

SAFETY DATA SHEETS

This SDS packet was issued with item:

078073682

N/A



Schering-Plough Animal Health Corporation
1095 Morris Ave
Union, NJ 07083

MATERIAL SAFETY DATA SHEET

Schering-Plough urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

MSDS NAME: Gentocin Durafilm Ophthalmic Solution

SYNONYM(S): None

MSDS NUMBER: SP000373

EMERGENCY NUMBER(S): Schering-Plough Security Control Center (908) 820-6921 (24 hours)

Transportation Emergencies -
CHEMTREC: (800) 424-9300 (Inside Continental USA)
(703) 527-3887 (Outside Continental USA)

Rocky Mountain Poison Center (For Human Exposure):
(303) 595-4869

Animal Health Technical Services:
For Animal Adverse Events: Small Animals and Horses: (800) 224-5318
For Animal Adverse Events: Livestock: (800) 211-3573
For Animal Adverse Events: Poultry: (800) 219-9286

INFORMATION: Animal Health Technical Services:
For Small Animals and Horses: (800) 224-5318
For Livestock: (800) 211-3573
For Poultry: (800) 219-9286

SCHERING-PLOUGH MSDS HELPLINE: (800) 770-8878 (US and Canada)
(908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Veterinary product

CHEMICAL FORMULA: Mixture.

The formulation for this product is 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 Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 3.

CHEMICAL COMPOSITION

CHEMICAL NAME	CAS NUMBER	PERCENT
Gentamicin Sulfate	1405-41-0	0.33
Betamethasone Acetate	987-24-6	0.1
Polyethylene Glycol Usp	9004-99-3	< 10

ADDITIONAL INFORMATION: This MSDS 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 MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

SECTION 3. HAZARDS IDENTIFICATION

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Published Date: 08-Jun-2004

EMERGENCY OVERVIEW

Clear, Light yellow

Solution

Odor unknown

Irritating to eyes.

May be toxic by inhalation.

May cause dermal sensitization.

May be irritating to respiratory system.

May be absorbed through the skin.

May be a reproductive toxicant.

May cause developmental effects.

Causes effects to:

- skin
- endocrine system

May cause effects to:

- nervous system
- gastrointestinal tract
- immune system
- liver
- kidney
- reproductive system
- fetus

POTENTIAL HEALTH EFFECTS:

The toxicological properties of the mixture(s) have not been fully characterized in humans or animals. However, there are data to describe the toxicological properties of the individual ingredients. The following summary is based upon available information about the individual ingredients of the mixture(s), or of the expected properties of the mixture(s).

Reported occupational effects for some corticosteroids include nasal irritation or burning, occasional sneezing, runny or bloody nose, and allergic skin reactions such as dermatitis and rash. Rare instances of nasal ulceration, septum perforation and increased intraocular pressure have been reported. Persons with pre-existing skin conditions including dermatitis and acne, a history of asthma, or those taking or those with a history of taking systemic steroids are more susceptible to allergic reactions from exposure to steroids.

Betamethasone is an anti-inflammatory corticosteroid used in the treatment of various disease states. As a class, corticosteroids are known to cause systemic effects such as reversible suppression of the hypothalamic-pituitary-adrenal (HPA) axis, increased blood sugar, sugar in the urine, impairment of glucose tolerance, and changes in general metabolism, bone metabolism, white blood cell counts, and some blood serum chemistry levels. The clinical relevance of these changes in healthy adults is unknown. Cushing's syndrome may occur from excessive exposure to corticosteroids. Use of aerosolized corticosteroid inhalers has caused nasal irritation or burning, occasional sneezing, runny or bloody nose. Rare instances of nasal ulceration, septum perforation and increased intraocular pressure have been reported following prolonged use of or overexposure to aerosolized corticosteroids. Prolonged use of systemic steroids is also known to be associated with the formation of cataracts and glaucoma. Corticosteroids may mask some signs of infection, and opportunistic infections may appear during their use due to effects on immune system. Persons with pre-existing skin conditions including dermatitis and acne, a history of asthma, or those taking or those with a history of taking systemic steroids are more susceptible to allergic reactions from exposure to steroids. Serious health effects including death have occurred in asthmatic patients during transfer from systemic corticosteroid to topical corticosteroid clinical use.

