



Merck & Co., Inc.
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Whitehouse Station, NJ 08889

MATERIAL SAFETY DATA SHEET

Merck Animal Health 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:	OTOMAX
SYNONYM(S):	Otomax CGB ointment Malotic ointment Otomax ointment
MSDS NUMBER:	SP000063
EMERGENCY NUMBER(S):	(908) 423-6000 (24/7/365) English Only Emergencies - CHEMTREC: (800) 424-9300 (Inside Continental USA) (703) 527-3887 (Outside Continental USA)
MERCK MSDS HELPLINE:	(800) 770-8878 (US and Canada) (908) 473-3371 (Worldwide) Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Viscous suspension
Light beige
Oil odor
May be absorbed through the skin.
May be harmful if absorbed through skin or if swallowed.
May cause dermal sensitization.
May be a reproductive toxicant.
May cause developmental effects.
Causes effects to:
skin
endocrine system

May cause effects to:
nervous system
musculoskeletal 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). Only information about the ingredients that are expected to contribute significantly to the potential health hazard profile of the formulation(s) are presented.

Clotrimazole is a broad-spectrum anti-fungal agent used for the treatment of dermal infections. Clotrimazole is poorly absorbed by skin or mucous membranes in humans. Clinical effects reported following the application of clotrimazole, as a 1% cream, on the skin included stinging, itching, redness, swelling, blisters, burning, peeling, itching eruptions (urticaria), and general irritation of the skin. Clotrimazole may cause sensitization of the skin in sensitive individuals. Reversible liver effects have also occurred in patients following clotrimazole treatment.

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.

Reported occupational effects include allergic skin reactions such as dermatitis and rash.

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.

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.

Ingestion of mineral oil may cause laxative effect, nausea, dehydration or lipid pneumonia. Long-term dermal exposure to mineral oil may cause dermatitis and oil acne.

LISTED CARCINOGENS

INGREDIENT	CAS NUMBER	OSHA	IARC	NTP	ACGIH
Mineral Oil	8012-95-1				A2

This product contains a highly refined grade of mineral oil which is not classified as a carcinogen by IARC or NTP.

SECTION 3. 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 2.

CHEMICAL COMPOSITION

INGREDIENT	CAS NUMBER	PERCENT
Betamethasone Valerate	2152-44-5	0.12
Ethene Homopolymer (Polyethylene)	9002-88-4	29.88
Gentamicin Sulfate (Preservative)	1405-41-0	0.5
Clotrimazole	23593-75-1	1
Mineral Oil	8012-95-1	65-75

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 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 unless under the direction of a qualified medical professional or Poison Control Center. If symptoms persist, consult a physician.

NOTE TO PHYSICIAN: This product contains clotrimazole, a broad spectrum antifungal agent, and betamethasone dipropionate, a steroid hormone. This product is indicated for the topical treatment of dermal infections. 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 exposure to this product. 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: Not determined (liquids) or not applicable (solids).

SPECIAL FIRE FIGHTING PROCEDURES:

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

SUITABLE EXTINGUISHING MEDIA:

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

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SECTION 5. FIRE FIGHTING MEASURES

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:

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

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. Wash face, hands, and any exposed skin after handling. Do not eat, drink, or smoke when using this substance or mixture.

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 in a cool, dry, well ventilated area.

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.

OCCUPATIONAL EXPOSURE BAND (OEB):

OEB 4: 1-10 mcg/m³. Materials in an OEB 4 category are considered high health hazards. The OEB is range of airborne concentrations expressed as an 8-hour Time Weighted Average (8-hr. TWA) and is intended to be used with Industrial Hygiene Risk Assessment to assist with industrial hygiene sampling and selection of proper controls for worker protection. Consult your site safety and industrial hygiene staff for guidance on handling and control strategies.

OCCUPATIONAL EXPOSURE GUIDELINE (OEG):

An Occupational Exposure Guideline of 5 mcg/m³ (8-hr TWA) has been established for betamethasone (base).

