1. PRODUCT AND COMPANY IDENTIFICATION

Product Name: Hormone Replacement Products

Common Name: Not available

Chemical Name: Not applicable

Synonyms: Premarin, Premarin Cream, Premarin Intravenous, Premphase, Prempro, Conjugated Estrogens, Medroxyprogesterone Acetate, 17ß Estratriol, Totelle, Premia, Trimegestone, Premique, Premique Low Dose, Premelle 2.5/5, Premelle Cycle 5, Gen-Medroxy, Premplus

Product Use: Pharmaceutical product

Classification: Hormones and Synthetic Substitutes

Supplier: Wyeth

P.O. Box 8299
Philadelphia, PA 19101 USA.
Telephone: 1-610-688-4400

Emergency Telephone Number: Chemtrec USA, Puerto Rico, Canada 1-800-424-9300
Chemtrec International 1-703-527-3887

2. HAZARDS IDENTIFICATION

Emergency Overview
This contains an active pharmaceutical ingredient that can affect body functions; handle with caution.

Appearance: Pharmaceutical tablet, powder, or cream

Physical State: Solid

Odor: Odorless

Potential Physical Hazards
Powders and solids are presumed to be combustible.

Potential Health Effects

Eyes: May cause mechanical eye irritation.

Skin: Not available

Inhalation: Not available

Ingestion:
The most common effects may include, vaginal bleeding irregularities, change in menstrual flow, breast changes (tenderness, pain, enlargement, secretion, lumps), vaginal secretion, headache, vaginal yeast infections, changes in reproductive organs, skin rash, joint pain, diarrhea, dizziness, fatigue, nausea, vomiting, hair loss, and stomach/abdominal cramps/bloating. Increased risks of endometrial cancer, heart attack, pulmonary emboli, deep vein thrombosis, coronary heart disease, stroke, venous thromboembolism, breast cancer, ovarian cancer, dementia, gallbladder disease, mental depression, colitis, central nervous system effects.

May impair fertility. May cause harm to the unborn child. Excreted in breast milk. May cause cancer.

Please see Patient Package Insert for further information.

Therapeutic Target Organ(s): Reproductive System.

Potential Environmental Effects: See Section 12.
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Common Name</th>
<th>CAS-No</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone Acetate</td>
<td>71-58-9</td>
<td>0 - 10 mg/tablet</td>
</tr>
<tr>
<td>Congugated Estrogens</td>
<td>12126-59-9</td>
<td>0.3 - 25 mg/tablet or vial or gram</td>
</tr>
<tr>
<td>Trimegestone</td>
<td>74531-62-5</td>
<td>0 - 500 mg/tablet</td>
</tr>
<tr>
<td>17ß Estradiol</td>
<td>50-28-2</td>
<td>0 - 2 mg/tablet</td>
</tr>
<tr>
<td>Inactive Ingredients</td>
<td>Not applicable</td>
<td>Remainder</td>
</tr>
</tbody>
</table>

4. FIRST AID MEASURES

Eye Contact: In the case of contact with eyes, rinse immediately with plenty of water for 15 minutes and seek medical advice.

Skin Contact: Take off contaminated clothing and shoes immediately. Wash off immediately with soap and plenty of water. If skin irritation persists, call a physician.

Inhalation: Move to fresh air. Artificial respiration and/or oxygen may be necessary. If symptoms persist, call a physician.

Ingestion: If symptoms persist, call a physician. Do not induce vomiting without medical advice. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Flammable Properties: Presumed to be a combustible particulate solid.

Extinguishing Media

<table>
<thead>
<tr>
<th>Suitable Extinguishing Media</th>
<th>Unsuitable Extinguishing Media</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use water spray, foam, dry chemical or carbon dioxide.</td>
<td>Do NOT use water jet.</td>
</tr>
</tbody>
</table>

Fire Fighting: Evacuate area and fight fire from a safe distance. Cool closed containers exposed to fire with water spray. In the event of fire and/or explosion do not breathe fumes.

Hazardous Combustion Products: Carbon oxides, nitrogen oxides.

Protective Equipment and Precautions for Firefighters: In the event of fire, wear self-contained breathing apparatus and special protective equipment for fire fighters.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions: Refer to protective measures listed in Sections 7 and 8.

Environmental Precautions: Prevent product from entering drains. Local authorities should be advised if a significant spill cannot be contained.

Methods for Containment: Not available

Methods for Cleaning up: Take up mechanically and collect in suitable container for disposal. Clean contaminated surface thoroughly. Avoid formation of dust and aerosols.
7. HANDLING AND STORAGE

Handling
For personal protection see Section 8. Handle in accordance with good industrial hygiene and safety practice. Skin should be washed after contact. Avoid formation of dust and aerosols.

Storage
No special safety precautions required. Keep container tightly closed.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Common Name | Exposure Guideline
--- | ---
Medroxyprogesterone Acetate | 1.5 mcg/m³
Congugated Estrogens | 0.15 mcg/m³
Trimegestone | 0.06 mcg/m³
17ß Estradiol | 0.5 mcg/m³

Engineering Controls
Apply technical measures to comply with the occupational exposure guideline. Enclose operations to prevent aerosol generation. General ventilation shall not be used as the primary control system. Isolators, fume hoods, or biological safety cabinets may be used based on a risk assessment.

Personal Protective Equipment
Eye/face Protection
Provide eye protection based on risk assessment.

Skin Protection
Wear nitrile or latex gloves. Wear protective garment.

Respiratory Protection
Base respirator selection on a risk assessment.

General Hygiene
When using, do not eat, drink or smoke. General industrial hygiene practice. Wash hands before breaks and at the end of workday.

Other
Limit access to only personnel trained in the safe handling of this material. Consult a health and safety professional for specific PPE, respirator, and risk assessment guidance.

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaporation Rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Partition Coefficient (n-octanol/water)</td>
<td>Not available</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Water Solubility</td>
<td>Not available</td>
</tr>
<tr>
<td>Solubility</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation Rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>pH</td>
<td>Not available</td>
</tr>
<tr>
<td>Vapor Pressure</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Appearance</td>
<td>Pharmaceutical tablet, powder, or cream</td>
</tr>
<tr>
<td>Physical State</td>
<td>Solid</td>
</tr>
<tr>
<td>Color</td>
<td>Various</td>
</tr>
<tr>
<td>Odor</td>
<td>Odorless</td>
</tr>
<tr>
<td>Melting Point</td>
<td>Not available</td>
</tr>
<tr>
<td>Explosion Limits in Air</td>
<td>Upper: Not applicable; Lower: Not applicable</td>
</tr>
<tr>
<td>Boiling Point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flash Point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability Limits in Air</td>
<td>Upper: Not applicable; Lower: Not applicable</td>
</tr>
<tr>
<td>Autoignition Temperature Method</td>
<td>None</td>
</tr>
<tr>
<td>Flash Point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Melting Point</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Revision Date: 31-Mar-2008
10. STABILITY AND REACTIVITY

Chemical Stability  Stable at room temperature.

Conditions to Avoid  None under normal use.

Materials to Avoid  No materials to be especially mentioned.

Hazardous Decomposition Products  None under normal use.

Possibility of Hazardous Reactions  None under normal use.

11. TOXICOLOGICAL INFORMATION

The following effects are based on the Active Pharmaceutical Ingredient.

Acute Toxicity

Medroxyprogesterone Acetate

| LD50 Oral | >6400 mg/kg rats |
|          | >4000 mg/kg mice |
|          | >5 g/kg dogs     |

Acute Dermal Irritation  Not a skin irritant.
Primary Eye Irritation  Mild eye irritant.
Sensitization  Not available

Congugated Estrogens

| LD50 Oral | >5000 mg/kg rats |
| IP 325 mg/kg rats |
| IR 1740 mg/kg mice |

Acute Dermal Irritation  Not available
Primary Eye Irritation  Severe irritation effects in rabbits.
Sensitization  Not available

Trimegestone

| LD50 Oral | >2000 mg/kg rats |

Acute Dermal Irritation  Not available
Primary Eye Irritation  Not available
Sensitization  Not available

17β Estradiol

| LD50 Oral | Not available |
|          | Not available |
|          | Not available |
|          | Not available |

Multiple Dose Toxicity

Medroxyprogesterone Acetate

No Toxicologic Effect
Dose/Species/Study Length:  See Carcinogenicity

Congugated Estrogens
**Hormone Replacement Products**

**Maximum Tolerated Dose (MTD), Oral**

- **Medroxyprogesterone Acetate**
  - **Carcinogenicity**: In a two-year oral study in female rats, a dose-related increase in pancreatic islet cell tumors occurred, and a decreased incidence of spontaneous mammary gland was observed in all treated groups. Dogs treated with MPA developed mammary nodules, some of which were malignant. In humans, results of a multinational case-control study in developing countries over a 9-year period indicated that the use of MPA did not increase the risk of breast cancer.
  - **Genetic Toxicity**: Not mutagenic in AMES Test. Non-mutagenic in the mouse micronucleus assay.
  - **Reproductive Toxicity**: Animal studies have reported no impairment of fertility in first or second generation studies.
  - **Developmental Toxicity**: Studies in humans have shown that MPA may decrease intrauterine growth. No evidence of teratogenic effects.

