



SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Par Sterile Products
870 Parkdale Road
Rochester, M.I. 48307
T: +1 (800) 828-9393
F: +1 (201) 829-9222
drugsafety@parpharm.com

Emergency telephone
number (Chemtrec):

1-(800) 424-9300 (US
and Canada)
1-(703) 527-3887 (collect
calls accepted)

| | |
|--|---|
| Product identifier | Dantrium® (dantrolene sodium) capsules |
| Synonyms | Dantrolene Sodium |
| Trade names | Dantrium® |
| Chemical family | Mixture containing a hydrated 1-{{5-(4-nitrophenyl)-2-furanyl}methylene}amino}-2-4-imidazolidinedione sodium salt |
| Relevant identified uses of the substance or mixture and uses advised against | Bulk formulated pharmaceutical product/ Formulated pharmaceutical product packaged in final form for patient use; indicated for the treatment of manifestation of chronic muscle stiffness/tightness. |
| Note | This SDS is written to address potential worker health and safety issues associated with the handling of the formulated product. Workers manufacturing this product should consult the SDSs of each hazardous ingredient for hazard information and handling recommendations. |
| Issue Date | 7 May 2014 |

SECTION 2 - HAZARDS IDENTIFICATION

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| Classification of the substance or mixture | Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada. Please consult the prescribing/packaging information. The classification and labelling listed below is for bulk Dantrium® capsules |
| Regulation (EC) 1272/2008 [GHS] | Specific Target Organ Toxicity (repeated exposure) - Category 2, Carcinogenic - Category 2 |
| Directive 67/548/EEC or 1999/45/EC | Xn - R48/22; R40 (Carc. Cat. 3) |

SECTION 2 - HAZARDS IDENTIFICATION ...continued

Label elements

CLP/GHS hazard pictogram



CLP/GHS signal word

Warning

CLP/GHS hazard statements

H373 - May cause damage to liver and kidneys through prolonged or repeated exposure. H351 - Suspected of causing cancer.

CLP/GHS precautionary statements

P201: Obtain special instructions before use. P202: Do not handle until all safety precautions have been read and understood. P281: Use personal protective equipment as required. P260 - Do not breathe dust. P308 + P313 - If exposed or concerned: get medical advice/attention. P314 - Get medical advice/attention if you feel unwell. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

EU symbol/indication of danger



Xn - Harmful

Risk (R) Phrase(s)

R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed. R40 - Limited evidence of a carcinogenic effect.

Safety Advice

S36/37 - Wear suitable protective clothing and gloves.

Other hazards

Dantrolene is muscle relaxant with a direct action on skeletal muscle. Commonly reported adverse effects include drowsiness, dizziness, fatigue, weakness and general tiredness. Gastrointestinal effects (diarrhea, abdominal cramps) have also been reported. Dantrolene has also been reported to cause an increase in liver enzymes and other liver effects.

US Signal word

Warning

US Hazard overview

May cause liver or kidney damage. Suspected of causing cancer.

Note

This mixture is classified as dangerous/hazardous according to directive 1999/45/EC, Regulation EC No 1272/2008 (EU CLP) and applicable US regulations. See Section 16 for full text of EU and GHS classifications. The GHS classifications are based on Regulation (EC) 1272/2008. The EU symbol/indicator of danger, R Phrases and Safety Advice are based on Directive 1999/45/EC.

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

| <u>Ingredient</u> | <u>CAS #</u> | <u>EINECS/ ELINCS#</u> | <u>Amount</u> | <u>EU Classification</u> | <u>GHS Classification</u> |
|--------------------|--------------|----------------------------|---------------|--|--|
| Dantrolene sodium | 24868-20-0 | 238-706-8 | 10-30% | Harmful - Xn: R48/22; Car. Cat. 3: R40 | STOT-R2: H373; Car. Cat. 2: H351 |
| Starch | 9005-25-8 | 232-679-6 | 10-20% | Not classified | Not classified |
| Talc | 14807-96-6 | 238-877-9 | 5-10% | Xi: R37 | STOT-S3: H335 |
| Magnesium Stearate | 557-04-0 | 209-150-3 | 1-2% | Not classified | Not classified |

Note The ingredient(s) listed above are considered dangerous/hazardous. Starch and magnesium stearate are included because they have OELs. The remaining components are non-dangerous/not hazardous and/or present at amounts below reportable limits. See Section 16 for full text of EU and GHS classifications. The EU classification is based on Directive 67/548/EEC and the GHS classification is based on Regulation (EC) 1272/2008.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures

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| Immediate Medical Attention Needed | Yes |
| Eye Contact | If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor. |
| Skin Contact | Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor. |
| Inhalation | Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor. |
| Ingestion | Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor. |
| Protection of first aid responders | See Section 8 for Exposure Controls/Personal Protection recommendations. |
| Most important symptoms and effects, both acute and delayed | See Sections 2 and 11. |
| Indication of immediate medical attention and special treatment needed, if necessary | Medical conditions aggravated by exposure: liver disease or dysfunction. Treat symptomatically and supportively. If accidental exposure occurs to an individual who is also taking one or more concomitant medications, consult the respective package or prescribing information for potential drug interactions. |

