PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] Dantrolene Sodium for Injection, USP

Dantrolene Sodium for Injection

Powder for solution, 20 mg / vial, Intravenous

USP

Skeletal Muscle Relaxant

Hikma Canada Limited
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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, Hepatic/Biliary/Pancreatic	08/2024

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

DANTROLENE SODIUM FOR INJECTION, USP (dantrolene sodium for injection) is indicated in:

- the management of malignant hyperthermia crisis.

1.1 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of DANTROLENE SODIUM FOR INJECTION, USP in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use in this subpopulation (see 7.1.3 Pediatrics).

1.2 Geriatrics

Geriatrics (≥65 years of age): The use in geriatric population may be associated with differences in safety or effectiveness (see 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

Patients with known hypersensitivity to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see 6 DOSAGE FORMS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- **Preoperatively:** If after suitable evaluation of the patient, including family history relative to malignant hyperthermia, it is felt that a malignant hyperthermia crisis may develop during anesthesia and surgery, oral dantrolene sodium may be used prophylactically 1-2 days prior to surgery (refer to dantrolene sodium capsules Product Monograph for further information). DANTROLENE SODIUM FOR INJECTION, USP could also be used preoperatively at a starting dose of 2.5 mg/kg, approximately 75 minutes before anticipated anesthesia and infused over approximately 1 hour. This dose should prevent or attenuate the development of clinical and laboratory signs of malignant hyperthermia provided that the usual precautions, such as avoidance of established malignant hyperthermia triggering agents, are followed.
- **Post Crisis Follow-up:** Oral dantrolene sodium should also be administered following a malignant hyperthermia crisis for a one- to three-day period to prevent recurrence of the manifestations of malignant hyperthermia (refer to dantrolene sodium capsules Product Monograph for further information).

4.2 Recommended Dose and Dosage Adjustment

During the crisis: DANTROLENE SODIUM FOR INJECTION, USP should be administered by continuous rapid intravenous push beginning at a minimum dose of 1 mg/kg and continuing until symptoms subside or the maximum cumulative dose of 10 mg/kg has been reached. If the physiologic and metabolic abnormalities reappear, the regimen may be repeated. It is important to note that administration of DANTROLENE SODIUM FOR INJECTION, USP should be continuous until symptoms subside.
The effective dose to reverse the crisis is directly dependent upon the individual's degree of susceptibility to malignant hyperthermia, the amount and time of exposure to the triggering agent, and the time elapsed between onset of the crisis and initiation of treatment.

Pediatrics (<18 years of age): Experience to date indicates that the dose for children is the same as for adults.

4.3 Reconstitution

Parenteral Products:

- Each vial of ANTRIUM INTRAVENOUS should be reconstituted by adding 60 mL of sterile water for injection USP (without a bacteriostatic agent), and the vial shaken until the solution is clear. **Store reconstituted solution between 15°C to 30°C, protected from light. The reconstituted solution must be used within 6 hours after reconstitution** (see 11 STORAGE, STABILITY AND DISPOSAL).

4.4 Administration

As soon as the crisis is recognized (i.e., tachycardia, tachypnea, central venous desaturation, central venous hypercarbia, metabolic acidosis, fever, skeletal muscle rigidity or cyanosis and mottling of the skin), anesthetics should be discontinued, then cooling procedures should be instituted and DANTROLENE SODIUM FOR INJECTION, USP should be administered by continuous rapid intravenous push. It is also important that appropriate supportive measures be instituted for treatment of the physiologic and metabolic abnormalities.

DANTROLENE SODIUM FOR INJECTION, USP is available only for use in hospitals or in dental clinics that are equipped to provide the necessary supportive measures used in the treatment of the malignant hyperthermia crisis.

5 OVERDOSAGE

There is no known constellation of symptoms with acute overdose. Drowsiness and generalized muscle weakness have been reported following very large doses of oral dantrolene sodium and would be expected as the major symptoms of overdosage. Other symptoms, which may occur in case of overdose include, but are not limited to, alterations in the state of consciousness (e.g., lethargy, coma), vomiting, diarrhea and crystalluria.

For acute overdosage, general supportive measures should be employed. Intravenous fluids should be administered in fairly large quantities to avert the possibility of crystalluria. An adequate airway should be maintained and artificial resuscitation equipment made available.

