MATERIAL SAFETY DATA SHEET

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

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Material Name: Estropipate Vaginal Cream, USP
Trade Name: Ogen (R) Vaginal Cream
Chemical Family: Mixture
Intended Use: Pharmaceutical product used for hormone replacement therapy

2. COMPOSITION/INFORMATION ON INGREDIENTS

### Hazardous

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerin, USP</td>
<td>56-81-5</td>
<td>200-289-5</td>
<td>*</td>
</tr>
<tr>
<td>Citric acid</td>
<td>77-92-9</td>
<td>201-069-1</td>
<td>*</td>
</tr>
<tr>
<td>Mineral oil</td>
<td>8012-95-1</td>
<td>232-384-2</td>
<td>*</td>
</tr>
<tr>
<td>Glyceryl monostearate</td>
<td>31566-31-1</td>
<td>250-705-4</td>
<td>*</td>
</tr>
<tr>
<td>Estropipate</td>
<td>7280-37-7</td>
<td>230-696-3</td>
<td>0.15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-(3-Chloroallyl)hexaminium chloride</td>
<td>4080-31-3</td>
<td>223-805-0</td>
<td>*</td>
</tr>
<tr>
<td>Polyethylene glycol ether complex of higher fatty alcohols</td>
<td>Not Assigned</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Piperazine hexahydrate</td>
<td>142-63-2</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>DIPHOSPHORIC ACID, TETRASODIUM SALTS</td>
<td>7722-88-5</td>
<td>231-767-1</td>
<td>*</td>
</tr>
<tr>
<td>Methylparaben</td>
<td>99-76-3</td>
<td>202-785-7</td>
<td>*</td>
</tr>
<tr>
<td>Propylparaben</td>
<td>94-13-3</td>
<td>202-307-7</td>
<td>*</td>
</tr>
<tr>
<td>Lanolin</td>
<td>8006-54-0</td>
<td>232-348-6</td>
<td>*</td>
</tr>
<tr>
<td>Cetyl alcohol</td>
<td>36653-82-4</td>
<td>253-149-0</td>
<td>*</td>
</tr>
<tr>
<td>Water, purified</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

3. HAZARDS IDENTIFICATION

Appearance: White cream
Signal Word: DANGER

Statement of Hazard: May cause cancer.
May damage fertility or the unborn child

Additional Hazard Information:
Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on the developing fetus. Occupational studies have shown that males working with estrogen-like compounds have shown clinical signs of hyperestrogenism including enlarged breasts and milk secretion. Loss of libido, breast tenderness, and changes in sex hormone levels have also occurred. Occupational exposure in females has resulted in menstrual irregularities (breakthrough bleeding, menstrual flow changes, spotting and amenorrhea).

Known Clinical Effects: Clinical use of estrogens has resulted in breast changes (enlargement, tenderness, and secretion), along with effects on the genitourinary (changes in vaginal bleeding), and GI systems. Effects on the skin, eyes, and CNS have also been reported. Clinical use has caused clotting abnormalities which may lead to stroke, heart attack, and pulmonary embolism.

EU Indication of danger: Carcinogenic: Category 1
Toxic to reproduction: Category 1

EU Hazard Symbols:

EU Risk Phrases:

R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

4. FIRST AID MEASURES

Eye Contact: Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Remove clothing and wash affected skin with soap and water. If irritation occurs or persists, get medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: This material produces toxic fumes of nitrogen and sulfur oxides, carbon dioxide, and carbon monoxide during fires.

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

Fire / Explosion Hazards: Not applicable
6. ACCIDENTAL RELEASE MEASURES

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

Measures for Environmental Protections: Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

General Handling: Avoid contact with eyes, skin and clothing. Wash thoroughly after handling.

Storage Conditions: Store as directed by product packaging. Keep out of reach of children.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Glycerin, USP
OSHA - Final PELS - TWAs:
ACGIH Threshold Limit Value (TWA) = 15 mg/m³ TWA total
ACGIH Threshold Limit Value (TWA) = 5 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA

Mineral oil
OSHA - Final PELS - TWAs:
ACGIH Threshold Limit Value (TWA) = 5 mg/m³ TWA
ACGIH Threshold Limit Value (STEL) = 10 mg/m³ STEL
ACGIH OELs - Notice of Intended Changes
Australia TWA = 5 mg/m³ TWA

Glyceryl monostearate
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA except stearates of toxic metals
Australia TWA = 10 mg/m³ TWA

DIPHOSPHORIC ACID, TETRASODIUM SALT
Australia TWA = 5 mg/m³ TWA

Estropipate
Pfizer OEL TWA-8 Hr: 1 ug/m³
The exposure limit(s) listed for solid components are only relevant if dust or mist may be generated.

Engineering Controls: Engineering controls should be used as the primary means to control exposures.