SECTION 5 - FIREFIGHTING MEASURES

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| Extinguishing media | Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials. |
| Specific hazards arising from the substance or mixture | No information identified. May emit toxic fumes of carbon monoxide, carbon dioxide, sodium, magnesium, and oxides of nitrogen. |
| Flammability/Explosivity | No information identified. High concentrations of finely divided organic particles can explode if ignited. |
| Advice for firefighters | Wear full protective clothing and a self-contained breathing apparatus with a full facepiece operated in the pressure demand or other positive pressure mode. Decontaminate all equipment after use. |

SECTION 6 - ACCIDENTAL RELEASE MEASURES

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| Personal precautions, protective equipment and emergency procedures | If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment (see section 8). Area should be adequately ventilated. Do not breathe dust. Consider the use of appropriate respiratory protection. |
| Environmental precautions | Do not empty into drains. Avoid release to the environment. |
| Methods and material for containment and cleaning up | If capsules are broken or crushed, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice. |
| Reference to other sections | See Sections 8 and 13 for more information. |

SECTION 7 - HANDLING AND STORAGE

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| Precautions for safe handling | If capsules are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Follow recommendations for handling bulk formulated/packaged pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Wash thoroughly after handling. Avoid breathing dust. Wash thoroughly after handling. |
| Conditions for safe storage including any incompatibilities | Store at controlled room temperature (20 to 25° C) |
| Specific end use(s) | Muscle relaxant |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

**Control Parameters/
Occupational Exposure
Limit Values**

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|-------------------|---|---------------|---|
| Dantrolene sodium | -- | -- | -- |
| Starch | ACGIH, Belgium, Bulgaria, Portugal, Spain, Singapore | TWA-8 HR | 10 mg/m ³ |
| | Czech Republic, Slovak Republic | TWA-8 HR | 4 mg/m ³ |
| | Greece, NIOSH | TWA-8 HR | 10 mg/m ³ (inhalable fraction); 5 mg/m ³ (respirable fraction) |
| | Ireland, United Kingdom | TWA-8 HR | 10 mg/m ³ (inhalable fraction); 4 mg/m ³ (respirable fraction) |
| | OSHA | TWA-8 HR | 15 mg/m ³ (total dust); 5 mg/m ³ (respirable fraction) |
| | United Kingdom | STEL | 30 mg/m ³ (inhalable fraction); 12 mg/m ³ (respirable fraction) |
| | NIOSH | TWA-10 HR | 10 mg/m ³ (total dust); 5 mg/m ³ (respirable fraction) |
| Talc | ACGIH, Austria, NIOSH, Portugal, Spain | TWA-8 HR | 2 mg/m ³ (respirable fraction; containing no asbestos and <1% crystalline silica) |
| | Australia | TWA-8 HR | 2.5 mg/m ³ (containing no asbestos) |
| | Belgium, Greece, Hungary | TWA-8 HR | 2 mg/m ³ (respirable fraction) |
| | Ireland | TWA-8 HR | 0.8 mg/m ³ (respirable dust) |
| | Netherlands | TWA-8 HR | 0.25 mg/m ³ |
| | Poland | TWA-8 HR | 1 mg/m ³ (respirable dust) |
| | Romania | TWA-8 HR | 2 mg/m ³ (total dust) |
| | United Kingdom | TWA-8 HR/STEL | 1 mg/m ³ /3 mg/m ³ (respirable dust) |
| | Magnesium Stearate | ACGIH | TWA-8 HR |

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION ...continued

**Control Parameters/
Occupational Exposure
Limit Values ...continued**

| <u>Compound</u> | <u>Issuer</u> | <u>Type</u> | <u>OEL</u> |
|-----------------|---------------|-------------|---------------------|
| | Lithuania | TWA-8 HR | 3 mg/m ³ |
| | Sweden | TWA-8 HR | 5 mg/m ³ |

DNELs/PNECs None identified.

Exposure/Engineering controls None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken. Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Open handling should not be performed when handling potent substances, or substances of unknown toxicity. Material should be handled inside a closed process, ventilated enclosure, isolator or device of equivalent or better control that is suitable for dusts and/or aerosols.

Respiratory protection None required for normal handling of packaged product. If handling bulk capsules or capsules are crushed or broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. For routine powder handling tasks, an approved and properly worn powered air-purifying respirator equipped with HEPA filters or combination filters should provide ancillary protection based on the known or foreseeable limitations of existing engineering controls. Use a positive-pressure air-supplied respirator if there is any potential for an uncontrolled release, when exposure levels are not known, or in any other circumstances where air purifying respirators may not provide adequate protection.

