDICATIONS**).
2-5 Years of age: 0.25 – 0.5 mL (12.5 - 25 mg) every 6 – 8 hours. Dosage should not exceed 75 mg/day.
6-11 Years of age: 0.5 – 1 mL (25 - 50 mg) every 6 – 8 hours. Dosage should not exceed 150 mg/day.
12-17 Years of age: 0.5 – 2 mL (25 - 100 mg) every 4 – 6 hours. Dosage should not exceed 300 mg/day (see adult administration information above).

Intravenous (IV) administration:
The same doses as indicated above diluted in a 1:10 ratio and injected over 2 minutes (see **DOSAGE AND ADMINISTRATION, Intravenous Dilution Instructions**).

Intravenous Dilution Instructions
For IV administration, each 1 mL of product must be diluted in 9 mL of 0.9% sodium chloride solution and injected over 2 minutes (dilution ratio 1:10). Diluted solutions can be stored up to 24 hours at room temperature. Dimenhydrinate is never to be injected intra-arterially. Always inspect the solution visually for particulate matter and discolouration prior to administration. Discard any unused portions.

OVERDOSAGE

Symptoms: Accidental antihistamine overdose occurs frequently in infants and children. Symptoms of dimenhydrinate toxicity in children may resemble atropine overdosage and include dilated pupils, flushed face, excitation, hallucinations, confusion, ataxia, intermittent clonic convulsions, coma, cardiorespiratory collapse, and death. **Symptoms may be delayed up to 2**

hours after ingestion; death may occur within 18 hours.

In adults, 500 mg or more of dimenhydrinate may cause extreme difficulty in speech and swallowing, and produces a psychosis indistinguishable from that of atropine poisoning. CNS excitation may be preceded by sedation, leading to a cycle of CNS excitation, seizures, and postictal depression.

Treatment: Treatment of dimenhydrinate toxicity is symptomatic and supportive. Emetics are usually ineffective, but in the absence of seizures, early gastric lavage (with an endotracheal tube with cuff inflate in place to prevent aspiration of gastric contents) may be beneficial. Patients should be kept quiet, to minimize CNS stimulation; seizures may be treated with diazepam in adults and phenobarbital in children (additional methods may include IV sodium bicarbonate, or IV physostigmine salicylate in children). Mechanical respiratory assistance may be required.

Positive and negative mode of ion mobility spectrometry (IMS) and ion mobility spectrometry/mass spectrometry (IMS/MS) have shown efficacy for the preliminary screening of emergency patients suspected of dimenhydrinate and other drug overdose.

For management of suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

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).

Pharmacokinetics

Dimenhydrinate is well absorbed after oral administration. Antiemetic effects occur almost immediately after IV administration, and within 20-30 minutes after IM administration and 15-30 minutes after oral administration. In a study of 9 healthy volunteers given a single dose of each dosage form (separated by a washout period), T_{max} and C_{max} are given in the following table.

Product	T_{max} (h)	C_{max} (ng/mL serum)
Dimenhydrinate film-coated tablets 50 mg	2.7	72.6
Dimenhydrinate long action capsules 75 mg	4.0	68.4
Dimenhydrinate suppositories 100 mg	5.3	112.2

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 0.1mcg/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 diphenyl-methoxy-N-methylamine.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dimenhydrinate Injection USP, 1 mL single use ampoules:
Each mL of sterile solution contains dimenhydrinate USP 50 mg in a mixture of propylene glycol (50%) and water for injection. Also contains hydrochloric acid to adjust pH. Available in 1 mL ampoules packaged in boxes of 10.

Dimenhydrinate Injection USP, 5 mL multidose vials:
Each mL of sterile solution contains dimenhydrinate USP 50 mg in a mixture of propylene glycol (50%), and water for injection. Also contains hydrochloric acid to adjust pH, and the preservatives, methylparaben 1 mg/mL (as sodium methylparaben) and propylparaben 0.1 mg/mL (as sodium propylparaben). Available in 5 mL multidose vials in boxes of 10.

STORAGE AND STABILITY

Dimenhydrinate Injection USP should be stored at room temperature (15 to 30°C). Protect from freezing. The 5 mL multidose vial should also be protected from light.

Keep out of reach and sight of children.

The Handbook on Injectable Drugs should be consulted prior to mixing dimenhydrinate with other drugs.

SPECIAL HANDLING INSTRUCTIONS

Do not use product if mixture (solution) shows haziness, particulate matter, discolouration, or leakage.

Dimenhydrinate Injection USP, packaged in 1 mL ampoules, is for single use only. Unused portions must be discarded.

