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

Product identifier
Product Name Estrace

Other means of identification
Product Code FG00088
Synonyms Estradiol Cream

Recommended use of the chemical and restrictions on use
Recommended Use Vulvar and vaginal atrophy

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.

Details of the supplier of the safety data sheet
Manufacturer Allergan plc
5 Giralda Farms
Madison, NJ USA 07940
+1-800-272-5525
E-mail address SDS@Allergan.com

Emergency telephone number
Emergency Telephone Call CHEMTREC Day or Night
Within USA or Canada: 1-800-424-9300
Outside USA and Canada: +1-703-741-5970 (collect calls accepted)

2. HAZARDS IDENTIFICATION

Classification

OSHA Regulatory Status
This chemical is not considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.122)

Not a dangerous substance or mixture according to the Globally Harmonized System (GHS)

Label elements

Emergency Overview

The product contains no substances which at their given concentration, are considered to be hazardous to health

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Physical state</th>
<th>Odor</th>
</tr>
</thead>
<tbody>
<tr>
<td>cream</td>
<td>Solid</td>
<td>No information available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP</td>
<td>1. Genitourinary systemChanges in vaginal bleeding pattern and abnormal withdrawal bleeding or flow; breakthrough bleeding, spotting, dysmenorrhea; increase in size of uterine leiomyomata; vaginitis, including vaginal candidiasis; change in amount of cervical secretion; changes in cervical ectropion; ovarian cancer; endometrial</td>
</tr>
</tbody>
</table>

_____________________________________________________________________________________________
hyperplasia; endometrial cancer. 2. Breasts: Tenderness, enlargement, pain, nipple discharge, galactorrhea; fibrocystic breast changes; breast cancer. 3. Cardiovascular: Deep and superficial venous thrombosis; pulmonary embolism; thrombophlebitis; myocardial infarction; stroke; increase in blood pressure. 4. Gastrointestinal: Nausea, vomiting; abdominal cramps, bloating; cholestatic jaundice; increased incidence of gallbladder disease; pancreatitis; enlargement of hepatic hemangiomas. 5. Skin: Chloasma or melasma that may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; pruritus, rash. 6. Eyes: Retinal vascular thrombosis, steepening of corneal curvature, intolerance to contact lenses. 7. Central Nervous System: Headache, migraine, dizziness; mental depression; chorea; nervousness, mood disturbances, irritability; exacerbation of epilepsy; dementia. 8. Miscellaneous: Increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; arthralgias; leg cramps; changes in libido; urticaria, angioedema, anaphylactoid/anaphylactic reactions; hypocalcemia; exacerbation of asthma; increased triglycerides.

OVERDOSAGE: Serious ill effects have not been reported following acute ingestion of large doses of estrogen-containing oral contraceptives by young children. Overdosage of estrogen may cause nausea and vomiting, and withdrawal bleeding may occur in females.

Chemical Name
Estradiol USP

Medical Conditions Aggravated by Exposure

BOXED WARNING: ESTROGENS INCREASE THE RISK OF ENDOMETRIAL CANCER. Close clinical surveillance of all women taking estrogens is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. There is no evidence that the use of "natural" estrogens results in a different endometrial risk profile than "synthetic" estrogens at equivalent estrogen doses. (See WARNINGS, Malignant neoplasms, Endometrial cancer.)

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 oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) relative to placebo. (See CLINICAL PHARMACOLOGY, Clinical Studies.) The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported increased risk of developing probable dementia in postmenopausal 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 or to women taking estrogen alone therapy. (See CLINICAL PHARMACOLOGY, Clinical Studies.) Other doses of oral conjugated estrogens with medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Estrogens should not be used in individuals with any of the following conditions: Undiagnosed abnormal genital bleeding. Known, suspected, or history of cancer of the breast except in appropriately selected patients being treated for metastatic disease. Known or suspected estrogen-dependent neoplasia. Active deep vein thrombosis, pulmonary embolism or history of these conditions. Active or recent (e.g., within the past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction). Liver dysfunction or disease. Estradiol tablets should not be used in patients with known hypersensitivity to its ingredients. Known or suspected pregnancy. There is no indication for estradiol in pregnancy. There appears to be little or no increased risk of birth defects in children born to women who have used estrogens and progestins from oral contraceptives inadvertently during early pregnancy.