Electrocardiographic monitoring should be instituted, and the patient carefully observed. No experience has been reported with dialysis; hence its value in DANTROLENE SODIUM FOR INJECTION, USP overdosage is not known.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	Lyophilized powder for injection 20 mg / vial	Mannitol, sodium hydroxide

DANTROLENE SODIUM FOR INJECTION, USP is available in 100 mL vials with Bromobutyl (FM257/2) stoppers. The vial stoppers are not made with natural rubber latex. Each vial contains a sterile lyophilized mixture of 20 mg dantrolene sodium, 3000 mg mannitol, and sufficient sodium hydroxide to yield a pH of approximately 9.5 when reconstituted. These are single dose vials. Available in cartons of 6 vials.

7 WARNINGS AND PRECAUTIONS

General

The use of DANTROLENE SODIUM FOR INJECTION, USP in the management of malignant hyperthermia crisis is not a substitute for supportive measures.

Since the effect of disease state and other drugs on dantrolene sodium related skeletal muscle weakness, including possible respiratory depression, cannot be predicted, patients who receive intravenous dantrolene sodium preoperatively should have vital signs monitored.

Caution is also indicated at meals on the day of administration, because difficulty swallowing and choking have been reported.

Because of the high pH of the intravenous formulation of DANTROLENE SODIUM FOR INJECTION, USP and potential for tissue necrosis, care must be taken to prevent extravasation of the intravenous solution into the surrounding tissues.

When mannitol is used for prevention or treatment of renal complication of malignant hyperthermia, the 3 g of mannitol contained in each 20 mg vial of intravenous dantrolene sodium should be taken into consideration.

Carcinogenesis and Mutagenesis

Toxicity studies in animals provided evidence of low-grade carcinogenic activity of dantrolene sodium in the rat (see 16 NON-CLINICAL TOXICOLOGY, Carcinogenicity). In view of the animal

findings, potential carcinogenicity in humans cannot be disregarded. Therefore, the potential benefits of the drug should be weighed against the possible risks of drug use for the individual patient. Consideration should be given as to whether the patient has responded to other medication and to benefits of the trial administration of DANTROLENE SODIUM FOR INJECTION, USP as recommended. In assessing risk acceptability, the age of the patient, the degree of disability and life expectancy should also be considered. The long-term safety of DANTROLENE SODIUM FOR INJECTION, USP has not yet been established.

Driving and Operating Machinery

After the administration of DANTROLENE SODIUM FOR INJECTION, USP, symptoms of muscle weakness should be expected postoperatively (i.e., decrease in grip strength and weakness of leg muscles, especially walking down stairs). In addition, symptoms such as “lightheadedness”, dizziness and/or drowsiness may be noted. Since some of these symptoms may persist for up to 48 hours, patients must not operate an automobile or engage in other hazardous activity during this time. Caution should be exercised in the concomitant administration of alcohol and/or tranquilizing agents (such as central nervous system (CNS) medication).

Hepatic/Biliary/Pancreatic

Hepatic dysfunction, including fatal hepatic failure, can occur with dantrolene sodium use, and is related to dose and duration of therapy. There have been reported cases of hepatotoxicity following the use of intravenous dantrolene products. Elevated liver enzymes have occurred hours to days following use of intravenous dantrolene, though many of these cases were observed in patients with comorbidities (e.g., critical illness). Dantrolene sodium should be used in conjunction with appropriate individualized monitoring of hepatic function, as deemed medically necessary after surgery, for symptoms of hepatotoxicity and determination of SGOT or SGPT.

Patients should be instructed to contact their physician should signs or symptoms of hepatotoxicity (e.g., discoloured feces, generalized pruritus, jaundice, anorexia, nausea, vomiting) occur after therapy.

Monitoring and Laboratory Tests

Dantrolene sodium should be used in conjunction with appropriate individualized monitoring of hepatic function, as deemed medically necessary after surgery, for symptoms of hepatotoxicity and determination of SGOT or SGPT.

Peri-Operative Considerations

If patients judged malignant hyperthermia susceptible are administered intravenous dantrolene sodium preoperatively, anesthetic preparation must still follow a standard malignant hyperthermia susceptible regimen, including the avoidance of known triggering agents (see 4.1 Dosing Considerations). Monitoring for early clinical and metabolic signs of malignant hyperthermia is indicated because attenuation of malignant hyperthermia, rather than prevention, is possible. These signs usually call for the administration of additional intravenous dantrolene sodium.

