PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr CHLORAL HYDRATE SYRUP ODAN

Chloral Hydrate Oral Solution, Odan Std

Syrup, 500 mg / 5 mL, for oral administration

Sedative - Hypnotic

Odan Laboratories Ltd.

325 Stillview Ave.

Pointe Claire, Quebec

Canada H9R 2Y6

Date of Initial Authorization:
May 13, 2003

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February 14, 2023

Submission Control Number: 268836

RECENT MAJOR LABEL CHANGES

None at time of the most recent authorization	06 / 2022

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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

CHLORAL HYDRATE SYRUP ODAN (Chloral Hydrate Oral Solution, Odan Std.) is indicated:

- For treatment of insomnia for short-term use; it has been shown to lose its effectiveness for both inducing and maintaining sleep after 2 weeks of administration.
- As a preoperative sedative that allays anxiety and induces sleep in candidates for surgery.
- In postoperative care and control of pain, as an adjunct to opiates and analgesics.

1.1 Pediatrics

Pediatrics (0-18 years of age): Health Canada has not authorized an indication for pediatric use (see 4.2 Recommended Dose and Dosage Adjustment, Children and 7.1.3 Pediatrics).

1.2 Geriatrics

Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see 4.1 Dosing Considerations).

2 CONTRAINDICATIONS

CHLORAL HYDRATE SYRUP ODAN is contraindicated in patients:

- with marked hepatic or renal impairment.
- who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Dosage must be individualized. Avoid in patients with moderate to severe renal failure (creatinine clearance < 0.8 ml/s). No dosage adjustment is necessary for patients with mild renal failure. Avoid in patients with severe hepatic dysfunction. (See 2 CONTRAINDICATIONS)

4.2 Recommended Dose and Dosage Adjustment

Adults:

- The usual hypnotic dose is 500 mg to 1 g, taken 15 to 30 minutes before bedtime or ½ hour before surgery.
- The usual sedative dose is 250 mg 3 times daily after meals. Generally, single doses or daily dosage should not exceed 2 g.

Children:

- The usual daily hypnotic dosage is 50 mg/kg, with a maximum of 1g per single dose. Daily dosage may be given in divided doses, if indicated.
- The sedative dosage is half of the hypnotic dosage. Maximum children sedative dose is 500 mg.
- The usual premedicant dose is 25 to 50 mg/kg, 30 minutes prior to procedure. May be repeated in 30 minutes using half the dose. Maximum children premedicant single dose is 1000 mg.

Geriatric:

- The usual hypnotic dose is 250 mg, 15 to 30 minutes before bedtime.

4.4 Administration

CHLORAL HYDRATE SYRUP ODAN may be administered in half a glass of water, fruit juice, or ginger ale.

4.5 Missed Dose

If a dose is missed, the next dose should be taken at the usual time. However, if it is almost time for the next dose, then the missed dose is to be skipped and not take two doses at once.

5 OVERDOSAGE

Symptoms: The signs and symptoms of chloral hydrate overdosage resemble those of barbiturates overdosage and especially affect the CNS and cardiovascular system: CNS depression, deep coma, respiratory depression, hypotension, cardiac arrhythmias. They may include: hypothermia, pinpoint pupils, blood pressure falls, comatose state, slow or rapid and shallow breathing. Gastric irritation may result in vomiting and even gastric necrosis. If the patient survives, icterus due to hepatic damage and albuminuria from renal irritation may appear.

The toxic oral dose of chloral hydrate for adults is approximately 10 g; however, death has been reported from a dose of 4 g and some patients have survived after taking as much as 30 g.

Treatment: Accidental overdosage should be treated by inducing vomiting with Ipecac syrup to empty the stomach; or by giving charcoal with sorbitol. Supportive measures, including respiratory and cardiovascular assistance and maintenance of body temperature and circulation, may be used. The airway should be protected in obtunded or unconscious patients. Cardiac monitoring is important, especially in patients with pre-existing cardiac disease. Hypotension should be treated with appropriate i.v. fluids and electrolytes; dopamine or norepinephrine may be required. Baseline hepatic and renal function tests should be obtained. Hemodialysis removes both the parent drug and the trichloroethanol metabolite.

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

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Solution; 500 mg / 5 mL	Citric Acid, D&C Yellow #10, FD&C Red #40, Flavor Blood Orange, Glycerin, Methylparaben, Propylene Glycol, Purified Water, Sodium Benzoate, Sodium Citrate, Sodium Hydroxide, Sucrose.

Description

Each 5 ml of orange flavored syrup contains 500 mg of chloral hydrate USP. Available in bottles of 500 ml.

7 WARNINGS AND PRECAUTIONS

Cardiovascular

Continued use of therapeutic doses of chloral hydrate has been shown to be without deleterious effect on the heart. Large doses of chloral hydrate, however, should not be used in patients with severe cardiac disease due to the possibility of cardiac arrhythmias and hypotension associated with larger doses.

Dependence/Tolerance

Chloral hydrate may be habit-forming: Long-term use or larger than usual therapeutic doses may result in tolerance and in physical and/or psychological dependence. Therefore, caution must be exercised when administering the drug to patients susceptible to drug abuse, mentally depressed, or suicidal.

Withdrawal: Sudden withdrawal may result in hallucinations and symptoms similar to delirium tremens (sometimes fatal), therefore chloral hydrate should be tapered gradually. Patients should be warned against sudden discontinuation of chloral hydrate except under the advice of the physician; they should also be informed of symptoms that would suggest potential adverse effects.

Driving and Operating Machinery

Chloral hydrate may cause drowsiness; therefore patients should be instructed to use caution when driving, operating a vehicle, potentially dangerous machinery or performing any hazardous task.

Endocrine and Metabolism

Chloral hydrate has been reported to precipitate attacks of acute intermittent porphyria and should be used with caution in susceptible patients.

Gastrointestinal

Because of its irritant properties, oral use of chloral hydrate should be avoided in patients with gastritis, esophagitis or gastric or duodenal ulcer.

Respiratory

Careful monitoring is required in patients with respiratory insufficiency.

Skin

Chloral hydrate is an irritant when applied to the skin and mucous membranes (See 8.1 Adverse Reaction Overview, Skin and subcutaneous tissue disorders).

7.1 Special Populations

7.1.1 Pregnant Women

Animal reproduction studies have not been conducted with chloral hydrate. Chloral hydrate crosses the placental barrier and chronic use during pregnancy may cause withdrawal symptoms in the neonate. It is not known whether chloral hydrate can affect reproduction capacity. Chloral hydrate should be given to a pregnant woman only if clearly needed. FDA Pregnancy Category C.

7.1.2 Breast-feeding

Chloral hydrate is excreted in human milk; use by nursing mothers may cause sedation in the infant.

7.1.3 Pediatrics

Gastric irritation and vomiting may occur following administration of the oral liquid. It should be well diluted with water or other liquid such as fruit juice or ginger ale. Due to the prolonged half-lives of the chloral hydrate's metabolites, excessive CNS depression may occur due to accumulation following repeated dosing. The degree of sedation should be monitored and caregivers cautioned against exceeding prescribed dosage. Neonates should be monitored for increased bilirubin concentrations as hyperbilirubinemia may occur due to the competition of chloral hydrate metabolites with bilirubin for hepatic glucuronidation.

Patients should be monitored for CNS and respiratory depressive effects. Deaths associated with the use of chloral hydrate for sedation prior to diagnostic or therapeutic procedures have been reported, particularly in pediatric patients. In addition, particular care must be taken in calculating and administering the proper dose. Sedation with chloral hydrate in children with adenoidal hypertrophy and obstructive sleep apnea has been reported to cause episodes of life-threatening respiratory obstruction. Children with obstructive sleep apnea from other causes may be at risk as well. Laryngeal edema resulting in severe respiratory difficulty in a child has also been reported.

7.1.4 Geriatrics

In geriatric patients likely to have age-related hepatic/renal function impairment, and in debilitated patients or those patients prone to CNS depression, reduction of dose may be necessary to avoid oversedation or other adverse effects. (See 2 CONTRAINDICATIONS)

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Blood and lymphatic system disorders: Leukopenia and eosinophilia have occasionally occurred.

Cardiac disorders: Large doses of chloral hydrate have been reported to produce hypotension, ventricular and atrial arrhythmias, torsades de pointes, depression of myocardial contractility, and shortening of refractory periods.

Ear and labyrinth disorders: Increases in middle ear pressure in infants and children have been reported.

Eye disorders: Chloral hydrate has produced oculotoxicities manifesting as ptosis, allergic conjunctivitis and keratoconjunctivitis.

Gastrointestinal disorders: Ileus in infant has been reported. Some patients experience gastric irritation and occasionally nausea and vomiting, flatulence, diarrhea, and unpleasant taste occur. These effects can be minimized by taking chloral hydrate with a full glass of fluid.

