



# MATERIAL SAFETY DATA SHEET

Revision date: 05-Dec-2011

Version: 2.0

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

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### Material Name: Estradiol Tablets

Trade Name:	RONFASE
Chemical Family:	Steroid
Intended Use:	Pharmaceutical product used for hormone replacement therapy

## 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 amenorrhea).

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.

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## 2. HAZARDS IDENTIFICATION

Australian Hazard Classification (NOHSC):

R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Hazardous Substance. Non-Dangerous Goods.

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

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Estradiol	50-28-2	200-023-8	Carc.Cat.1;R45 Repr.Cat.1;R60 Repr.Cat.1;R61 N;R50/53	1 or 2 mg ***
Magnesium stearate	557-04-0	209-150-3	Not Listed	*
Maize starch	9005-25-8	232-679-6	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Lactose NF, monohydrate	64044-51-5	Not Listed	Not Listed	*
Hydroxypropyl methylcellulose	9004-65-3	Not Listed	Not Listed	*

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.

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**Hazardous Combustion Products:** May include oxides of carbon

**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:** 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. 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/m<sup>3</sup>, Skin

#### Magnesium stearate

ACGIH Threshold Limit Value (TWA) 10 mg/m<sup>3</sup>  
Lithuania OEL - TWA 5 mg/m<sup>3</sup>  
Sweden OEL - TWAs 5 mg/m<sup>3</sup>

#### Maize starch

ACGIH Threshold Limit Value (TWA) 10 mg/m<sup>3</sup>  
Australia TWA 10 mg/m<sup>3</sup>  
Belgium OEL - TWA 10 mg/m<sup>3</sup>  
Bulgaria OEL - TWA 10.0 mg/m<sup>3</sup>  
Czech Republic OEL - TWA 4.0 mg/m<sup>3</sup>  
Greece OEL - TWA 10 mg/m<sup>3</sup>  
5 mg/m<sup>3</sup>

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### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Ireland OEL - TWAs	10 mg/m <sup>3</sup> 4 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	15 mg/m <sup>3</sup>
Portugal OEL - TWA	10 mg/m <sup>3</sup>
Slovakia OEL - TWA	4 mg/m <sup>3</sup>
Spain OEL - TWA	10 mg/m <sup>3</sup>

#### Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m <sup>3</sup>
Australia TWA	10 mg/m <sup>3</sup>
Belgium OEL - TWA	10 mg/m <sup>3</sup>
Estonia OEL - TWA	10 mg/m <sup>3</sup>
France OEL - TWA	10 mg/m <sup>3</sup>
Ireland OEL - TWAs	10 mg/m <sup>3</sup> 4 mg/m <sup>3</sup>
Latvia OEL - TWA	2 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	15 mg/m <sup>3</sup>
Portugal OEL - TWA	10 mg/m <sup>3</sup>
Romania OEL - TWA	10 mg/m <sup>3</sup>
Spain OEL - TWA	10 mg/m <sup>3</sup>

#### 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.

#### 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

<b>Physical State:</b>	Film-coated tablets	<b>Color:</b>	White
<b>Molecular Formula:</b>	Mixture	<b>Molecular Weight:</b>	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

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### 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/m<sup>3</sup>

##### **Hydroxypropyl methylcellulose**

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 NOEL 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 LOEL Reproductive toxicity  
Embryo / Fetal Development Rat Intramuscular 30 mg/kg/day LOEL 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

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### 11. TOXICOLOGICAL INFORMATION

#### Estradiol

IARC: Group 1 (Carcinogenic to Humans)  
NTP: Listed  
OSHA: Listed

### 12. ECOLOGICAL INFORMATION

**Environmental Overview:** Environmental properties have not been investigated. Releases to the environment should be avoided. See aquatic toxicity data, below:

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

#### Estradiol

Fish LC50 96 Hours 2 mg/L

### 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

**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.  
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

#### **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.

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## 15. REGULATORY INFORMATION

### 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
	Schedule 5
EU EINECS/ELINCS List	200-023-8

### Lactose NF, monohydrate

Australia (AICS):	Present
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### Magnesium stearate

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

### Maize starch

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

### Hydroxypropyl methylcellulose

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

### Microcrystalline cellulose

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

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### 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:** Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 7 - Handling and Storage. Updated Section 12 - Ecological Information. Updated Section 15 - Regulatory Information.

**Prepared by:** Product Stewardship Hazard Communication  
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**