MATERIAL SAFETY DATA SHEET

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Astra USA, Inc.
50 Otis Street
Westborough, Massachusetts 01581

General Information Phone Numbers:
800/225-6333
508/366-1100

CHEMTREC(R) Emergency Telephone Numbers (24-HOURS):
United States: 1-800/424-9300
International: (202/483-7616(collect)

These CHEMTREC(R) numbers are to be used ONLY IN THE EVENT OF A CHEMICAL EMERGENCY INVOLVING A SPILL, LEAK, FIRE, EXPOSURE OR ACCIDENT.

MSDS NUMBER: 1 EFFECTIVE DATE: 16 August 1994

Product Name: Rhinocort(R) (budesonide) Nasal Inhaler

Synonyms/Chemical Name: 16a, 17 a-butylidenedioxypregna-1,4-diene-11B, 21-diol-3,20-dione
Therapy Category: Topical anti-inflammatory glucocorticosteroid for treatment of rhinitis

2. COPOSITION/INFORMATION ON INGREDIENTS

COMPONENT	CAS REGISTRY NO.	EINICS	PERCENT	MOL.WT.
Budesonide C25H34O6	51333-22-3	257-139-7	0.14	430.5
Sorbitan trioleate C60H104O8	26266-58-0	247-569-3	0.5	952
Pll:Trichloromonofluoromethane CC13F	75-69-4	200-892-3	25	137.4
Pl2:Dichlorodifluoromethane CC12F2	75-71-8	200-893-9	50	120.9
Pl14:Dichlorotetrafluoroethane C2C12F4	76-14-2	200-937-7	25	170.9

(See Section 8 for exposure guidelines)

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

POTENTIAL HEALTH EFFECTS
Rhinocort Nasal Inhaler is a pressurized aerosol unit containing a suspension of micronized budesonide in a mixture of propellants and sorbitan trioleate. Potential routes of exposure include nasal and oral inhalation and absorption through the oral mucosa (surface of the mouth), skin and eyes. Budesonide is a potent corticosteroid. Long-term exposure to doses greater than are recommended may product a variety of effects related to systemic corticosteroid therapy. The propellant mixture poses an inhalation hazard only if used in an abusive, non-intended fashion. Direct contact of the aerosol with the eyes or skin may cause slight to moderate irritation.

4. FIRST AID MEASURES

EYE: First check victim for contact lenses and remove if present. Flush victim's eyes with large quantities of water and contact a physician.
SKIN: Wash with water while removing all contaminated clothing. If rash or irritation develop, contact a physician. For frostbite burns, rapidly

rewarm area by washing with 40 - 42o C water until flush has returned.
INGESTION: Unlikely route of exposure with this preparation. What little budesonide is swallowed is rapidly inactivated by the liver. Do not give anything by mouth or induce vomiting if victim is convulsing or unconscious.
INHALATION: If solvent abuse is suspected, keep patient quiet, provide oxygen if necessary, and get immediate medical attention.
NOTE TO PHYSICIAN: If victim is not breathing, maintain an adequate airway and administer oxygen by artificial respiration. Caution is advised with the use of adrenalin because of the possibility of inducing cardiac arrythmias.
ANTIDOTE: Dilantin (phenytoin) may be useful in the management of ventricular arrhythmias.

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5. FIRE FIGHTING MEASURES

FLAMMABLE PROPERTIES
FLASH POINT: NA
FLAMMABLE LIMITS:
LOWER FLAMMABLE LIMIT: NA
UPPER FLAMMABLE LIMIT: NA

NA = Not applicable

EXTINGUISHING MEDIA: For small fires, dry chemical or carbon dioxide; for large fires, water spray, fog, or foam.
UNUSUAL FIRE OR EXPLOSION HAZARDS: Containers may explode in the heat of fire. Propellant gases are heavier than air and may accumulate in low-lying areas creating a potential health hazard.
FIREFIGHTING INSTRUCTIONS: Firefighters should use self-contained breathing apparatus with a full facepiece operated in pressure-demand or positive-pressure mode and protective clothing. If feasible and without risk, move containers from fire area. Otherwise, cool fire-exposed containers with water spray until well after fire is out.
HAZARDOUS COMBUSTION PRODUCTS: In contact with flame or very hot surfaces, toxic decomposition products include fluoride, chloride, hydrogen chloride, hydrogen fluoride, carbonyl fluoride, phosgene, and carbon dioxide fumes.

