SAFETY DATA SHEET

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

Contact information

General

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Product identifier	Dantrium® Intravenous (Dantrolene Sodium for Injection)
Synonyms	Dantrolene Sodium
Trade names	Dantrium®
Chemical family	Mixture containing 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	30 September 2014

SECTION 2 - HAZARDS IDENTIFICATION

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® Intravenous.**

SECTION 2 - HAZARDS IDENTIFICATION …continued

Regulation (EC) 1272/ 2008 [GHS]	Not classified
Directive 67/548/EEC or 1999/45/EC	Not classified

Label elements

CLP/GHS hazard pictogram	None required
CLP/GHS signal word	None required
CLP/GHS hazard statements	None required
CLP/GHS precautionary statements	None required
EU symbol/indication of danger	None required
Risk (R) Phrase(s)	None required
Safety Advice	None required

Other hazards	Dantrolene is a 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	None required
US Hazard overview	Not classified.
Note	This mixture is not 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

Ingredient	CAS #	EINECS/ ELINCS#	Amount	EU Classification	GHS Classification
Dantrolene sodium	24868-20-0	238-706-8	0.03-0.05%	Harmful - Xn: R48/22; R40	STOT-R2: H373; Carc2: H351

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS …continued

Note	The ingredient(s) listed above are considered dangerous/hazardous. 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

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: none identified. 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

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 carbon monoxide, carbon dioxide, sodium, and oxides of nitrogen.

SECTION 5 - FIREFIGHTING MEASURES …continued

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

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	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

Precautions for safe handling	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 the unreconstituted product at controlled room temperatures 20° to 25°C (68° to 77°F) and protect from light.
Specific end use(s)	Muscle relaxant

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
Dantrolene sodium	--	--	--

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Exposure/Engineering controls	None required for normal handling of packaged product. If handling bulk powder or vials are crushed or broken. Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use local exhaust and/or enclosure at dust-generating points. Emphasis is to be placed on closed material transfer systems and process containment, with limited open handling of powders. High-energy operations such as milling, particle sizing, spraying or fluidizing should be done within an approved emission control or containment system.
Respiratory protection	None required for normal handling of packaged product. If handling bulk powder or vials 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

Appearance	Lyophilized powder

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Color	Pale, orange-yellow powder cake.
Odor	Odorless
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	225-226° C
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	791 mg/L
Solvent solubility	No information identified.
Partition coefficient (*n-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.

Other information

Molecular weight	Not applicable (Mixture)
Molecular formula	Not applicable (Mixture)

SECTION 10 - STABILITY AND REACTIVITY

Reactivity No information identified.

Chemical stability Chemically stable; pharmacological stability not guaranteed beyond expiration date imprinted on package.

Possibility of hazardous reactions Not expected to occur.

Conditions to avoid Avoid extreme temperatures.

Incompatible materials No information identified.

Hazardous decomposition products No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Note **The following data describe the active ingredient.**

Information on toxicological effects

Route of entry May be absorbed by inhalation, skin contact and ingestion.

Acute toxicity

Compound	Type	Route	Species	Dose
Dantrolene sodium	LD_{50}	Oral	Rat	7432 mg/kg
	LD_{50}	Oral	Mouse	1188 mg/kg

Irritation/Corrosion No data available.

Sensitization No data available.

STOT-single exposure Clinical signs of acute toxicity in rats treated orally with doses of up to 18,000 mg/kg of dantrolene sodium included inactivity, lethargy, weakness, gasping, diarrhea, yellowing of the skin, and decreased growth rate or weight loss. Kidney toxicity was also observed.

STOT-repeated exposure/Repeat-dose toxicity Repeat-dose studies were carried out with dantrolene sodium 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.

SECTION 11 - TOXICOLOGICAL INFORMATION …continued

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. None of the 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

Compound	Type	Species	Concentration
Dantrolene sodium	--	--	--

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

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.

SECTION 14 - TRANSPORT INFORMATION

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

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	No
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.
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

Full text of R phrases and EU Classifications	R48/22 - Danger of serious damage to health by prolonged exposure if swallowed. 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. 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	This is the first version of this SDS.
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 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

Disclaimer …continued

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.