Material Safety Data Sheet

200R Medique Diamode

LOPERAMIDE TABLETS

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING	
Material	Loperamide Hydrochloride
Empirical Chemical Formula	$C_{29}H_{34}Cl_2N_2O_2$
Synonyms	-
Manufacturer	Ohm Laboratories, Inc., 1385 Livingston Ave. North Brunswick, NJ, 08907, USA.
Distributor	Ranbaxy Pharmaceuticals Inc., 9431, Florida Mining Blvd. East, Jacksonville, FL, 32257

2. COMPOSITION / INFORMATION ON INGREDIENTS		
Ingredients	CAS Number	Percentage
Loperamide Hydrochloride	34552-83-5	1.30%
Non-Hazardous Ingredients	–	98.70%

3. HAZARDS IDENTIFICATION	
Fire and Explosion	This material is assumed to be combustible.
Health	Adverse effects may include bloating, abdominal pain, nausea, vomiting, dizziness, dry mouth, skin rash, drowsiness, and constipation. Possible allergic reaction to material if inhaled, ingested or in contact with skin.
Environment	No environmental hazards have been identified for this material.

4. FIRST-AID MEASURES	
Ingestion	Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.
Inhalation	Remove to fresh air and keep patient at rest. Seek medical attention immediately.
Skin Contact	Wash skin with soap and water. If irritation occurs or persists, get medical attention.
Eye Contact	Flush eye(s) immediately with plenty of water. If irritation occurs or persists, get medical attention.
NOTES TO PHYSICIANS / HEALTH PROFESSIONALS	
Medical Treatment	Treat according to locally accepted protocol. For additional guidance, refer to the current prescribing information or to the local poison control information center.

	Treatment of overdose may include the following: 1. Administer activated charcoal promptly following ingestion. If vomiting has occurred spontaneously following ingestion, slurry of activated charcoal should be administered as soon as fluids can be retained. 2. Perform gastric lavage if vomiting has not occurred. 3. Use narcotic antagonists, such as Naloxone, to treat adverse effects as necessary. 4. Support respiration and provide prolonged and careful monitoring.
Medical Conditions Caused or Aggravated by Exposure	Refer to prescribing information for detail description of medical conditions caused by or aggravated by overexposure to this product. Hypersensitivity to the material, dehydration, severe colitis, antibiotic-associated diarrhea, and acute dysentery.
Antidotes	Naloxone (narcotic antagonists) may be used as an antidote.

5. FIRE-FIGHTING MEASURES	
Fire and Explosion Hazards	Not expected for the product, although the packaging is combustible.
Extinguishing Media	Use carbon dioxide, dry chemical, or water spray.
Special Firefighting Procedures	For single units (packages) – No special requirements needed. For larger amounts (multiple packages/pallets) of product – Since toxic or flammable vapours/fumes might be evolved from fires involving this product and associated packaging, self contained breathing apparatus and full protective equipment are recommended for firefighters. If possible, contain and collect firefighting water for later disposal.
Hazardous Combustion Products	May emit toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, hydrogen chloride, and other chlorine-containing compounds.

6. ACCIDENTAL RELEASE MEASURES	
Personal Precautions	Wear protective clothing and equipment consistent with the degree of hazard.
Environmental Precautions	For large spills, take precautions to prevent entry into waterways, sewers, or surface drainage systems.
Clean-up Methods	Collect and place it in a suitable, properly labelled container for recovery or disposal. Avoid raising dust. Ventilate area and wash spill site after pick-up complete.
Decontamination Procedure	No specific decontamination or detoxification procedures have been identified for this product. Water can be used for clean-up and decontamination operations.

7. HANDLING AND STORAGE	
Safe Handling and Use	Avoid breaking or crushing tablets.
Storage	No storage requirements necessary for occupational hazards. Follow product information storage instructions to maintain efficacy.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION	
PERSONAL PROTECTIVE EQUIPMENT	
Eye Protection	None required for consumer use of this product. Avoid eye contact.
Respirators	None required for consumer use of this product. If respiratory protective equipment (RPE) is used, the type of RPE will depend upon air concentrations present, required protection factor as well as hazards, physical properties and warning properties of substances present.
Other Equipment or Procedures	None required for consumer use of this product.
Work / Hygienic Practices	Follow good Industrial & Personal Hygiene practices.

9. PHYSICAL AND CHEMICAL PROPERTIES	
Physical Form (Appearance)	Color and Shape: Green capsule shaped tablets debossed with 123 on one side and bisect on the other side.

10. STABILITY AND REACTIVITY	
Stability	Stable
Conditions to Avoid	n/k

11. TOXICOLOGICAL INFORMATION	
This material contains active pharmaceutical ingredient Loperamide, the specific information on which is provided below.	
Oral Toxicity	Oral Rat : LD50: 185 mg/kg Oral Mouse : LD50: 105 mg/kg
Inhalation Toxicity	n/k

Skin Effects	n/k
Eye Effects	n/k
Target Organ Effects	n/k
Sensitisation	n/k
Genetic Toxicity	Non-mutagenic in Ames test, in *in vitro* transformation test using mammal cells, in *in vitro* SOS chromotest using E. coli, and in *in vitro* mammal tests.
Carcinogenicity	In an 18-month rat study with oral doses up to 40 mg/kg/day (21 times the maximum human dose of 16 mg/day, based on a body surface area comparison), there was no evidence of carcinogenesis.
Reproductive Effects	Fertility and reproductive performance was evaluated in rats using oral doses of 2.5, 10, and 40 mg/kg/day in one study, and 1, 5, 10, 20, and 40 mg/kg/day (females only) in a second study. Oral administration of 20 mg/kg/day (approximately 11 times the human dose based on a body surface area comparison) and higher produced strong impairment of female fertility. Treatment of female rats with up to 10 mg/kg/day p.o. (approximately 5 times the human dose based on a body surface area comparison) had no effect on fertility. Treatment of male rats with 40 mg/kg/day p.o. (approximately 21 times the human dose based on a body surface area comparison) produced impairment of male fertility, whereas administration of up to 10 mg/kg/day (approximately 5 times the human dose based on a body surface area comparison) had no effect.
Gastrointestinal Reactions	n/k
Hypersensitivity Reactions	n/k
Pharmacological Effects	*In vitro* and animal studies show that Loperamide hydrochloride acts by slowing intestinal motility and by affecting water and electrolyte movement through the bowel. Loperamide binds to the opiate receptor in the gut wall. Consequently, it inhibits the release of acetylcholine and prostaglandins, thereby reducing peristalsis, and increasing intestinal transit time. Loperamide increases the tone of the anal sphincter, thereby reducing incontinence and urgency. In man, Loperamide HCl prolongs the transit time of the intestinal contents. It reduces the daily fecal volume, increases the viscosity and bulk density, and diminishes the loss of fluid and electrolytes. Tolerance to the antidiarrheal effect has not been observed. Clinical studies have indicated that the apparent elimination half-life of Loperamide in man is 10.8 hours with a range of 9.1 - 14.4 hours. Plasma levels of unchanged drug remain below 2 nanograms per mL after the intake of a 2mg capsule of Loperamide HCl. Plasma levels are highest approximately five hours after administration of the capsule and 2.5 hours after the liquid. The peak plasma levels of Loperamide were similar for both formulations. Elimination of Loperamide mainly occurs by oxidative N-