Hand protection Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

Skin protection Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

Eye/face protection Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

Environmental Exposure Controls Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

Other protective measures Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

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| Appearance | Capsules |
| Color | Pale, orange-yellow powder cake inside an opaque orange and tan capsule. |
| Odor | Odorless |
| Odor threshold | No information identified. |
| pH | No information identified. |
| Melting point/ freezing point | No information identified. |
| Initial boiling point and boiling range | No information identified. |
| Flash point | No information identified. |
| Evaporation rate | No information identified. |
| Flammability (solid, gas) | No information identified. |
| Upper/lower flammability or explosive limits | No information identified. |
| Vapor pressure | No information identified. |
| Vapor density | No information identified. |
| Relative density | No information identified. |
| Water solubility | Slightly soluble in water. |
| Solvent solubility | No information identified. |
| Partition coefficient (<i>n</i>-octanol/water) | No information identified. |
| Auto-ignition temperature | No information identified. |
| Decomposition temperature | No information identified. |
| Viscosity | No information identified. |
| Explosive properties | No information identified. |
| Oxidizing properties | No information identified. |

SECTION 11 - TOXICOLOGICAL INFORMATION ...continued

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| STOT-repeated exposure/Repeat-dose toxicity | Repeat-dose studies were carried out in rats for up to 18 months, and monkeys and dogs for up to 12 months. Lower body weight gains were observed in all three species. Target organs of toxicity included liver, kidney, blood and mammary tissues (rats only). Toxicity was observed at ≥ 30 , ≥ 15 , and ≥ 120 mg/kg/day, in dogs, rats, and monkeys, respectively, but was reversible upon the discontinuation of treatment. |
| Reproductive toxicity | Dantrolene sodium administered to rats at doses up to 45 mg/kg/day showed no adverse effects on fertility or general reproductive performance. |
| Developmental toxicity | Dantrolene sodium induced minor skeletal variations in the offspring of pregnant rats and rabbits treated orally with 60 mg/kg/day during gestation days 7-17 and 6-18, respectively. In rats, maternal and fetal weights were also reduced at that dose. |
| Genotoxicity | Dantrolene sodium tested positive in the Ames bacterial mutagenesis assay with or without metabolic activation. |
| Carcinogenicity | Dantrolene sodium produced benign and malignant mammary tumors in female rats orally treated with 15 mg/kg/day for 18 months. Increased incidence of benign hepatic tumors were also observed. No other components of the product present at levels greater than or equal to 0.1% are listed by NTP, IARC, ACGIH or OSHA as a carcinogen. |
| Aspiration hazard | No data available. |
| Human health data | See "Section 2 - Other Hazards" |

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

| <u>Compound</u> | <u>Type</u> | <u>Species</u> | <u>Concentration</u> |
|--------------------|-------------|----------------|----------------------|
| Dantrolene sodium | -- | -- | -- |
| Starch | -- | -- | -- |
| Talc | -- | -- | -- |
| Magnesium Stearate | -- | -- | -- |

Persistence and Degradability No data available.

Bioaccumulative potential No data available.

Mobility in soil No data available.

Results of PBT and vPvB assessment Not performed.

Other adverse effects No data available.

Note The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

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| Waste treatment methods | Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility. |
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SECTION 14 - TRANSPORT INFORMATION

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| Transport | Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG. |
| UN number | None assigned. |
| UN proper shipping name | None assigned. |
| Transport hazard classes and packing group | None assigned. |
| Environmental hazards | Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant. |
| Special precautions for users | Avoid release to the environment. |
| Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code | Not applicable. |

SECTION 15 - REGULATORY INFORMATION

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| Safety, health and environmental regulations/legislation specific for the substance or mixture | This SDS complies with the requirements under US, EU and GHS (EU CLP - Regulation EC No 1272/2008) guidelines. Consult your local/regional authorities for more information. |
| Chemical safety assessment | Not conducted. |
| OSHA Hazardous | Yes. Warning. May cause liver or kidney damage. Suspected of causing cancer. |
| WHMIS classification | Not required. Drugs are not subject to WHMIS. This substance has been classified in accordance with the hazard criteria of the Controlled Products Regulations and the SDS contains all of the information required by those regulations. |

SECTION 15 - REGULATORY INFORMATION ...continued

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| TSCA status | Drugs are exempt from TSCA. |
| SARA section 313 | Not listed. |
| California proposition 65 | Not listed. |
| Additional information | No other information identified. |

SECTION 16 - OTHER INFORMATION

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| Full text of R phrases and EU Classifications | Xn - Harmful. R48/22 - Danger of serious damage to health by prolonged exposure. Xi - Irritant. R37 - Irritating to respiratory system. Carc. Cat. 3 - Carcinogenic Category 3. R40 - Limited evidence of a carcinogenic effect. |
| Full text of H phrases, P phrases and GHS classification | STOT-R2 - Specific Target Organ Toxicity Following Repeated Exposure Category 2. H373 - May cause damage to liver and kidneys. STOT-S3 - Specific Target Organ Toxicity Following Single Exposure Category 3. H335 - May cause respiratory irritation. Carc2 - Carcinogenicity Category 2. H351 - Suspected of causing cancer. |
| Sources of data | Information from published literature and internal company data. |
| Abbreviations | ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; WHMIS - Workplace Hazardous Materials Information System |
| Revisions | Updated contact information in Section 1. |

SECTION 16 - OTHER INFORMATION ...continued

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a potent pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.