

SAFETY DATA SHEET

NFPA Rating: Health: 1 Flammability: 2 Reactivity: 0 Special: 0

TELEPHONE CONTACTS:
Product Technical and Medical Information: (800) 433-8871
Transportation Emergency 24-Hour Response (CHEMTREC): (800) 424-9300

SECTION 1: PRODUCT IDENTIFICATION

Compound Name: **ESTRASORB® Estradiol Topical Emulsion**
Chemical Class: Steroid
Manufacturer's Name: Manufactured by Novavax, Malvern, PA for Allergan, Inc.
Address: 2525 Dupont Drive
Irvine, CA 92612
Revision Date: December 18, 2007

SECTION 2: HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW: Repeated exposure to estrogens may result in an increased risk of endometrial and breast cancer as well as cardiovascular disease leading to myocardial infarction, stroke and pulmonary embolism. Exposure to elevated levels of estrogens has reportedly resulted in birth defects associated with mutagenic and teratogenic effects in humans. **Women of child-bearing potential and nursing mothers should avoid contact with this material. Product is flammable. Do not open containers or use product near open flame or other ignition sources.**

Hazard Classification (GHS): Flammable liquid (Category 3)
Target organ systemic toxicity – Repeated exposure (Category 2)



Signal Word and Hazard Statements (GHS): Warning – Flammable liquid. Prolonged or repeated exposure may cause increased risk of cancer, cardiovascular effects, reproductive impairment, and fetal abnormalities.

Potential Health Effects:

EYE CONTACT: Contact with the eyes may result in mild irritation (burning or stinging) in sensitive individuals. Avoid contact with the eyes.

SKIN CONTACT: Prolonged contact with the skin may result in mild irritation.

INHALATION: The product is non-volatile and inhalation is not likely to occur.

INGESTION: Serious ill effects have not been reported following acute ingestion of large doses of estrogen-containing products by young children. May cause irritation, nausea and vomiting.

CHRONIC EFFECTS: Repeated exposure may increase risk of cancers of the uterus, breasts, ovaries, and other endometrial tissues. May cause cardiovascular damage resulting in increased risk of heart attacks, stroke or embolism. May cause reproductive impairment and birth defects in the developing fetus.

SECTION 3: COMPOSITION/HAZARDOUS INGREDIENTS

Chemical Name	CAS Number	Percent (By Weight)	Exposure Limits in Air (8 hr. TWA)		
			OSHA PEL	ACGIH TLV	ALLERGAN OEL
Estradiol Hemihydrate	35380-71-3	0.25	N/E	N/E	N/E
Ethyl alcohol	64-17-5	7.6	1000 ppm	1000 ppm	N/E

N/E: Not Established

SECTION 4: FIRST AID MEASURES

Eye Contact: Flush eyes with plenty of water for at least 15 minutes. Obtain medical attention if irritation or other symptoms occur.

Skin Contact: Wash skin thoroughly with soap and water if unintended contact occurs. If irritation develops consult a physician.

Wash contaminated clothing before reuse.

Inhalation: Inhalation is not likely to occur. If symptoms occur, move to fresh air and obtain medical attention. Treat symptomatically.

Ingestion: No information is available on overdosage in humans. Treatment of an oral overdose includes supportive and symptomatic therapy. Consult a physician or poison control center immediately if symptoms develop.

SECTION 5: FIRE FIGHTING MEASURES

Flash Point and Method: No data for product (Ethanol: 55 °F, Closed Cup)

Flammable Limits (Ethanol): LEL: 3.3% UEL: 19%

Autoignition Temperature: No data for this product

Fire-Extinguishing Materials: Use extinguishing media suitable for materials supporting combustion such as water fog, CO₂, foam or dry chemical

Fire fighting Procedures: Use self-contained breathing apparatus in enclosed or confined spaces or as otherwise needed.

Unusual Fire and Explosion Hazards: None known

SECTION 6: ACCIDENTAL RELEASE MEASURES

Wipe up spilled liquid with absorbent material and wash area with water. If large quantities are spilled, flush spill area with water.

SECTION 7: HANDLING AND STORAGE

Handling: Avoid unintentional contact with skin surfaces. Wash thoroughly after handling or in the event of unintended skin contact. Observe all precautions contained on product label and package insert.

Storage: Store in a cool, dry location out of direct sunlight. Keep container closed when not in use.

SECTION 8: EXPOSURE CONTROLS AND PERSONAL PROTECTION

Engineering Controls: None necessary for normal product handling.

Respiratory Protection: None necessary for normal product handling.

Eye Protection: None required for normal product handling.

Protective Clothing: None required for normal product handling.

Hygienic Work Practices: Wash hands thoroughly after handling. If working with large quantities of material (such as spill clean-up), use latex or chemical resistant gloves and appropriate eye protection. No eating, drinking or smoking in area.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

Appearance and Odor: White lotion in sealed foil pouch; alcohol odor

pH: 6.0 - 8.0

Melting Point/ Freezing Point: Not Determined

Boiling Point: Not Determined

Vapor Pressure (mm Hg at 20° C): No data for this product

Vapor Density (Air = 1): No data for this product

Solubility in Water: Miscible

Specific Gravity: Approximately 1.0

Partition coefficient: n-octanol/water: Not Determined

SECTION 10: STABILITY AND REACTIVITY

General: This product is stable and hazardous polymerization will not occur.

Incompatible Materials and Conditions to Avoid: Store away from oxidizers and heat. Store below 25 °C

Hazardous Decomposition: None known

SECTION 11: TOXICOLOGICAL INFORMATION

Acute Toxicity: Topical administration of a single dose of estradiol to rhesus monkeys (1.0 mg in 0.42 mL of vehicle) and to rabbits (0.4 mL of Estrasorb) resulted in no significant localized reactions or toxicity.

Topical administration to rabbits once per week over a 91 day period (13 doses) produced a mild to moderate inflammatory response at the site of dermal application. In addition, an estrogenic-related decrease in food consumption and an increased spleen size resulted, without apparent histopathologic changes in the spleen. These effects were not considered toxicologically relevant, and no other systemic adverse effects were noted in the animals.

During the phase III human clinical trials, human subjects daily applied Estrasorb at a dose 15 times the dose used in the rabbit dermal trial for a period of 12 weeks. Of 100 subjects in each group, only five subjects in the test group and four in the placebo group developed dermal reactions (identified as skin rashes). Two of the subjects in the test group and one of the subjects in the placebo group withdrew from the trial because of the localized skin reaction.

Chronic Toxicity: The Women's Health Initiative (WHI) study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during 5 years of treatment with estrogens relative to placebo. In addition, the report indicated an increased risk of developing probable dementia in post-menopausal women 65 years of age or older during 4 years of treatment with oral conjugated estrogens plus medroxyprogesterone acetate relative to placebo. It is unknown whether this finding applies to younger postmenopausal women.

Chronic exposure to estrogens may increase the risk of liver damage and hypothyroidism, and may cause exacerbation of endometriosis, asthma, diabetes mellitus, epilepsy, migraine or porphyria, systemic lupus erythematosus, and hepatic hemangiomas.

Carcinogenicity: Use of estrogens in women with intact uteri has been associated with an increased risk of endometrial cancer. The reported endometrial cancer risk among estrogen users is about 2- to 12-fold greater than in nonusers, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with the use of estrogens for less than 1 year. The greatest risk appears associated with prolonged use, with increased risks of 15- to 24-fold for use over 5 to 10 years or more, and this risk has been shown to persist at least 8 to 15 years after estrogen therapy is discontinued.

Use of estrogens has been reported to increase the risk of breast cancer. The WHI study reported an increased risk of breast cancer in women receiving estrogen therapy for a mean follow-up of 5.6 years. The overall relative risk of invasive breast cancer was 1.24 (95% confidence interval 1.01-1.54), and the overall absolute risk was 41 vs 33 cases per 10,000 women-years compared with placebo. Observational studies have also reported an increased risk for estrogen/progestin combination therapy, and a smaller increased risk for estrogen alone therapy, after several years of use. In the WHI trial and from observational studies, the excess risk increased with duration of use. From observational studies the risk appeared to return to baseline in about five years after stopping treatment. In addition, observational studies suggest that the risk of breast cancer was greater, and became apparent earlier, with estrogen/progestin combination therapy as compared to estrogen alone therapy.

Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.09, and the absolute risk was 40 vs 36 cases per 10,000 women-years compared with placebo. In the same substudy, invasive breast cancers were larger and diagnosed at a more advance stage compared with the placebo group.

Mutagenicity: Mutagenic and teratogenic affects associated with exposure to estrogens have been reported in humans.

Reproductive Toxicity: Impairment of fertility associated with repeated or prolonged exposure to estrogens has been reported in humans.

SECTION 12: ECOLOGICAL INFORMATION

No ecological information is available for the product.

SECTION 13: DISPOSAL CONSIDERATIONS

For small quantities of **ESTRASORB® Estradiol Topical Emulsion**, discard as ordinary trash. For large quantities, contact Allergan for information on disposal options.

SECTION 14: TRANSPORT INFORMATION

Domestic (Land, D.O.T.)

Consumer Commodity (containing flammable solution), ORM-D

International (Air, I.C.A.O.)

ID 8000 Consumer Commodity (containing flammable solution), Class 9

International (Water, I.M.O.)

UN 1993 Flammable Liquid, N.O.S. (Ethyl Alcohol Solution), Class 3.3, Pkg. Group III, Limited Quantity

SECTION 15: REGULATORY INFORMATION

TSCA (Toxic Substances Control Act):

As defined by U.S. Code Title 15, Chapter 53 (TSCA), Section 2602 and TSCA Regulations at 40CFR, Subchapter R, Part 710, this drug product is exempt from regulations under TSCA.

CERCLA (Comprehensive Environmental Response, Compensation, and Liability Act):

This product contains no components subject to reporting or notification requirements.

SARA Title III (Superfund Amendments and Reauthorization Act):

311/312 Hazard Categories: Chronic Health

313 Reportable Ingredients: None

WHMIS (Workplace Hazardous Materials Information System - Canada):

Not Regulated (Product is regulated by the Food and Drugs Act)

California Proposition 65:

This product contains Estradiol hemihydrate, a substance known to the State of California to cause cancer.

SECTION 16: OTHER INFORMATION

Revision Summary: Prepared December 21, 2007

The preceding information is based on available data and is believed to be correct. However, no warranty is expressed or to be implied regarding the accuracy of this information, the results to be obtained from the use thereof or the hazards connected with the use of the material. Since the information contained herein may be applied under conditions beyond our control and with which we may be unfamiliar, Allergan does not assume any responsibility for the results of its use. This information is furnished upon the condition that the persons receiving it shall make their own determinations of the effects, properties, and protections which pertain to their particular conditions.