



## Material Safety Data Sheet

# Granisetron Hydrochloride Injection

### 1. PRODUCT IDENTIFICATION

**Product Name** Granisetron Hydrochloride Injection  
**Product Use** Medical Treatment; Antinausea and Antiemetic  
**Manufacturer** Teva Parenteral Medicines, Inc.  
**Address** 11 Hughes  
 Irvine, CA 92618-1902  
  
**Chemtrec Emergency No.** 1-800-424-9300 (United States)  
 1-202-483-7617 (International Collect)  
**Business Phone** 1-800-729-9991  
**Website Address** <http://www.newsicor.com>  
  
**Common Names** Kytril®  
**Chemical Name** 1*H*-Indazole-3-carboxamide, 1-methyl-*N*-(9-methyl-9-azabicyclo(3,3,1)Non-3-yl)-monohydrochloride, endo-  
**Chemical Formula** C<sub>18</sub>H<sub>24</sub>N<sub>4</sub>O \* ClH  
**Chemical Family** Anti-Nauseant and Antiemetic  
**How Supplied** 1mL sterile aqueous solution in a 2mL vial  
  
**Date of Preparation:** February 7, 2005

### 2. COMPOSITION AND INGREDIENTS

CHEMICAL NAME	CAS#	Wt%	EXPOSURE LIMITS IN AIR				
			ACGIH		OSHA		Other
			TL	CEIL	PEL	CEIL	
Granisetron Hydrochloride	107007-99-8	0.0112 –0.112	NE	NE	NE	NE	NE
Sodium Chloride	7647-14-5	0.9	NE	NE	NE	NE	NE
Water (for injection)	7732-18-5	Balance	NE	NE	NE	NE	NE

NE - Not Established

C - Ceiling Limit

NOTE: All WHMIS required information is included. It is located in appropriate sections based on the ANSI Z400.1 – 1998 format  
 CHEMTREC NUMBER: Use only in the event of a chemical emergency involving a spill, leak, fire, exposure or accident involving this drug.

### 3. HAZARD IDENTIFICATION

**EMERGENCY OVERVIEW:** Material is a clear, colorless, odorless liquid. Avoid contact with eyes, skin and clothing. Do not taste or swallow. Wash thoroughly after handling.

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### 3. HAZARD IDENTIFICATION cont.

Symptoms of Overexposure by Route of Exposure: This material is intended for intravenous injection under the supervision of physicians.

Inhalation: Inhalation of significant amounts of the product is not anticipated to occur because of the small size of individual containers.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness and swelling of the eyes and redness and a burning sensation on the skin.

Ingestion: Ingestion is not an anticipated route of occupational exposure. However, the active ingredient, Granisetron Hydrochloride is toxic if ingested. Symptoms similar to those identified under injection may occur.

Injection: Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Medical personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, therapeutic effects including headache, sleepiness, agitation, anxiety, central nervous system stimulation, insomnia, extrapyramidal syndrome, diarrhea, constipation, hypertension, hypotension, arrhythmias (e.g., sinus bradycardia, atrial fibrillation, ventricular ectopy including non-sustained tachycardia, ECG abnormalities), hypersensitivity reactions (anaphylaxis), sometimes severe, with skin rashes, weakness and fever may occur. See package insert for other adverse reactions associated with therapeutic doses of this product.

#### Health Effects or Risks From Exposure (An explanation in lay terms):

Acute: The primary health effects anticipated in an occupational setting include mild irritation of eyes and skin as well as redness and local swelling after accidental injection. In case of over-exposure by injection, effects such as headache, sleepiness, agitation, anxiety, central nervous system stimulation, insomnia, diarrhea, constipation, hypertension (high blood pressure), hypotension (low blood pressure), arrhythmias and hypersensitivity reactions (anaphylaxis), sometimes severe, with skin rashes, weakness and fever may occur.

Cancer: Granisetron Hydrochloride has demonstrated carcinogenic effects in laboratory animals (see Section 11).

Chronic: Based on animal data, Granisetron Hydrochloride, the active ingredient, is not considered a potential reproductive or developmental toxicant (see Section 11).

Pre-Existing Medical Conditions: Pre-existing central nervous system disorders may be aggravated by exposure to this material.



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**6. ACCIDENTAL RELEASE MEASURES**

Spill and Leak Response:

For small releases of this product, wear latex or nitrile gloves and safety glasses. Absorb spilled liquid and rinse area thoroughly with soap and water.

For large or uncontrolled releases, stay away from spill. Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Wear appropriate protective equipment including respiratory protection as conditions warrant (see Section 8). Prevent spilled material from entering sewers, storm drains, other unauthorized treatment drainage systems, and natural waterways. Dike far ahead of spill for later recovery or disposal. Spilled material may be absorbed into an appropriate absorbent material. Notify appropriate federal, state, and local agencies. Immediate cleanup of any spill is recommended.