The most common side effects in studies with betamethasone-containing topical preparations were local, including erythema, steroid-induced rosacea (redness, acne-like reaction on face), mild burning, itching, skin dryness and irritation. Betamethasone has been shown to decrease collagen synthesis in human skin following treatment with topical cream. Adverse reactions reported following injection of betamethasone include effects on fluid and electrolytes, musculoskeletal, gastrointestinal, dermatologic, neurological, endocrine, ophthalmic and metabolic parameters.

In animal studies, betamethasone acetate was shown to be toxic by inhalation.

Corticosteroids are teratogenic in laboratory animals and may be considered teratogenic in non-human primates as well. Widespread clinical use of corticosteroids has resulted in very few reports of teratogenic activity in humans. There is no evidence of impaired fertility in humans treated with corticosteroids although hypo-adrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy.

Gentamicin sulfate, an active ingredient, is an aminoglycoside antibiotic that acts by inhibiting normal protein synthesis in susceptible bacteria. Gentamicin sulfate may be irritating to the eyes and skin. It may cause damage to the nervous system and kidneys. Balance and hearing problems may occur as well as numbness and convulsions. Gentamicin sulfate may produce severe reactions in persons allergic or sensitized to aminoglycoside antibiotics. Exposure to gentamicin sulfate by individuals already using potent diuretics should be avoided.

Aminoglycosides, the class to which gentamicin sulfate belongs, are associated with significant nephrotoxicity (kidney damage) and neurotoxicity (nervous system damage), the latter manifested by ototoxicity (ear damage), numbness, and convulsions. Aminoglycosides can cause fetal harm since they can cross the placenta. Animal reproduction studies did not reveal evidence of impaired fertility or harm to the fetus due to gentamicin sulfate. It is not known; however, whether fetal harm or effects on the reproductive capacity can be caused by exposure to gentamicin sulfate by pregnant women.

LISTED CARCINOGENS

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

SECTION 4. FIRST AID MEASURES

INHALATION:	Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.
SKIN CONTACT:	In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.
EYE CONTACT:	In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.
INGESTION:	Rinse mouth and drink a glass of water. Do not induce vomiting. If symptoms persist, consult a physician.
NOTE TO PHYSICIAN:	Gentamicin sulfate is a aminoglycoside antibiotic. Allergic reactions may occur in susceptible individuals. Exposure to gentamicin sulfate by individuals already using potent diuretics should be avoided. This product contains a steroid hormone. Persons with a prior history of asthma, treatment with systemic steroids, or pre-existing skin conditions, such as acne and dermatitis, may be more susceptible to the adverse effects of steroid exposure. Serious health effects including death have occurred in asthmatic patients during transfer from systemic corticosteroid to topical corticosteroid clinical use.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

FLASH POINT: 93.3 deg C (200 deg F)

SPECIAL FIRE FIGHTING PROCEDURES:

Wear full protective clothing and self-contained breathing apparatus (SCBA).

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SUITABLE EXTINGUISHING MEDIA:

Carbon dioxide (CO₂), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES**PERSONAL PRECAUTIONS:**

Keep personnel away from the clean-up area. Wear appropriate personal protective equipment as specified in Section 8.

SPILL RESPONSE / CLEANUP:

All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. For laboratories and small-scale operations, incidental spills within a hood or enclosure should be cleaned by using a HEPA filtered vacuum or wet cleaning methods as appropriate. For large dry or liquid spills or those spills outside enclosure or hood, appropriate emergency response personnel should be notified. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7. HANDLING AND STORAGE**HANDLING:**

Keep containers adequately sealed during material transfer, transport, or when not in use.

Appropriate handling of this material is dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:

Store between 2 and 30 deg C (36 and 86 deg F).

See Section 8 for exposure controls and additional safe handling information.

SECTION 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

The following guidance applies to the handling of the active ingredient(s) in this formulation.

S-P OCCUPATIONAL EXPOSURE GUIDELINE (OEG):

Schering-Plough Corporation has established an Occupational Exposure Guideline of 5 mcg/m³ (8-hr TWA) for betamethasone (base).

