MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
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Contact E-Mail: pfizer-MSDS@pfizer.com

Material Name: Reboxetine Methanesulfonate Tablets
Trade Name: Edronax; Integrex; Norebox; Prolift; Solvax; Reboxetine
Chemical Family: Mixture
Intended Use: Pharmaceutical active used as antidepressant, chronic neuropathic pain

2. HAZARDS IDENTIFICATION

Appearance: White tablets
Signal Word: WARNING

Statement of Hazard: Harmful if swallowed.
May cause damage to central nervous system, liver through prolonged or repeated exposure.
Suspected of damaging the unborn child.
May cause harm to breastfed babies.

Additional Hazard Information:
Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on liver, kidneys, blood, bone marrow, reproductive system.

Known Clinical Effects: Adverse effects most commonly reported in clinical use include dry mouth, constipation, insomnia, increased sweating, increased heart rate (tachycardia), vertigo, impotence. Other less common effects include nausea, vomiting and headache.

EU Indication of danger: Toxic to Reproduction: Category 2

EU Hazard Symbols:

EU Risk Phrases:
R61 - May cause harm to the unborn child.
R64- May cause harm to breastfed babies.

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.
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reboxetine Methanesulfonate</td>
<td>98769-84-7</td>
<td>Not listed</td>
<td>Xn;R22</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R48/22</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr.Cat2;R61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R64</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>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Silicon dioxide, NF</td>
<td>7631-86-9</td>
<td>231-545-4</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EEC No. 418-260-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crospovidone</td>
<td>9003-39-8</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Dibasic calcium phosphate, dihydrate USP</td>
<td>7789-77-7</td>
<td>Not listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

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.

**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:**
Not available

**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, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Releases to the environment should be avoided.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Reboxetine Methanesulfonate
- Pfizer OEL TWA-8 Hr: 25µg/m³

Microcrystalline cellulose
- ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA
- Australia TWA = 10 mg/m³ TWA
- Belgium OEL - TWA = 10 mg/m³ TWA
- Estonia OEL - TWA = 10 mg/m³ TWA
- France OEL - TWA = 10 mg/m³ TWA
- Ireland OEL - TWAs = 10 mg/m³ TWA
- Latvia OEL - TWA = 4 mg/m³ TWA
- OSHA - Final PELS - TWAs: = 15 mg/m³ TWA total = 5 mg/m³ TWA
- Portugal OEL - TWA = 10 mg/m³ TWA
- Romania OEL - TWA = 10 mg/m³ TWA
- Spain OEL - TWA = 10 mg/m³ VLA-ED

Magnesium stearate
- ACGIH Threshold Limit Value (TWA) = 10 mg/m³ TWA except stearates of toxic metals
- Australia TWA = 10 mg/m³ TWA
- Belgium OEL - TWA = 10 mg/m³ TWA
- Ireland OEL - TWAs = 10 mg/m³ TWA except lead stearate
- Lithuania OEL - TWA = 3 mg/m³ IPRV
- Portugal OEL - TWA = 10 mg/m³ TWA does not include stearates of toxic metals
- Spain OEL - TWA = 10 mg/m³ VLA-ED not including stearates of toxic metals
- Sweden OEL - TWAs = 5 mg/m³ LLV

Silicon dioxide, NF
- Australia TWA = 2 mg/m³ TWA
- Austria OEL - MAKs = 4 mg/m³ MAK
Material Name: Reboxetine Methanesulfonate Tablets
Revision date: 20-Dec-2007

Refer to available public information for specific member state Occupational Exposure Limits. 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. 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 gloves 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 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:

<table>
<thead>
<tr>
<th>Physical State</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula</td>
<td>Mixture</td>
</tr>
<tr>
<td>Color</td>
<td>White</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Stability: Stable under normal conditions of use.
Conditions to Avoid: None known
Incompatible Materials: No data available

11. TOXICOLOGICAL INFORMATION

General Information: The information in this section includes the potential hazards of the individual ingredients, the active ingredients and/or of a chemically-related material.