Personal Protective Equipment:

Hands: Rubber gloves
Eyes: Not required under normal conditions of use. Wear safety glasses or goggles if eye contact is possible.
Skin: Not required for the normal use of this product. Wear protective clothing when working with large quantities.
Respiratory protection: None required under normal conditions of use. If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

9. PHYSICAL AND CHEMICAL PROPERTIES:

Physical State: Cream  
Color: White  
Molecular Formula: Mixture  
Molecular Weight: Mixture  
Solubility: Soluble: Water

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.  
Conditions to Avoid: None for the normal use of this material  
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers.

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

Acute Toxicity: (Species, Route, End Point, Dose)

**Glycerin, USP**
- Mouse Oral LD50 4090 mg/kg
- Rat Oral LD50 12.6 g/kg
- Rabbit Dermal LD50 > 10 g/kg
- Rat Inhalation LC50 1hr > 570 mg/m³
- Rat Dermal LD 50 > 21.9 g/kg

**Glyceryl monostearate**
- Mouse IP LD50 200 mg/kg

**Cetyl alcohol**
- Rat Oral LD50 5000 mg/kg
- Rabbit Dermal LD50 > 2,600 mg/kg
- Mouse Oral LD50 3200 mg/kg

**N-(3-Chloroallyl)hexaminium chloride**
- Rat Oral LD 50 500 mg/kg
- Rabbit Dermal LD 50 565 mg/kg

**Propylparaben**
- Mouse Oral LD 50 633 mg/kg
- Mouse Intraperitoneal LD 50 200 mg/kg

**Methylparaben**
- Mouse Oral LD50 > 8000 mg/kg
- Rat Oral LD50 2280 mg/kg

**Citric acid**
Rat   Oral   LD50   3000 mg/kg

Piperazine hexahydrate
Mouse   Oral   LD 50   11,200 mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Glycerin, USP
Eye Irritation   Rabbit   Mild

Mineral oil
Eye Irritation   Rabbit   Moderate
Skin Irritation   Rabbit   Mild

N-(3-Chloroallyl)hexaminium chloride
Skin Irritation   Rabbit   Mild

Propylparaben
Eye Irritation   Rabbit   Severe
Skin Irritation   Rabbit   Mild

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Estropipate
30 Day(s)   Dog   Vaginal   10 mg/day   LOAEL   Female reproductive system
2 Year(s)   Dog   Oral   0.1-1 mg/kg/day   LOAEL   Male reproductive system
2 Year(s)   Rat   Oral   0.1-1.0 mg/kg   LOAEL   Male reproductive system

Propylparaben
3 Week(s)   Rat   Oral   27.1 g/kg   LOAEL   Endocrine system
4 Week(s)   Rat   Oral   347.2 g/kg   LOAEL   Male reproductive system

Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))

Estropipate
Embryo / Fetal Development   Mouse   Intraperitoneal   0.2 mg/day   LOAEL   Teratogenic

Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Estropipate
2 Year(s)   Rat   Oral   0.1-1 mg/kg/day   LOAEL   Pituitary gland, Female reproductive system, Tumors

Carcinogen Status: See below

Estropipate
IARC: Group 1 (Conjugated Estrogens)
NTP: Known (Steroidal Estrogens)
OSHA: Present

Mineral oil
IARC: Group 3
12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been investigated. Releases to the environment should be avoided.

Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Glycerin, USP
Onchorhynchus mykiss (Rainbow Trout) LC-50 96 Hours 50 mg/L
Daphnia Magna (Water Flea) EC-50 24 Hours >500 mg/L

Aquatic Toxicity Comments: A greater than symbol (>) indicates that aquatic toxicity was not observed at the maximum dose tested.

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations.

14. TRANSPORT INFORMATION

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

15. REGULATORY INFORMATION

EU Symbol: T
EU Indication of danger: Carcinogenic: Category 1
Toxic to reproduction: Category 1

EU Risk Phrases: R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

EU Safety Phrases: S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
DANGER
May cause cancer.
May damage fertility or the unborn child

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision A
N-(3-Chloroallyl)hexaminium chloride
  CERCLA/SARA 313 Emission reporting = 1.0 % de minimis concentration
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 223-805-0

Piperazine hexahydrate
  Australia (AICS): Present

Glycerin, USP
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 200-289-5

Citric acid
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 201-069-1

Mineral oil
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 232-384-2

Glyceryl monostearate
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 250-705-4

DIPHOSPHORIC ACID, TETRASODIUM SALT
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
  EU EINECS List 231-767-1

Methylparaben
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 202-785-7

Propylparaben
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 202-307-7

Lanolin
  Inventory - United States TSCA - Sect. 8(b) Present
  Australia (AICS): Present
  EU EINECS List 232-348-6
16. OTHER INFORMATION

Reasons for Revision:
Updated Section 3 - Hazard Identification. Updated Section 11 - Toxicology Information.
Updated Section 12 - Ecological Information. Updated Section 13 - Disposal Considerations.

Prepared by:
Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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End of Safety Data Sheet