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

Material Name: Estradiol Vaginal Ring
Trade Name: ESTRING; ELLESTE; OESTRING
Chemical Family: Steroid
Intended Use: Pharmaceutical product used as hormone replacement therapy

2. HAZARDS IDENTIFICATION

Appearance: Whitish solid
Signal Word: DANGER

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

Additional Hazard Information:
- Short Term: May be absorbed through the skin and cause systemic effects.
- Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on reproductive system, 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 this drug has caused headache, menstrual irregularities, changes in cervical erosion and secretion, breast enlargement, breast pain, nausea, vomiting, abdominal cramping, weight changes, fluid retention, loss of hair, mental depression. Other less common effects include breast cancer, uterine cancer, stroke, blood clots, mental confusion, and gallbladder disease.

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

EU Hazard Symbols: T

EU Risk Phrases:
2. HAZARDS IDENTIFICATION

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

Australian Hazard Classification (NOHSC):

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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>200-023-8</td>
<td>Carc.Cat.1,R45</td>
<td>2 mg****</td>
</tr>
<tr>
<td>Barium sulfate USP</td>
<td>7727-43-7</td>
<td>231-784-4</td>
<td>Not Listed</td>
<td></td>
</tr>
</tbody>
</table>

For the full text of the R phrases mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Eye Contact:
Rinse thoroughly with plenty of water, also under the eyelids. If irritation occurs or persists, get medical attention.

Skin Contact:
Wash hands and arms thoroughly after handling this material. Obtain medical assistance if skin effects occur.

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:
Due to the nature of this material first aid is not normally required. If discomfort occurs, get medical attention.

Symptoms and Effects of Exposure:
For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

5. FIRE FIGHTING MEASURES

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

Hazardous Combustion Products:
May include oxides of carbon, silicone.
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 spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. 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. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Storage Conditions:
Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Estradiol
- Pfizer OEL TWA-8 Hr: 0.2 µg/m³, Skin

Barium sulfate USP
- ACGIH Threshold Limit Value (TWA) 0.5 mg/m³ TWA
- 10 mg/m³ TWA
- Australia TWA 0.5 mg/m³
- 10 mg/m³
- Austria OEL - MAKs Listed
- Belgium OEL - TWA Listed
- Bulgaria OEL - TWA Listed
- Cyprus OEL - TWA Listed
- Czech Republic OEL - TWA Listed
- Denmark OEL - TWA Listed
- Estonia OEL - TWA Listed
- Finland OEL - TWA Listed
- France OEL - TWA Listed
- Germany - TRGS 900 - TWAs 0.5 mg/m³
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Analytical Method:
Analytical method available. Contact Pfizer Inc for further information.

Engineering Controls:
Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Environmental Exposure Controls:
Refer to specific Member State legislation for requirements under Community environmental legislation.

Personal Protective Equipment:
Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

- Hands:
  Impervious, disposable gloves (double suggested) are recommended if skin contact with drug product is possible and for bulk processing operations.

- Eyes:
  Wear safety glasses or goggles if eye contact is possible.

- Skin:
  Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

- Respiratory protection:
  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:
  Solid

- Color:
  Whitish

- Molecular Formula:
  Mixture

- Molecular Weight:
  Mixture

10. STABILITY AND REACTIVITY

- Chemical Stability:
  Stable under normal conditions of use.

- Conditions to Avoid:
  Fine particles (such as dust and mists) may fuel fires/explosions.

- 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 active ingredient(s).

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

Estradiol
90 Day(s)  Rat  Oral  0.003 mg/kg/day  NOAEL  Blood, Female reproductive system, Male reproductive system, Endocrine system, Liver

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

Estradiol
Reproductive & Fertility-Females  Rat  Oral  0.003 mg/kg/day  LOAEL  Reproductive toxicity
Embryo / Fetal Development  Rat  Intramuscular  30 mg/kg/day  LOAEL  Fetotoxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Estradiol
Sister Chromatid Exchange  Human Lymphocytes  Positive
Micronucleus  Human  Positive
Chromosomal Aberration  Human  Negative
In Vivo Direct DNA Damage  Hamster  Positive
In Vivo Micronucleus  Rodent Bone Marrow  Negative

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

Estradiol
2 Year(s)  Female Mouse  Oral  0.1 mg/kg  LOEL  Tumors, Mammary gland, Female reproductive system

Carcinogen Status: See below

Estradiol
IARC: Group 1
NTP: Listed
OSHA: Present

12. ECOLOGICAL INFORMATION

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

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.
14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

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

15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>EU Symbol:</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU Indication of danger:</td>
<td>Carcinogenic: Category 1</td>
</tr>
<tr>
<td></td>
<td>Toxic to reproduction: Category 1</td>
</tr>
<tr>
<td>EU Risk Phrases:</td>
<td>R45 - May cause cancer.</td>
</tr>
<tr>
<td></td>
<td>R60 - May impair fertility.</td>
</tr>
<tr>
<td></td>
<td>R61 - May cause harm to the unborn child.</td>
</tr>
<tr>
<td>EU Safety Phrases:</td>
<td>S22 - Do not breathe dust.</td>
</tr>
<tr>
<td></td>
<td>S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.</td>
</tr>
<tr>
<td></td>
<td>S53 - Avoid exposure - obtain special instructions before use.</td>
</tr>
</tbody>
</table>

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

Estradiol
California Proposition 65: carcinogen, initial date 1/1/88
Australia (AICS): Listed
Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
EU EINECS/ELINCS List: 200-023-8

Barium sulfate USP
CERCLA/SARA 313 Emission reporting: 1.0% de minimis concentration does not include Barium sulfate
Inventory - United States TSCA - Sect. 8(b): Listed
15. REGULATORY INFORMATION

Australia (AICS):
Listed

Standard for the Uniform Scheduling for Drugs and Poisons:
Schedule 6

EU EINECS/ELINCS List
231-784-4

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3
R45 - May cause cancer.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

Data Sources: The data contained in this MSDS may have been gathered from confidential internal sources, raw material suppliers, or from the published literature.

Reasons for Revision: New data sheet.

Prepared by: Product Stewardship Hazard Communications
Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet