

ANTITUSSIVE

HYCODAN[®]

(Hydrocodone Bitartrate and Homatropine Methylbromide)

TABLETS AND ORAL SOLUTION

CII

R_x only

WARNING: RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death (see WARNINGS, PRECAUTIONS – Drug Interactions). Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol.

DESCRIPTION

HYCODAN contains hydrocodone (dihydrocodeinone) bitartrate, a semisynthetic centrally-acting opioid antitussive. Homatropine methylbromide is included in a subtherapeutic amount to discourage deliberate overdose.

Each HYCODAN tablet or teaspoonful (5 mL) contains:

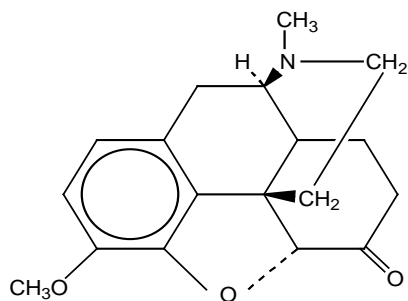
Hydrocodone Bitartrate, USP 5 mg

Homatropine Methylbromide, USP 1.5 mg

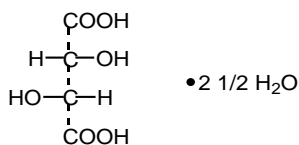
HYCODAN tablets also contain: calcium phosphate dibasic, colloidal silicon dioxide, lactose, magnesium stearate, starch and stearic acid.

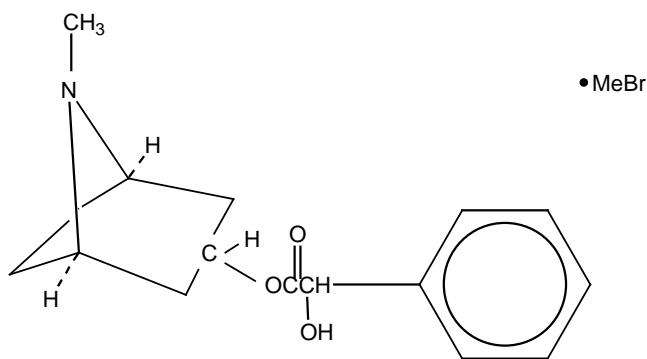
HYCODAN oral solution also contains: caramel coloring, FD&C Red 40, liquid sugar, methylparaben, propylparaben, sorbitol solution and wild cherry imitation flavor.

The hydrocodone component is 4,5 α -epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5), a fine white crystal or crystalline powder, which is derived from the opium alkaloid, thebaine, has a molecular weight of (494.50), and may be represented by the following structural formula:



$C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2 \frac{1}{2} H_2O$
HYDROCODONE BITARTRATE





$C_{17}H_{24}BrNO_3$
HOMATROPINE METHYLBROMIDE

Homatropine methylbromide is 8-Azoniabicyclo [3.2.1]octane,3-[(hydroxyphenyl-acetyl)oxy]-8,8-dimethyl-,bromide, endo-; a white crystal or fine white crystalline powder, with a molecular weight of (370.29).

CLINICAL PHARMACOLOGY

Hydrocodone is a semisynthetic opioid antitussive and analgesic with multiple actions qualitatively similar to those of codeine. The precise mechanism of action of hydrocodone and other opiates is not known; however, hydrocodone is believed to act directly on the cough center. In excessive doses, hydrocodone, like other opium derivatives, will depress respiration. The effects of hydrocodone in therapeutic doses on the cardiovascular system are insignificant. Hydrocodone can produce miosis, euphoria, physical and physiological dependence.

Following a 10 mg oral dose of hydrocodone administered to five adult male subjects, the mean peak concentration was 23.6 ± 5.2 ng/mL. Maximum serum levels were achieved at 1.3 ± 0.3 hours and the half-life was determined to be 3.8 ± 0.3 hours. Hydrocodone exhibits a complex pattern of metabolism including O-demethylation, N-demethylation and 6-keto reduction to the corresponding 6- α - and 6- β -hydroxymetabolites.

INDICATIONS AND USAGE

HYCODAN (hydrocodone bitartrate and homatropine methylbromide) is indicated for the symptomatic relief of cough in adults and children 6 years of age and older.

CONTRAINDICATIONS

HYCODAN should not be administered to patients who are hypersensitive to hydrocodone or homatropine methylbromide.

