



IN CASE OF EMERGENCY Emergency Phone: (614) 276-4000

Material Safety Data Sheet

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION			
Common/Trade Name: Granisetron Hydrochloride Tablets			
Chemical Name: endo-N-(9-methyl-9-azabicyclo [3.3.1] non-3-yl)-1-methyl-1H-indazole-3-carboxamide hydrochloride			
Synonyms: Not applicable			
Molecular Formula: C ₁₈ H ₂₄ N ₄ O·HCl			
Molecular Weight: 348.9			
CAS No: 107007-99-8			
Chemical Family: Selective serotonin receptor antagonist			
Product Use: Antinauseant and antiemetic			
Manufacturer's Name: Roxane Laboratories Inc.			
Address: 1809 Wilson Road Columbus, Ohio 43228			
2. COMPOSITION / INFORMATION ON INGREDIENTS			
Composition	CAS#	Mg/Tablet	Exposure Limit
Granisetron Hydrochloride	107007-99-8	1.12	None established
<i>REFER to PHYSICIAN'S DESK REFERENCE for common components present as <1%</i>			
3. HAZARDS IDENTIFICATION			
Emergency Overview	Physical State: Round, biconvex 1 mg tablet debossed with product identification "54 922" on one side and plain on the other (1 blister card of 2 unit dose tablets each, or 2 blister cards of 10 unit dose tablets each). Color: White Odor: No data available WARNING! May be harmful if swallowed. Accidental ingestion of large amounts may be harmful.		
Primary Route(s) of Entry	Ingestion		
Potential Health Effects:	Inhalation: Not expected to be an inhalation hazard in final pharmaceutical form. Eye Contact: Not expected to be a hazard to the eye in final pharmaceutical form. Skin Contact: Not expected to be a hazard to the skin. Can cause hypersensitive reactions resulting in rash, redness, itching and inflammation. Ingestion: May be harmful if ingested. Ingestion may cause headache, constipation, weakness, diarrhea, abdominal pain, gastrointestinal upset, central nervous system effects, and other systemic effects.		
WARNINGS	Granisetron hydrochloride is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction. The use of granisetron hydrochloride in patients following abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distention. In most human studies, granisetron has had little effect on blood pressure, heart rate or ECG. No evidence of an effect on plasma prolactin or aldosterone concentrations has been found in other studies. In clinical studies, the safety and effectiveness of granisetron hydrochloride were maintained with increasing age.		

