MATERIAL SAFETY DATA SHEET

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

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ChemSafe (24 hours): +44 (0)208 762 8322

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

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Reboxetine Methanesulfonate	98769-84-7	Not listed	Xn;R22 Xn;R48/22 Repr.Cat2;R61 R64	2.6
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*
Silicon dioxide, NF	7631-86-9	231-545-4 EEC No. 418-260-2	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	Classification	%
Crospovidone	9003-39-8	Not listed	Not Listed	*
Dibasic calcium phosphate, dihydrate USP	7789-77-7	Not listed	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.

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/m^3

Microcrystalline cellulose

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
Estonia OEL - TWA	= 10 mg/m^3 TWA
France OEL - TWA	= 10 mg/m^3 VME
Ireland OEL - TWAs	= 10 mg/m^3 TWA = 4 mg/m^3 TWA
Latvia OEL - TWA	= 2 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
Romania 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

Silicon dioxide, NF

Australia TWA	= 2 mg/m^3 TWA
Austria OEL - MAKs	= 4 mg/m^3 MAK

Czech Republic OEL - TWA	= 0.1 mg/m^3 TWA = 4.0 mg/m^3 TWA
Estonia OEL - TWA	= 2 mg/m^3 TWA
Germany - TRGS 900 - TWAs	= 4 mg/m^3 TWA
Ireland OEL - TWAs	= 2.4 mg/m^3 TWA = 6 mg/m^3 TWA
Latvia OEL - TWA	= 1 mg/m^3 TWA containing more than 70% SiO2 (quartz) = 2 mg/m^3 TWA containing 10-70% SiO2 (granite, mica) = 4 mg/m^3 TWA containing 2-10% SiO2 (copper sulfate ores)
OSHA - Final PELs - Table Z-3 Mineral D:	(80)/(% SiO2) mg/m^3 TWA = 20 mppcf TWA
Slovakia OEL - TWA	= 4.0 mg/m^3 TWA
Slovenia OEL - TWA	= 4 mg/m^3 TWA

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.

Analytical Method: Analytical method available for Reboxetine. 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 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:

Physical State:	Tablets	**Color:**	White
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

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

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

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m^3

Silicon dioxide, NF
Rat Oral LD50 10 g/kg

Reboxetine Methanesulfonate
Rat Intraperitoneal Minimum Symptomatic Dose 0.3 mg/kg
Mouse Intraperitoneal Minimum Symptomatic Dose 7.5 mg/kg

Reboxetine
Rat Oral LD50 977 mg/kg
Rat Intravenous LD50 51.2 mg/kg
Mouse Intravenous LD50 67.2 mg/kg
Mouse Oral Minimum Lethal Dose 200 mg/kg
Dog Oral Minimum Symptomatic Dose >= 60 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

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 Subcutaneous 182 mg/kg/day LOAEL Blood
28 Day(s) Dog No route specified 1260 mg/kg/day LOAEL Central Nervous System

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

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.

Crospovidone
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

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