Dimenhydrinate Injection USP, packaged in 5 mL vials, can be stored up to 28 days following first puncture.

The 5 mL vial stopper is not made with natural rubber latex.

PART II: SCIENTIFIC INFORMATION

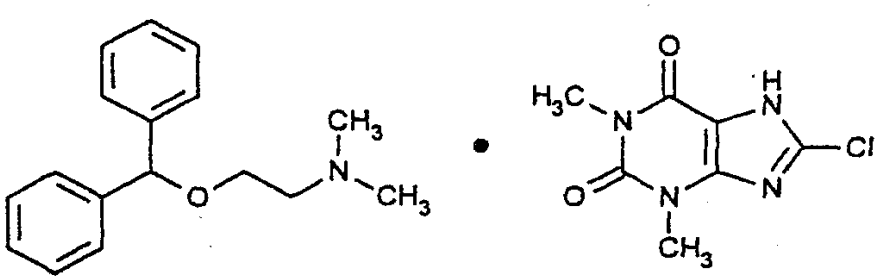
PHARMACEUTICAL INFORMATION

Proper Name: Dimenhydrinate

Chemical Name: 8-chlorotheophyllinate of 2-[diphenylmethoxy]-n,n-dimethylethylamine

Other Names: IS = Anautinum; Dommanate, Dramamine®, Gravol®

Chemical Structure:



Molecular Formula: $C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$

Molecular Weight: 469.97 g/mol

Physical Properties:

Physical Form: White, crystalline, odorless powder

Solubility: Slightly soluble in water; freely soluble in ethanol and in chloroform; sparingly soluble in ether

pH Value: 6.8 – 7.3

Melting Point Range: 102°C – 107°C

TOXICOLOGY

Acute toxicity was determined by administering dimenhydrinate to mice PO and IP, and in rats PO and IV. The results are shown in the following table.

Species	**Oral**	**IP**	**IV**
Mice	203 mg/kg	110 mg/kg 149 mg/kg	--
Rats	831 mg/kg 1320 mg/kg	--	200 mg/kg

REFERENCES

1. **Scavone JM,** Luna BG, Harmatz JS, Moltke von L, Greenblatt DJ: Diphenhydramine kinetics following intravenous, oral and sublingual dimenhydrinate administration. Biophamaceut Drug Dispos 1990, 11: 185-189

2. **Farrell M,** Heinrichs M, Tilelli JA: Response of life threatening dimenhydrinate intoxication to sodium bicarbonate administration. Clin Toxicol 1991, 29(4): 527-535

3. Le traitement des nausées et vomissement causés par la radiothérapie et la chimiothérapie. **Gravol:** p. 15, 31-33. Gouvernement du Québec 1993 ISBN 2-550-28418-6

4. **Kovac AL:** Prevention and treatment of postoperative nausea and vomiting. Dimenhydrinate p.225 Drugs 2000, 59(2): 213-243.

5. **Albert KS,** Hallmark MR, Sakmar E, Weidler DJ, Wagner JG: Pharmacokinetics of diphenhydramine in man. J Pharmacokinet Biopharm 1975, 3(3): 159-170 (**168-169**)

6. **Carruthers SG,** Shoeman DW, Hignite ChE, Azarnoff DL: Correlation between plasma diphenhydramine level and sedative and antihistamine effects. Clin Pharmacol Ther 1978, 23(4): 375-382.

7. **Winn RE,** McDonnell KP: Fatality secondary to massive overdose of dimenhydrinate. Ann Emerg Med 1993, 22(9): 154/1481-157/1484 (**155/1482**)

8. **Craig DF,** Mellor CS: Dimenhydrinate dependence and withdrawal. C M A J 1990, 142(9): 970-973

9. **Gardner DM,** Kutcher St: Dimenhydrinate abuse among adolescents. Can J Psychiatr 1993, 38: 113-116.

10. **Rowe C,** Verjee Z, Koren G: Adolescent dimenhydrinate abuse: resurgence of an old problem. J Adolescents Health 1997, 21(1): 47-49

11. **Krenzelok EP,** Anderson GM, Mirick M: Massive diphenhydramine overdose resulting in death. Ann Emerg Med 1982, 11(Apr): 212-213.