	<p>The safety and efficacy of granisetron hydrochloride have not been established in pediatric patients.</p> <p>Medical conditions aggravated by exposure: None known.</p> <p>Granisetron does not induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system in vitro. There have been no definitive drug-drug interaction studies to examine pharmacokinetic or pharmacodynamic interaction with other drugs; however, in humans, granisetron injection has been safely administered with drugs representing benzodiazepines, neuroleptics, and anti-ulcer medications commonly prescribed with antiemetic treatments. Granisetron injection also does not appear to interact with emetogenic cancer chemotherapies. Because granisetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes, inducers or inhibitors of these enzymes may change the clearance and, hence, the half-life of granisetron. No specific interaction studies have been conducted in anesthetized patients. In addition, the activity of the cytochrome P-450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) is not modified by granisetron in vitro. In in vitro human microsomal studies, ketoconazole inhibited ring oxidation of granisetron. However, the clinical significance of in vivo pharmacokinetic interactions with ketoconazole is not known. In a human pharmacokinetic study, hepatic enzyme induction with phenobarbital resulted in a 25% increase in total plasma clearance of intravenous granisetron. The clinical significance of this change is not known.</p>
Contraindications	Hypersensitivity to granisetron hydrochloride or any other component of the therapeutic system.
Adverse Reactions to Product:	The common side effects include mild to moderate headache, constipation, weakness, diarrhea, and abdominal pain. Additional adverse events reported include nausea, vomiting, and insomnia. Rare cases of hypersensitivity reactions, sometimes severe (eg, anaphylaxis, shortness of breath, hypotension, urticaria) have been reported.
Toxicity Data:	See Section 11
Effects of Overexposure:	The potential for exposure is reduced in finished pharmaceutical form. The signs of overdosage may include abdominal pain, gastrointestinal upset and dizziness.
Target Organs:	Central nervous system
4. FIRST AID MEASURES	
Eye Exposure	Any material that contacts the eye should be washed out immediately with water. If easy to do, remove contact lenses if worn. Get medical attention if symptoms persist.
Skin Exposure	Wash with soap and water. Get medical attention if symptoms occur.
Ingestion	Call a physician or poison control center immediately. Only induce vomiting at the instruction of medical personnel. Never give anything by mouth to an unconscious person.
Inhalation	Should not pose a hazard in the final form. Move to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.
Notes to Physician	There is no specific treatment for granisetron hydrochloride overdosage. In case of overdosage, symptomatic treatment should be given. Overdosage of up to 38.5 mg of granisetron hydrochloride injection has been reported without symptoms or only the occurrence of a slight headache.
5. FIRE AND EXPLOSION HAZARDS	
Flammability	Lower: N/A Upper: N/A
Flash Point	Not Applicable
Extinguishing Media	Use water spray chemical, carbon dioxide or material appropriate for fire in surrounding area
Special Fire Fighting Procedures	Wear full protective clothing and self-contained breathing apparatus.
Unusual Fire/Explosion Hazards	Not Applicable
Hazardous Combustion Products	Carbon dioxide, carbon monoxide, oxides of nitrogen, hydrogen chloride
6. ACCIDENTAL RELEASE INFORMATION	

STEPS TO BE TAKEN IF SIGNIFICANT QUANTITIES OF TABLETS ARE BROKEN: Use appropriate protective equipment (see Section 8). Sweep/wipe up and containerize spill material in a compatible container. Dispose according to applicable regulations. Incineration of the waste at an approved facility is recommended.					
7. PRECAUTIONS FOR SAFE HANDLING AND USE					
Precautions Handling Significant Quantities of Broken Tablets:		Avoid contact with eyes, skin and clothing. Wash thoroughly after handling.			
Storage		Store between 15° and 30°C (59° and 86°F). Keep container closed tightly. Protect from light. Store away from foodstuffs.			
8. CONTROL MEASURES AND PERSONAL PROTECTIVE EQUIPMENT					
Exposure Limits		None			
Engineering Controls		Not required when handling tablets or containers. Good ventilation (typically 10 air changes per hour) should be used. Ventilation should be matched to conditions.			
Respiratory Protection		Not required when handling tablets or containers. NIOSH/MSHA approved respirators for protection should be used if respirators are found to be necessary. Ventilation should be matched to conditions.			
Personal Protection		Not required when handling tablets. If containers are compromised or exposure is likely wear: Goggles, Lab Coat, Gloves			
Recommended Facilities		Eye wash, washing facilities			
9. PHYSICAL / CHEMICAL CHARACTERISTICS					
Appearance	Round, white, biconvex tablets	Melting point	Not available	Solubility in water	Not available
Odor	Not available	Boiling point	Not available	Specific Gravity	Not available
Taste	Not available	Vapor Pressure	Not available	Flashpoint	Not applicable
pH	Not available	Density	Not available	Flammability Limits	Not applicable
10. STABILITY AND REACTIVITY DATA					
Stability		Stable			
Incompatibility		None known			
Hazardous Decomposition		Oxides of carbon, oxides of nitrogen, hydrogen chloride			
Conditions to Avoid		Excessive heat, light			
Hazardous Polymerization		Will not occur.			
11. TOXICOLOGICAL INFORMATION					
Acute Toxicity:					
Active Ingredient:					
LD50 Oral (rat): 350 mg/kg					
LD50 Oral (mouse): 350 mg/kg					
Product:					
No data available.					
Teratogenicity: Pregnancy Category B: Reproduction studies have been performed in pregnant rats at oral doses up to 125 mg/kg/day (750 mg/m ² /day, 507 times the recommended human dose based on body surface area) and pregnant rabbits at oral doses up to 32 mg/kg/day (378 mg/m ² /day, 255 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to granisetron.					