Sensitivity

The possibility of cross-sensitivity with compounds of related chemical structure exists; however, no such reactions were reported in clinical trials.

7.1 Special Populations

7.1.1 Pregnant Women

Pregnancy and Lactation: The safety of DANTROLENE SODIUM FOR INJECTION, USP in women who are or who may become pregnant has not been established; in such patients it should be given when the potential benefits have been weighed against possible hazard to mother and child. Dantrolene crosses the placenta.

Breast-feeding

Dantrolene sodium has been detected in human milk at low concentrations (less than 2 micrograms per milliliter) during repeat intravenous administration over 3 days. DANTROLENE SODIUM FOR INJECTION, USP should be used by nursing mothers only if the potential benefit justifies the potential risk to the infant.

7.1.2 Pediatrics

Pediatrics (<18 years of age): Experience to date indicates that the dose for children is the same as for adults.

7.1.3 Geriatrics

Geriatrics (≥65 years of age): The use in the geriatric population could be associated with differences in safety and effectiveness.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

There have been occasional reports of death following malignant hyperthermia crisis even when treated with intravenous dantrolene sodium. Most of these deaths can be accounted for by late recognition, delayed treatment, inadequate dosage, lack of supportive therapy, intercurrent disease and/or the development of delayed complications such as renal failure or disseminated intravascular coagulopathy. In some cases, there are insufficient data to completely rule out therapeutic failure of dantrolene sodium.

There are rare reports of fatality in malignant hyperthermia crisis, despite initial satisfactory response to intravenous dantrolene sodium, which involve patients who could not be weaned from dantrolene sodium after initial treatment.

The following serious reactions were reported use of oral dantrolene sodium for 60 days or longer: hepatitis, seizures and pleural effusions with pericarditis. For a list of adverse reactions reported with the use of dantrolene sodium capsules, please consult the appropriate Product

Monograph.

The administration of intravenous dantrolene sodium to human volunteers is associated with loss of grip strength and weakness in the legs, as well as subjective central nervous system complaints.

There have been reports of the effects listed below by systems following administration of intravenous dantrolene sodium:

Cardiovascular System: thrombophlebitis, injection site reactions

Digestive System: choking, difficulty swallowing

Hepatobiliary: hepatotoxicity (see 7 WARNINGS AND PRECAUTIONS, Hepatic/Biliary/ Pancreatic)

Integumentary System: erythema (rare), urticaria (rare)

Musculoskeletal System: loss of grip strength, muscular weakness

Nervous System: lightheadedness

Respiratory System: pulmonary edema (rare) (diluent volume and mannitol needed to deliver intravenous dantrolene may contribute to the event)

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

See the WARNINGS AND PRECAUTIONS, Hepatic/Biliary/Pancreatic

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

Dantrolene sodium causes dizziness, drowsiness, and weakness; alcohol and other central nervous system (CNS) medications may intensify this effect.

9.4 Drug-Drug Interactions

Dantrolene sodium is metabolized by the liver, and it is theoretically possible that its metabolism may be enhanced by drugs known to induce hepatic microsomal enzymes. However, neither phenobarbital nor diazepam appears to affect dantrolene sodium metabolism. Binding to plasma protein is not significantly altered by diazepam, diphenylhydantoin, or phenylbutazone. Binding to plasma proteins is reduced by warfarin and clofibrate and increased by tolbutamide.

The combination of therapeutic doses of intravenous dantrolene sodium and verapamil in halothane/α-chloralose anesthetized swine has resulted in ventricular fibrillation and cardiovascular collapse in association with marked hyperkalemia. Hyperkalemia and myocardial depression have been observed in malignant hyperthermia-susceptible patients receiving intravenous dantrolene and concomitant calcium channel blockers. It is

recommended that the combination of intravenous dantrolene sodium and calcium channel blockers, such as verapamil, not be used during the reversal of a malignant hyperthermia crisis.

Administration of dantrolene may potentiate vecuronium-induced neuromuscular block.

Caution should be exercised in the concomitant administration of alcohol and tranquilizing agents (such as central nervous system (CNS) medication).

The effects of non-depolarizing muscle relaxants may be potentiated in patients administered dantrolene sodium. Caution should be exercised in the concomitant administration of tranquilizing agents.