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6. ACCIDENTAL RELEASE MEASURES

SPILLS: Remove all heat and ignition sources, and ventilate the area of spill or leak. Stop leak if it can be done without risk. Promptly clean up spills using appropriate protective equipment. Place in a suitable, properly labeled container for disposal. Wash area with soap and water.
DECONTAMINATION PROCEDURES: Propellants will rapidly vaporize. Do not release leaking cylinder gas to the atmosphere because of propellants' role in ozone depletion.

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7. HANDLING AND STORAGE

HANDLING: Avoid contact with eyes, skin and clothing. Do not eat, drink, or smoke in areas where chemicals are present. Wash thoroughly after handling. Wash contamianted clothing before reuse.
STORAGE: Protect containers agains physical damage. Store in a cool, dry, well-ventilated area away from heat and ignition sources and incompatibles.

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8. EXPOSURE CONTROLS/PERSONAL PROTECTION

EXPOSURE GUIDELINES:

	EXPOSURE LIMITS		
	OSHA PEL	ACGIH TLV	SUPPLIER
Budesonide			0.01 mg/m3 (skin)
P11	Ceiling: 1000 ppm	Ceiling: 1000 ppm	
P12	8-hr TWA: 1000 ppm	TWA: 1000 ppm	
P114	8-hr TWA: 1000 ppm	TWA: 1000 ppm	

ENGINEERING CONTROLS: General and/or local exhaust to maintain airborne concentrations below PEL and TLV levels. Good general ventilation should be sufficient for most conditions.
RESPIRATORY PROTECTION: Not required if used according to Package Insert.
SKIN PROTECTION: Rubber gloves to prevent prolonged or repeated contact.
EYE PROTECTION: Use chemical safety goggles to prevent liquid contact with eyes where splashing is possible. Emergency eyewash stations should be accessible to the work areas.

OTHER: A laboratory coat or apron appropriate for the work situation to minimize skin contact with the liquid.

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE: A grayish white to cream-colored suspension filled into aerosol vials of aluminum.
ODOR: ND
PHYSICAL STATE: Aerosol
BOILING POINT: ND
VAPOR PRESSURE: Volatile
VAPOR DENSITY: ND
SOLUBILITY IN WATER: Budesonide: 14 ug/ml
SPECIFIC GRAVITY: ND
pH: ND
MELTING POINT: Budesonide: 224 - 232oC
OCTANOL/WATER COEFFICIENT: ND

10. STABILITY AND REACTIVITY

STABILITY: Stable under normal storage and handling conditions.
INCOMPATIBILITY: Acids and chemically-active metals such as sodium, potassium, calcium, barium, lithium and powdered aluminum, zinc, or magnesium.
HAZARDOUS DECOMPOSITION PRODUCTS: When heated to decomposition, emits toxic and irritating fumes, such as fluoride, chloride, hydrogen chloride, hydrogen fluoride, carbonyl fluoride, phosgene, and CO2.
HAZARDOUS POLYMERIZATION: Will not occur.

