



MATERIAL SAFETY DATA SHEET

While we believe the information provided herein is accurate and current, JHP Pharmaceuticals makes no representation or warranties, either explained or implied, and assume no responsibility for any damage or injuries of any kind, which may result from use or reliance upon this information

SECTION 1 MATERIAL IDENTIFICATION

PRODUCT NAME: Dantrium[®] Intravenous (Dantrolene Sodium for Injection) **DATE OF ISSUE:** 9/2/2009

FORMULA: Lyophilized Solid **SUPERCEDES:** 4/17/2009 **REVISION:** 3.0
SYNONYMS: Dantrolene Sodium, F-440 (active ingredient)

NDC #: 42023-123-06

DISTRIBUTION: JHP Pharmaceuticals, LLC. **ADDRESS:** 870 Parkdale Road, Rochester, MI 48307 **PHONE:** Emergency: 248-656-5400, Medical Affairs: 866-923-2547

SECTION 2 INGREDIENT (S)

Component	CAS No.	EINECS No.
Hydrated 1-{{5-(4-nitrophenyl)-2-furanyl}methylene}amino}-2-4-imidazolidinedione sodium salt (F-440, Dantrolene Sodium)	24868-20-0	238-706-8
Mannitol	69-65-8	200-711-8
Sodium Hydroxide	1310-73-2	215-185-5

NA – Not available

SECTION 3 HAZARD IDENTIFICATION

HMIS: 2-Health, 1-Flammability, 1-Reactivity.

EMERGENCY OVERVIEW: Caution. This MSDS is written to address potential worker health and safety issues associated with the handling of formulated final product which is a lyophilized cake, e.g., during the transportation, distribution, and use by medical personnel. For worker health and safety information during the manufacture of Dantrium IV, please refer to the MSDS on each component. Accidental ingestion of large quantities may cause muscle weakness, lethargy, GI signs, hepatotoxicity, and crystalluria. See Section 11 for detailed information.

SECTION 3**HAZARD IDENTIFICATION cont.****POTENTIAL HEALTH EFFECTS:**

INHALATION: Unknown effect from direct contact with material; however, effects may be similar to ingestion.

EYE CONTACT: Unknown effect from direct contact with material.

SKIN CONTACT: Unknown effect from direct contact with material.

INGESTION: Muscle weakness, drowsiness, respiratory depression, lethargy, GI signs, hepatotoxicity and crystalluria.

SECTION 4**FIRST AID INFORMATION**

INHALATION: Remove the exposed person to fresh air. Give artificial respiration if not breathing. Seek medical aid.

EYE CONTACT: Flush eyes with copious amounts of water for at least 15 minutes. Seek medical attention.

SKIN CONTACT: Remove any contaminated clothing and wash area thoroughly with soap and water for at least 15 minutes. Get medical attention if irritation occurs.

INGESTION: Never give anything by mouth to someone who is unconscious or convulsive. Do not induce vomiting. Seek medical attention immediately.

SECTION 5**FIRE AND EXPLOSION DATA**

FLASH POINT AND METHOD: Not applicable.

EXTINGUISHING MEDIUM: Water spray, carbon dioxide, dry chemical

HAZARDOUS DECOMPOSITION OR COMBUSTION PRODUCTS: Oxides of Carbon, Carbon Monoxide and Nitrogen Oxides

EXPLOSION HAZARDS: May form explosive dust clouds in air (Mannitol). For active ingredient only: Fine dust suspended in air in the presence of an ignition source is a potential explosion hazard. St-1 combustible dust ($K_{st} = 134 \text{ bar-m/sec}$, $P_{max} = 9.3 \text{ bar}$, $dP/dt_{max} = 492 \text{ bar/sec}$).

SPECIAL FIRE PROCEDURES: Move container from fire area if it can be done without risk. Avoid inhalation of material or combustion by-products. Stay upwind and keep out of low areas. An explosion and fire hazard may result if the material is exposed to heat, flame, spark, and/or oxidizers. Wear a self-contained breathing apparatus and full bunker gear when fighting these fires. All equipment should be thoroughly decontaminated after use. Do not release the material into sewers or waterways

HAZARDOUS DECOMPOSITION OR COMBUSTION PRODUCTS: Fire may produce irritating, corrosive, and/or toxic gases, such as carbon monoxide and nitrogen oxides.

SECTION 6**ACCIDENTAL RELEASE MEASURES**

ACTION TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED: Immediately notify appropriate emergency response, safety and environmental personnel of any spills or leaks. Cleanup personnel need protection against inhalation and skin contact (see Section 8). Contain the spill and pick up material for recovery or disposal when feasible. Avoid creating a dust cloud, wet down with water spray or use a vacuum equipped with HEPA filters. Do not dispose of the material in any sanitary sewer, storm sewer, sink, toilet, or floor drain. Contact a licensed waste-disposal contractor for detailed disposal recommendations.

