MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Femhrt® - 1/5 and 1/10 Tablets (Norethindrone Acetate/Ethinyl Estradiol Tablets)

Trade Name: Femhrt®
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as hormone replacement therapy

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS List	%
Norethindrone Acetate	51-98-9	200-132-0	1.43
Ethinyl Estradiol	57-63-6	200-342-2	<1.0
Calcium stearate	1592-23-0	216-472-8	*
Corn Starch	9005-25-8	232-679-6	*
Microcrystalline cellulose	9004-34-6	232-674-9	*

Ingredient	CAS Number	EU EINECS List	%
Lactose NF, monohydrate	64044-51-5	Not listed	*

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

3. HAZARDS IDENTIFICATION

Appearance: White D-shaped tablets
Signal Word: WARNING

Statement of Hazard: Carcinogen
May cause reproductive system effects.
May cause harm to the unborn child.

Additional Hazard Information:
Short Term: Dust may be absorbed through the skin and cause systemic effects. Accidental ingestion may cause effects similar to those seen in clinical use.
Long Term: Occupational exposure to components of this mixture has resulted in menstrual irregularities in women and breast changes (enlargement, mammary secretions), loss of libido, and changes in sex hormone levels in men.

Known Clinical Effects: Hormone replacement therapy is associated with increased risks of myocardial infarction, thromboembolism, stroke, cancer of the breast and endometrium, and gallbladder disease. The most common adverse effects seen during clinical use of Femhrt® are nausea, vomiting, abdominal pain, nervousness, depression, breast pain, urinary tract infection, headache, and changes in vaginal bleeding patterns.

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 product or its ingredients 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: Immediately flush eyes with water 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. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder. If irritation occurs or persists, get medical attention.

Ingestion: Get medical attention. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention.

5. FIRE FIGHTING MEASURES

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

Hazardous Combustion Products: No data available

Fire Fighting Procedures: Wear approved positive pressure, self-contained breathing apparatus and full protective turn out gear.

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: If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing.

Storage Conditions: Store in a cool, dry, well-ventilated area.

Storage Temperature: Store below 30°C

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Norethindrone Acetate

Pfizer OEL TWA-8 Hr:	0.8 ug/m^3, Skin	

Ethinyl Estradiol

Pfizer OEL TWA-8 Hr:	40 ng/m^3, Skin	

Calcium stearate

ACGIH Threshold Limit Value (TWA)	= 10 mg/m^3 TWA	except stearates of toxic metals
Australia TWA	= 10 mg/m^3 TWA	

Corn Starch

OSHA - Final PELS - TWAs:	= 15 mg/m^3 TWA = 5 mg/m^3 TWA	total
ACGIH Threshold Limit Value (TWA)	= 10 mg/m^3 TWA	
Australia TWA	= 10 mg/m^3 TWA	

Microcrystalline cellulose

OSHA - Final PELS - TWAs:	= 15 mg/m^3 TWA = 5 mg/m^3 TWA	total
ACGIH Threshold Limit Value (TWA)	= 10 mg/m^3 TWA	
Australia TWA	= 10 mg/m^3 TWA	

The exposure limit(s) listed for solid components are only relevant if dust may be generated.

Analytical Method: Analytical method available for norethindrone acetate; ethinyl estradiol. Contact Pfizer Inc for further information.

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

Personal Protective Equipment:

Hands:	Rubber gloves
Eyes:	Safety glasses or goggles
Skin:	Wear protective clothing with long sleeves to avoid skin contact. Wash hands and arms thoroughly after handling this product.
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:	Tablet	**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

Hazardous Decomposition Products: 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)

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

Norethindrone Acetate
Rat Oral LD50 > 5010 mg/kg
Mouse Oral LD50 > 5010 mg/kg

Ethinyl Estradiol
Mouse Oral LD50 1737 mg/kg
Rat Oral LD50 1200 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

Chronic Effects/Carcinogenicity The combination of ethinyl estradiol and norethindrone acetate was tested for carcinogenicity in mice, rats, and monkeys. Mice exhibited pituitary tumors. Rats developed mammary and benign liver-cell tumors along with endometrial carcinomas, hyperplastic nodules of the liver, and hepatocellular carcinoma. Monkeys treated for 10 years did not develop malignant tumors. Hormone replacement therapy is associated with an increased risk of developing endometrial and breast cancers.

