

MATERIAL SAFETY DATA SHEET

Section I - IDENTITY

Common/Trade Name: Granisetron Hydrochloride Injection (0.1 mg/mL and 1 mg/mL)
Single Dose Vial

Chemical Names: 1*H*-Indazole-3-carboxamide, 1-methyl-*N*-(9-methyl-9-azabicyclo(3,3,1)Non-3-yl)-monohydrochloride, endo-

Manufacturer's Name: Wockhardt Limited, Mumbai ,India.

Emergency Telephone Number: +91-22-2653 4444

Section II - HAZARDOUS INGREDIENTS/COMPOSITION INFORMATION

Chemical Name	CAS#	%w/w	%w/w	OSHA PEL	ACGIH TLV	IDLH
Granisetron Hydrochloride	107007-99-8	0.0112	0.112	NE	NE	NE
Sodium Chloride	7647-14-5	0.9	0.9	NE	NE	NE
Citric Acid monohydrate	5949-29-1	0.2	0.2	NE	NE	NE
Water (for injection)	7732-18-5	Balance	Balance	NE	NE	NE
NE= Not Established						

Section III - 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.

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.

Section IV - FIRST AID MEASURES
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Skin Exposure: Remove contaminated shoes and clothing and cleanse affected area(s) thoroughly by washing with mild soap and water. If irritation or redness develops and persists, seek medical attention.

Eye Exposure: If irritation or redness develops, move victim away from exposure and into fresh air. Flush eyes with clean water and seek medical attention.

Inhalation: If respiratory symptoms develop, move victim away from source of exposure and into fresh air. If symptoms persist, seek medical attention. If victim is not breathing, clear airway and immediately begin artificial respiration. If breathing difficulties develop, oxygen should be administered by qualified personnel. Seek immediate medical attention.

Ingestion: If swallowed, seek emergency medical attention. If victim is drowsy or unconscious and vomiting, place on the left side with the head down and DO NOT give anything by mouth. If not vomiting and professional advice is not available, DO NOT induce vomiting. If possible, do not leave victim unattended and observe closely for adequacy of breathing.

Victims of chemical exposure must be taken for medical attention. Take a copy of the MSDS to the physician or health professional with victim. Physicians should refer to Section 11 (Toxicological Information) as well as the Physicians Desk Reference for additional treatment information.

Section V - FIRE AND EXPLOSION HAZARD DATA

Flash Point: Non-flammable Autoignition Temperature: Not applicable

Flammable Limits (in air by volume, %): Lower: Not applicable Upper: Not applicable

Fire Extinguishing Equipment: Use extinguishing agent suitable for type of surrounding fire.

Water Spray: OK Carbon Dioxide: OK Halon: OK

Foam: OK Dry Chemical: OK Other: Any "ABC" Class

Unusual Fire and Explosion Hazards: No unusual fire or explosion hazards are expected.

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

Special Fire Fighting Procedures.: For fires beyond the incipient stage, emergency responders in the immediate hazard area should wear bunker gear. When the potential chemical hazard is unknown, in enclosed or confined spaces, or when explicitly required by DOT, a self-contained breathing apparatus should be worn. In addition, wear other appropriate protective equipment as conditions warrant (see Section 8). Isolate immediate hazard area and keep unauthorized personnel out. Contain spill if it can be done with minimal risk. Move undamaged containers from immediate hazard area if it can be done with minimal risk. Cool equipment exposed to fire with water, if it can be done with minimal risk.

NFPA HAZARD CLASS: Health: 1 (Slight)

Flammability: 0 (Least)

Reactivity: 0 (Least)

Section VI - ACCIDENTAL RELEASE INFORMATION

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.

Section VII - PRECAUTIONS FOR SAFE HANDLING AND USE

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.

Section VIII - EXPOSURE CONTROLS - PERSONAL PROTECTION

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

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.

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

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

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

Section IX - PHYSICAL/CHEMICAL CHARACTERISTICS

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:	4.0-6.0
Odor Threshold: ND			
Appearance and Color: Clear, colorless liquid			

ND = No Data

Section X - STABILITY AND REACTIVITY DATA

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.

Section XI - 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/m²/day). The 50 mg/kg/day dose was reduced to 25 mg/kg/day (150 mg/m²/day) during week 59 due to toxicity. For a 50 kg person of average height (1.46 m² body surface area), these doses represent 16, 81 and 405 times the recommended clinical dose (0.37 mg/m², 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/m²/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/m²/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/m²/day, 16 times the recommended human dose based on body surface area) in males and 5 mg/kg/day (30 mg/m²/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/m²/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.

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.

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.

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.

Section XII - ENVIRONMENTAL IMPACT 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.

Section XIII - DISPOSAL INFORMATION

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

Section XIV - 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)

Section XV - OTHER DATA

The information in this document is believed to be correct as of the date issued. However, no warranty of merchantability, fitness for any particular purpose, or any other warranty is expressed or is to be implied regarding the accuracy or completeness of this information, the results to be obtained from the use of this information or the product, the safety of this product, or the hazards related to its use. This information and product are furnished on the condition that the person receiving them shall make his own determination as to the suitability of the product for his particular purpose and on the condition that he assume the risk of his use thereof.