- **17ß Estradiol**
  - **Carcinogenicity**: In mice studies, there was an increased incidence of mammary, pituitary, uterine, cervical, vaginal, testicular, lymphoid and bone tumors. In rat studies, there was an increased risk of mammary and/or pituitary tumors. In hamster studies there was a high incidence of malignant kidney tumors in males and in ovariectomized females, but not in intact females. In guinea pig studies, diffuse fibromyomatous uterine and abdominal lesions were observed.
  - **Genetic Toxicity**: No evidence of mutagenicity was observed in a battery of *in vitro* and *in vivo* assays.
  - **Reproductive Toxicity**: No data available
  - **Developmental Toxicity**: No data available

- **Trimegestone**
  - **Carcinogenicity**: No data available
  - **Genetic Toxicity**: AMES Test: Non-mutagenic
  - **Reproductive Toxicity**: In in rat studies, did not cause maternal effects at doses up to 25 mg/kg/day. Doses of 30-480 mg/kg/day caused maternal effects. Studies in rabbits resulted in maternotoxicity and fetotoxicity at doses of 40-160 mg/kg/day.
  - **Developmental Toxicity**: No data available

- **Congugeted Estrogens**
  - **Carcinogenicity**: In certain animal species, long-term continuous administration of estrogens increases the frequency of cancers in the breast, cervix, liver, pancreas, testes, uterus, and vagina. Results of animal studies may not apply to humans because of the general hormonal differences of sex steroids among species.
  - **Genetic Toxicity**: No specific mutagenic information available.

- **Reproductive Toxicity**: No data available

- **Developmental Toxicity**: No data available

**Revision Date**: 31-Mar-2008

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**Medroxyprogesterone Acetate**

**Target Organ(s) of Toxicity**: No data available
Congugated Estrogens
  Target Organ(s) of Toxicity  No data available

Trimegestone
  Target Organ(s) of Toxicity  No data available

17ß Estradiol
  Target Organ(s) of Toxicity  No data available
12. ECOLOGICAL INFORMATION

The following effects are based on the Active Pharmaceutical Ingredient.

Chemical Fate Information

**Medroxyprogesterone Acetate**
- Mobility: Not available
- Biodegradability: Not readily biodegradable.
- Stability in Water: Not available
- Bioaccumulation: Not available

**Congugated Estrogens**
- Mobility: Not available
- Biodegradability: Considered to be biodegradable under aerobic conditions.
- Stability in Water: Not available
- Bioaccumulation: Not available

**Trimegestone**
- Mobility: Not available
- Biodegradability: Not readily biodegradable.
- Stability in Water: Not available
- Bioaccumulation: May bioaccumulate in organisms.

**17β Estradiol**
- Mobility: Not available
- Biodegradability: Not available
- Stability in Water: Not available
- Bioaccumulation: Not available

Ecotoxicity

**Congugated Estrogens**
- Microorganisms: Inhibition > 150 mg carbon/liter
- Algae: Not available
- Daphnia: Not available
- Fish: Not available

**Medroxyprogesterone Acetate**
- Microorganisms: Not available
- Algae: Not available
- Daphnia: Not available
- Fish: Not available

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method
Dispose of in accordance with local and national regulations.

14. TRANSPORT INFORMATION
15. REGULATORY INFORMATION

USA

Federal Regulations

OSHA Regulatory Status
This material is not considered hazardous by the OSHA Hazard Communication Standard (29 CFR 1910.1200)

SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40n of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazardous Categorization
- Acute Health Hazard: No
- Chronic Health Hazard: Yes
- Fire Hazard: No
- Sudden Release of Pressure Hazard: No
- Reactive Hazard: No

This product does not contain any HAPs.

State Regulations

California Proposition 65
This product contains the following Proposition 65 chemicals:

<table>
<thead>
<tr>
<th>Common Name</th>
<th>CAS-No</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congugated Estrogens</td>
<td>12126-59-9</td>
<td>Cancer, Developmental Toxicity</td>
</tr>
<tr>
<td>Medroxyprogesterone Acetate</td>
<td>71-58-9</td>
<td>Cancer, developmental</td>
</tr>
<tr>
<td>17ß Estradiol</td>
<td>50-28-2</td>
<td>Cancer</td>
</tr>
</tbody>
</table>

Canada
Not classified

WHMIS Hazard Class
Non-controlled
In accordance with EC directives or respective national laws, the product does not need to be classified nor labeled.

## 16. OTHER INFORMATION

<table>
<thead>
<tr>
<th>Prepared By</th>
<th>Wyeth Department of Environment, Health &amp; Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Format</td>
<td>This MSDS was prepared in accordance with ANSI Z400.1-2004.</td>
</tr>
<tr>
<td>List of References</td>
<td>Product Package Insert</td>
</tr>
<tr>
<td>Revision Summary</td>
<td>Changes to Section 2</td>
</tr>
</tbody>
</table>

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End of MSDS