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

Material Name: Levonorgestrel and Ethinyl Estradiol Tablets

- Trade Name: LYBREL
- Chemical Family: Synthetic estrogen, Synthetic progestogen
- Intended Use: Pharmaceutical product used as oral contraceptive

2. HAZARDS IDENTIFICATION

Appearance: Yellow Tablet
Signal Word: DANGER

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:

- T

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.
2. HAZARDS IDENTIFICATION


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

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethinyl Estradiol</td>
<td>57-63-6</td>
<td>200-342-2</td>
<td>Carc. Cat.1;R45 N;R50/53</td>
<td>20 mcg***</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr. Cat.1;R60/61 Xn;R22</td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>797-63-7</td>
<td>212-349-8</td>
<td>Repr.Cat.1;R60 Carc.Cat.3;R40 Repr.Cat.2;R61-64</td>
<td>90 mcg***</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Iron oxide</td>
<td>1309-37-1</td>
<td>215-168-2</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>25322-68-3</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>236-675-5</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>Lactose NF, monohydrate</td>
<td>64044-51-5</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Polacrilin potassium</td>
<td>39394-76-8</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Fatty acids, montan-wax, ethylene esters</td>
<td>73138-45-1</td>
<td>277-291-8</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Hydroxypropyl methycellulose</td>
<td>9004-65-3</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: * Proprietary  
*** 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: 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.
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: Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, restrict access to work area. 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. 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.

Ethinyl Estradiol
Pfizer OEL TWA-8 Hr: 0.04µg/m³, Skin

Levonorgestrel
Pfizer OEL TWA-8 Hr: 0.05µg/m³

Magnesium stearate
ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA
Australia TWA 10 mg/m³
### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Material Name: Levonorgestrel and Ethinyl Estradiol Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revision date:</strong> 09-Mar-2011</td>
</tr>
<tr>
<td><strong>Version:</strong> 1.0</td>
</tr>
</tbody>
</table>

#### Iron oxide
- **ACGIH Threshold Limit Value (TWA)**
  - 1 mg/m³ TWA
  - 5 mg/m³ TWA
- **OSHA - Final PELS - TWAs:**
  - 10 mg/m³ total

#### Polyethylene glycol
- **Austria OEL - MAKs**
  - Listed
- **Germany - TRGS 900 - TWAs**
  - 1000 mg/m³
- **Germany (DFG) - MAK**
  - 1000 mg/m³ MAK
- **Slovenia OEL - TWA**
  - Listed

#### Titanium dioxide
- **ACGIH Threshold Limit Value (TWA)**
  - 10 mg/m³ TWA
- **Austria OEL - MAKs**
  - Listed
- **Belgium OEL - TWA**
  - Listed
- **Bulgaria OEL - TWA**
  - Listed
- **Denmark OEL - TWA**
  - Listed
- **Estonia OEL - TWA**
  - Listed
- **France OEL - TWA**
  - Listed
- **Germany (DFG) - MAK**
  - Listed
- **Ireland OEL - TWAs**
  - Listed
- **Latvia OEL - TWA**
  - Listed
- **Lithuania OEL - TWA**
  - Listed
- **OSHA - Final PELS - TWAs:**
  - 15 mg/m³ total
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

- Physical State: Tablet
- Molecular Formula: Mixture
- Color: Yellow
- Molecular Weight: 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.

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA
Australia TWA 10 mg/m³
Belgium OEL - TWA Listed
Estonia OEL - TWA Listed
France OEL - TWA Listed
Ireland OEL - TWAs Listed
Latvia OEL - TWA Listed
OSHA - Final PELS - TWAs: 15 mg/m³ total
5 mg/m³
Portugal OEL - TWA Listed
Romania OEL - TWA Listed
Spain OEL - TWA Listed

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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/m³

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

Titanium dioxide
Rat Oral LD50 > 7500 mg/kg
Rat Subcutaneous LD 50 50 mg/kg

Hydroxypropyl methylcellulose
Rat Oral LD50 > 10,000 mg/kg

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

Levonorgestrel
Rat Oral LD50 > 4000 mg/kg
Mouse Oral LD50 > 4000 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

Polyethylene glycol
Eye Irritation Rabbit Mild
Skin Irritation Rabbit Mild

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

Levonorgestrel
Reproductive & Fertility Rat Oral 10 ug/kg/day LOAEL Fertility
Reproductive & Fertility Rabbit Oral 1875 ug/kg/day LOAEL Fertility

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

Ethinyl Estradiol
11. TOXICOLOGICAL INFORMATION

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

Levonorgestrel
Bacterial Mutagenicity (Ames)  *Salmonella*  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

Carcinogen Status:  See below

**Titanium dioxide**
- IARC:  Group 3 (Not Classifiable)

**Iron oxide**
- IARC:  Group 3

**Ethinyl Estradiol**
- IARC:  Group 1
- NTP:  Listed
- OSHA:  Present

**Levonorgestrel**
- IARC:  Group 2B
- 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**
- *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

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.

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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:
S36/37 - Wear suitable protective clothing and gloves.
S22 - Do not breathe dust.
S53 - Avoid exposure - obtain special instructions before use.
S57 - Use appropriate containment to avoid environmental contamination.

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
15. REGULATORY INFORMATION

**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)**: Listed
- **Australia (AICS)**: Listed
- **Standard for the Uniform Scheduling for Drugs and Poisons**: Schedule 4
- **EU EINECS/ELINCS List**: 200-342-2

**Levonorgestrel**
- **California Proposition 65**: female reproductive toxicity, initial date 5/15/98 (implants)
- **Inventory - United States TSCA - Sect. 8(b)**: Listed
- **Australia (AICS)**: Listed
- **EU EINECS/ELINCS List**: 212-349-8

**Lactose NF, monohydrate**
- **Australia (AICS)**: Listed

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

**Fatty acids, montan-wax, ethylene esters**
- **Inventory - United States TSCA - Sect. 8(b)**: Listed
- **Australia (AICS)**: Listed
- **EU EINECS/ELINCS List**: 277-291-8

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

**Iron oxide**
- **Inventory - United States TSCA - Sect. 8(b)**: Listed
- **Australia (AICS)**: Listed
- **Standard for the Uniform Scheduling for Drugs and Poisons**: Schedule 2
  Schedule 4
  Schedule 5
  Schedule 6
- **EU EINECS/ELINCS List**: 215-168-2

**Polyethylene glycol**
- **Inventory - United States TSCA - Sect. 8(b)**: Listed
- **Australia (AICS)**: Listed

**Titanium dioxide**
- **Inventory - United States TSCA - Sect. 8(b)**: Listed
- **Australia (AICS)**: Listed
- **EU EINECS/ELINCS List**: 236-675-5
15. REGULATORY INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect
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: Product Stewardship Hazard Communications
Pfizer Global Environment, Health, and Safety Operations

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End of Safety Data Sheet