



MATERIAL SAFETY DATA SHEET

Revision date: 25-Jul-2007

Version: 1.0

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

Pfizer Inc
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Contact E-Mail: Contact E-Mail: pfizer-MSDS@pfizer.com This e-mail address should not be used to report suspected adverse events.

Material Name: Norethisterone/Ethinylloestradiol tablets

Trade Name:	BREVINOR; SYNPHASE; NORIMIN
Chemical Family:	Mixture
Intended Use:	Pharmaceutical product used as oral contraceptive

2. HAZARDS IDENTIFICATION

Appearance: White or Blue Tablet
Signal Word: WARNING

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

Additional Hazard Information:

Short Term:	Dust may be absorbed through the skin and cause systemic effects. May be harmful if swallowed. (based on components) . 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: The use of oral contraceptives is associated with increased risks of myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease. The most common adverse effects seen during clinical use of oral contraceptives are menstrual irregularities.

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

EU Hazard Symbols:



EU Risk Phrases:

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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.
Hazardous Substance. Non-Dangerous Goods.

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 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.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Ethinyl Estradiol	57-63-6	200-342-2	Carc. Cat.1;R45 N;R50/53 Repr. Cat.1;R60/61 Xn;R22	< 1.0
Norethisterone	68-22-4	200-681-6	Carc. Cat.2;R45 N;R50/53 Repr. Cat.1;R60/61	1.3-2.0
Starch	9005-25-8	232-679-6	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	*
Povidone	9003-39-8	Not listed	Not Listed	*
FD & C Blue No. 1	3844-45-9	223-339-8	Not Listed	*

Additional Information: * Proprietary
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: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek 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.

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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: Formation of toxic gases is possible during heating or fire.

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: Restrict access to work area. 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. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Ethinyl Estradiol	
Pfizer OEL TWA-8 Hr:	0.04µg/m ³ , Skin
Norethisterone	
Pfizer OEL TWA-8 Hr:	0.8µg/m ³ , Skin
Starch	
ACGIH Threshold Limit Value (TWA)	= 10 mg/m ³ TWA
Australia TWA	= 10 mg/m ³ TWA
Belgium OEL - TWA	= 10 mg/m ³ TWA
Bulgaria OEL - TWA	= 10.0 mg/m ³ TWA
Czech Republic OEL - TWA	= 4.0 mg/m ³ TWA
Greece OEL - TWA	= 10 mg/m ³ TWA
	= 5 mg/m ³ TWA

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Ireland OEL - TWAs	= 10 mg/m ³ TWA
	= 4 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
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	

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

Analytical Method: Analytical method available for Ethinyl Estradiol and Norethisterone. 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:	Tablet	Color:	White, or Blue
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

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General Information: The information included in this section describes the potential hazards of the individual ingredients, except where noted.

Acute Toxicity: (Species, Route, End Point, Dose)

Magnesium stearate

Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m³

Starch

Mouse IP LD50 6600 mg/kg

Ethinyl Estradiol

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

Norethindrone Acetate

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

Povidone

Rat Oral LD50 100 g/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.

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

Ethinyl Estradiol

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

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

Reproductive Effects

This product is an oral contraceptive and as such, may adversely effect fertility. 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 oral contraceptives to cause genital anomalies in exposed human fetuses.

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

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

Norethindrone Acetate

Bacterial Mutagenicity (Ames) *Salmonella* Negative
In Vitro Chromosome Aberration Human Lymphocytes Positive
In Vitro Sister Chromatid Exchange Human Lymphocytes Negative

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In Vivo Unscheduled DNA Synthesis Rat Hepatocyte Positive
In Vivo Direct DNA Damage Mouse Negative

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

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

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

Carcinogen Status: See below

FD & C Blue No. 1

IARC: Group 3

Ethinyl Estradiol

IARC: Group 1

NTP: Listed

OSHA: Present

Norethindrone Acetate

IARC: Group 2B

NTP: Listed

OSHA: Present

Povidone

IARC: Group 3

Norethisterone

IARC: Group 2B

NTP: Reasonably Anticipated To Be A Carcinogen

OSHA: Present

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this mixture have not been fully evaluated. Releases to the environment should be avoided. See Aquatic toxicity data of the active ingredient, below:

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

Ethinyl Estradiol

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Oncorhynchus mykiss (Rainbow Trout) LC50 96 Hours 1.6 mg/L
Daphnia magna (Water Flea) EC50 48 Hours 5.7 mg/L
Algae EC50 0.84 mg/L

Norethisterone

Oncorhynchus mykiss (Rainbow Trout) OECD LC50 96 Hours > 4.3 mg/L
Scenedesmus subspicatus (Green Alga) OECD EC50 Hours 0.12 mg/L

Aquatic Toxicity Comments: A greater than (>) symbol indicates that acute ecotoxicity was not observed at the maximum solubility. Since the substance is insoluble in aqueous solutions above this concentration, an acute ecotoxicity value (i.e. LC/EC50) is not achievable.

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.
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 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.
S57 - Use appropriate containment to avoid environmental contamination.

OSHA Label:
WARNING
May cause cancer.
May damage fertility or the unborn child.

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Canada - WHMIS: Classifications

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



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/ELINCS List	200-342-2

Norethisterone

California Proposition 65	carcinogen, initial date 10/1/89 developmental toxicity, initial date 4/1/90
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	200-681-6

Lactose NF, monohydrate

Australia (AICS):	Present
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Povidone

Inventory - United States TSCA - Sect. 8(b)	XU
Australia (AICS):	Present

FD & C Blue No. 1

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	223-339-8

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

Magnesium stearate

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

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16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.

R45 - May cause cancer.

R60 - May impair fertility.

R61 - May cause harm to the unborn child.

R50 - Very toxic to aquatic organisms.

R53 - May cause long-term adverse effects in the aquatic environment.

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

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

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End of Safety Data Sheet