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

Microcrystalline cellulose

Reboxetine Methanesulfonate Tablets
MATERIAL SAFETY DATA SHEET

Material Name: Reboxetine Methanesulfonate Tablets
Revision date: 20-Dec-2007
Version: 1.3

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

Reboxetine
Antigenicity- Delayed skin reaction Guinea Pig Negative

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

Reboxetine Methanesulfonate
4 Week(s) Rat Intraperitoneal Minimum Symptomatic Dose 0.3 mg/kg
Mouse Intraperitoneal Minimum Symptomatic Dose 7.5 mg/kg

Reboxetine
4 Week(s) Dog Oral 15 mg/kg/day NOAEL Liver, Heart, Blood
26 Week(s) Rat Oral 25 mg/kg/day NOAEL Thymus, Liver, Bone Marrow
26 Week(s) Dog Oral 3.75 mg/kg/day NOAEL Blood, Liver
52 Week(s) Rat Oral 10 mg/kg/day NOAEL Bone Marrow, Liver
52 Week(s) Dog Oral 3 mg/kg/day NOAEL Liver, Female reproductive system

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

Reboxetine
Reproductive & Fertility Rat Oral 100 mg/kg/day NOAEL No effects at maximum dose
2 Generation Reproductive Toxicity Rat Oral 10 mg/kg/day LOAEL Fetotoxicity, Reproductive toxicity
Embryo / Fetal Development Rabbit Oral 50 mg/kg/day NOAEL Fetotoxicity, Not Teratogenic
Peri-/Postnatal Development Rat Oral 5 mg/kg/day NOAEL Fetotoxicity
Peri-/Postnatal Development Rat Oral 25 mg/kg/day LOAEL Fetotoxicity, Neonatal toxicity

REBOXETINE METHANESULFONATE TABLETS
**Genetic Toxicity: (Study Type, Cell Type/Organism, Result)**

**Reboxetine**
- Bacterial Mutagenicity (Ames) *Salmonella, E. coli* Negative
- *In Vitro* Direct DNA Damage Chinese Hamster Ovary (CHO) cells Negative
- *In Vitro* Chromosome Aberration Human Lymphocytes Negative at cytotoxic levels
- *In Vitro* Direct DNA Damage Rat Hepatocyte Fungi Negative
- *In Vivo* Micronucleus Mouse Bone Marrow Negative

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

**Reboxetine**
- 2 Year(s) Mouse Oral 45 mg/kg/day NOAEL Not carcinogenic
- 2 Year(s) Rat Oral 90 mg/kg/day NOAEL Not carcinogenic

**Carcinogen Status:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

**Crospondione**
- IARC: Group 3

**Silicon dioxide, NF**
- IARC: Group 3

**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. 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:** Toxic to Reproduction: Category 2

REBOXETINE METHANESULFONATE TABLETS
EU Risk Phrases:  
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.

EU Safety Phrases:  
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:  
WARNING  
Harmful if swallowed.
May cause damage to central nervous system, liver through prolonged or repeated exposure.
Suspected of damaging the unborn child.
May cause harm to breastfed babies.

Canada - WHMIS: Classifications  
WHMIS hazard class:  
D2a very toxic materials
D2b toxic materials

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

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

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

Silicon dioxide, NF  
Inventory - United States TSCA - Sect. 8(b) Present  
Australia (AICS): Present  
EU EINECS/ELINCS List 231-545-4  
EEC No. 418-260-2

Dibasic calcium phosphate, dihydrate USP  
Australia (AICS): Present
16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

Data Sources:

Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision:

Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 4 - First Aid Measures. Updated Section 5 - Fire Fighting Measures. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 11 - Toxicology Information. Updated Section 15 - Regulatory Information.

Prepared by:

Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet