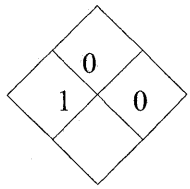
NOVARTIS




**MATERIAL SAFETY DATA SHEET**

**NOVARTIS PHARMACEUTICALS CORPORATION**
One Health Plaza
East Hanover, NJ 07936

**24-Hour Emergency Telephone Number:** 1-862-778-7000
**Customer Interaction Center (MSDS requests):** 1-888-669-6682
**For Technical Information:** 1-862-778-3680 (9:00 AM – 5:00 PM E.S.T.)

## SECTION 1. PRODUCT IDENTIFICATION

| | |
|---|---|
| PRODUCT NAME: | **Exelon® Patch** |
| SYNONYMS: | Rivastigmine transdermal system |
| THERAPEUTIC CATEGORY: | Treatment of mild to moderate dementia of the Alzheimer's type and that associated with Parkinson's disease. |
| GENERIC NAME: | None |
| CHEMICAL NAME: | (S)-N-Ethyl-N-methyl-3-[1-(dimethylamino)ethyl]phenyl carbamate |
| CHEMICAL FORMULA: | $C_{14}H_{22}N_2O_2$ |
| MOLECULAR WEIGHT: | 250.34 |

## SECTION 2. INFORMATION ON HAZARDOUS INGREDIENTS

| COMPOSITION | CAS # | CONCENTRATION |
|---|---|---|
| Rivastigmine | 123441-03-2 | 9 mg per 5 $cm^2$ patch; 18 mg per 10 $cm^2$ patch |

## SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

**********

**FINISHED PHARMACEUTICAL PRODUCT**
**REFER TO PHYSICIANS' DESK REFERENCE**
**CENTRAL NERVOUS SYSTEM EFFECTS**
**MAY CAUSE NAUSEA, VOMITING, DIARRHEA**

**********

PRIMARY ROUTE(S) OF ENTRY: Dermal

| | |
|---|---|
| EFFECTS OF OVEREXPOSURE: | Finished pharmaceutical product. Potential for exposure is reduced in this form. Based on acetylcholinesterase inhibitors overdosing can include severe nausea and vomiting, salivation, sweating, bradycardia, hypotension, labored respiration, collapse and convulsions. Increase muscle weakness is a possibility and may result in death, if the respiratory muscles are involved. |
| Skin: | No hazard is expected from normal clinical use. |
| Eye: | No hazard is expected from normal clinical use. |
| Inhalation: | No hazard is expected from normal clinical use. |
| Ingestion: | No hazard is expected from normal clinical use. |
| THERAPEUTIC SIDE EFFECTS: | Nausea, vomiting, headaches, dizziness, tiredness, anorexia and diarrhea. |
| TARGET ORGAN EFFECTS: | Central nervous system. |
| REPRODUCTIVE HAZARDS: | None identified. (see section 11) |
| CARCINOGENICITY: | No carcinogenic potential was demonstrated. (see section 11) |
| MUTAGENICITY: | Clastogenic in two *in vitro* assays; non-mutagenic *in vitro* and *in vivo* and non-clastogenic *in vivo*. (see section 11) |

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Clinically significant gastrointestinal and cardiovascular conditions, CNS/psychiatric symptoms and neurological symptoms; patients with known hypersensitivity to rivastigmine, other carbamate derivatives or other components of the formulation.

## SECTION 4. EMERGENCY AND FIRST AID MEASURES

| | |
|---|---|
| **Skin Contact:** | Wash contaminated area with soap and water. |
| **Eye Contact:** | Flush with running water for 15 minutes holding eyelids open. |
| **Inhalation:** | No specific treatment is necessary since this product is not likely to be hazardous by inhalation. |
| **Ingestion:** | Get medical attention immediately. |
| **Note to Physician:** | Antidote: Atropine |

## SECTION 5. FIRE FIGHTING MEASURES

**Flash Point:** not applicable **Method Used**: not applicable
**Flammable Limits (% in air)**
Lower: not applicable Upper: not applicable

| | |
|---|---|
| **Autoignition Temperature:** | Not available |
| **Extinguishing Media:** | Use media suitable for fire in surrounding area. |
| **Special Fire Fighting Procedures and Precautions:** | Evacuate area and fight fire from safe distance. |
| **Fire and Explosion Hazards:** | Not available |
| **Fire-Fighting Equipment:** | Wear full protective clothing and positive pressure self-contained breathing apparatus. |
| **Hazardous Products of Combustion** | COx, NOx |

NFPA Ratings: Health = 1 Flammability = 1 Reactivity = 0 Special Hazard = None
Hazard Rating Scales: 0 = Minimal 1 = Slight 2 = Moderate 3 = Serious 4 = Severe U = Unknown

## SECTION 6. ACCIDENTAL RELEASE MEASURES

**Steps to be taken if Material is Released or Spilled:** Using appropriate protective equipment, absorb/sweep up and containerize spilled material. All wastes must be disposed of in accordance with local, state and federal laws and regulations. Avoid disposal in sewers and waterways.