The concomitant administration of dantrolene and therapies with estrogens or other potentially hepatotoxic substances may increase the risk of developing hepatotoxicity (liver damage). While a definite drug interaction with dantrolene and estrogen therapy has not been established, caution should be observed if the two drugs are to be given concomitantly. Hepatotoxicity has occurred more often in women over 35 years of age receiving concomitant estrogen therapy.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Dantrolene sodium is a muscle relaxant acting specifically on skeletal muscles.

Dantrolene sodium may prevent the increase in myoplasmic calcium and the acute catabolism within the muscle cell associated with anesthetic-induced malignant hyperthermia syndrome by interfering with the release of calcium from the sarcoplasmic reticulum to the myoplasm. Thus, the physiologic, metabolic and biochemical changes associated with the crisis may be reversed or attenuated.

10.2 Pharmacodynamics

Based on limited information obtained from study patients with malignant hyperthermia, it is estimated that therapeutic efficacy of the drug is obtained at a serum concentration of dantrolene of about 1 mcg/mL.

Dantrolene sodium causes marked, dose-dependent skeletal muscle relaxation in laboratory animals with a long duration of action. The pharmacologic profile of dantrolene sodium in

animals is unlike neuromuscular blocking agents in that total muscle paralysis and/or respiratory depression do not occur.

Various studies *in vivo* and *in vitro* demonstrated the apparent selectivity of action of dantrolene sodium for skeletal muscle. There were some non-specific depressant effects seen in several smooth muscle studies and insignificant effects in cardiac muscle in doses which cause skeletal muscle relaxation. Nerve transmission was not affected by dantrolene sodium in several animal studies.

Intravenous dantrolene sodium has no appreciable effect on the cardiovascular system or on respiratory function. A transient inconsistent effect on smooth muscles has been observed at high doses.

10.3 Pharmacokinetics

Distribution: Based on assays of whole blood and plasma, slightly greater amounts of dantrolene are associated with red blood cells than with the plasma fraction of blood. Significant amounts of dantrolene are bound to plasma proteins, mostly albumin, and this binding is readily reversible.

Metabolism: In humans, dantrolene metabolism is rapid via hepatic microsomal enzymes. The major metabolites in body fluids are the 5-hydroxy analog and the acetylamino analog. Dantrolene sodium also undergoes a minor metabolic pathway of hydrolysis and subsequent oxidation to form nitrophenylfuroic acid.

Elimination: Urinary excretion of dantrolene sodium and its metabolites occurs in an initially rapid phase (t-1/2, 2.5 to 3 hours) followed by a slower phase over a 24-hour period. Dantrolene sodium is also removed by biliary excretion and through the feces. The mean biologic half-life of dantrolene sodium after intravenous administration is about 5 hours.

11 STORAGE, STABILITY AND DISPOSAL

Unreconstituted vials: Store at controlled room temperature (15°C to 30°C) and protected from light.

Reconstituted vials: Store reconstituted solution between 15°C to 30°C, protected from light. The reconstituted solution must be used within 6 hours after reconstitution.

Disposal: Discard any portion of the reconstituted solution that remains unused. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

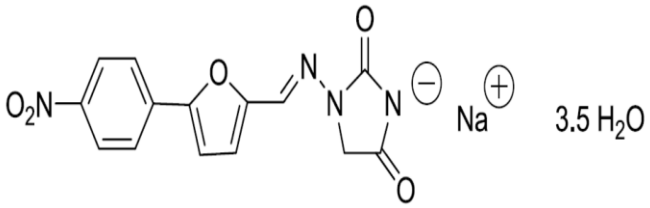
Drug Substance

Proper name: dantrolene sodium

Chemical name: 1- {[5-(p-nitrophenyl)-furturylidene] amino}-hydantoin sodium hydrate

Molecular formula and molecular mass: $C_{14}H_9N_4NaO_5 \cdot 3½\ H_2O$
399.29 (hydrous)
336.23 (anhydrous)

Structural formula:



Physicochemical properties: orange powder, slightly soluble in water, but due to its slightly acidic nature the solubility increases somewhat in alkaline solution.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Because of the low drug concentration (0.5 mg/mL) requiring the administration of large volumes of fluid, acute toxicity of intravenous dantrolene sodium could not be assessed. In 14-day (subacute) studies, dantrolene sodium was relatively non-toxic to rats at doses of 10 and 20 mg/kg/day. While 10 mg/kg/day in dogs for 14 days evoked little toxicity, 20 mg/kg/day for 14 days caused hepatic changes of questionable biologic significance.