WARNINGS

Risks from Concomitant Use with Benzodiazepines or other CNS Depressants

Concomitant use of opioids, including HYCODAN, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedations, respiratory depression, coma, and death. Because of these risks, avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol (see **PRECAUTIONS – Drug Interactions**).

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol.

Advise both patients and caregivers about the risks of respiratory depression and sedation if HYCODAN is used with benzodiazepines, alcohol, or other CNS depressants (see **PRECAUTIONS – Information for Patients**).

Hydrocodone can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of HYCODAN and it should be prescribed and administered with the same degree of caution appropriate to the use of other opioid drugs (see **DRUG ABUSE AND DEPENDENCE**).

Respiratory Depression

The use of HYCODAN is not recommended for use in children less than 6 years of age because of the risk of fatal respiratory depression (see **ADVERSE REACTIONS –Respiratory Depression**). HYCODAN produces dose-related respiratory depression by directly acting on brain stem respiratory centers. If respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride and other supportive measures when indicated.

Head Injury and Increased Intracranial Pressure

The respiratory depression properties of opioids and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, opioids produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions

The administration of HYCODAN or other opioids may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Pediatric Use

In pediatric patients, as well as adults, the respiratory center is sensitive to the depressant action of opioid cough suppressants in a dose-dependent manner. Caution should be exercised when administering HYCODAN to pediatric patients 6 years of age and older because of the potential for fatal respiratory depression. Overdose or concomitant administration of HYCODAN with other respiratory depressants may increase the risk of respiratory depression in pediatric patients. Benefit to risk ratio should be carefully considered especially in the pediatric population with respiratory embarrassment (e.g., croup) (see **PRECAUTIONS**).

PRECAUTIONS

General

Before prescribing medication to suppress or modify cough, it is important to ascertain that the underlying cause of cough is identified, that modification of cough does not increase the risk of clinical or physiological complications, and that appropriate therapy for the primary disease is provided.

Special Risk Patients

HYCODAN (hydrocodone bitartrate and homatropine methylbromide) should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal functions, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture, asthma, and narrow-angle glaucoma.

Information for Patients

Inform patients and caregivers that potentially fatal additive effects may occur if HYCODAN is used with benzodiazepines or other CNS depressants, including alcohol. Because of this risk, patients should avoid concomitant use of HYCODAN with benzodiazepines or other CNS depressants, including alcohol (see **WARNINGS, PRECAUTIONS – Drug Interactions**).

Hydrocodone may produce marked drowsiness and impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using HYCODAN should be cautioned accordingly.

Patients should be advised to measure HYCODAN oral solution with an accurate measuring device. A household teaspoon is not an accurate measuring device and could lead to overdose, especially when a half a teaspoon is measured. A pharmacist can recommend an appropriate measuring device and can provide instructions for measuring the correct dose. Keep out of the reach of children.

Drug Interactions

The use of benzodiazepines, opioids, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with HYCODAN may cause an additive CNS depressant effect, profound sedation, respiratory depression, coma, and death and should be avoided (see **WARNINGS**).

The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies of HYCODAN in animals to evaluate the carcinogenic and mutagenic potential and the effect on fertility have not been conducted.

Pregnancy

Teratogenic Effects: Pregnancy Category C:

Animal reproduction studies have not been conducted with HYCODAN. It is also not known whether HYCODAN can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. HYCODAN should be given to a pregnant woman only if clearly needed.

Nonteratogenic Effects:

Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes,

increased respiratory rate, increased stools, sneezing, yawning, vomiting and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose.

Labor and Delivery

As with all opioids, administration of HYCODAN to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from HYCODAN, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of HYCODAN in pediatric patients under six have not been established. The use of HYCODAN in children less than 6 years of age has been associated with cases of fatal respiratory depression (see **ADVERSE REACTIONS – Respiratory Depression**). HYCODAN should be used with caution in pediatric patients 6 years of age and older (see **WARNINGS – Pediatric Use**).

ADVERSE REACTIONS

Central Nervous System

Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychic dependence, mood changes.

Gastrointestinal System

Nausea and vomiting may occur; they are more frequent in ambulatory than in recumbent patients. Prolonged administration of HYCODAN may produce constipation.

Genitourinary System

Ureteral spasm, spasm of vesicle sphincters and urinary retention have been reported with opiates.