SECTION 7

HANDLING AND STORAGE

HANDLING: Keep the material away from heat, sparks, static discharge, and open flame. Keep container closed when not in use. Avoid contact with skin and eyes, and avoid generating dust. Use only in well-ventilated areas and wear appropriate personal protective equipment (PPE). Never eat, drink or smoke in work areas. Practice good personal hygiene (e.g., wash hands and other potentially exposed skin) after using this material.

STORAGE: Store the unreconstituted product at controlled room temperatures 20° to 25°C (68° to 77°F) and protect from light. [See USP Controlled Room Temperature].

SECTION 8

SPECIAL PROTECTION INFORMATION

Composition					
Component	CAS No.	OSHA PEL	ACGIH TLV	NIOSH REL	Other limits
Hydrated 1-{{5-(4-nitrophenyl)-2-furanyl}methylene}amino}-2-4-imidazolidinedione sodium salt	24868-20-01	NA	NA	NA	0.2 mg/m ³ *
Mannitol	69-65-8	NA	NA	NA	NA
Sodium hydroxide	1310-73-2	2 mg/m ³ Ceiling	2 mg/m ³ Ceiling	2 mg/m ³ Ceiling	NA

NA – Not available

*Occupational exposure limit proposed by Proctor and Gamble Pharmaceuticals

VENTILATION: To maintain airborne levels of components of this product in compliance with airborne concentration limits, use appropriate ventilation and/or enclose the process to control emissions during handling and other dust producing operations.

EYE PROTECTION: Wear safety goggles or safety glasses in compliance with OSHA regulations in 29 CFR 1910.133. Provide an emergency eye wash fountain and quick drench shower in the immediate work area.

CLOTHING: Wear appropriate chemical resistant clothing. Refer to 29 CFR 1910.133.

GLOVES: Standard rubber or polymer gloves that are impermeable to solid powder materials are adequate for prolonged exposure to all the components of this material. Refer to 29 CFR 1910.132.

RESPIRATOR: Under conditions of frequent use or heavy exposure, respiratory protection may be needed. Ensure compliance with airborne concentration limits. Respiratory protection is ranked in order from minimum to maximum. Consider warning properties before use.

Any chemical cartridge respirator with appropriate organic vapor and particulate filter cartridges(s)

Any chemical cartridge respirator with a full face piece and appropriate organic vapor and particulate filter cartridge(s).

Any air-purifying respirator with a full face piece and appropriate organic vapor and particulate filter canister

For Unknown Concentrations or Immediately Dangerous to Life or Health*

Any supplied-air respirator with full face piece and operated in a pressure-demand or other positive –pressure mode in combination with a separate escape supply.

Any self-contained breathing apparatus with a full face piece.

SECTION 9**PHYSICAL AND CHEMICAL DATA**

Appearance:	Pale orange-yellow powder cake inside a clear glass vial.
Physical State:	Lyophilized powder
Odor:	Odorless
Odor threshold:	Not Available
pH:	Not Available
Boiling or Melting Point:	225 to 226 degrees Celsius
Vapor Pressure @ 20°C:	Not Available
Vapor Density (air = 1):	Not Available
Solubility in Water:	791 mg/L
Specific Gravity (water = 1):	Not Available
Volatile organic compound (VOC) content:	Not Available
Evaporation Rate:	Not Available
Octanol/Water Partition Coefficient:	Not Available
Flammability:	Not Available
Flammability/explosion limits:	Not Available
Flashpoint:	Not Available
Auto-ignition temperature:	Not Available
Decomposition temperature:	Not Available

SECTION 10**STABILITY AND REACTIVITY**

REACTIVITY: Stable at normal temperature and pressure when properly stored (refer to section 7).

CONDITIONS TO AVOID: Avoid heat, flames, sparks and other sources of ignition. Avoid dust generation.

INCOMPATIBLES: Avoid contact with incompatible materials such as strong oxidizers.

POLYMERIZATION: Hazardous polymerization will not occur.

SECTION 11**TOXICOLOGY**

Note: Refer to packaging insert for additional information. Oral or systemic toxicity and effects data are available for this material as a whole due to its use as a pharmaceutical product. However, some toxic effects described in this section are those that might be expected, based on data for the components of the material. Many of these effects are only associated with very high levels of exposure based on tests in animals or by routes of exposure (e.g., ingestion) that are of minimal relevance for occupational situations. Furthermore, exposure to bulk material could result in health effects that may not be a concern for the formulated material distributed as tablets, since exposure to the final product (outside its intended pharmaceutical use) would be limited. Based on this information the material is unlikely to pose a significant hazard to human health if appropriate handling procedures, protective clothing and ventilation practices are followed.

EYE: Unknown effect on eyes from direct contact by material.

SKIN: Unknown effect on skin from direct contact material.