Other Information
Unknown Acute Toxicity
4% of the mixture consists of ingredient(s) of unknown toxicity
Over the counter drugs in their solid form are considered exempt under the criteria of the Federal OSHA Hazard Communication Standard 20 CFR 1910.1200. However, in an industrial setting where a component's occupational exposure limit may be surpassed, than can be considered hazardous.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>CAS No.</th>
<th>EINECS</th>
<th>Weight-%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PURIFIED WATER USP</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>60 - 100*</td>
</tr>
<tr>
<td>PROPYLENE GLYCOL USP</td>
<td>57-55-6</td>
<td>200-338-0</td>
<td>7 - 13*</td>
</tr>
<tr>
<td>White Cresin Wax</td>
<td>8002-74-2</td>
<td>232-315-6</td>
<td>5 - 10*</td>
</tr>
<tr>
<td>Stearyl Alcohol</td>
<td>112-92-5</td>
<td>204-017-6</td>
<td>5 - 10*</td>
</tr>
<tr>
<td>ESTRADIOL USP</td>
<td>50-28-2</td>
<td>200-023-8</td>
<td>&lt;0.1*</td>
</tr>
</tbody>
</table>

*The exact percentage (concentration) of composition has been withheld as a trade secret.

### 4. FIRST AID MEASURES

**First aid measures**

**Eye contact**
Rinse immediately with plenty of water and seek medical advice.

**Skin Contact**
Wash off immediately with soap and plenty of water while removing all contaminated clothes and shoes.

**Inhalation**
Remove to fresh air.

**Ingestion**
Consult a physician if necessary.

**Chemical Name**
ESTRADIOL USP

**Note to physicians**
This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product. Treat symptoms and eliminate exposure.

### 5. FIRE-FIGHTING MEASURES

**Suitable extinguishing media**
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

**Unsuitable extinguishing media**
None known.

**Specific hazards arising from the chemical**
Fire may produce irritating, corrosive and/or toxic gases.

**Explosion data**

**Sensitivity to Mechanical Impact**
Not impact sensitive.

**Sensitivity to Static Discharge**
Fine dust dispersed in air, in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.

**Protective equipment and precautions for firefighters**
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

### 6. ACCIDENTAL RELEASE MEASURES

**Personal precautions**
Use personal protection recommended in Section 8. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing.

**Environmental precautions**
See Section 12 for additional ecological information.
**Methods for containment**
Prevent further leakage or spillage if safe to do so.

**Methods for cleaning up**
Use personal protective equipment as required. Cover powder spill with plastic sheet or tarp to minimize spreading and keep powder dry. Take up mechanically, placing in appropriate containers for disposal. Avoid creating dust. Clean contaminated surface thoroughly.

**7. HANDLING AND STORAGE**

**Advice on safe handling**
Avoid contact with skin, eyes or clothing. Avoid generation of dust. Do not eat, drink or smoke when using this product.

**Storage Conditions**
Keep containers tightly closed in a dry, cool and well-ventilated place. Store away from incompatible materials.