OEB/OEL NOTATION(S):

Betamethasone: This material has a notation of "S" for its ability to cause systemic toxicity through skin absorption.

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. 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 may be required based on hazard, potential for contact, or level of exposure. 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

INGREDIENT	CAS NUMBER	ACGIH TLV (TWA)	OSHA PEL (TWA)
Mineral Oil	8012-95-1	5 mg/m ³	5 mg/m ³

Fields in the above table(s) that do not contain data indicate that exposure limits are not available for those endpoints.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM: Viscous suspension
 COLOR: Light beige
 ODOR: Oil odor
 SOLUBILITY: Not determined
 Water:

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. Oxidizers. Strong acids and bases.

HAZARDOUS DECOMPOSITION PRODUCTS / REACTIONS:
 Carbon oxides (CO_x).

SECTION 12. ECOLOGICAL INFORMATION

ECOTOXICITY DATA

There are no ecotoxicity data available for these products or their components.

ENVIRONMENTAL DATA

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

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:

Rats dosed with clotrimazole at 0.73 mg/L (maximum attainable level) for 4 hours exhibited lacrimation, salivation, nasal discharge, ano-genital staining, stool changes, and dried black material on extremities. Significant weight loss was observed the day after exposure and continued for a week after treatment. One animal died six days after exposure. All other animals appeared normal by the end of the observation period. At necropsy, discolored liver, nasal turbinates, and dilated renal pelvis were noted; however, it was unclear if these were treatment related effects.

In an acute inhalation toxicity study in rats at 0.59 mg/l betamethasone dipropionate (maximum attainable concentration), animals exhibited labored breathing, eye closure and decreased activity during exposure. All animals recovered within one day after exposure.

Rats and mice were exposed by inhalation to an aerosol containing 0.3 mg of betamethasone dipropionate per liter over a 5-hour period. Both species exhibited body weight decreases during the 4 day post treatment period. During exposure the mice exhibited transient central nervous system stimulation including excitation, tremors and convulsions. Recovery was prompt. Upon microscopic examination, partial thymic involution was seen in both species. This finding together with the loss in body weight was attributed to the known pharmacological activity of a corticosteroid.

Ethene homopolymer: Practically not toxic.

SKIN:

Clotrimazole was practically not irritating to rabbit skin.

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.

Mineral oil was slightly irritating to the skin of rabbits.

EYE:

OTOMAX is minimally irritating to the eyes of rabbits.

ORAL:

Clotrimazole: Oral LD50: 708 mg/kg (rat); 761-923 mg/kg (mouse); >1000 mg/kg (rabbit); >1000 mg/kg (dog)

Betamethasone dipropionate: Oral LD50: >1000 mg/kg (dog); >5000 mg/kg (rat); >50 mg/kg (mice)

One male and one female dog were each administered a single oral dose of 1000 mg/kg of betamethasone dipropionate and observed for five weeks. Urine output and water consumption were increased and eosinophil counts decreased during the week post treatment.

Ethene homopolymer: Practically not toxic.

Mineral Oil: Oral LD50: 22,000 mg/kg (mouse)

DERMAL AND RESPIRATORY 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.

Mineral oil was not a skin sensitizer in guinea pigs.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:

Clotrimazole was fed to rats at doses of 10, 25, 50, or 150 mg/kg/day in the diet for 18 months. The only clinical effect observed during the study was decreased body weight in the 50 (females) and 150 mg/kg/day dosage groups; however, reversal of body weight loss was noted in rats not dosed during the last 25 weeks of the study. Chemical and pathological effects observed during the study included decreases in hematocrit and hemoglobin values (50 and 150 mg/kg/day), increases in serum chemistry levels (150 mg/kg/day males), dose- and treatment-related incidences of liver mottling, nodular enlargement, pigmentation of the renal cortices, fatty metamorphosis and regenerative hyperplasia of the liver, and deposits of intracellular fat in the adrenal glands. Reversal of liver effects were observed in rats not dosed during the last 25 weeks of the study. A NOEL was not determined for this study.