Respiratory Depression

HYCODAN may produce dose-related respiratory depression by acting directly on brain stem respiratory centers (see **OVERDOSAGE**). Use of HYCODAN in children less than 6 years of age has been associated with fatal respiratory depression. Overdose with HYCODAN in children 6 years of age and older, in adolescents, and in adults has been associated with fatal respiratory depression.

Postmarketing events seen in children under 6 years of age include accidental overdose, bronchopneumonia, coma, cyanosis, death, death neonatal, dyspnea, pulmonary edema, respiratory arrest, and respiratory depression.

Postmarketing events seen in patients older than 6 years of age include accidental overdose, cardio-respiratory arrest, death due to drug toxicity, non-accidental overdose, and overdose.

Dermatological

Skin rash, pruritus.

DRUG ABUSE AND DEPENDENCE

HYCODAN (hydrocodone bitartrate and homatropine methylbromide) is a Schedule II opioid. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of opioids; therefore, HYCODAN should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when HYCODAN is used for a short time for the treatment of cough. Physical dependence, the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome, assumes clinically significant proportions only after several weeks of continued oral opioid use, although some mild degree of physical dependence may develop after a few days of opioid therapy.

OVERDOSAGE

Signs and Symptoms

Serious overdosage with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur. The ingestion of very large amounts of HYCODAN may, in addition, result in acute homatropine intoxication.

Treatment

Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The opioid antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdosage or unusual sensitivity to opioids including hydrocodone. Therefore, an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. For further information, see full prescribing information for naloxone hydrochloride. An antagonist should not be administered in the absence of clinically significant respiratory depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug.

DOSAGE AND ADMINISTRATION

It is important that HYCODAN oral solution is measured with an accurate measuring device (see **PRECAUTIONS – Information for Patients**). A household teaspoon is not an accurate measuring device and could lead to overdosage, especially when a half a teaspoon is to be measured. It is strongly recommended that an accurate measuring device be used. A pharmacist can provide an appropriate measuring device and can provide instructions for measuring the correct dose.

Adults and Adolescents 12 Years of Age and Older

One (1) tablet or 5 mL (1 teaspoonful) of the oral solution every 4 to 6 hours as needed; do not exceed six (6) tablets or 30 mL (6 teaspoonfuls) in 24 hours.

Children 6 to 11 Years of Age

One-half (1/2) tablet or 2.5 mL (1/2 teaspoonful) of the oral solution every 4 to 6 hours as needed; do not exceed three (3) tablets or 15 mL (3 teaspoonfuls) in 24 hours.

HOW SUPPLIED

HYCODAN is supplied as a white, biconvex tablet, one face bisected and debossed with “HYCODAN”, and the other face plain, available in:

Bottles of 100 NDC 63481-042-70
Bottles of 500 NDC 63481-042-85

Store tablets at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature.]

Dispense in a tight, light-resistant container, as defined in the USP, with a child-resistant closure (as required).

HYCODAN is also available as a clear red colored, wild cherry flavored oral solution in:

Bottles of one pint NDC 63481-234-16

Store oral solution at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature.]

Oral prescription where permitted by state law.

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MEDICATION GUIDE

HYCODAN (hy-kə-dan)

(hydrocodone bitartrate and homatropine methylbromide) tablets and oral solutions, CII

What is the most important information I should know about HYCODAN?

- Taking HYCODAN with benzodiazepines or other central nervous system depressants, including alcohol can cause severe drowsiness, breathing problems (respiratory depression), coma, and death.
- HYCODAN can cause you to be drowsy. Avoid driving a car or operating machinery during treatment with HYCODAN.
- Women who breastfeed should talk to their healthcare provider before taking HYCODAN.
- Call your healthcare provider or get emergency medical help right away if anyone taking HYCODAN has any of the symptoms below:
 - increased sleepiness
 - confusion
 - difficulty breathing
 - shallow breathing
 - limpness
 - your baby has difficulty breastfeeding
- Keep HYCODAN in a safe place away from children. Accidental use by a child is a medical emergency and can cause death. If a child accidentally takes HYCODAN, get emergency medical help right away.
- HYCODAN can cause serious side effects including death.
- Take HYCODAN exactly as prescribed by your healthcare provider. If you take the wrong dose of HYCODAN, you could overdose and die.
- HYCODAN is not for children under 6 years of age.

What is HYCODAN?