**Incompatible materials**
None known based on information supplied.

**8. EXPOSURE CONTROLS/PERSONAL PROTECTION**

**Control parameters**

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>ACGIH TLV</th>
<th>OSHA PEL</th>
<th>NIOSH IDLH</th>
<th>Allergan OEL (ug/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Cresin Wax</td>
<td>TWA: 2 mg/m³ fume</td>
<td>(vacated) TWA: 2 mg/m³</td>
<td>TWA: 2 mg/m³ fume</td>
<td>N/A</td>
</tr>
<tr>
<td>8002-74-2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESTRADIOL USP</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>0.02 ug/m³^3</td>
</tr>
<tr>
<td>50-28-2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NIOSH IDLH Immediately Dangerous to Life or Health**

**Other Information**
Vacated limits revoked by the Court of Appeals decision in AFL-CIO v. OSHA, 965 F.2d 962 (11th Cir., 1992).

**Appropriate engineering controls**
The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

**Individual protection measures, such as personal protective equipment**

**Eye/face protection**
No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, safety glasses should be considered.

**Skin and body protection**
During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. Use appropriate protective clothing for the task (e.g., lab coat, etc.).

**Respiratory protection**
Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

**9. PHYSICAL AND CHEMICAL PROPERTIES**

**Information on basic physical and chemical properties**
10. STABILITY AND REACTIVITY

Reactivity
Not defined As Reactive substance

Chemical stability
Stable under normal conditions.

Possibility of Hazardous Reactions
None under normal processing.

Conditions to avoid
Aerosol formation.

Incompatible materials
None known based on information supplied.

Hazardous Decomposition Products
None known based on information supplied.

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Acute toxicity

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Inhalation</th>
<th>Eye contact</th>
<th>Skin Contact</th>
<th>Ingestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP</td>
<td>Inhalation of airborne dusts generated by this product may slightly irritate the nose, throat, and lungs. Symptoms are generally alleviated upon breathing fresh air.</td>
<td>Irritating to eyes.</td>
<td>May cause skin irritation and/or dermatitis.</td>
<td>Ingestion is not a significant route of occupational overexposure. Acute ingestion of large quantities of this product or chronic ingestion caused by poor hygiene practices may</td>
</tr>
</tbody>
</table>
cause adverse symptoms. Symptoms of ingestion overexposure may include nausea, vomiting, and diarrhea.

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Oral LD50</th>
<th>Dermal LD50</th>
<th>Inhalation LC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>PURIFIED WATER USP</td>
<td>&gt; 90 mL/kg</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>PROPYLENE GLYCOL USP</td>
<td>= 19000 mg/kg (Dog)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>White Cresin Wax</td>
<td>&gt; 5000 mg/kg (Rat)</td>
<td>&gt; 3600 mg/kg (Rabbit)</td>
<td>N/A</td>
</tr>
<tr>
<td>Stearyl Alcohol</td>
<td>&gt; 5 g/kg (Rat)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Delayed and immediate effects as well as chronic effects from short and long-term exposure

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Germ cell mutagenicity</th>
<th>Carcinogenicity</th>
<th>Reproductive toxicity</th>
<th>Effects on or via lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP</td>
<td>Not Suspected of being a Mutagen.</td>
<td>Confirmed human carcinogen.</td>
<td>Presumed to produce significant toxicity to specific target organ(s).</td>
<td>Detectable amounts of this compound have been identified in the milk of nursing women receiving this drug. Caution should be exercised when taking this compound is administered to nursing women.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>STOT - single exposure</th>
<th>STOT - repeated exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP</td>
<td>No information available.</td>
<td>Presumed to produce significant toxicity to specific target organ(s).</td>
</tr>
</tbody>
</table>

Target Organ Effects

Eyes, Respiratory system, Skin.

Numerical measures of toxicity - Product Information

Unknown Acute Toxicity

4% of the mixture consists of ingredient(s) of unknown toxicity

The following values are calculated based on chapter 3.1 of the GHS document

ATEmix (oral) 19305 mg/kg
ATEmix (dermal) 41267 mg/kg

12. ECOLOGICAL INFORMATION

Ecotoxicity

Toxic to aquatic life with long lasting effects

11.52% of the mixture consists of components(s) of unknown hazards to the aquatic environment

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Algae/aquatic plants</th>
<th>Fish</th>
<th>Crustacea</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROPYLENE GLYCOL USP 57-55-6</td>
<td>19000: 96 h Pseudokirchneriella subcapitata mg/L EC50</td>
<td>41 - 47: 96 h Oncorhynchus mykiss mL/L LC50 static 51600: 96 h Oncorhynchus mykiss mg/L LC50 static 51400: 96 h Pimephales promelas mg/L LC50 static 710: 96 h Pimephales promelas mg/L LC50</td>
<td>1000: 48 h Daphnia magna mg/L EC50 Static 10000: 24 h Daphnia magna mg/L EC50</td>
</tr>
<tr>
<td>Stearyl Alcohol 112-92-5</td>
<td>235: 96 h Desmodesmus subspicatus mg/L EC50</td>
<td>10000: 96 h Brachydanio rerio mg/L LC50</td>
<td>1666: 48 h Daphnia magna mg/L EC50</td>
</tr>
<tr>
<td>ESTRADIOL USP 50-28-2</td>
<td>N/A</td>
<td>.002 micrograms/L</td>
<td>2040 micrograms/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Persistence and degradability</th>
<th>Bioaccumulation</th>
<th>Mobility</th>
<th>Partition coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stearyl Alcohol 112-92-5</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>7.19</td>
</tr>
<tr>
<td>ESTRADIOL USP 50-28-2</td>
<td>Slow</td>
<td>N/A</td>
<td>Immobile</td>
<td>4.01</td>
</tr>
</tbody>
</table>

Other adverse effects

No information available
13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes  
Disposal should be in accordance with applicable regional, national and local laws and regulations.

Contaminated packaging  
Do not reuse container. Dispose of contents/containers in accordance with local regulations.

14. TRANSPORT INFORMATION

DOT  
Not regulated

TDG  
Not regulated

ICAO (air)  
Not regulated

IATA  
Not regulated

IMDG  
Not regulated

ADR  
Not regulated

ADN  
Not regulated

15. REGULATORY INFORMATION

International Inventories

<table>
<thead>
<tr>
<th>TSCA</th>
<th>Not Listed</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSL/NDSL</td>
<td>Listed</td>
</tr>
<tr>
<td>EINECS/ELINCS</td>
<td>Not Listed</td>
</tr>
</tbody>
</table>

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances

US Federal Regulations

Carcinogenicity  
This product contains one or more substances which are classified by IARC as carcinogenic to humans (Group I), probably carcinogenic to humans (Group 2A) or possibly carcinogenic to humans (Group 2B)

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>ACGIH</th>
<th>IARC</th>
<th>NTP</th>
<th>OSHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP 50-28-2</td>
<td>-</td>
<td>Group 1</td>
<td>-</td>
<td>X</td>
</tr>
</tbody>
</table>

SARA 313  
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312 Hazard Categories

- Acute health hazard  
  No
- Chronic Health Hazard  
  No
- Fire hazard  
  No
- Sudden release of pressure hazard  
  No
- Reactive Hazard  
  No

CWA (Clean Water Act)
This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

**CERCLA**
This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

**US State Regulations**

**California Proposition 65**
This product contains the following Proposition 65 chemicals:

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>California Proposition 65</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTRADIOL USP - 50-28-2</td>
<td>Carcinogen</td>
</tr>
</tbody>
</table>

**U.S. State Right-to-Know Regulations**

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>New Jersey</th>
<th>Massachusetts</th>
<th>Pennsylvania</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROPYLENE GLYCOL USP</td>
<td>X</td>
<td>-</td>
<td>X</td>
</tr>
<tr>
<td>57-55-6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Creosin Wax</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>8002-74-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESTRADIOL USP</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>50-28-2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**16. OTHER INFORMATION**

Revision Date 02-Oct-2018
Revision Note No information available
Disclaimer
The information provided in this Material Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

End of Safety Data Sheet