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

Norethindrone Acetate

Embryo / Fetal Development	Rat	No route specified	1 mg/kg/day	LOEL	Teratogenic
Embryo / Fetal Development	Mouse	No route specified	0.5 mg/kg/day	LOEL	Teratogenic
Embryo / Fetal Development	Rat	No route specified	3.5 mg/kg/day	NOAEL	Not Teratogenic

Ethinyl Estradiol

Embryo / Fetal Development	Mouse	No route specified	0.02 mg/kg/day	LOEL	Embryotoxicity, Not teratogenic

Reproductive Effects Reproductive toxicity has been reported in male animals exposed to estradiol. Effects included a decrease in testicular size and a reduction in testosterone levels. Norethindrone acetate has been shown to effectively inhibit ovulation in rats.

Teratogenicity Rhesus monkeys given norethindrone acetate and ethinyl estradiol in combination exhibited embryo lethality and virilization of female offspring. There are conflicting reports concerning the ability of estrogen/progestin combinations to cause genital anomalies in exposed human fetuses.

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

Norethindrone Acetate

Bacterial Mutagenicity (Ames)	*Salmonella*	Negative
In Vitro Chromosome Aberration	Human Lymphocytes	Positive
In Vitro Sister Chromatid Exchange	Human Lymphocytes	Negative
In Vivo Unscheduled DNA Synthesis	Rat Hepatocyte	Positive
In Vivo Direct DNA Damage	Mouse	Negative

Ethinyl Estradiol

Bacterial Mutagenicity (Ames)	*Salmonella*	Negative
Chromosome Aberration	Human Lymphocytes	Positive
Sister Chromatid Exchange	Human Lymphocytes	Positive
Chromosome Aberration	Chinese Hamster Ovary (CHO) cells	Positive
In Vivo Micronucleus	Mouse Bone Marrow	Positive

Mutagenicity Genotoxicity testing results indicate that EE and NA do not directly interact with DNA but that they may produce non-specific chromosome damage.

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

Norethindrone Acetate

2 Year(s)	Male Rat	Oral	3-4 mg/kg/day	LOEL	Malignant tumors, Liver
2 Year(s)	Female Rat	Oral	3-4 mg/kg/day	LOEL	Tumors, Female reproductive system
104 Week(s)	Male Rat	Intramuscular	10 mg/kg/day	LOEL	Malignant tumors, Mammary gland, Liver, Endocrine system
104 Week(s)	Female Rat	Intramuscular	10 mg/kg/day	LOEL	Malignant tumors, Liver, Mammary gland

Ethinyl Estradiol

80 Week(s)	Mouse	Oral, in feed	0.07 mg/kg/day	LOEL	Tumors, Pituitary gland
104 Week(s)	Rat	No route specified	0.07 mg/kg/day	LOEL	Malignant tumors, Liver
105 Week(s)	Rat	Oral, in feed	0.053 mg/kg/day	NOEL	Not carcinogenic

Carcinogen Status: See below

Norethindrone Acetate

IARC: Group 2B
NTP: Listed
OSHA: Present

Ethinyl Estradiol

IARC: Group 1

NTP:	Listed
OSHA:	Present

At increase risk from exposure: Cigarette smoking increases the risk of serious cardiovascular side effects from estrogen/progestin combination use.

Additional Information: Small amounts of estrogens and progestins have been identified in the milk of nursing mothers, and a few adverse effects on the child have been reported. In addition, estrogens given in the postpartum period may interfere with lactation by decreasing the quantity and quality of breast milk.

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided.

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:

S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING

Carcinogen
May cause reproductive system effects.
May cause harm to the unborn child.

Canada - WHMIS: Classifications

WHMIS hazard class:
Class D, Division 2, Subdivision A

Norethindrone Acetate

California Proposition 65	developmental toxicity, initial date 10/1/91
Australia (AICS):	Present
EU EINECS List	200-132-0

Ethinyl Estradiol

California Proposition 65	carcinogen, initial date 1/1/88 developmental toxicity, initial date 4/1/90 (when mixed with Norethisterone)
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	200-342-2

Calcium stearate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	216-472-8

Corn Starch

Inventory - United States TSCA - Sect. 8(b)	XU
Australia (AICS):	Present
EU EINECS List	232-679-6

Microcrystalline cellulose

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

Lactose NF, monohydrate

Australia (AICS):	Present

16. OTHER INFORMATION

Reasons for Revision: Updated Section 3 - Hazard Identification. Updated Section 5 - Fire Fighting Measures. Updated Section 6 - Accidental Release Measures. Updated Section 7 - Handling and Storage. Updated Section 10 - Stability and Reactivity. Updated Section 11 - Toxicology Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

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

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End of Safety Data Sheet