	demethylation. Cytochrome P450 (CYP450) isozymes, CYP2C8 and CYP3A4, are thought to play an important role in Loperamide N-demethylation process since quercetin (CYP2C8 inhibitor) and ketoconazole (CYP3A4 inhibitor) significantly inhibited the N- demethylation process *in vitro* by 40% and 90%, respectively. In addition, CYP2B6 and CYP2D6 appear to play a minor role in Loperamide N-demethylation. Excretion of the unchanged Loperamide and its metabolites mainly occurs through the feces. In those patients in whom biochemical and hematological parameters were monitored during clinical trials, no trends toward abnormality during Loperamide HCl therapy were noted. Similarly, urinalyses, EKG and clinical ophthalmological examinations did not show trends toward abnormality.
Over Dosage	In cases of overdosage, urinary retention, paralytic ileus and CNS depression may occur. Children may be more sensitive to CNS effects than adults. Clinical trials have demonstrated that a slurry of activated charcoal administered promptly after ingestion of Loperamide hydrochloride can reduce the amount of drug which is absorbed into the systemetic ciculation by as much as ninefold. If vomiting occurs spontaneously upon ingestion, a slurry of 100 gms of activated charcoal should be administered orally as soon as fluids can be retained. If vomiting has not occurred, gastric lavage should be performed followed by administration of 100 gms of the activated charcoal slurry through the gastric tube. In the event of overdosage, patients should be monitored for signs of CNS depression for at least 24 hours. If symptoms of overdose occur, Naloxone can be given as an antidote. If responsive to Naloxone, vital signs must be monitored carefully for recurrence of symptoms of drug overdose for at least 24 hours after the last dose of Naloxone. In view of the prolonged action of Loperamide and the short duration (one to three hours) of Naloxone, the patient must be monitored closely and treated repeatedly with Naloxone as indicated. Since relatively little drug is excreted in the urine, forced diuresis is not expected to be effective for Loperamide hydrochloride overdosage. In clinical trials an adult who took three 20mg doses within a 24 hour period was nauseated after the second dose and vomited after the third dose. In studies designed to examine the potential for side effects, intentional ingestion of up to 60 mg of Loperamide hydrochloride in a single dose to healthy patient resulted in no significant adverse effects.

Contraindications	Loperamide HCl is contraindicated in patients with a known hypersensitivity to Loperamide hydrochloride or to any of the excipients. Loperamide HCl is contraindicated in patients with abdominal pain in the absence of diarrhea. Loperamide HCl is not recommended in infants below 24 months of age. Loperamide HCl should not be used as the primary therapy: - in patients with acute dysentery, which is characterized by blood in stools and high fever, - in patients with acute ulcerative colitis, - in patients with bacterial enterocolitis caused by invasive organisms including Salmonella, Shigella, and Campylobacter, - in patients with pseudomembranous colitis associated with the use of broad-spectrum antibiotics.
Other Information	n/k

12. ECOLOGICAL INFORMATION
This material contains an active pharmaceutical ingredient that has been tested, and no environmental effects have been identified. Local regulations and procedures should be consulted prior to environmental release. DO NOT discharge into sewer or waterways.

13. DISPOSAL CONSIDERATIONS	
Disposal Recommendations	Material should be disposed of in keeping with all local and national legislation. Packaging should be disposed of in keeping with all local and national legislation. Handle contaminated containers as product.
Regulatory Requirements	Observe all local and national regulations when disposing of this product.

14. TRANSPORT INFORMATION	
The MSDS should accompany all shipments for reference in the event of spillage or accidental release. Only authorized persons trained and competent in accordance with appropriate national and international regulatory requirements may prepare dangerous goods for transport.	
Transport Information	Transportation and shipping of this product is not restricted. It has no known, significant hazards requiring special packaging or labelling for air, maritime, US or European ground transport purposes.

15. REGULATORY INFORMATION	
EU Classification and Labelling	n/k
US OSHA Standard (29 CFR Part 1910.1200)	n/k
OTHER US REGULATIONS	
	n/k

16. OTHER INFORMATION
The above information and recommendations are believed to be correct as on date but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose. Ranbaxy shall not be held liable for any damage resulting from handling or from contact with the above product. Ranbaxy reserves the right to revise this MSDS.