ND = No Data

11. TOXICOLOGICAL INFORMATION

GENERAL PHARMACOLOGICAL EFFECTS AND HUMAN DATA:
Budesonide is a potent corticosteroid used for the treatment of seasonal rhinitis ("hay fever") and perennial rhinitis (like hay fever, but all year long). Long-term exposure to doses greater than are recommended may produce a variety of effects related to systemic corticosteroid therapy including edema (holding excessive water), weight gain, high blood pressure, fatigue, emotional changes, peptic ulcers, demineralization ("thinning") of bones and adrenocortical suppression. In short-term studies slower growth rate has been observed in children with asthma but in long-term studies no effect on growth in children has been observed. There are a few reports in the literature of allergic reactions to budesonide. The propellant mixture is composed of chlorofluorocarbons P11, P12, and P114 and poses an inhalation hazard only if used in an abusive, non-intended fashion. Human TCLo's for P11 and P12 are 50,000 ppm and 200,000 ppm for 30 minutes, respectively. No TCLo's are available for P114, budesonide, or sorbitan trioleate.
ORAL TOXICITY: The oral LD50 in rats for budesonide is greater than 400 mg/kg; ingestion of budesonide can cause similar symptoms as inhalation exposure. The oral LD50 in rats for P114 is greater than 2250 mg/kg and for sorbitan trioleate is greater than 39.8 g/kg. No oral LD50's for P11 or P12 are available. Accidental ingestion of large amounts of propellant components may cause necrosis and perforation of the stomach.
INHALATION TOXICITY: Prolonged or repeated inhalation of budesonide may cause the corticosteroid effects as described above. The propellants are central nervous system depressants at very high concentrations, causing dizziness and unconsciousness. Intentionally sniffing very high concentrations of these propellants can cause cardiac arrhythmias which are potentially lethal. Inhalation LC50's for P11, P12, and P114 in rats are 13%/15 min; 80%/30 min; and 72%/30 min, respectively.
EYE: No data, but contact with eyes may cause slight irritation based on irritation potential of the components. Prolonged exposure of budesonide to the eye can cause corticosteroid symptoms similar to that caused by inhalation exposure.
SKIN: Budesonide can be absorbed through the skin and cause systemic effects similar to that following prolonged inhalation or oral exposure. Accidental contact with the liquid propellants may cause frostbite. Prolonged or repeated contact of the skin with these propellants can dry and defat the skin.
SENSITIZATION: Hypersensitivity reactions have been reported in rare instances with budesonide, and the propellants P11 and P12.

CHRONIC/CARCINOGENICITY: No ingredient is listed as a carcinogen by NTP, IARC, or OSHA. Long-term studies conducted in mice using orally administered budesonide found no evidence of a carcinogenic effect when budesonide was administered orally for 91 weeks to mice at doses up to 200 ug/kg/day (600 ug/m2/day). In a 104-week study of budesonide in Sprague Dawley rats a statistically significant increase in the incidence of gliomas was observed in male rats receiving 50 ug/kg/day (300 ug/m2/day) orally; no such changes were seen in male rats receiving dosts of 10 and 25 ug/kg/day (60 and 150 ug/m2/day) or in female

rats at any dose. Two other 104-week studies of oral budesonide at doses of 50 ug/kg/day (300 ug/m2/day) in male Sprague-Dawley and Fischer rats did not demonstrate an increased glioma incidence in budesonide-treated animals as compared with concurrent controls or reference groups treated with prednisolone and triamcinolone acetonide. Compared with concurrent control male Sprague-Dawley rats there was a statistically significant increase in the incidence of hepatocellular tumors. However, this finding was confirmed in all three steroid groups (budesonide, prednisolone, triamcinolone acetonide) in the second study in male Sprague-Dawley rats. Chronic and carcinogenicity studies on the propellants revealed no significant chronic effects and negative carcinogenicity results.

MUTAGENICITY: The mutagenic potential of budesonide was evaluated in six different test systems: Ames Salmonella/microsome plate test, mouse micronucleus test, mouse lymphoma test, chromosome aberration test in human lymphocytes, sex-linked recessive lethal test in Drosophila melanogaster, and DNA repair analysis in rat hepatocyte culture. No mutagenic or clastogenic properties of budesonide were found in any of these tests. Mutagenicity studies on the propellants have in general been negative.

REPRODUCTIVE/DEVELOPMENTAL EFFECTS: There are no adequate and well-controlled studies in pregnant women. Thus, budesonide is catagorized as a Pregnancy Category C drug. Budesonide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. As with other glucocorticoids budesonide has been shown to be teratogenic and embryocidal in rabbits and rats when given subcutaneously in high doses. In rats, there was increased fetal loss, decreased pup weights and skeletal abnormalities. No teratogenic or embryocidal effects have been seen in rats when budesonide was administered by inhalation at doses of approximately 27 times the human recommended starting doe based on ug/kg/day or 4 times the human dose based on ug/m2/day. Experience with oral glucocorticosteroids since their introduction in pharmacologic, as opposed to physiologic, doses suggests that rodents are more prone to teratogenic effects from glucocorticosteroids than humans. Reproductive/developmental studies of the propellants have given negative results.