Metabolism and nutrition disorders: Chloral hydrate has been reported to precipitate attacks of acute intermittent porphyria.

Nervous system disorders: Occasionally, a patient becomes somnambulistic and may be disoriented and incoherent and show paranoid behavior. Rarely, excitement, tolerance, addiction, delirium, drowsiness, staggering gait, ataxia, lightheadedness, vertigo, dizziness, nightmares, malaise, mental confusion, and hallucinations have been reported. Hangover effect can occur, although it is less commonly observed than with barbiturates and some benzodiazepines.

Other: Chronic poisoning may manifest with symptoms of gastritis, skin rash, peripheral vasodilation, hypotension, renal damage and myocardial depression.

Renal and urinary disorders: Rarely, ketonuria have been reported.

Respiratory, thoracic and mediastinal disorders: Life-threatening respiratory obstruction episodes have been reported in young children.

Skin and subcutaneous tissue disorders: Allergic skin rashes including hives, exzematoid dermatitis, urticaria, scarlatiniform exanthems, bulbous reactions, non-thrombocytopenic purpurea and erythema multiforme, have occasionally been reported. Some cutaneous reactions are accompanied by fever. Chloral hydrate is an irritant when applied to the skin and mucous membranes.

8.2 Clinical Trial Adverse Reactions

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

9 DRUG INTERACTIONS

9.3 Drug-Behaviour Interactions

CHLORAL HYDRATE SYRUP ODAN may produce additive CNS depressant effects when co-administered with alcohol.

9.4 Drug-Drug Interactions

Alcohol or CNS Depressants: Concurrent use may increase the CNS depressant effects of either these medications or chloral hydrate, cautions recommended and dosage of one or both agents should be reduced.
(A disulfiram-like reaction may occur in patients receiving chloral hydrate and alcohol, including tachycardia, facial flushing, and dysphoria.)

Anticoagulants, coumarin – or indandione-derivative: Chloral hydrate may transiently enhance the hypoprothrombinemic response to these medications, especially within the first 2 weeks of therapy, by displacing the anticoagulant from plasma protein binding sites. When chloral hydrate is added or removed from the therapeutic regimen, or when dosage changes are made, frequent prothrombin time determinations are recommended.

Furosemide, intravenous: Use caution if administering i.v. furosemide within 24 hours of chloral hydrate. Administration of chloral hydrate followed by intravenous furosemide within 24 hours may result in diaphoresis, hot flashes, and variable blood pressure, including hypertension.

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

Chloral hydrate may produce false-positive results for urine glucose determinations utilizing cupric sulfate as Benedict's solution and possibly with cupric sulfate tablets but the drug does not interfere with urine glucose tests utilizing glucose oxidase.

Chloral hydrate may interfere with fluorometric tests for urine catecholamines, and it has been recommended that the drug not be administered for 48 hours preceding the test.

Chloral hydrate administration may also interfere with the Reddy, Jenkins, and Thorn procedure for determining urinary 17-hydroxycorticosteroids. Administration of chloral Hydrate can result in erroneously high values for vitamin B12 in some radioassay procedure.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The mechanism of action by which the CNS is affected is not known. Chloral hydrate is readily absorbed from the gastrointestinal tract following oral administration; however, significant amounts of chloral hydrate have not been detected in the blood after oral administration. It is generally believed that the central depressant effects are due to the principal pharmacologically active metabolite trichloroethanol.

Hypnotic dosage produces mild cerebral depression and quiet, deep sleep with little or no "hangover". Chloral hydrate decreases sleep latency and nighttime awakenings with minimal effects on REM sleep REM rebound does not occur with drug withdrawal.

Blood pressure and respiration are depressed only slightly more than in normal sleep and reflexes are not significantly depressed, so the patient can be awakened and completely aroused. Higher doses may lead to depression of respiratory and vasomotor centers.

Chloral hydrate has little analgesic activity and may produce excitement or delirium in the presence of pain. Sedative or hypnotic doses have little anticonvulsant activity.

10.2 Pharmacodynamics

Following a hypnotic dose, drowsiness occurs within 10 to 15 minutes, and sleep usually occurs within 30 to 60 minutes, which lasts about 4 to 8 hours. When used as a premedication in infants and children, sedation usually occurs within 15 minutes and sleep by 40 minutes, with most fully awake within 2 hours.

10.3 Pharmacokinetics

Absorption:

Chloral hydrate is readily absorbed from the gastrointestinal tract after oral administration.

Distribution:

Chloral hydrate has been detected in CSF, umbilical cord blood, fetal blood, and amniotic fluid. Following therapeutic doses of chloral hydrate, only small, clinically insignificant amounts of the active metabolite are distributed into milk.

Metabolism:

Chloral hydrate is rapidly and extensively metabolized in the liver and erythrocytes by alcohol dehydrogenase to active trichloroethanol. A small amount of chloral hydrate and a larger portion of trichloroethanol are oxidized to an inactive metabolite, trichloroacetic acid, in the liver and kidneys. This metabolite is excreted in the urine and bile, together with trichloroethanol in free or conjugated form.

Elimination:

The average half-life of trichloroethanol in adults is 8 hours, ranging from 4 to 12 hours. The half-life is prolonged in children and infants, averaging 10 hours in children and 37 hours in pre-term infants. Trichloroethanol is 70 to 80% bound to plasma proteins and is widely distributed to all tissues including CSF, breast milk and placenta.

The half-life of trichloroacetic acid approaches 100 hours. It is highly plasma protein bound (94%), primarily to albumin.

11 STORAGE, STABILITY AND DISPOSAL

Temperature:

Store CHLORAL HYDRATE SYRUP ODAN below 40°C; preferably between 15 and 30°C.

Protect from freezing.

Light:

Store in a light-resistant container.

Moisture:

Store in a tight container.

Others:

Keep out of reach and sight of children.

12 SPECIAL HANDLING INSTRUCTIONS

None

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

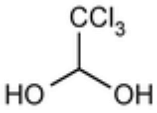
Drug Substance

Proper name: Chloral Hydrate

Chemical name: 1,1-Ethanediol,2,2,2-trichloro-

Molecular formula and molecular mass: $CCl_3CH(OH)_2$ 165.4 g/mol

Structural formula:



Physicochemical properties: Colorless, transparent, or white crystals having an aromatic, penetrating, and slightly acrid odor, and a slightly bitter, caustic taste. Melts at about 55°, and slowly volatilizes when exposed to air. Very soluble in water and in olive oil; freely soluble in alcohol, in chloroform, and in ether.

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

Information not available.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]CHLORAL HYDRATE SYRUP ODAN

Chloral Hydrate Oral Solution, Odan Std.

Read this carefully before you start taking **CHLORAL HYDRATE SYRUP ODAN** 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 **CHLORAL HYDRATE SYRUP ODAN**.

What is CHLORAL HYDRATE SYRUP ODAN used for?

CHLORAL HYDRATE SYRUP ODAN is used in adults:

- for short term (less than 2 weeks) treatment of insomnia. This is a sleep disorder that makes it hard to fall asleep, hard to stay asleep, or causes you to wake up too early.
- to reduce anxiety and help put you to sleep before surgery.
- to help control pain after you have had surgery.

How does CHLORAL HYDRATE SYRUP ODAN work?

CHLORAL HYDRATE SYRUP ODAN works by producing a hypnotic effect in the brain. This induces a deep sleep. It also helps you fall asleep faster and decreases nighttime awakenings.

What are the ingredients in CHLORAL HYDRATE SYRUP ODAN?

Medicinal ingredients: chloral hydrate

Non-medicinal ingredients: citric acid, D&C yellow #10, FD&C red #40, flavor blood orange, glycerin, methylparaben, propylene glycol, purified water, sodium benzoate, sodium citrate, sodium hydroxide, sucrose.

CHLORAL HYDRATE SYRUP ODAN comes in the following dosage forms:

Orange flavored syrup: 500 mg / 5 mL

Do not use CHLORAL HYDRATE SYRUP ODAN if:

- you are allergic to chloral hydrate or any of the ingredients in CHLORAL HYDRATE SYRUP ODAN
- you have liver or kidney problems

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CHLORAL HYDRATE SYRUP ODAN. Talk about any health conditions or problems you may have, including if you:

- have ever had a problem with:
    - substance use, including prescribed or illegal drugs, or
    - alcohol
- have heart disease
- have or have had porphyria (a blood disease)
- have digestive problems, such as ulcers or inflammation of the stomach or esophagus
- have lung or breathing problems
- are pregnant or plan to become pregnant. You could harm your baby if you take CHLORAL HYDRATE SYRUP ODAN while you are pregnant.
- are breastfeeding or plan to breastfeed. CHLORAL HYDRATE SYRUP ODAN passes into breastmilk.
- are 65 years of age or older

Other warnings you should know about:

Addiction, Abuse and Misuse: If you take CHLORAL HYDRATE SYRUP ODAN, you are at risk for abuse, misuse, addiction, physical dependence and withdrawal. Abuse and misuse can result in overdose or death.

Withdrawal: If you suddenly stop your treatment, lower your dose too fast, or switch to another medication, you can experience withdrawal symptoms that can be life threatening, such as:

- severe confusion, shivering, irregular heartrate and excessive sweating (delirium tremens)
- seeing or hearing things that are not there (hallucinations)

To reduce your chances of going through withdrawal:

- always contact your healthcare professional before stopping or reducing your dose of CHLORAL HYDRATE SYRUP ODAN or changing medications
- always follow your healthcare professional's instructions on how to reduce your dose carefully and safely
- tell your healthcare professional **right away** if you experience any unusual symptoms after changing or stopping your treatment

Driving and Using Machines: CHLORAL HYDRATE SYRUP ODAN may make you drowsy. Give yourself time after taking CHLORAL HYDRATE SYRUP ODAN to see how you feel before driving a vehicle or using machinery.

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 CHLORAL HYDRATE SYRUP ODAN:

- alcohol. Do not take CHLORAL HYDRATE SYRUP ODAN if you drink alcohol.

- depressants, including other hypnotics or sedative that are used to help with sleeping
- medicines used to prevent blood clots such as, coumarin, indandione-derivative
- furosemide, a diuretic or “water pill”, when given intravenously (IV)

How to take CHLORAL HYDRATE SYRUP ODAN:

- Always take CHLORAL HYDRATE SYRUP ODAN exactly as your healthcare professional tells you to. Do not change your dose without taking to your healthcare professional.
- Your healthcare professional will slowly decrease your dose and will tell you when to stop taking the medicine. Always follow your healthcare professional’s instructions on how to lower your dose carefully and safely to avoid experiencing withdrawal symptoms.
- Your healthcare professional will ensure the lowest effective dose of CHLORAL HYDRATE SYRUP ODAN is used for the shortest amount of time.
- CHLORAL HYDRATE SYRUP ODAN can be taken in half a glass of water, fruit juice, or ginger ale.

Usual dose:

Adults:
- Insomnia: 500 mg (5 mL) to 1 g (10 mL), taken 15 to 30 minutes before bedtime.
- Surgery: 500 mg (5 mL) to 1 g (10 mL), taken 30 minutes before surgery.
- Pain control after surgery: 250 mg (2.5 mL) 3 times a day after meals.
- Maximum dose: 2 g (20 mL), either as a single dose or total daily dose.

Children:
- Your healthcare professional will decide on the dose that is right for your child based on their body weight and the reason CHOLORAL HYDRATE SYRUP ODAN has been prescribed.

Elderly (65 years or older):
- Insomnia: 250 mg (2.5 mL), 15 to 30 minutes before bedtime.

Overdose:

Accidental overdosage should be treated by inducing vomiting with Ipecac syrup to empty the stomach; or by taking charcoal with sorbitol.

If you think you, or a person you are caring for, have taken too much CHLORAL HYDRATE SYRUP ODAN, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, skip the missed dose and take your next dose at your usual time. Do not take two doses at once.

What are possible side effects from using CHLORAL HYDRATE SYRUP ODAN?

These are not all the possible side effects you may have when taking CHLORAL HYDRATE SYRUP ODAN. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- difficulty with coordination
- nausea, vomiting
- gas
- diarrhea
- unpleasant taste
- dizziness, lightheadedness
- drowsiness
- nightmares

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**	
Overdose: slow reflexes, slow shallow breathing, coma, and low blood pressure.			√
Respiratory Depression: slow, shallow or weak breathing.			√
Withdrawal, severe symptoms include: **Delirium Tremens:** severe confusion, shivering, irregular heartrate and excessive sweating **Hallucinations:** seeing or hearing things that are not there		√	
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing, fever.			√

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:

Store CHLORAL HYDRATE SYRUP ODAN below 40°C; preferably between 15 and 30°C. Store in a tight, light-resistant container. Protect from freezing.

Keep out of reach and sight of children.

If you want more information about CHLORAL HYDRATE SYRUP ODAN:

- 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://health-products.canada.ca/dpd-bdpp/index-eng.jsp); or by calling the manufacturer at 1-888-666-6326.

This leaflet was prepared by Odan Laboratories Ltd.

Last Revised February 14, 2023