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

Material Name: Spironolactone and Hydroflumethiazide Tablets
Trade Name: Aldactide(R)
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as antihypertensive, diuretic.

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>52-01-7</td>
<td>200-133-6</td>
<td>25 / 50 mg ***</td>
</tr>
<tr>
<td>Hydroflumethiazide</td>
<td>135-09-1</td>
<td>205-173-8</td>
<td>25 / 50 mg ***</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>236-675-5</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>*</td>
</tr>
<tr>
<td>Maize starch</td>
<td>9005-25-8</td>
<td>232-679-6</td>
<td>*</td>
</tr>
<tr>
<td>Calcium sulfate</td>
<td>7778-18-9</td>
<td>231-900-3</td>
<td>*</td>
</tr>
<tr>
<td>Iron oxide</td>
<td>1309-37-1</td>
<td>215-168-2</td>
<td>*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS List</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Povidone</td>
<td>9003-39-8</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Hypromellose</td>
<td>9004-65-3</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Peppermint flavor</td>
<td>8006-90-4</td>
<td>Not listed</td>
<td>*</td>
</tr>
<tr>
<td>Macrogol 400</td>
<td>Not assigned</td>
<td>Not listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information:

*** per tablet/capsule/lozenge/suppository
* Proprietary

Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

3. HAZARDS IDENTIFICATION

Appearance: Tablets: buff, film-coated
Signal Word: WARNING
Statement of Hazard:  Antihypertensive drug: has blood pressure-lowering properties
Suspected of damaging fertility.
Suspected of causing cancer.
May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

Additional Hazard Information:
Long Term:  Repeat-dose studies in animals have shown a potential to cause adverse effects on blood, kidneys, reproductive system.
Known Clinical Effects:  Signs and symptoms might include nausea, vomiting, cramps, dizziness, headache, vertigo, low blood pressure on standing, rash, urticaria, photosensitivity, electrolyte imbalance, muscle spasm, weakness, and restlessness. Hypersensitivity reactions may also occur in susceptible individuals. Effects on blood and blood-forming organs have also occurred.

EU Indication of danger:  Harmful
Toxic to Reproduction: Category 2
Carcinogenic: Category 3

EU Hazard Symbols:

EU Risk Phrases:
R40 - Limited evidence of a carcinogenic effect
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R60 - May impair fertility.

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.

4. FIRST AID MEASURES

Eye Contact:  Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact:  Wash skin with soap and 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.

5. FIRE FIGHTING MEASURES

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

Hazardous Combustion Products:  Emits toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides, sulfur oxides, and other fluorine- and sulfur-containing compounds.

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

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Spironolactone
Pfizer OEL TWA-8 Hr: 0.09 mg/m³, Skin

Titanium dioxide
OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA

Magnesium stearate
ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA except stearates of toxic metals
Australia TWA = 10 mg/m³ TWA

Maize starch
OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total
ACGIH Threshold Limit Value (TWA) = 5 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA

Calcium sulfate
OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total
ACGIH Threshold Limit Value (TWA) = 5 mg/m³ TWA
Australia TWA = 10 mg/m³ TWA

Iron oxide
OSHA - Final PELS - TWAs: = 10 mg/m³ TWA
ACGIH Threshold Limit Value (TWA) = 5 mg/m³ TWA
Australia TWA = 5 mg/m³ TWA

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

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

Personal Protective Equipment:

- **Hands:** Not required for the normal use of this product. Wear protective gloves when working with large quantities.
- **Eyes:** Not required under normal conditions of use. Wear safety glasses or goggles if eye contact is possible.
- **Skin:** Not required for the normal use of this product. Wear protective clothing when working with large quantities.
- **Respiratory protection:** Not required for the normal use of this product. 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:

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Film-coated tablets</th>
<th>Color:</th>
<th>Buff-colored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight: Mixture</td>
<td></td>
</tr>
</tbody>
</table>

### 10. STABILITY AND REACTIVITY

**Stability:** Stable under normal conditions of use.

**Conditions to Avoid:** None known

**Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers.

### 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)**

- **Spironolactone**
  - Rat Oral LD 50 4121 mg/kg
  - Mouse Oral LD 50 >1000 mg/kg
  - Rabbit Oral LD 50 >1000 mg/kg
  - Rat Intraperitoneal LD 50 786 mg/kg

- **Povidone**
  - Rat Oral LD50 100 g/kg

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

- **Hydroflumethiazide**
  - Mouse Oral LD 50 > 10,000
  - Mouse Intraperitoneal LD 50 6280
Material Name: Spironolactone and Hydroflumethiazide Tablets
Revision date: 15-Dec-2006

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)

Spironolactone
Skin Sensitization - GPMT  Guinea Pig  No effect

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Spironolactone
13 Week(s)  Rat  Oral  50 mg/kg  LOAEL  Blood
78 Week(s)  Rat  Oral  50 mg/kg/day  LOAEL  Liver, Male reproductive system

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

Spironolactone
Reproductive & Fertility  Rat  Oral  15 mg/kg/day  NOAEL  Fetotoxicity
Reproductive & Fertility  Rat  Intraperitoneal  100 mg/kg/day  LOAEL  Fertility
Embryo / Fetal Development  Mouse  Intraperitoneal  100 mg/kg/day  LOAEL  Maternal Toxicity
Embryo / Fetal Development  Rat  Oral  50 mg/kg/day  LOAEL  Fetotoxicity
Embryo / Fetal Development  Rabbit  Oral  20 mg/kg/day  LOAEL  Fetotoxicity

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

Spironolactone
Bacterial Mutagenicity (Ames)  Salmonella, E. coli  Negative
Mammalian Cell Mutagenicity  Negative without activation

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

Spironolactone
104 Week(s)  Rat  Oral  10 mg/kg/day  LOAEL  Benign tumors
52 Week(s)  Non-human Primate  Oral  20 mg/kg/day  LOAEL  Reproductive System

Carcinogen Status: See below

Spironolactone
IARC: Group 3

Povidone
IARC: Group 3

Iron oxide
IARC: Group 3

Titanium dioxide
IARC: Group 2B
12. ECOLOGICAL INFORMATION

Environmental Overview: Environmental properties have not been thoroughly investigated. 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: Harmful
Toxic to Reproduction: Category 2
Carcinogenic: Category 3

EU Risk Phrases:
- R40 - Limited evidence of a carcinogenic effect
- R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
- R60 - May impair fertility.

EU Safety Phrases:
- S22 - Do not breathe dust.
- S24 - Avoid contact with skin.
- S36/37 - Wear suitable protective clothing and gloves.
- S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING
Antihypertensive drug: has blood pressure-lowering properties
Suspected of damaging fertility.
Suspected of causing cancer.
May cause damage to: blood and blood forming organs through prolonged or repeated exposure.

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 2, Subdivision A

Spironolactone
- California Proposition 65: carcinogen, initial date 5/1/97
- 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: 200-133-6

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

Hypermellose
- Inventory - United States TSCA - Sect. 8(b): XU
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4

Hydroflumethiazide
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
- EU EINECS List: 205-173-8

Titanium dioxide
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS List: 236-675-5

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

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

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

Calcium sulfate
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS List: 231-900-3
Iron oxide
  Inventory - United States TSCA - Sect. 8(b)  Present
  Australia (AICS):  Present
  EU EINECS List  215-168-2

16. OTHER INFORMATION

Reasons for Revision:  Updated Section 2 - Composition / Information on Ingredients. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 11 - Toxicology Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

Prepared by:  Corporate Occupational Toxicology & Hazard Assessment

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End of Safety Data Sheet