PHARMACOLOGICAL EFFECTS: The pharmacological effects of the corticosteroid budesonide have been described above. The propellants are asphyxiants and CNS depressants at high concentrations and can sensitize the myocardium to epinephrine. P11 is one of the more potent cardiac sensitizers and P12 and P114 have moderate potential. Cardiotoxicity is unlikely to occur with Rhinocort when the Inhalers are used at intended.

METABOLISM: Follow nasal administration, budesonide reaches its peak plasma concentration in less than an hour. It is transformed in the liver to less active metabolites which are excreted via the urine and feces. The propellants are very rapidly eliminated unchanged via the exhaled air.
MEDICAL CONDITIONS ENHANCING TOXICITY: People with underlying cardiac or respiratory disorders may be more susceptible to the pharmacological effects of the propellants. Consult the Product Package Insert for additional information.

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12. ECOLOGICAL INFORMATION

ECTOXICOLOGICAL INFORMATION: Budesonide: EC20 growth rate inhibition of green algae: 18.6 mg/l; LC50 (48 hr) Ceriodaphnia: 20 mg/l;
LC50 (96 hr) Zebra fish: > 18.6 mg/l.
CHEMICAL FATE: Budesonide: Biodegradability: BOD (7 days) < 3mg/l: not readily biodegradable. Exhibits slight potential for bioaccumulation. The propellants P11, P12, and P114 are class 1, group 1 ozone depleting substances.

The contribution to emissions from the use of this drug product is minor compared to the total emissions of CFC's and their use is required for the medical action of the drug product. These materials will rapidly volatilize from soil and water and do not readily bio- or abiotically degrade.

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13. DISPOSAL CONSIDERATIONS

Dispose of material by sending to a RCRA licensed facility, retrofitted for incinerating aerosols with CFC's. Disposal should be conducted by approved disposal companies in accordance with local, state and federal environmental regulations. P11: RCRA Code: U121; P12: RCRA Code: U075.

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14. TRANSPORT INFORMATION

TRANSPORTATION AND HAZARDOUS MATERIALS DESCRIPTION:

Description	Medicine, N.O.S., in small inner packaging
Class	9
ID	ID 8008

Packing Group: None assigned
Label MISC
Limitations 25 kg gross weight: passenger aircraft or railcar
25 kg gross weight: cargo aircraft

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15. REGULATORY INFORMATION

OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). Labelling regulated by FDA.
CERCLA/SUPERFUND: Contains Reportable Quantity (RQ) substances, P11 and P12, with RQ's of 5000 lbs.
SARA HAZARD CATEGORY (311/312): Immediate, chronic health hazard; sudden release of pressure physical hazard. Exempted from reporting since material is regulated by FDA.
SARA 313 INFORMATION: Contains CFC11, CFC12, and CFC144, chemicals subject to the reporting requirements of Section 313.
TSCA: Drugs exempted from TSCA Chemical Substance Inventory
CALIFORNIA PROPOSITION 65: Contains no chemicals know to the state of California to cause cancer, birth defects, or other reproductive harm.

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16. OTHER INFORMATION

PACKAGING DESCRIPTION: Aerosol dispenser
ADDITIONAL INFORMATION: Refer to manufacturer's package insert.
HAZARD LABEL TEXT: WARNING: Contains trichloromonofluoromethane, dichlorodifluoromethane, and dichlorotetrafluoro-methane, substances which harm public health and environment by destroying ozone in the upper atmosphere. Your physician has determined that this product is likely to help your personal health. USE THIS PRODUCT AS DIRECTED, UNLESS INSTRUCTED TO DO OTHERWISE BY YOUR PHYSICIAN.
NFPA RATING: Health = 2 Fire = 0 Reactivity = 0
REVISIONS/DATE: