SAFETY DATA SHEET

1 PRODUCT AND COMPANY IDENTIFICATION

Product name: Ribavirin Capsules

SDS No: P00000021745

Synonyms, Trade Names:
Ribavirina Capsulas, Cotronak Capsules, Rebetol Capsules, Rebetron Capsules, Rebetron Terapia Combinada, SP001487, SP000313, MK-8908 Capsules

Class:
Anti-viral purine nucleoside

Manufacturer:
Merck
One Merck Drive P.O. Box 100
Whitehouse Station, NJ, USA 08889-0100

Telephone: 908-423-1000 (General Information Only)
Fax: 908-735-1496

Contact Person: EHS Data Steward
e-mail: MSDS@merck.com

Emergency telephone: 1-908-423-6000 (24/7/365) English Only

Intended Use: Finished pharmaceutical product: Intended for the treatment of hepatitis C.

2 HAZARDS IDENTIFICATION

Emergency Overview:

Appearance:
Color: White
Form : Capsule
Odor: Unknown

Signal words WARNING!

Potential Health Effects:
General Finished pharmaceutical product. Exposure to crushed tablets or capsules may cause irritation. Suspected of causing genetic defects. Suspected of damaging fertility. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure. Do not breathe dust or vapor. Do not get in eyes, on skin, on clothing. Wash thoroughly after handling.

Potential Physical / Chemical Effects: None expected with normal handling of finished product.

Inhalation: Exposure to crushed tablets or capsules may cause irritation. Avoid breathing mists or vapors.

skin: Exposure to crushed tablets or capsules may cause irritation. Avoid contact with skin.

eye: Exposure to crushed tablets or capsules may cause irritation. Avoid contact

with eyes.

Ingestion: Intended route for clinical use. May be harmful if swallowed.

Routes of Exposure: Inhalation, Ingestion

Target Organs: blood, gastrointestinal tract

OSHA Regulatory Status This product is hazardous according to OSHA 29CFR 1910.1200.

Environment: The product is not expected to be hazardous to the environment.

OTHER INFORMATION No additional information

3 COMPOSITION / INFORMATION ON INGREDIENTS

General information: The formulations for these products are proprietary information. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the composition table. Active ingredients in any concentration are listed.

Hazardous Component(s):

Chemical name	CAS-No.	Concentration
Ribavirin	36791-04-5	66.7%
Cellulose Microcrystalline	9004-34-6	16.7%

* All concentrations are percent by weight unless ingredient is a gas. Gas concentrations are in percent by volume.

4 FIRST AID MEASURES

Inhalation: Move to fresh air. For breathing difficulties, oxygen may be necessary. If breathing stops, provide artificial respiration. Get medical attention.

Skin contact: Wash skin thoroughly with soap and water. Get medical attention if irritation persists after washing.

Eye contact: Immediately flush with plenty of water for at least 15 minutes. If easy to do, remove contact lenses. Get medical attention if symptoms occur.

Ingestion: Do not induce vomiting. Get medical attention if symptoms occur.

Notes to the physician:
Hazards: See Sections 2 and 11.See current prescribing information. Minor abnormalities in pulmonary function or exacerbation of bronchospasm or chest pain in workers with pre-existing reactive airway disease were also observed.
Treatment: Treat supportively and symptomatically.

5 FIRE-FIGHTING MEASURES

Extinguishing media: Water spray, fog, CO2, dry chemical, or alcohol resistant foam.

Unsuitable extinguishing media: None known.

Unusual Fire & Explosion Hazards: Emits toxic fumes under fire conditions.

Special Fire Fighting Procedures: Self-contained breathing apparatus and full protective clothing must be worn in case of fire.

Protective Measures: Prevent runoff from fire control or dilution from entering streams, sewers, or drinking water supply.

6 ACCIDENTAL RELEASE MEASURES

Personal precautions: Use personal protective equipment. Keep unnecessary personnel away.

Environmental precautions: Do not release into the environment.

Spill Cleanup Methods: Use a vacuum cleaner. If not possible, moisten dust with water before it is collected with shovel, broom or the like. Avoid dusty conditions and prevent wind dispersal. Collect in containers and seal securely. For waste disposal, see section 13 of the MSDS. Prevent runoff from entering drains, sewers, or streams.

7 HANDLING AND STORAGE

Handling: No specific hazard with intact tablets or capsules. In case of exposure to crushed or broken tablets/capsules, avoid contact with eyes and avoid prolonged or repeated contact with skin. Wash thoroughly after handling.

Storage: Store in a cool, dry and ventilated location

8 EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure limits:

Chemical name	Type	Exposure Limit values	Source
Cellulose Microcrystalline	TWA	10 mg/m3	US. ACGIH Threshold Limit Values (2009)
Cellulose Microcrystalline - Total dust.	PEL	15 mg/m3	US. OSHA Table Z-1 Limits for Air Contaminants (29 CFR 1910.1000) (02 2006)
Cellulose Microcrystalline - Respirable fraction.	PEL	5 mg/m3	US. OSHA Table Z-1 Limits for Air Contaminants (29 CFR 1910.1000) (02 2006)
Ribavirin	TWA	100 ug/m3 (OEB 2)	Merck

OEB (Occupational Exposure Band) is an internal Merck control band.

Protective Measures: No special containment required with normal handling of finished product. Use local exhaust ventilation to control residual dust from broken or crushed tablets when handling in bulk quantities.

Respiratory Protection: No specific recommendation made, but respiratory protection must be used if the general level exceeds the Recommended Occupational Exposure Limit

Hand protection: Disposable chemical resistant gloves wherever the potential exists for direct exposure to residual dust from crushed or broken tablets or capsules.

Eye protection: If contact is likely, safety glasses with side shields are recommended.

Skin and Body Protection: Work uniform or laboratory coat when there is potential for direct contact with

the residual dust from crushed or broken tablets.

Hygiene measures: Wash skin thoroughly with soap and water.

9 PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance:

Physical State:	Solid
Form:	Capsule
Color:	White
Odor:	Unknown

10 STABILITY AND REACTIVITY

Stability: Stable

Possibility of hazardous reactions: Stable

Conditions to avoid: Moisture. Open flames and high temperatures.

Incompatible materials: Oxidizers Strong acids. Bases.

Hazardous decomposition products: Thermal decomposition or combustion may liberate carbon oxides and other toxic gases or vapors.

11 TOXICOLOGICAL INFORMATION

General information: The information presented below pertains to the individual ingredients, and not to the mixture(s) or final formulations.

Specified substance(s):

Acute Toxicity (Oral);

Name	Test results
Ribavirin	LD50 (Rat): 5.3 g/kg LD50 (Mouse): 2,000 mg/kg LD50 (Dog): < 1,500 mg/kg Effects observed include: hemorrhage (bleeding).
Cellulose Microcrystalline	LD50 (Rat): > 5,000 mg/kg

Acute Toxicity (Dermal):

Name	Test results
Ribavirin	No data available.
Cellulose Microcrystalline	LD50 (Rabbit): > 2,000 mg/kg

Acute Toxicity (Inhalation):

Name	Test results
Ribavirin	No data available.
Cellulose Microcrystalline	LC50 (Rat, 4 h): > 5.05 mg/l

Repeated dose toxicity:

Name	Test results
Ribavirin	LOAEL (Monkey, Intramuscular, 10 d, daily): 30 mg/kg (Target Organ(s): blood, gastrointestinal tract) NOAEL (Rat, Inhalation, 90 d, daily): 7.6 mg/kg (Target Organ(s): blood, lungs) NOAEL (Dog, Oral, 365 d, daily): 5 mg/kg (Target Organ(s): blood, gastrointestinal tract) NOAEL (Mouse, Oral, 540 - 720 d, daily): 20 mg/kg (Target Organ(s): blood) NOAEL (Rat, Oral, 540 - 720 d, daily): 10 mg/kg (Target Organ(s): blood, eye) Effects observed include: retinal degeneration and cataracts. In this case, the retinal observations were specific to the rat and were not seen in other animals tested. Ribavirin appears to reduce the number of circulating red blood cells and red blood cell survival as well as inhibit the release of late stage erythrocytes from the bone marrow. All effects were reversible (weeks to months) after cessation of drug treament.
Cellulose Microcrystalline	No data available.

Inhalation: Exposure to crushed tablets or capsules may cause irritation. Avoid breathing mist or vapor.

Ingestion: Intended route for clinical use. May be harmful if swallowed.

Skin corrosion/irritation: Exposure to crushed tablets or capsules may cause irritation. Avoid contact with skin.

Serious eye damage/eye irritation: Exposure to crushed tablets or capsules may cause irritation. Avoid contact with eyes.

Respiratory sensitizer/Skin sensitizer: No data available.

Carcinogenicity: Active pharmaceutical ingredient: No evidence of carcinogenicity was observed in a two-year study in rats.

Mutagenesis: Active pharmaceutical ingredient: Equivocal results were observed in genotoxicity assays.

Reproductive toxicity: Active pharmaceutical ingredient: Decreased fertility was observed in male rats. Decreased fertility was reported in male rats. Caused adverse developmental effects in rats and rabbits.