**7. HANDLING and STORAGE**

Work and Hygiene Practices: As with all chemicals, avoid getting this product ON YOU or IN YOU. Do not eat, drink, smoke or apply cosmetics while handling the product. Wash hands thoroughly after handling.

Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this product, and during patient administration. Precautions should be taken during the following activities:

- Withdrawal of needles from drug vials.
- Drug transfers using syringes and needles or filter straws.
- Expulsion of air from drug-filled syringes.

Storage and Handling Practices: Employees must be trained to properly use the product. Ensure vials are properly labeled. Store only in approved containers. Keep away from sources of ignition and any incompatible materials or conditions (see Section 10). Store at room temperature 15-30°C (59-86°F). Protect from light. Do not use discolored solutions.

Protective Practices During Maintenance of Contaminated Equipment: When cleaning non-disposable equipment, wear latex or nitrile gloves (double gloving is recommended), goggles, and lab coat. Wash equipment with soap and water. All needles, syringes, vials and other disposable items contaminated with this product should be disposed of properly.



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### 8. EXPOSURE CONTROLS - PERSONAL PROTECTION

Ventilation and Engineering Controls: Use with adequate ventilation. Follow standard medical product handling procedures.

Respiratory Protection: Not normally required for routine, medical administration of this product. A NIOSH certified air-purifying respirator with a type 95 filter may be used under conditions where airborne concentrations are expected to be excessive. Protection provided by air purifying respirators is limited (see manufacturer's respirator selection guide). Use a positive pressure air supplied respirator if there is potential for uncontrolled release, exposure levels are not known, or any other circumstances where air-purifying respirators may not provide adequate protection. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions warrant a respirator's use.

Eye Protection: Approved eye protection to safeguard against potential eye contact, irritation or injury is recommended. Depending on conditions of use, a face shield may be necessary.

Hand Protection: Use latex, nitrile, or rubber gloves. Check gloves for leaks. Wash hands before and after using gloves.

Body Protection: No special body protection required for routine, medical administration of this product. Wear lab coat, gown, or smock, as appropriate for procedure.

Product Preparation Instructions for Medical Personnel: Follow standard procedure for handling pharmaceutical materials and recommendations presented on the Package Insert.

### 9. PHYSICAL and CHEMICAL PROPERTIES

Relative Vapor Density (air = 1):	ND	Evaporation Rate (n-BuAc=1):	ND
Specific Gravity (water = 1):	ND	Melting/Freezing Point:	0°C (32°F)
Solubility in Water:	Complete	Boiling Point:	100°C (212°F)
Vapor Pressure, mm Hg @ 25°C.	ND	pH:	4.7 – 7.3
Odor Threshold: ND			
Appearance and Color: Clear, colorless liquid			

ND = No Data

### 10. STABILITY and REACTIVITY

Stability: Stable under normal conditions of storage and handling.

Materials With Which Substance is Incompatible: This product is generally compatible with other common materials in a medical facility. Keep away from strong oxidizers, strong acids, some metals and substances that are incompatible with water..

Hazardous Polymerization: Will not occur.

Hazardous Combustion Products: Oxides of carbon and nitrogen and hydrogen chloride.

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**11. TOXICOLOGICAL INFORMATION**

Toxicity Data: The following information is for Granisetron Hydrochloride, the active ingredient

IV LD50(rat) = 14 mg/kg                      Oral LD50(rat) = 350 mg/kg  
 IV LD50(mouse) = 17 mg/kg                Oral LD50(mouse) = 350 mg/kg

Carcinogenicity: Data indicates some carcinogenic potential in rodents, although at doses exceeding human clinical dose. In a 24-month carcinogenicity study, rats were treated orally with Granisetron Hydrochloride 1, 5 or 50 mg/kg/day (6, 30 or 300 mg/m<sup>2</sup>/day). The 50 mg/kg/day dose was reduced to 25 mg/kg/day (150 mg/m<sup>2</sup>/day) during week 59 due to toxicity. For a 50 kg person of average height (1.46 m<sup>2</sup> body surface area), these doses represent 16, 81 and 405 times the recommended clinical dose (0.37 mg/m<sup>2</sup>, IV) on a body surface area basis. There was a statistically significant increase in the incidence of hepatocellular carcinomas and adenomas in males treated with 5 mg/kg/day (30 mg/m<sup>2</sup>/day, 81 times the recommended human dose based on body surface area) and above, and in females treated with 25 mg/kg/day (150 mg/m<sup>2</sup>/day, 405 times the recommended human dose based on body surface area). No increase in liver tumors was observed at a dose of 1 mg/kg/day (6 mg/m<sup>2</sup>/day, 16 times the recommended human dose based on body surface area) in males and 5 mg/kg/day (30 mg/m<sup>2</sup>/day, 81 times the recommended human dose based on body surface area) in females. In a 12-month oral toxicity study, treatment with Granisetron Hydrochloride 100 mg/kg/day (600 mg/m<sup>2</sup>/day, 1622 times the recommended human dose based on body surface area) produced hepatocellular adenomas in male and female rats while no such tumors were found in the control rats. A 24-month mouse carcinogenicity study of Granisetron Hydrochloride did not show a statistically significant increase in tumor incidence, but the study was not conclusive. It is not listed as carcinogenic by NTP, IARC or OSHA.

Irritancy of Product: This product is expected to be mildly irritating to contaminated skin, eyes and other tissues. The active ingredient is irritating to the eyes and the skin.

Sensitization to the Product: Rare cases of hypersensitivity reactions, sometimes severe (e.g., anaphylaxis, shortness of breath, hypotension, urticaria) have been reported. In addition, hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other selective 5-HT 3 receptor antagonists.

Reproductive Toxicity Information: Listed below is information concerning the effects of Granisetron Hydrochloride on human and animal reproductive systems. This material is classified as a Pregnancy Category B (No Evidence of Risk)

Mutagenicity: Equivocal. Granisetron Hydrochloride is not mutagenic in the Ames gene mutation assay and mouse lymphoma gene mutation assay, mouse micronucleus and hepatocyte DNA assay. Mutagenic in unscheduled DNA synthesis and human lymphocyte chromosomal assay.

Embryotoxicity/Teratogenicity Toxicity: Not a developmental toxicant nor did it cause malformations in rats at doses 405 times the human recommended clinical dose based on body surface area.

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**11. TOXICOLOGICAL INFORMATION cont..**

Reproductive Toxicity: Not a reproductive toxicant (affect fertility) in male or female rats at doses 405 times the human recommended clinical dose based on body surface area. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

ACGIH Biological Exposure Indices: Currently there are no Biological Exposure Indices (BEIs) associated with the components of this product.

**12. ECOLOGICAL INFORMATION**

All work practices must be aimed at eliminating environmental contamination.

Environmental Stability: The components of this product will degrade in the environment into organic and inorganic constituents, especially upon exposure to light.

Effect of Materials on Plants or Animals: No specific information is available on the effect of Granisetron Hydrochloride on plants or animals in the environment. Due to the small product size and dilute concentration of the components, this product is not anticipated to cause adverse effects.

Effect of Chemicals on Aquatic Life: No specific information is available on the effect of Granisetron Hydrochloride on plants or animals in the aquatic environment. Due to the small product size and dilute concentration of the components, this product is not anticipated to cause adverse effects.

**13. DISPOSAL CONSIDERATIONS**

Preparing Wastes for Disposal: This material, if discarded as produced, is not a RCRA “listed” or “characteristic” hazardous waste. Use resulting in chemical or physical change or contamination may subject it to regulation as a hazardous waste. Along with properly characterizing all waste materials consult state and local regulations regarding the proper disposal of this material.

U.S. EPA Waste Number: None

**14. TRANSPORTATION INFORMATION**

This Materials is not Hazardous as Defined by 49 CFR 172.101 by the U. S. Department of Transportation

Proper Shipping Name: Not applicable

Hazard Class Number and Description: Not applicable

UN Identification Number: Not applicable

Packing Group: Not applicable

DOT Label(s) Required: Not applicable

North American Emergency Response Guidebook Number (1996): Not applicable.

MARINE POLLUTANT: No component of this product is listed as a Marine Pollutant (49 CFR 172.101, Appendix B)

Transport Canada Transportation of Dangerous Goods Regulations: Not applicable



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### 15. REGULATORY INFORMATION

#### U.S. REGULATIONS:

U.S. SARA Reporting Requirements: The components of this product are not subject to the reporting requirements of Sections 302, 304 and 313 of Title II of the Superfund Amendments and Reauthorization Act.

U.S. SARA Threshold Planning Quantity: Not applicable

U.S. TSCA Inventory Status: Granisetron Hydrochloride is a "drug" as defined by the Federal Food, Drug and Cosmetic Act and is therefore not a chemical substance under TSCA.

California Safe Drinking Water and Toxic Enforcement Act (Proposition 65): This product does NOT contain a chemical known to the State of California to cause developmental and reproductive effects.

Other U.S. Federal Regulations: Based on this product's use, the requirements of the OSHA Bloodborne pathogen Standard (29 CFR 1910.1030) are applicable.

#### CANADIAN REGULATIONS:

Canadian DSL/NDSL Status: Granisetron Hydrochloride is regulated by the Food and Drug Administration of Health Canada and is therefore exempt from the requirements of CEPA.

ANSI Labeling (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): Granisetron Hydrochloride should be administered under the supervision of a qualified physician. Avoid over-exposure. Avoid contact with eyes, skin and clothing. Do not eat, drink or smoke when handling Granisetron Hydrochloride. Do not taste or swallow. Wash thoroughly after handling. Clean up spills promptly.

### 16. OTHER INFORMATION

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