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

Material Name: Estradiol Tablets

<table>
<thead>
<tr>
<th>Trade Name:</th>
<th>RONFASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Family:</td>
<td>Steroid</td>
</tr>
<tr>
<td>Intended Use:</td>
<td>Pharmaceutical product used for hormone replacement therapy</td>
</tr>
</tbody>
</table>

2. HAZARDS IDENTIFICATION

Appearance: White tablets
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 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 amenorrhrea).

Known Clinical Effects:
- Clinical use of this drug has caused menstrual irregularities, lack of menstrual periods (amenorrhea), changes in cervical erosion and secretion, breast enlargement, breast pain, breast development in males (gynecomastia), nausea, vomiting, abdominal cramping, weight changes, fluid retention, changes in sexual desire (libido), loss of hair, mental depression.

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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>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 Repr.Cat.1;R60 Repr.Cat.1;R61</td>
<td>1 or 2 mg ***</td>
</tr>
<tr>
<td>Maize starch</td>
<td>9005-25-8</td>
<td>232-679-6</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>9004-34-6</td>
<td>232-674-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose NF, monohydrate</td>
<td>64044-51-5</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Hypromellose</td>
<td>9004-65-3</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: *** per tablet/capsule/lozenge/suppository Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

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 off immediately with soap and plenty of 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.

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
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: Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling.

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

<table>
<thead>
<tr>
<th>Source</th>
<th>Limit Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer OEL TWA-8 Hr</td>
<td>0.2 µg/m³, Skin</td>
</tr>
</tbody>
</table>

Maize starch

<table>
<thead>
<tr>
<th>Source</th>
<th>Limit Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH Threshold Limit Value</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Australia TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Belgium OEL - TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Bulgaria OEL - TWA</td>
<td>10.0 mg/m³ TWA</td>
</tr>
<tr>
<td>Czech Republic OEL - TWA</td>
<td>4.0 mg/m³ TWA</td>
</tr>
<tr>
<td>Greece OEL - TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Ireland OEL - TWAs</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>OSHA - Final PELS - TWAs</td>
<td>15 mg/m³ TWA</td>
</tr>
<tr>
<td>Portugal OEL - TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Spain OEL - TWA</td>
<td>10 mg/m³ VLA-ED</td>
</tr>
</tbody>
</table>

Microcrystalline cellulose

<table>
<thead>
<tr>
<th>Source</th>
<th>Limit Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH Threshold Limit Value</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Australia TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Belgium OEL - TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
<tr>
<td>Estonia OEL - TWA</td>
<td>10 mg/m³ TWA</td>
</tr>
</tbody>
</table>
Material Name: Estradiol Tablets
Revision date: 27-Sep-2007
Version: 1.0

Analytical Method:
Analytical method available for estradiol. 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.

Personal Protective Equipment:
- 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:

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Film-coated tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
</tr>
<tr>
<td>Color:</td>
<td>White</td>
</tr>
<tr>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.
Conditions to Avoid: None known
Incompatible Materials: None known

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)

Magnesium stearate
- Rat Oral LD50 > 2000 mg/kg
- Rat Inhalation LC50 > 2000 mg/m³

Hypermellose
- Rat Oral LD50 > 10,000 mg/kg

Microcrystalline cellulose
- Rat Oral LD50 > 5000 mg/kg
- Rabbit Dermal LD50 > 2000 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)

Microcrystalline cellulose
- Skin Irritation Rabbit Non-irritating
- Eye Irritation Rabbit Non-irritating

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
- Chromosome 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
12. ECOLOGICAL INFORMATION

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

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered.

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:
S22 - Do not breathe dust.
S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.
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

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

Lactose NF, monohydrate
- Australia (AICS): Present

Maize starch
- Inventory - United States TSCA - Sect. 8(b): XU
- Australia (AICS): Present
- REACH - Annex IV - Exemptions from the obligations of Register: Present
- EU EINECS/ELINCS List: 232-679-6

Microcrystalline cellulose
- Inventory - United States TSCA - Sect. 8(b): XU
- Australia (AICS): Present
- EU EINECS/ELINCS List: 232-674-9

Magnesium stearate
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 209-150-3

Hyprosmellose
- Inventory - United States TSCA - Sect. 8(b): XU
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 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: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety
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End of Safety Data Sheet