



MATERIAL SAFETY DATA SHEET

Revision date: 24-Mar-1998

Version: 1.1

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1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND THE COMPANY/UNDERTAKING

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CHEMTREC (24 hours): 1-800-262-8200

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Trovafloxacin mesylate film coated tablets

Trade Name: Not determined
Synonyms: TROVAN® tablets
Chemical Family: Fluoronaphthyridone
Intended Use: Antibiotic agent

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS List	%
Croscarmellose sodium	74811-65-7	Not listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	*
Magnesium stearate	557-04-0	209-150-3	*
Trovafloxacin mesylate	147059-75-4	Not listed	*

Additional Information: * Proprietary

3. HAZARDS IDENTIFICATION

Appearance: 100 mg: Blue, round convex, film coated tablets, debossed "Pfizer" on one side and "378" on the other side
200 mg: Blue, modified oval, film coated tablets, debossed "Pfizer" on one side and "379" on the other side

Signal Word: CAUTION

Statement of Hazard: Accidental ingestion of large amounts of this material may be harmful; see known clinical effects, below
May be a liver or reproductive toxin (based on animal data)

Eye Contact: None known

Skin Contact: None known

Inhalation: None known

Ingestion: Abdominal pain, constipation, fatigue, and drowsiness have also been reported.

Known Clinical Effects: Ingestion of this material may cause effects similar to those seen in clinical use including dizziness, nausea, headache, vomiting, vaginitis, diarrhea, and rash. Individuals sensitive to this material or other materials in its chemical class may develop allergic reactions.

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Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

4. FIRST AID MEASURES

Eye Contact: Immediately flush eyes with water for at least 15 minutes. Get medical attention.

Skin Contact: Wash skin with soap and water. Remove contaminated clothing and shoes. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder. If irritation occurs or persists, get medical attention.

Ingestion: Get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention immediately.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Emits toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, sulfur oxides, and other fluorine- and sulfur-containing compounds.

Fire Fighting Procedures: Wear approved positive pressure, self-contained breathing apparatus and full protective turn out gear. Evacuate area and fight fire from a safe distance.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting: Contain the source of the spill or leak. Wipe up with a damp cloth and place in container for disposal. Clean spill area thoroughly.

Measures for Environmental Protections: Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Additional Consideration for Large Spills: Review Sections 3, 8 and 12 before proceeding with clean up. Vacuum or sweep material into appropriate recovery container. Close container and move it to a secure holding area.

7. HANDLING AND STORAGE

General Handling: Eliminate possible ignition sources (e.g., heat, sparks, flame, impact, friction, electricity), and follow appropriate grounding and bonding procedures. Minimize dust generation and accumulation. Use only in a well-ventilated area. IF TABLETS OR CAPSULES ARE CRUSHED AND/OR BROKEN, AVOID BREATHING DUST AND AVOID CONTACT WITH EYES, SKIN AND CLOTHING.

Storage Conditions: Keep container tightly closed when not in use. Store out of direct sunlight in a well ventilated area at room temperature.

Storage Temperature 15 - 30 °C

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8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Microcrystalline cellulose

OSHA - Final PELs - TWAs

15 mg/m³ total dust

5 mg/m³ respirable fraction

ACGIH Threshold Limit Value (TWA)

10 mg/m³ TWA

Analytical Method: No method available

Engineering Controls: Good general ventilation should be sufficient to control airborne levels.

Personal Protective Equipment:

Hands: None required under normal and foreseeable conditions of use.

Eyes: Not required under normal conditions of use.

Skin: None required under normal and foreseeable conditions of use.

Respiratory protection: None required under normal conditions of use. Use dust mask for dusty conditions.

9. PHYSICAL AND CHEMICAL PROPERTIES:

Physical State: Tablet

Color: White

Molecular Formula: Mixture

Molecular Weight: Mixture

10. STABILITY AND REACTIVITY

Stability: Stable

Conditions to Avoid: High temperatures

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers.

Hazardous Decomposition Products: No data available

Polymerization: Will not occur

11. TOXICOLOGICAL INFORMATION

NTP: Not classified

IARC: Not classified

OSHA: No

Microcrystalline cellulose

Rat Oral LD50 > 5000 mg/kg

Rabbit Dermal LD50 > 2000 mg/kg

Magnesium stearate

Rat Oral LD50 > 2000 mg/kg

Rat Inhalation LC50 > 2000 mg/m³

Ingestion Acute Toxicity

The minimum lethal dose upon oral administration of trovafloxacin in rats or mice was found to be greater than 2000 mg/kg for either sex of either species. The intraperitoneal minimum lethal dose of this material was 250 mg/kg and 500 mg/kg in mice and rats, respectively. Signs of toxicity in acute studies included decreased activity and respiration, ptosis, piloerection, prone positioning, unsteady movements, and decreased body weight gain.

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Microcrystalline cellulose

Skin Irritation Rabbit Non-irritating

Eye Irritation Rabbit Non-irritating

Eye Irritation / Sensitization

A positive reaction characterized by moderate conjunctival reddening or iritis was seen after instillation of 0.1 mL of trovafloxacin into one eye of each rabbit.

Skin Irritation / Sensitization

No evidence of systemic toxicity associated with a topical dose of trovafloxacin at 2000 mg/kg in rabbits. A minimal skin response (very slight or well defined reddening) was seen following 24 hours of exposure to this material under an occlusive dressing. These results suggest that while minimally irritating trovafloxacin is not poisonous or corrosive upon dermal exposure.

Subchronic Effects

Repeat-dose and subchronic oral toxicity studies for trovafloxacin were conducted in rats and dogs for 1- and 6-months. In a 1-month rat study, there were no drug-related changes reported upon histopathologic examination. Salivation was observed immediately after dosing at the high dose (200 mg/kg/day) with decreased body weight gain in males. In a 6-month oral toxicity study, salivation was also noted in mid- and high-dose rats, with inhibition of weight gain in high-dose males. In this study, a slight increase in the amount of fat in the livers of mid- and high-dose males was reported, and testicular degeneration was observed at all dose levels. In dogs, oral administration of trovafloxacin at doses of 5, 15 and 50 mg/kg/day for 1-month, produced vomiting (50 mg/kg/day) and mild reddening of the ears, which was noted at all dose levels. In the 6-month study, liver changes and testicular degeneration were observed in the high-dose animals (50 mg/kg/day). In a separate study, the effects on the liver were seen to be reversible 2 months after cessation of treatment.

Chronic Effects/Carcinogenicity

No long-term toxicity studies have been conducted to evaluate the chronic toxicity or carcinogenic potential of this material.

Reproductive Effects

Trovafloxacin was evaluated in a maternal toxicity study and fertility study in rats at doses of 25, 75 or 200 mg/kg/day. In the maternal toxicity study, decreases in maternal body weight in conjunction with decreases in food consumption were observed at all dose levels. In the fertility study, the same findings were seen at the high dose only and the copulation rate was slightly lower than in the high dose group as compared to the control group. Slight decreases in the number of implantation sites, number of live fetuses, and fetal body weights were also seen in both studies in the high-dose animals. In males treated prior to mating, enlarged ceca were reported in all dose groups and the mean organ weights of the epididymides, prostate, and seminal vesicles were decreased at 75 and 200 mg/kg/day. In a study of the peri- and postnatal effects, abnormal birthing and increased number of pups found dead at birth were noted through the first pregnancy cycle, F0 to F1 mating, at 75 mg/kg; the mean length of gestation was also increased at all levels. Early appearance of certain developmental milestones was seen at 15 and 75 mg/kg/day and increased peri- and postnatal mortality was seen at 75 mg/kg/day. However, the second mating cycle, F1 to F2 mating, proceeded normally.

Teratogenicity

The teratogenic potential of trovafloxacin was evaluated in rats at doses of 5, 15, or 75 mg/kg/day during days 6 through 17 of gestation. No drug-related maternal toxicity, embryomortality, or effects on fertility were noted. The high-dose group, fetuses experienced a slight delay in skeletal ossification and an increase in skeletal variations. Pregnant rabbits were administered trovafloxacin at doses ranging from 5 to 125 mg/kg/day during organogenesis (pilot study 25, 75, 125 mg/kg/day, definitive study 5, 15, 45 mg/kg/day). Abortions occurred at doses greater than 45 mg/kg/day and decreases in body weight gain and food consumption were reported at doses greater than 25 mg/kg/day. There were no viable fetuses at the highest dose (125 mg/kg/day) and an increase in embryomortality and decreased fetal body weight were seen at 75 mg/kg/day. In these studies, the maternal No-Observed-Adverse-Effect Level (NOAEL) was 15 - 25 mg/kg/day and fetal NOAEL ranging from less than 25 - 45 mg/kg/day. Liver

Mutagenicity

No evidence of mutagenicity was observed for this substance when it was tested in the following in vitro and in vivo assays: the Ames test, the microbial mutation assay, the mammalian cell gene mutation assay using (CHO/HGPRT), and the chromosomal aberrations assay using human lymphocytes and mouse bone marrow cells. No chromosomal aberrations or gene mutations in mammalian cells were observed for neither compound.

Carcinogen Status:

Not listed as a carcinogen by IARC, NTP or US OSHA.

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At increase risk from exposure: Individuals with a known history of hypersensitivity to this material or other materials in its chemical class and individuals with liver conditions and/or impaired liver function may be more susceptible to toxicity in cases of overexposure.

Additional Information: FDA PREGNANCY CATEGORY C. No adequate and well-controlled studies in pregnant women. Animal studies have shown adverse effects on the fetus. In clinical usage, it is considered that potential therapeutic benefits to the pregnant women may be acceptable despite the risk to the fetus.

12. ECOLOGICAL INFORMATION

Environmental Overview: The use and/or disposal of this material, its metabolites and degradation products is not expected to cause adverse effects upon animals, plants, humans, other organisms, or the environment.

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Incineration is the recommended method of disposal for this material. This material may also be disposed in landfills. Observe all local and national regulations when disposing of this material.

14. TRANSPORT INFORMATION

Not regulated

Proper shipping name: Trovafloxacin mesylate tablets

15. REGULATORY INFORMATION

OSHA Label:

CAUTION

Accidental ingestion of large amounts of this material may be harmful; see known clinical effects, below May be a liver or reproductive toxin (based on animal data)

Canada - WHMIS: Classifications

WHMIS hazard class:

None required

Microcrystalline cellulose
EU EINECS List

232-674-9

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Inventory - United States TSCA - Sect. 8(b)	Listed
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Magnesium stearate	
EU EINECS List	209-150-3
Inventory - United States TSCA - Sect. 8(b)	Listed

16. OTHER INFORMATION

Prepared by: Corporate Occupational Toxicology & Hazard Assessment

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without a warranty of any kind, expressed or implied.

End of Safety Data Sheet