Carcinogenicity:

Lifetime tumorigenesis studies were conducted in Sprague-Dawley and Fischer 344 rats. The treated Sprague-Dawley rats received dantrolene sodium in the diet at levels of 15, 30, and 60 mg/kg daily for 18 months and the Fischer 344 rats received the same levels for 20 months. The animals subsequently were maintained on a standard diet until 90% of each treatment group died spontaneously. Dantrolene sodium produced in the female Sprague-Dawley rats a

linear, dose-related increase in the number of rats with malignant neoplasms, and a decrease in the time of onset of mammary neoplasms. There were also increased incidence of benign hepatic tumours including lymphangiomas and bile duct cystadenomas, and angiosarcomas. In Fischer rats, there was a significant, dose-related reduction in the times of onset of mammary and testicular tumours.

A two-year tumorigenesis study was conducted in Swiss mice (CD®-1 HaM/ICR). Dantrolene sodium was fed to mice at levels of 15, 30, and 60 mg/kg/day for 15 months and then the mice were maintained on a standard diet for 9 additional months. There was an increased incidence of benign angiomatous neoplasms.

Genotoxicity:

Dantrolene sodium has produced positive results in the *Ames S. Typhimurium* bacterial mutagenesis assay in the presence and absence of a liver activating system.

Reproductive and Developmental Toxicology:

Dantrolene sodium administered to male and female rats at dose levels up to 45 mg/kg/day showed no adverse effects on fertility or general reproductive performance of adult animals.

In rabbits receiving 45 mg/kg/day during the period of organogenesis, there was a statistically significant increase in the frequency of pelvic ribs. In rats receiving 20 mg/kg/day, there was an increased frequency of pelvic ribs, and in rats receiving 60 mg/kg/day, there was suppression of fetal weight.

17 SUPPORTING PRODUCT MONOGRAPH

1. PrDantrium® Intravenous (Dantrolene Sodium for Injection, Powder for solution, 20 mg / vial, Intravenous) Submission Control No. 282340, Product Monograph, Endo Par Innovation Company, LLC. (May 16, 2024).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

DANTROLENE SODIUM FOR INJECTION, USP

Dantrolene Sodium for Injection

Read this carefully before you start taking **DANTROLENE SODIUM FOR INJECTION, USP** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **DANTROLENE SODIUM FOR INJECTION, USP**.

What is DANTROLENE SODIUM FOR INJECTION, USP used for?

DANTROLENE SODIUM FOR INJECTION, USP is used in adults and children to manage malignant hyperthermia (MH).

MH is a severe reaction to certain anesthetic medicines and can be life-threatening. Symptoms include severe muscle contractions, dangerously high body temperature, and a rapid heartbeat, among others. You are at a higher risk of MH if you have certain gene mutations.

How does DANTROLENE SODIUM FOR INJECTION, USP work?

DANTROLENE SODIUM FOR INJECTION, USP belongs to a group of medicines called skeletal muscle relaxants. It helps to reduce excessive muscle contractions.

What are the ingredients in DANTROLENE SODIUM FOR INJECTION, USP?

Medicinal ingredient: dantrolene sodium.

Non-medicinal ingredients: mannitol and sodium hydroxide.

DANTROLENE SODIUM FOR INJECTION, USP comes in the following dosage forms:

Powder for solution: 20 mg / vial of dantrolene sodium.

Do not use DANTROLENE SODIUM FOR INJECTION, USP if:

- you are allergic to dantrolene sodium or any of the other ingredients in DANTROLENE SODIUM FOR INJECTION, USP.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take DANTROLENE SODIUM FOR INJECTION, USP. Talk about any health conditions or problems you may have, including if you:

- have a history of liver problems.
- are allergic to other medicines of the hydantoin family, including phenytoin, fosphenytoin, nitrofurantoin, or nilutamide.
- are pregnant or planning to become pregnant.
- are breastfeeding or planning to breastfeed.

Other warnings you should know about:

Muscle weakness: Dantrolene sodium, the active ingredient in DANTROLENE SODIUM FOR INJECTION, USP, can induce a decrease in the grip strength and weakness of leg muscles, especially walking downstairs. Caution is also indicated at meals on the day of administration because difficulty swallowing and choking have been reported.