ACUTE INGESTION: The compound is pharmacologically active producing muscle weakness and associated lethargy. The minimal clinical dose producing these effects is about 25 mg/day. In acute toxicity studies, lethality only occurred at extremely high oral doses (oral LD₅₀); 7432 mg/kg in rats, and 1188 mg/kg in mice. The intraperitoneal LD₅₀ in these two species was 413 mg/kg in rats and 534 mg/kg in mice (RTECS 2003).

ACUTE INHALATION: Not available.

CHRONIC TOXICITY: The pharmacological effect of the compound would be expected to be seen on repeated oral exposures to approximately 25.0 mg/day. Higher doses, i.e. 30 mg/kg/day (about 2.1 g/day for human) could product reversible or hepatic or renal toxicity.

SECTION 11

TOXICOLOGY cont.

SUB-CHRONIC TOXICITY: The pharmacological effect of the compound would be expected to be seen on repeated oral exposures to approximately 25.0 mg/day. Higher doses, i.e. 30 mg/kg/day (about 2.1 g/day for human) could produce reversible or hepatic or renal toxicity.

TARGET ORGAN SYSTEMS: Skeletal muscle, Liver

CARCINOGENICITY:

Chemical	ACGIH	NTP	IARC	EPA	OSHA
Dantrolene Sodium	Not listed	Not Listed	Not Listed	Not Listed	Not Listed
Mannitol	Not Listed	Not listed	Not Listed	Not Listed	Not Listed
Sodium Hydroxide	Not Listed	Not Listed	Not Listed	Not Listed	Not Listed

There is some indication from rodent life time feeding studies that Dantrolene Sodium might cause cancer in laboratory animals at very high doses that resulted in increased mortality. The relevance of these findings to humans is unknown. Dantrolene Sodium has been evaluated in rodent carcinogenicity studies: Sprague Dawley rats and Fisher (F-344) rats were each dosed at 0, 15, 30 and 60 mg/kg/day, and CD-1 mice were dosed at 0, 12.9, 23.7 and 50.5 mg/kg/day for fifteen months. Increases in the incidence of some types of tumors were reported. However, at the very high doses used there was increased mortality in the treated groups making the interpretation of the studies difficult. Therefore, the relevance of the tumor findings to man is not known.

REPRODUCTION and DEVELOPMENT: Dantrolene Sodium does not produce birth defects. Animal studies showed an increase in embryo lethality in rabbits and decreased pup survival in rats at dose at or above 15 mg/kg/day (1 g/day to humans). In both cases, the study reports conclude that there are confounding issues in the studies which make it unlikely that the effects are due to exposure to Dantrolene Sodium.

GENOTOXICITY: Dantrolene Sodium has produced positive results in Ames Assay in the presence and absence of a liver activating system.

SECTION 12

ECOLOGICAL INFORMATION

ECOLOGICAL EFFECTS

No ecological studies have been completed to date.

SECTION 13

DISPOSAL

RCRA Hazardous Waste (40 CFR 261): Product is not listed as a hazardous waste. Consult an expert on the management and disposal of recovered material. Do not dispose of the material in any sanitary sewer or storm sewer system, which includes sinks, toilets, and floor drains. Ensure conformity with Federal, state, and local disposal regulations.

SECTION 14

TRANSPORTATION

The final packaged product is considered to be non-hazardous for transport.

PROPER SHIPPING NAME: Not applicable

ID/UN NUMBER: Not applicable

HAZARD CLASS: Not applicable

PACKAGING GROUP: Not applicable

U.S REGULATIONS:

CERCLA SECTIONS 102a/103 HAZARDOUS SUBSTANCES (40 CFR 302.4): Not regulated.

SARA TITLE III SECTIONS 302/304 EXTREMELY HAZARDOUS SUBSTANCES: Not regulated.

SARA TITLE III SECTIONS 311/312 HAZARDOUS CATEGORIES: Not regulated.

SARA TITLE II SECTION 313: Not regulated.

STATE REGULATIONS:

California Proposition 65: Not listed.

NATIONAL INVENTORY STATUS:

U.S. INVENTORY (TSCA): All the components of this material are listed on the TSCA inventory

OSHA: The final product is not considered hazardous under the US Hazard Communication Standard.

EUROPEAN UNION REGULATIONS:**Risk Phrases**

R20	Harmful by inhalation
R21	Harmful in contact with skin
R22	Harmful if swallowed.

Symbols

Xn	Harmful
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NA – NOT APPLICABLE

ND – NO DATA FOUND

The information provided in this Material Safety Data Sheet has been compiled from our experience and the data presented in various technical publications. It is the user's responsibility to determine the suitability of this information for the adoption of safety precautions as may be necessary. We reserve the right to revise the Material Safety Data Sheets from time to time as new information becomes available. The user has the responsibility to contact the company to make sure the sheet is the latest one issued.