## SECTION 7. HANDLING AND STORAGE

| | |
|---|---|
| **Storage Temperature:** | Store between 59°F (15°C) and 86°F (30°C). |
| **Shelf Life:** | See container packaging. |
| **Special Sensitivity:** | Protect from light. |
| **Handling and Storage Precautions:** | None known. |

## SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

| | |
|---|---|
| **Eye Protection:** | Not required under normal conditions of therapeutic administration and use, however, the use of protective eyewear is recommended in the event of leakage of contents of patch.. |
| **Skin Protection:** | Not required under normal conditions of therapeutic administration and use, however, the use of protective gloves is recommended if there is a potential for skin contact with the contents of the patch. |
| **Respiratory Protection:** | Not required under normal conditions of therapeutic administration and use. |
| **Ventilation Requirements:** | Not required under normal conditions of therapeutic administration and use. |
| **Additional Measures:** | None |

**Exposure Limits (Definition of terms):**

NPIEL: Novartis Pharma Internal Exposure Limit

| **Component** | **Exposure Limit** |
|---|---|
| Rivastigmine | NPIEL = 0.01 $mg/m^3$ (8h TWA) |

## SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

| | | | |
|---|---|---|---|
| **Appearance:** | Patch | **Odor:** | not applicable |
| **Color:** | not available | **Vapor Pressure (mm Hg):** | not applicable |
| **pH:** | not applicable | **Vapor Density:** | not applicable |
| **Boiling Point:** | not applicable | **Specific Gravity:** | not available |
| **Melting Point/Range:** | not applicable | **% Volatile by Wt:** | not available |
| **Freezing Point:** | not applicable | **Viscosity:** | not available |
| **Soluble In:** | not applicable | **Log P:** | not applicable |
| | | **pKa:** | not available |

## SECTION 10. STABILITY AND REACTIVITY

| | |
|---|---|
| **Stable (yes/no):** | Yes |
| **Hazardous Polymerization:** | Will not occur. |
| **Conditions and Materials to Avoid:** | Protect from light. |
| **Incompatibility** | Not known. |
| **Hazardous Decomposition Products:** | Not known. |
| Dust Explosion Test: | Not known. |

## SECTION 11. TOXICOLOGICAL INFORMATION

No toxicological data on finished product; data are for drug substance.

| | |
|---|---|
| **Eye Irritation:** | Not irritating in rabbits. |
| **Skin Irritation/Sensitization:** | Not a sensitizer in guinea pigs and mice. Not irritating in rabbits. |
| **Oral Toxicity:** | **$LD_{50}$ (rat):** 13 mg/kg (males) |
| **Inhalation Toxicity:** | Not data available. |
| **Chronic/Carcinogenicity:** | In oral carcinogenicity studies conducted at doses up to 1.1 mg-base/kg/day in rats and 1.6 mg-base/kg/day in mice, rivastigmine was not carcinogenic. In a dermal carcinogenicity study conducted at doses up to 0.75 mg-base/kg/day in mice, rivastigmine was not carcinogenic. |
| **Mutagenicity:** | Rivastigmine was clastogenic in two *in vitro* assays in the presence, but not the absence, of metabolic activation. It caused structural chromosomal aberrations in V70 Chinese hamster lung cells and both structural and numerical (polyploidy) chromosomal aberrations in human peripheral blood lymphocytes. Rivastigmine was not genotoxic in three *in vitro* assays: the Ames test, the unscheduled DNA synthesis (UDS) test in rat hepatocytes (a test for induction of DNA repair synthesis), and the HGPRT test in V79 Chinese hamster cells. Rivastigmine was not clastogenic in the *in vivo* mouse micronucleus test. |
| **Reproductive Effects:** | No fertility or reproduction studies have been conducted in animals treated with dermal rivastigmine. Rivastigmine had no effect on fertility or reproductive performance in rats at oral doses up to 1.1 mg-base/kg/day. |