Pregnancy: There are 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.

Nursing Mothers: It is not known whether granisetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when granisetron is administered to a nursing woman.

Carcinogenesis/Mutagenesis: In a 24-month carcinogenicity study, rats were treated orally with granisetron 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 4, 20, and 101 times the recommended clinical dose (1.48 mg/m², oral) 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, 20 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, 101 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, 4 times the recommended human dose based on body surface area) in males and 5 mg/kg/day (30 mg/m²/day, 20 times the recommended human dose based on body surface area) in females. In a 12-month oral toxicity study, treatment with granisetron 100 mg/kg/day (600 mg/m²/day, 405 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 did not show a statistically significant increase in tumor incidence, but the study was not conclusive.

Granisetron was not mutagenic in in vitro Ames test and mouse lymphoma cell forward mutation assay, and in vivo mouse micronucleus test and in vitro and ex vivo rat hepatocyte UDS assays. It, however, produced a significant increase in UDS in HeLa cells in vitro and a significant increased incidence of cells with polyploidy in an in vitro human lymphocyte chromosomal aberration test.

Impairment of Fertility: Granisetron at oral doses up to 100 mg/kg/day (600 mg/m²/day, 405 times the recommended human dose based on body surface area) was found to have no effect on fertility and reproductive performance of male and female rats.

Carcinogenicity: Not listed as a carcinogen or potential carcinogen by NTP, IARC Monographs or OSHA.

12. ENVIRONMENTAL IMPACT INFORMATION

No information is currently available on the environmental impact of this product.

13. DISPOSAL INFORMATION

Waste Disposal Considerations: Dispose of material according to federal, state and local disposal regulations or company operating procedures. Disposal by incineration is recommended.
At home: Discard away from children's reach.

14. TRANSPORTATION INFORMATION

This product is not subject to the regulations for the safe transport of hazardous chemicals.

DOT: Not regulated

TDG: Not regulated

IATA: Not regulated

IMDG: Not regulated

15. REGULATORY INFORMATION

See package insert for NDC Numbers

DEA: Granisetron hydrochloride is not a controlled substance.

FDA: Granisetron hydrochloride is an approved antiemetic and anti-nausea prescription medication.

Canadian Controlled Products Regulations: This product has been classified in accordance with the hazard criteria of the Canadian Controlled Products Regulations, Section 33, and the MSDS contains all the required information.

WHMIS Classification for Product: Not controlled, exempt.

Inventory Status: This material is not listed on the US TSCA Inventory. Therefore, it can only be used for TSCA exempt purposes such as R&D or drug use.

This material is not on the DSL Inventory but is exempt.
16. OTHER DATA
ABBREVIATIONS: N/A – not applicable
Prepared by: Roxane Laboratories, Inc.
References: <ol style="list-style-type: none">1. Granisetron Hydrochloride Tablets, Package Insert, Roxane Laboratories, Inc. , Columbus, Ohio2. RTECS No. 200009 for 1H-Indazole-3-carboxamide, 1-methyl-N-(9-methyl-9-azabicyclo(3.3.1)non-3-yl)-, monohydrochloride, endo-3. Ariel Websight. Regulatory and ChemExpert Database.4. PDR – Physicians Desk Reference
Date: 12/17/07- New MSDS
SEE CURRENT PACKAGE INSERT FOR FURTHER INFORMATION

The information provided is believed to be complete and accurate. If this product is combined with other materials, deteriorates or becomes contaminated, it may pose hazards not mentioned in this MSDS. It is the users' responsibility to use the information according to the application. Roxane Laboratories Inc. assumes no responsibility or liability resulting from the use of this information.