Dogs were treated with clotrimazole at doses of 25, 50, or 150 mg/kg/day for six or twelve months. Dose-related clinical effects observed included emesis shortly after dosing, soft stool, transient increased salivation, conjunctivitis accompanied by lacrimation, and body weight loss (high-dose group). Most effects were not observed during the recovery period. Chemical and pathological effects were observed in the mid- or high-dose groups and included increases in serum chemistry levels (similar to those seen in rats) and increased fat deposits in the adrenal glands. A NOEL was not determined for this study.

Rabbits are the most sensitive species tested with betamethasone dipropionate in regards to repeated topical skin application. Serious effects including death, hypothalamic-pituitary-adrenal (HPA) axis suppression, skeletal muscle wasting, immune organ atrophy, and abdominal distention in more than 50% of animals tested were observed following application for 10 to 30 days with 0.05% betamethasone propionate cream, lotion or ointment formulations. However, rats and mice demonstrated only minimal systemic effects, principally thymic involution, when either 0.05% or 0.1% cream was applied to skin six days a week for up to eight weeks.

In a 14-day oral toxicity study testing the 0.1% betamethasone topical cream formulation in rats and mice, drug-related clinical signs including diarrhea, hypothermia and rough coat, were observed within three hours to six days after dosing. Hypoactivity and ptosis were also seen in rats. In a 28-day oral toxicity study in dogs treated with 0.05 to 1 mg/kg/day of betamethasone dipropionate, drug-related effects observed included reversible changes in hematological, biochemical and physiological data (increased fluid intake and urinary output, decreased hematocrit and hemoglobin values, alterations in white blood cell counts, increases in liver enzymes, thymic involution and adrenal atrophy) which were attributed to the known pharmacological activity of corticosteroid drugs.

Female rats received mineral oil in the diet at dosages up to 20,000 ppm for 90 days. Effects observed included increased liver, kidney, and spleen weights, and enlargement of the lymph nodes together with granulomatous lipid granules.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:

High oral doses of clotrimazole in rats and mice ranging from 50 to 120 mg/kg resulted in embryotoxicity (possibly secondary to maternal toxicity), impairment of mating, decreased litter size and number of viable young, and decreased pup survival to weaning. Clotrimazole was not teratogenic in rats, rabbits, or mice given oral doses up to 100, 180, or 200 mg/kg, respectively. Intravaginal dosing of 100 mg/kg in pregnant rats did not result in harm to the fetuses.

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.

MUTAGENICITY / GENOTOXICITY:

Clotrimazole (100 mg/kg/day) was negative in a chromosome spermatophore study in Chinese hamsters.

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.

CARCINOGENICITY:

Clotrimazole was not carcinogenic in rats exposed to oral doses for 18 months.

There was no evidence of carcinogenicity in animals exposed to mineral oil mist at 100 mg/m³ or higher for as long as two years.

SECTION 13. DISPOSAL CONSIDERATIONS
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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(s).

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, IATA, IMO, and the ADR.

SECTION 15. REGULATORY INFORMATION**TSCA LISTING**

INGREDIENT	TSCA
Ethene Homopolymer (Polyethylene)	X
Mineral Oil	X

Substances not included in the table above are TSCA exempt or not regulated under TSCA.

U.S. STATE REGULATIONS

INGREDIENT	California Proposition 65	CARTK	NJRTK	CTR TK	MARTK
Mineral Oil		X	1437		X

INGREDIENT	PARTK	MNRTK	MIRTK	RIRTK
Mineral Oil	X	X		X

Fields in the above tables that do not contain data indicate that those materials have not been listed by local regulations.

X: Listed on applicable state hazardous substance or right-to-know lists.

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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SIGNIFICANT CHANGES (US SUBFORMAT):

Complete rewrite
Conversion, OEG, OEB