Other Effects: The most common adverse events reported in clinical use include: hemolytic anemia. Patients receiving combination therapy experience injection site reaction, fatigue/asthenia, headache, rigors, fevers, nausea, myalgia and anxiety/emotional irritability. Adverse effects from occupational exposure by inhalation in health-care personnel include: headache, conjunctivitis, rhinitis or nasal congestion, nausea, rash, dizziness, pharyngitis, or lacrimation. Most reported effects in workers resolved within minutes to hours of removal from ribavirin exposure. Damage to soft contact lenses following repeated occupational exposure has been reported. Minor abnormalities in pulmonary function or exacerbation of bronchospasm or chest pain in workers with pre-existing reactive airway disease were also observed.

12 ECOLOGICAL INFORMATION

General information: The information presented below pertains to the individual ingredients, and not to the mixture(s) or final formulations.

Ecotoxicity: Active pharmaceutical ingredient: ASRIT (Activated Sludge Respiration Inhibition Test) (3 hours) EC 50 > 1000

Product:

Chronic Toxicity(Fish): No data available.

Chronic Toxicity(Aquatic invertebrates): No data available.

Specified substance(s):

Acute toxicity(Fish):

Name	Test results
Ribavirin	LC50 (Rainbow Trout (Oncorhynchus mykiss), 96 h): > 119 mg/l No effects seen up to highest concentration tested (reported).
Cellulose Microcrystalline	LC50 (Trout family (Salmonidae), 96 h): > 100% Saturated solution.

Acute toxicity(Aquatic invertebrates):

Name	Test results
Ribavirin	EC 50 (Water flea (Daphnia magna), 48 h): > 117 mg/l No effects seen up to highest concentration tested (reported).
Cellulose Microcrystalline	LC50 (Water Flea, 48 h): > 100 % Saturated solution.

Acute toxicity(Aquatic plants):

Name	Test results
Ribavirin	EC 50 (Green algae (Pseudokirchneriella subcapitata), 96 h): > 119 mg/l (growth) NOEC (Green algae (Pseudokirchneriella subcapitata), 96 h): 6.9 mg/l (growth)
Cellulose Microcrystalline	EC 50 (Algae, algal mat (Algae), 96 h): > 100% Saturated solution.

Persistence and degradability: No data available.

Bioaccumulative potential: Active pharmaceutical ingredient: Not likely to bioaccumulate based on log Kow

Mobility: No data available.

13 DISPOSAL CONSIDERATIONS

Disposal Methods: Do not allow runoff to sewer, waterway or ground. Discharge, treatment, or disposal may be subject to national, state, or local laws.

Measures for Avoidance and Recovery: Incineration is the most effective method of disposal in most instances. Do not allow runoff to sewer, waterway or ground. Operations that involve the crushing or shredding of waste materials or returned goods should take into account recommended exposure limits where they exist.

14 TRANSPORT INFORMATION

DOT
Not regulated.

IMDG - International Maritime Dangerous Goods Code
Not regulated.

IATA - International Air Transport Association
Not regulated.

15 REGULATORY INFORMATION

US Regulations

- **CERCLA Hazardous Substance List (40 CFR 302.4):**
  None

- **Clean Water Act Section 311 Hazardous Substances (40 CFR 117.3):**
  None

- **Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130):**
  None

SARA Title III

- **Section 302 Extremely Hazardous Substance (40 CFR 355, Appendix A):**
  None

- **Section 313 Toxic Release Inventory (40 CFR 372):**
  None present or none present in regulated quantities.

State Regulations

- **California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65):**
  Ribavirin — Hazard Designation: Developmental toxin.
  Hazard Designation: Male reproductive toxin.

- **Massachusetts Right-To-Know List:**
  Cellulose Microcrystalline — Listed

- **New Jersey Right-To-Know List:**
  Cellulose Microcrystalline — Listed

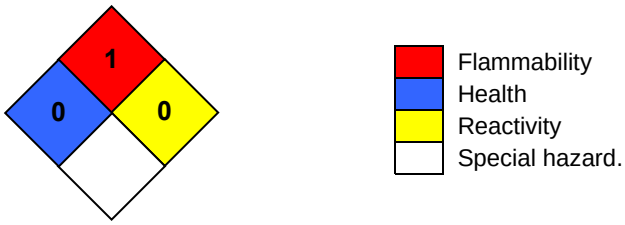
- **Pennsylvania Right-To-Know List:**
  Cellulose Microcrystalline Listed

16 OTHER INFORMATION

OTHER INFORMATION

This SDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate SDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

NFPA Hazard ID



Hazard rating: 0 - Minimal; 1 - Slight; 2 - Moderate; 3 - Serious; 4 - Severe

Revision Information: Not relevant.
Issue Date: 27.01.2014
Disclaimer: This information is provided without warranty. The information is believed to be correct. This information should be used to make an independent determination of the methods to safeguard workers and the environment.