EXPOSURE CONTROLS:

The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. However, PPE should not be used as a method of permanent or long-term exposure control. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection:	Respiratory protective equipment (RPE) may be required for certain laboratory and large-scale manufacturing tasks if potential airborne breathing zone concentrations of substances exceed the relevant exposure limit(s). Workplace risk assessment should be completed before specifying and implementing RPE usage. Potential exposure points and pathways, task duration and frequency, potential employee contact with the substance, and the ability of the substance to be rendered airborne during specific tasks should be evaluated. Initial and ongoing strategies of quantitative exposure measurement should be obtained as required by the workplace risk assessment. All RPE must conform to local and regional specifications for efficacy and performance. Consult your site or corporate health and safety professional for additional guidance.
Skin Protection:	Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.
Eye Protection:	Safety glasses with side shields. Use of goggles or full face protection is required if there is potential for contact with this material. Consult your site safety staff for guidance.

Body Protection:

In small-scale or laboratory operations, lab coats or equivalent protection is required. Disposable Tyvek or other dust impermeable suit should be considered based on procedure or level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

In large-scale or manufacturing operations, disposable Tyvek or other dust impermeable suit is recommended and based on level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

EXPOSURE LIMIT VALUES

See Schering-Plough occupational exposure guideline (OEG) listed above.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM: Solution
COLOR: Clear, Light yellow
ODOR: Odor unknown
pH: 5.5-7.0
SOLUBILITY:
Water: Not determined

See Section 5 for flammability/explosivity information.

SECTION 10. STABILITY AND REACTIVITY**STABILITY/ REACTIVITY:**

Stable under normal conditions.

INCOMPATIBLE MATERIALS / CONDITIONS TO AVOID:

Open flames and high temperatures.

SECTION 11. TOXICOLOGICAL INFORMATION

The toxicological properties of this material have not been fully characterized in humans or animals. The information presented below pertains to the following individual ingredients in this formulation, unless indicated otherwise.

ACUTE TOXICITY DATA**INHALATION:**

Gentamicin sulfate: LC50: > 0.20 mg/L (rat)

In an acute inhalation toxicity study in rats at 0.20 mg/L, animals exhibited labored breathing and eye closure during exposure to gentamicin sulfate. Nasal discharge was noted for several days followed by recovery.

In an acute inhalation toxicity study in rats, betamethasone acetate has an LC50 of 0.28 mg/L (maximum obtainable dose). Gross toxic effects observed included reduced activity and eye closure during exposure. Emaciation and nasal discharge, with some mortality, occurred during the second week after exposure. Recovery from these effects was not seen in this study.

No mortalities were reported in rats following a 4-hour exposure to polyethylene glycol generated at 170 deg C.

SKIN:

Gentamicin sulfate was slightly irritating to the skin of rabbits (PII 1.0).

Betamethasone produced erythema which was present five hours after dosing in a skin irritation study in rabbits but resolved by 96 hours after dosing. There were no adverse skin changes detected in dermal toxicity studies of betamethasone dipropionate cream (0.05% or 0.1%) in hairless mice, rats, rabbits or dogs.

Polyethylene glycols (200-9000): Dermal LD50: >20 g/kg (unspecified species).

Polyethylene glycol was not irritating to the skin of rabbits and guinea pigs.

Polyethylene glycol was not irritating in a human patch test.

EYE:

Eye irritation studies using Gentamicin Ophthalmic Solutions (0.1% and 0.3%) were performed in rabbits. The concentrations tested were non-irritating, no significant changes were observed in the cornea, iris or conjunctivae of any of the animals tested.

ORAL:

In acute oral toxicity studies in rats and mice, using Gentocin Durafilm Ophthalmic Solution, mortality occurred in 0/0 mice in the 100 ml/kg group and 1/6 rats in the 50 ml/kg group. In mice, no changes in behavior or appearance were seen following treatment. The maximum tolerated dose was in excess of 100 ml/kg. In rats, one death occurred in the treated group eight days after treatment and no abnormalities were observed upon necropsy of the animal. At necropsy, two rats from the treated group exhibited pale kidneys. These effects were not observed in rats in the non-treated group.

SENSITIZATION:

A betamethasone dipropionate (0.05%) ointment formulation was determined to be a potentially weak sensitizer in guinea pigs. Local irritation at the intradermal injection sites was observed during the induction phase.

Polyethylene glycols did not produce skin sensitization in guinea pigs.