12. **Leathem AM:** Safety and efficacy of antiemetics used to treat nausea and vomiting in pregnancy. (Therapy reviews antiemetics) Clin Pharm 1986, 5: 660-668

13. **Lemay M,** Samaan M, St. Michel P, Granger L, Pigeon R: Effets immédiats du dimenhydrinate sur la contraction utérine et le rythme cardiaque foetal durant le travail. C M A J 1982, 127: 606-607

14. **Mazzotta P,** Magee LA: A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. p.785, 787, 795-796

Drugs 2000, 59(4): 781-800

15. **Ito Sh,** Blajchman A, Stephenson M, Elipoulos Ch, Koren G: Prospective follow-up of adverse reactions in breast-fed infants exposed to maternal medication. Am J Obstet Gynecol 1993, 168(5): 1393-1399

16. **Manning C**, Scandale L, Manning EJ, Gengo FM: Central nervous system effects of meclizine and dimenhydrinate: evidence of acute tolerance to antihistamines. J Clin Pharmacol 1992, 32: 996-1002

17. **Luria SM,** Kinney JAS, McKay CL, Paulson HM, Ryan AP: Effects of aspirin and dimenhydrinate (dramamine) on visual processes. Br J Clin Pharmacol 1979, 7: 585-593

18. **Bamforth KJ,** Dagliesh K, Coughtrie MWH: Inhibition of human liver steroid sulfotransferase activities by drugs: a novel mechanism of drug toxicity. (Dimenhydrinate and diphenhydramine). Eur J Pharmacol (Environ Toxicol Pharmacol Sect) 1992, 228: 15-21

19. **Kivity S:** Fixed drug eruption to multiple drugs: Clinical and laboratory investigation. Int J Dermatol 1991, 30(2): 149-150

20. **Zavitz M,** Lindsay C, McGuigan MA: Acute diphenhydramine ingestion in children. Vet Hum Toxicol 1989, 31(4): 349 Abstr.#80

21. **Lawrence AH,** Nanji AA: Ion mobility spectrometry and ion mobility spectrometry/mass spectometric characterization of dimenhydrinate. Biomed Environ Mass Spectrom 1988, 16: 345- 347

22. **Guay DRP,** Meatherall RC, Macaulay PA, Yeung C: Activated charcoal adsorption of diphenhydramine. Int J Clin Pharmacol Ther Toxicol 1984, 22(8): 395-400

23. **Federal Register V,** Department of Health and Human Services, FDA 21 CFR Parts 310, 336, and 369: Antiemetic drug products for over-the-counter human use: **Final Rule.** Effective May 2, 1988 Federal Register 1987(30.04), 52(83): 15886-15893.

24. **Walker SE,** Iazzetta J, DeAngelis C, Lau DWC: Stability and compatibility of combinations of hydromorphone and dimenhydrinate, lorazepam or prochlorperazine. Can J Hosp Pharm 1993, 46: 61-65

25. **Oshiro Y,** Balwierz PS, Piper CE: Experimental design for the C3H/10T1/2 CL8 cell transformation assay. J Appl Toxicol 1988, 8(4): 255-260

26. **Church & Dwight Canada Corp.**, Product Monograph, GRAVOL™ IM (Dimenhydrinate), Control No. 188084, January 25, 2016.

PART III: PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

DIMENHYDRINATE INJECTION USP

Read this carefully before you start taking Dimenhydrinate Injection USP and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about Dimenhydrinate Injection USP.

What is Dimenhydrinate Injection USP used for?
Dimenhydrinate Injection USP is used to prevent and relieve symptoms such as:

- nausea
- vomiting and/or
- vertigo

These symptoms may be the result of:

- motion sickness
- radiation sickness
- postoperative recovery
- taking other drugs
- an ear condition (Menière's disease and other labyrinthine disturbances)

How does Dimenhydrinate Injection USP work?
Dimenhydrinate Injection USP belongs to a family of drugs called antiemetics. They work by:

- affecting the brain and inner ear to help prevent problems with the body's balance
- blocking processes that are involved in the vomiting reflex

What are the ingredients in Dimenhydrinate Injection USP?
Medicinal ingredient: dimenhydrinate

Non-medicinal ingredients:

Dimenhydrinate Injection USP, single use ampoules	50% propylene glycol, water for injection, and hydrochloric acid for pH adjustment
Dimenhydrinate Injection USP, multidose vials	50% propylene glycol, water for injection, hydrochloric acid for pH adjustment, and methylparaben (as sodium methylparaben) and propylparaben (as sodium propylparaben) as preservatives

Dimenhydrinate Injection USP comes in the following dosage forms:

- **50 mg / mL,** sterile solution for IM administration or IV administration if diluted, 1 mL single use ampoule
- **250 mg / 5 mL** (50 mg / mL), sterile solution for IM administration or IV administration if diluted, 5 mL multidose vial

Do not use Dimenhydrinate Injection USP if you:

- are allergic to dimenhydrinate or any of the other ingredients (see **What are the ingredients in Dimenhydrinate Injection USP)**
- take a Monoamine Oxidase Inhibitor (MAOI). Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid and methylene blue. **Do not**:
    - Take an MAOI within 2 weeks of stopping Dimenhydrinate Injection USP use unless told to do so by your doctor
    - Start taking Dimenhydrinate Injection USP if you stopped taking an MAOI in the last 2 weeks unless told to do so by your doctor
- Have glaucoma
- Have chronic lung disease including:
    - asthma
    - chronic obstructive pulmonary disease
    - lower respiratory tract symptoms
- Have difficulty urinating due to an enlarged prostate
- Are 2 years old or younger

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Dimenhydrinate Injection USP. Talk about any health conditions or problems you may have, including if you:

- have a history of heart problems, including high blood pressure
- have a history of seizures
- have problems with your thyroid
- have or had liver problems
- are pregnant or planning to become pregnant
- are breastfeeding or planning to breastfeed
- have porphyria (a condition that affects your hemoglobin)

Other warnings you should know about:

Do not take more than the recommended dose. At high doses, Dimenhydrinate Injection USP can cause:

- confusion
- hallucinations

- temporary amnesia
- paranoia

Abuse: chronic abuse of Dimenhydrinate Injection USP can lead to accidents, overdose, and in extreme cases to death. Dimenhydrinate Injection USP should not be used for prolonged periods except on the advice of your doctor.

Driving and using machines: Before doing tasks that require special attention, wait until you know how you respond to Dimenhydrinate Injection USP.

Pregnancy: Do not take Dimenhydrinate Injection USP for nausea or vomiting while pregnant unless told to do so by your doctor.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Dimenhydrinate Injection USP:

- Alcohol
- Some drugs used to treat depression (MAO inhibitors)
- Drugs used to help you sleep such as:
    - barbiturates
    - sedatives
    - hypnotics
- Drugs used to reduce tension or anxiety (such as tranquilizers)

To avoid an overdose, you should use caution when taking Dimenhydrinate Injection USP with these types of drugs.

- Drugs used to treat allergies or allergic reactions (antihistamines)
- Drugs that can cause damage to the ear (called ototoxic drugs). If you take dimenhydrinate in combination with certain antibiotics or other drugs that can cause damage to the ear, you may not be able to see the early symptoms of ototoxicity.

Dimenhydrinate Injection USP in 5 mL multidose vials contains the preservatives methylparaben and propylparaben. They are known to be associated with undesirable reactions produced by the normal immune system in single or repeated uses.

How to take Dimenhydrinate Injection USP:

Dimenhydrinate Injection USP is for intramuscular use only.

If used for intravenous (IV) administration, it must be diluted at least one to ten with a compatible physiological solution (such as sterile saline). Diluted Dimenhydrinate Injection

USP, prepared for IV use, should be administered by **SLOW INTRAVENOUS INJECTION ONLY** (over 2 minutes).

Adults:
Usual dose: 25 mg - 100 mg given IM or by IV every 4 to 6 hours.
Maximum daily dose: This dose can be given again up to 400 mg a day.

Children:
Usual dose for 2 to 5 years of age: 12.5 mg - 25 mg given IM or by IV every 6 to 8 hours. This dose can be given again up to 75 mg a day.
Usual dose for 6 to 11 years of age: 25 mg - 50 mg given IM or by IV every 6 to 8 hours. This dose can be given again up to 150 mg a day.
Usual dose for 12 to 17 years of age: 25 mg - 100 mg given IM or by IV every 4 – 6 hours. This dose can be given again up to 300 mg a day.

Overdose:

If you think you have taken too much Dimenhydrinate Injection USP, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed dose:
If you miss a dose and you are taking it regularly, take it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. Do not take 2 doses at once. Do not exceed the maximum daily dose.
What are possible side effects from using Dimenhydrinate Injection USP?

These are not all the possible side effects you may feel when taking Dimenhydrinate Injection USP. If you experience any side effects not listed here, contact your healthcare professional.

- drowsiness
- dizziness
- pain may occur at the site of IM injection
- dry mouth
- fatigue
- excitement
- nausea

Skin Rash: If you experience a skin rash after taking Dimenhydrinate Injection USP, you should contact your doctor or pharmacist for assessment and advice.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Dimenhydrinate Injection USP should be stored at controlled room temperature (15°C – 30°C). Protect from freezing. The 5 mL multidose vial should also be protected from light.

Keep out of reach and sight of children.

If you want more information about Dimenhydrinate Injection USP:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or by calling 1-800-656-0793.

This leaflet was prepared by Hikma Canada Limited, Mississauga, ON L5R 3P9

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