## SECTION 12. ECOLOGICAL INFORMATION

| | |
|---|---|
| Biological elimination: | 5 % (aerobic, HPLC), Initial concentration: 10 mg/l 28 day, not degradable in biol. waste water treatment plant. Method: test result of the active component. |
| Fish toxicity: | LC0: 8 mg/l, LC50: 31.8 mg/l, (Species: bluegill sunfish (lepomis macrochirus), Exp. time: (96 h) |
| Daphnia toxicity: | EC0: 1.1 mg/l, EC50: 1.4 mg/l, (Species: daphnia magna (water flea), Exp. time: 48 h) |
| Algae toxicity: | IC0: 10 mg/l, IC50: 37 - 49 mg/l, (Species: Selenastrum capricornutum ATCC 22662. Green algae, Exp. time: 72 h), Method: OECD 201 * 1984. Growth inhibition |
| Bacteria toxicity: | IC50: > 1000 mg/l (Species: pseudomonas fluorescens) |

## SECTION 13. DISPOSAL CONSIDERATIONS

**Waste Disposal Method:** Using appropriate protective equipment, absorb/sweep up and containerize spilled material. All wastes must be disposed of in accordance with local, state and federal laws and regulations. Avoid disposal in sewers and waterways.

**EPA Hazardous Waste Number:** None

## SECTION 14. TRANSPORTATION INFORMATION

**Ground Regulations:**

| | |
|---|---|
| **Proper Shipping Description:** | Drugs, N.O.I., NMFC Item 60000 |
| **DOT Proper Shipping Name:** | Not Applicable |
| **DOT Hazard Class:** | Not Applicable |
| **DOT Identification Number:** | Not Applicable |
| **Packing Group:** | Not Applicable |
| **Hazard Label:** | Not Applicable |
| **Package Weight Limits:** | Not Applicable |
| **Special Requirements:** | Not Applicable |
| **Exceptions:** | Not Applicable |
| **Non-Bulk Requirements:** | Not Applicable |
| **Bulk Requirements:** | Not Applicable |
| **Reportable Quantity (lbs.):** | Not Applicable |
| **Stowage:** | Not Applicable |
| **Other Requirements:** | Not Applicable |

**Air Regulations:**

| | |
|---|---|
| **Proper Shipping Description:** | Drugs, N.O.I., NMFC Item 60000 |
| **IATA Proper Shipping Name:** | Not Applicable |
| **IATA Hazard Class:** | Not Applicable |
| **IATA Identification Number:** | Not Applicable |
| **Packing Group:** | Not Applicable |
| **Hazard Label:** | Not Applicable |
| **Special Requirements:** | Not Applicable |
| **Max. wgt/pkg - Passgr. Aircraft:** | Not Applicable |
| **Max. wgt/pkg - Cargo Only Air:** | Not Applicable |

## SECTION 15. REGULATORY INFORMATION

**OSHA (Occupational Safety & Health Administration):** This Material Safety Data Sheet contains the information required by the Federal Hazard Communication Standard (29 CFR 1910.1200).

**OSHA PSM (Process Safety Management):** Not listed (29 CFR 1910.119, Appendix A).

**NJ TCPA (Toxic Catastrophe Prevention Act):** This product contains NONE of the substances subject to the reporting requirements of Section N.J.A.C. 7:31 of this act.

**TSCA (Toxic Substance Control Act):** Not applicable

**CERCLA (Comprehensive Response Compensation & Liability Act):** Not listed

**SARA Title III (Superfund Amendments & Reauthorization Act):**

| | |
|---|---|
| Section 302 Extremely Hazardous Substances: | Not listed |
| Section 311/312 Hazard Categories: | Not listed |
| Section 313 Reportable Ingredients: | Not listed |

**RCRA (Resource Conservation & Recovery Act):** Not listed

**Other State Regulatory Information:**

**New Jersey:** NJ RTK Threshold Planning Quantity = 10,000 lbs.

**Other USA Regulations:** None

**California Proposition 65:** The following statement is made in order to comply with the California Safe Drinking Water and Toxic Enforcement Act of 1986. *This product contains no chemicals known to the State of California to cause cancer or reproductive toxicity.*

**Canada:** WHMIS Ingredient Disclosure List
Not listed

**EU Classification (European Union):**
**Warning Symbol:** Not Available
**Risk Phrases:** Not Available
**Safety Phrases:** Not Available

## SECTION 16. OTHER INFORMATION

**Reason for Issue:** New

| | | | |
|---|---|---|---|
| **Written By:** | C. Perino | **Date:** | 27 July 07 |
| **Approved By:** | G. King | **Date:** | 03 August 07 |

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**To the best of our knowledge, the information contained herein is accurate. However, Novartis Pharmaceuticals Corporation does not assume any liability whatsoever for the accuracy or completeness of the information contained herein except for the product's administration/use as intended. Final determination of the suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards, which exist.**