REPEAT DOSE TOXICITY DATA**SUBCHRONIC / CHRONIC TOXICITY:**

In a 7-day comparative eye irritation study in rabbits using domestic and international vehicles alone and with 0.3% Gentamicin, no significant changes were observed in the cornea, iris or conjunctivae of any animals tested. No diffuse or persisting redness, chemosis, discharge of the conjunctivae or evidence of irritation was observed. In a 21-day ocular toxicity study, Ophthalmic Durafilm Gentamicin with Celestone Solution was not irritating when applied to the eyes of rabbits. Another 21-day ocular toxicity study was conducted in rabbits using Betamethasone-Gentamicin eye drops. Except for the sporadic mild hyperemia of the conjunctivae and a slight discharge observed during the first week of testing, the treated eyes did not exhibit any inflammatory signs or abnormalities of the cornea, iris, lens, or fundus oculi.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:

A reproduction study with gentamicin sulfate was conducted in rabbits. On gestation days 6-16, dose levels of 0.8 and 3.6 mg/kg were injected intramuscularly. There were no adverse findings in the offspring noted. In rats and guinea pigs, fetal renal abnormalities have been reported after administration of gentamicin to the dam. In guinea pigs, transient renal abnormalities were observed in the fetus after the administration of 4 mg/kg of gentamicin to the mother. In two reproduction studies, rats were administered 75 mg/kg of gentamicin in saline by intraperitoneal or intramuscular injection for 12 days from day 10 of gestation to delivery or on days 7-11 and 14-18 of pregnancy, respectively. Adverse effects reported included focal tubular lesions in the developing kidney, reduced rate of early nephrogenesis, general growth retardation, and alterations of the glomeruli and proximal tubules. Other animal reproduction studies in rats and rabbits did not exhibit any evidence of impaired fertility or harm to the fetus following exposure to gentamicin sulfate.

Corticosteroids are known teratogens in rodent species with some teratogenic effects having been observed in non-human primates. They are generally teratogenic in laboratory animals when administered systemically at low dosages.

Subcutaneous administration of up to 0.42 mg of a mixture of betamethasone/sodium phosphate and betamethasone/acetate suspension, on days 12 and 13 of gestation in pregnant rats, caused decreases in maternal and fetal weight gain, occurrence of cleft palate and omphalocele (umbilical hernia), and impaired growth of fetal heart, liver, adrenals, kidneys, and skeletal muscle. Dose-related increases in fetal resorptions in rabbits and mice following single intramuscular doses up to 1 and 33 mg/kg, respectively were observed. Additionally, betamethasone dipropionate has been shown to produce umbilical hernias, cephalocele (cranial protrusion) and cleft palate in rabbits when given intramuscular doses of 0.05 mg/kg/day during gestation. Suppression of adrenocorticotrophic hormone (ACTH), following intramuscular administration of betamethasone in monkeys during gestation resulted in decreases in fetal adrenal weight, cortical cell size, appearance of apoptosis and cellular disorganization.

Polyethylene glycol 200 was developmentally toxic in mice, causing malformations and other fetotoxicity, but elicited no similar response in rats at higher doses.

MUTAGENICITY / GENOTOXICITY:

Betamethasone was negative in a bacterial mutagenicity study (Ames) and mammalian cell mutagenicity assay (CHO/HGPRT) and positive in the in vitro human lymphocyte chromosome aberration assay. Equivocal results were seen in the in vivo mouse bone marrow micronucleus assay.

Polyethylene glycol was negative in a bacterial mutagenicity study (Ames), results were inconclusive in a bacterial DNA repair study.

CARCINOGENICITY:

This material has not been evaluated for carcinogenicity.

SECTION 12. ECOLOGICAL INFORMATION**ECOTOXICITY DATA**

There are no ecotoxicity data available for this product or its components.

ENVIRONMENTAL DATA

There are no environmental data available for this product or its components.

SECTION 13. DISPOSAL CONSIDERATIONS**MATERIAL WASTE:**

Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the recommended exposure limit.

PACKAGING AND CONTAINERS:

Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SECTION 14. TRANSPORT INFORMATION

This material is not subject to the transportation regulations of DOT, ICAO, IMO, and the ADR.

SECTION 15. REGULATORY INFORMATION**TSCA LISTING**

CHEMICAL NAME	TSCA
Polyethylene Glycol Usp	Listed

U.S. STATE REGULATIONS

Check state requirements for ingredient listing.

SECTION 16. OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

DEPARTMENT ISSUING MSDS:

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Monday to Friday, 9am to 5pm (US Eastern Time)

MSDS CREATION DATE:

16-Mar-1992

SUPERSEDES DATE:

01-Jan-1993