Pregnancy: Dantrolene sodium, the active ingredient in DANTROLENE SODIUM FOR INJECTION, USP, can cross the placenta. It is not known if it can harm an unborn baby. DANTROLENE SODIUM FOR INJECTION, USP should not be taken during pregnancy unless your healthcare professional has determined the expected benefits outweigh the possible risks to your health and that of your baby.

Breastfeeding: Dantrolene sodium, the active ingredient in DANTROLENE SODIUM FOR INJECTION, USP, can pass into breast milk. It is not known if it can harm a breastfed baby. Talk to your healthcare professional about the best way to feed your baby during this time.

Driving and using machines: DANTROLENE SODIUM FOR INJECTION, USP can cause dizziness, lightheadedness, drowsiness, and weakness. Alcohol and medicines that affect the central nervous system (CNS) may increase this effect. You should **not** drive or do tasks that require special attention for 48 hours after administration.

Check-ups and testing: You may have regular visits with your healthcare professional, before and during your treatment. They may do tests to monitor the health of your kidneys and liver, and the profile of your blood.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with DANTROLENE SODIUM FOR INJECTION, USP:

- other muscle relaxants used to treat muscle spasms and back pain (such as vecuronium).
- tranquilizing agents used to treat anxiety, panic and sleep disorders.
- anesthetic agents used during surgery and other procedure.
- alcohol.
- calcium channel blockers used to lower blood pressure and relieve chest pain (such as verapamil).
- anticoagulant agents used to treat and prevent blood clots (such as warfarin).
- lipid-lowering agents used for controlling the high cholesterol and triacylglyceride level in the blood (such as clofibrate).
- medicines use to help reduce blood sugar level (such as tolbutamide).
- estrogen-containing therapies used for birth control and hormone replacement.

How to take DANTROLENE SODIUM FOR INJECTION, USP:

- Your healthcare professional will prepare and give you or child DANTROLENE SODIUM FOR INJECTION, USP in a hospital or medical setting.
- You or your child will receive DANTROLENE SODIUM FOR INJECTION, USP through your veins (i.e.,“intravenously” or “IV”).

- Follow all instructions given to you by your healthcare professional.

Usual dose:

Your healthcare professional will decide on the right dose for you or your child. This may depend on you or child's current health, weight, if other medicines are taken, and the reaction to DANTROLENE SODIUM FOR INJECTION, USP.

Overdose:

Signs of an overdose with DANTROLENE SODIUM FOR INJECTION, USP may include:

- muscle weakness,
- drowsiness,
- altered state of consciousness (e.g., lack of energy or coma),
- vomiting
- diarrhea
- crystals in urine (crystalluria).

If you think you, or a person you are caring for, have taken too much DANTROLENE SODIUM FOR INJECTION, USP, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using DANTROLENE SODIUM FOR INJECTION, USP?

These are not all the possible side effects you may have when taking DANTROLENE SODIUM FOR INJECTION, USP. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- choking,
- difficulty swallowing,
- loss of grip strength,
- muscle weakness,
- injection site reactions,
- redness of the skin,
- hives,
- lightheadedness.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Pulmonary edema (excess fluid in the lungs): Coughing up blood or bloody froth, trouble breathing, shortness of breath,			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
wheezing, noisy breathing, or quick, shallow breathing.			
UNKNOWN FREQUENCY			
Liver problems: Jaundice (yellowing of the skin or whites of eyes), unusual dark urine, light-colored stool, loss of appetite, nausea, vomiting, abdomen pain, abdomen swelling, unusual tiredness, mental disorientation, confusion, sleepiness, coma, or itchiness.			√
Thrombophlebitis (inflamed or swollen vein from a blood clot): Swelling in the part of the body affected, pain in the part of the body affected, or skin redness, warmth and tenderness over the vein.			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health- products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Your healthcare professional will store DANTROLENE SODIUM FOR INJECTION, USP

for you. The unreconstituted vials of DANTROLENE SODIUM FOR INJECTION, USP will be stored between 15°C to 30°C and the reconstituted solution will be stored between 15°C to 30°C, protected from light.

- Keep out of reach and sight of children.

If you want more information about DANTROLENE SODIUM FOR INJECTION, USP:

- Talk to your healthcare professional;
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website https://www.hikma.com/, or by calling 1-888-656-0793.

This leaflet was prepared by Hikma Canada Limited.

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