



MATERIAL SAFETY DATA SHEET

Revision date: 27-Sep-2007

Version: 1.0

Page 1 of 8

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.

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 2 of 8
Version: 1.0

Australian Hazard Classification (NOHSC):

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

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Lactose NF, monohydrate	64044-51-5	Not listed	Not Listed	*
Hypromellose	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.
- Hazardous Combustion Products:** May include oxides of carbon

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 3 of 8
Version: 1.0

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.

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

Maize starch

ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA
Belgium OEL - TWA = 10 mg/m³ TWA
Bulgaria OEL - TWA = 10.0 mg/m³ TWA
Czech Republic OEL - TWA = 4.0 mg/m³ TWA
Greece OEL - TWA = 10 mg/m³ TWA
Ireland OEL - TWAs = 5 mg/m³ TWA
OSHA - Final PELs - TWAs: = 10 mg/m³ TWA
Portugal OEL - TWA = 4 mg/m³ TWA
Spain OEL - TWA = 15 mg/m³ TWA total
= 5 mg/m³ TWA
= 10 mg/m³ TWA
= 10 mg/m³ VLA-ED

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA
Belgium OEL - TWA = 10 mg/m³ TWA
Estonia OEL - TWA = 10 mg/m³ TWA

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 4 of 8
Version: 1.0

France OEL - TWA	= 10 mg/m ³ VME	
Ireland OEL - TWAs	= 10 mg/m ³ TWA	
	= 4 mg/m ³ TWA	
Latvia OEL - TWA	= 2 mg/m ³ TWA	
OSHA - Final PELs - TWAs:	= 15 mg/m ³ TWA	total
	= 5 mg/m ³ TWA	
Portugal OEL - TWA	= 10 mg/m ³ TWA	
Romania OEL - TWA	= 10 mg/m ³ TWA	
Spain OEL - TWA	= 10 mg/m ³ VLA-ED	

Magnesium stearate

ACGIH Threshold Limit Value (TWA)	= 10 mg/m ³ TWA	except stearates of toxic metals
Australia TWA	= 10 mg/m ³ TWA	
Belgium OEL - TWA	= 10 mg/m ³ TWA	
Ireland OEL - TWAs	= 10 mg/m ³ TWA	except lead stearate
Lithuania OEL - TWA	= 3 mg/m ³ IPRV	
Portugal OEL - TWA	= 10 mg/m ³ TWA	does not include stearates of toxic metals
Spain OEL - TWA	= 10 mg/m ³ VLA-ED	not including stearates of toxic metals
Sweden OEL - TWAs	= 5 mg/m ³ LLV	

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:

Physical State:	Film-coated tablets	Color:	White
Molecular Formula:	Mixture	Molecular Weight:	Mixture

10. STABILITY AND REACTIVITY

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

11. TOXICOLOGICAL INFORMATION

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 5 of 8
Version: 1.0

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

Hypromellose

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

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 6 of 8
Version: 1.0

OSHA: Present

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

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 7 of 8
Version: 1.0

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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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

Hypromellose

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

MATERIAL SAFETY DATA SHEET

Material Name: Estradiol Tablets
Revision date: 27-Sep-2007

Page 8 of 8
Version: 1.0

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