

Chloral Hydrate Syrup-Odan
(Chloral Hydrate Syrup 500 mg/5 ml, USP)

Sedative-Hypnotic

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Control: 072163

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Prescribing information

Chloral Hydrate-Odan Syrup

PHARMACOLOGY

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.

Pharmacokinetics:

Chloral hydrate is readily absorbed from the gastrointestinal tract after oral administration. 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. 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 premedicant in infants and children, sedation usually occurs within 15 minutes and sleep by 40 minutes, with most fully awake within 2 hours.

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.

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.

INDICATIONS

For treatment of insomnia. Chloral hydrate is effective as a hypnotic only for a short-term use; it has been shown to lose its effectiveness for both inducing and maintaining sleep after 2 weeks of administration.

In candidates for surgery, it is a satisfactory preoperative sedative that allays anxiety and induces sleep without depressing respiration or cough reflex.

In postoperative care and control of pain, it is a valuable adjunct to opiates and analgesics.

CONTRAINDICATIONS

Patients with marked hepatic or renal impairment.

Idiosyncrasy or hypersensitivity to chloral hydrate.

WARNINGS

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. Sudden withdrawal may result in hallucinations and symptoms similar to delirium tremens (sometimes fatal), therefore chloral hydrate should be tapered gradually.

Cardiac disorders: In patients with severe cardiac disease, chloral hydrate should be avoided due to the possibility of cardiac arrhythmias and hypotension associated with larger doses.

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

Children: 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.

PRECAUTIONS

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

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.

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

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.

Chloral hydrate may interfere with copper sulfate tests for glycosuria (suspected glycosuria should be confirmed by a glucose oxidase test when the patient is receiving chloral hydrate); fluorometric tests for urine catecholamines (it is recommended that the medication not be administered for 48 hours preceding the test); or urinary 17-hydroxycorticosteroid determinations (when using the Reddu, Jenkins, or Thorn procedures).

Pregnancy: 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.

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

Children: 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.

Geriatrics: In elderly 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.

Respiratory: Careful monitoring is required in patients with respiratory insufficiency.

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 agent 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 indandiono-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.

Laboratory Testing: Chloral hydrate may produce false-positive results for urine glucose determinations utilizing cupric sulfate as Benedict's solution and possibly with cupric sulfate tablets (Clinitest®) but the drug does not interfere with urine glucose tests utilizing glucose oxidase (e.g. Clinistix®, Tes-Tape®).

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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.

ADVERSE EFFECTS

CNS: 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.

Hematological: Leukopenia and eosinophilia have occasionally occurred.

Dermatological: Allergic skin rashes including hives, exzematoid dermatitis, urticaria, scarlatiniform exanthems, bulbous reactions, non-thrombocytopenic purpura 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.

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

Gastrointestinal: 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

Cardiovascular: 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.

Respiratory: Life-threatening respiratory obstruction episodes have been reported in young children.

Metabolic: Chloral hydrate has been reported to precipitate attacks of acute intermittent porphyria. Rarely, ketonuria have been reported.

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

Other: Increases in middle ear pressure in infants and children have been reported.

OVERDOSE

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 10g; however, death has been reported from a dose of 4g and some patients have survived after taking as much as 30g.

Treatment: Accidental overdosage should be treated with gastric lavage; 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.

DOSAGE

Dosage must be individualized. Avoid in patients with moderate to severe renal failure (creatinine clearance < 0.8ml/s). No dosage adjustment is necessary for patients with mild renal failure. Avoid in patients with severe hepatic dysfunction. The syrup may be administered in half a glass of water, fruit juice, or ginger ale.

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 2g.

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 500mg.

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

1000mg.

Geriatric:

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

SUPPLIED

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

Store below 40°C (104°F). preferably between 15 and 30°C (59 and 86°F). Store in a tight, light-resistant container. Protect from freezing.