- HYCODAN is a prescription medicine used to treat a cough in adults and children 6 years and older. HYCODAN contains hydrocodone and is a narcotic cough suppressant.
- **HYCODAN is a federal controlled substance (C-II) because it contains hydrocodone that can be abused or lead to dependence.** Keep HYCODAN in a safe place to prevent misuse and abuse. Selling or giving away HYCODAN may harm others, and is against the law. Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.
- HYCODAN is not for children under 6 years of age.

Who should not take HYCODAN?

- Do not take HYCODAN if you are allergic to hydrocodone or homatropine methylbromide. See the end of this Medication Guide for a complete list of ingredients.

Before you take HYCODAN, tell your healthcare provider about all of your medical conditions, including if you:

- have a drug dependence
- have lung or breathing problems
- have had a head injury
- have pain in your stomach-area (abdomen)
- have a history of severe or persistent cough
- have prostate problems
- have problems with your urinary tract (urethral stricture)
- are pregnant or plan to become pregnant. It is not known if HYCODAN can harm your unborn baby. You and your healthcare provider should decide if you should take HYCODAN while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if HYCODAN passes into your breast milk. You and your healthcare provider should decide if you will take HYCODAN or breastfeed. You should not do both.
- plan to have surgery
- drink alcohol
- have kidney or liver problems
- have diabetes
- have thyroid problems, such as hypothyroidism
- have Addison's disease
- have glaucoma (increased pressure in eyes)

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Taking HYCODAN with certain other medicines can cause side effects or affect how well HYCODAN or the other medicines work. Do not start or stop other medicines without talking to your healthcare provider. Especially tell your healthcare provider if you:

- take pain medicines such as narcotics
- take cold or allergy medicines that contain antihistamines or cough suppressants
- take medicines for mental illness (anti-psychotics, anti-anxiety)
- drink alcohol
- take medicines for depression, including monoamine oxidase inhibitors (MAOIs) and tricyclics Ask your healthcare provider if you are not sure if you take one of these medicines.

How should I take HYCODAN?

- Take HYCODAN exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much HYCODAN to take and when to take it. Do not change your dose without talking to your healthcare provider.
- Ask your pharmacist to give you a measuring device to help you measure the correct amount of HYCODAN. **Do not use a household teaspoon to measure your medicine. You may accidentally take too much.** If you take too much HYCODAN, call your healthcare provider or go to the nearest hospital emergency room right away.

What should I avoid while taking HYCODAN?

- **HYCODAN can cause you to be drowsy. Avoid driving a car or operating machinery during treatment with HYCODAN.**
- **Avoid drinking alcohol during treatment with HYCODAN. Drinking alcohol can increase your chances of having serious side effects.**

What are the possible side effects of HYCODAN?

HYCODAN may cause serious side effects, including:

- **See “What is the most important information I should know about HYCODAN?”**
- **Breathing problems (respiratory depression) which can lead to death.** Call your healthcare provider or get emergency treatment right away if you are sleeping more than usual, have shallow slow breathing, or confusion.
- **Physical dependence or abuse.** Take HYCODAN exactly as your healthcare provider tells you to take it. Stopping HYCODAN suddenly could cause withdrawal symptoms.
- **Bowel problems including constipation or stomach pain.**
- **Increased intracranial pressure**

The most common side effects of HYCODAN include:

- sleepiness
- confusion
- nausea and vomiting
- difficulty urinating
- trouble breathing

These are not all the possible side effects of HYCODAN.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store HYCODAN?

- Store HYCODAN tablets and oral solution at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep HYCODAN tablets in a tightly closed, child-resistant container and out of the light.
- **Keep HYCODAN tablets and oral solution, and all medicines out of the reach of children.**

General information about the safe and effective use of HYCODAN.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use HYCODAN for a condition for which it was not prescribed. Do not give HYCODAN to other people, even if they have the same symptoms that you have.

You can ask your pharmacist or healthcare provider for information about HYCODAN that is written for health professionals.

What are the ingredients in HYCODAN?

Active ingredient: hydrocodone bitartrate and homatropine methylbromide.

Inactive ingredients in HYCODAN tablets: calcium phosphate dibasic, colloidal silicon dioxide, lactose, magnesium stearate, starch and stearic acid.

Inactive ingredients in HYCODAN oral solution: caramel coloring, FDA&C Red 40, liquid sugar, methylparaben, propylparaben, sorbitol solution and wild cherry imitation flavor.

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This Medication Guide has been approved by the U.S. Food and Drug Administration.

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