HYDROCODONE BITARTRATE AND HOMATROPINE METHYLBROMIDE- hydrocodone bitartrate and homatropine methylbromide syrup
Morton Grove Pharmaceuticals, Inc.

HYDROCODONE BITARTRATE
and HOMATROPINE METHYLBROMIDE SYRUP
CIII

Rx only

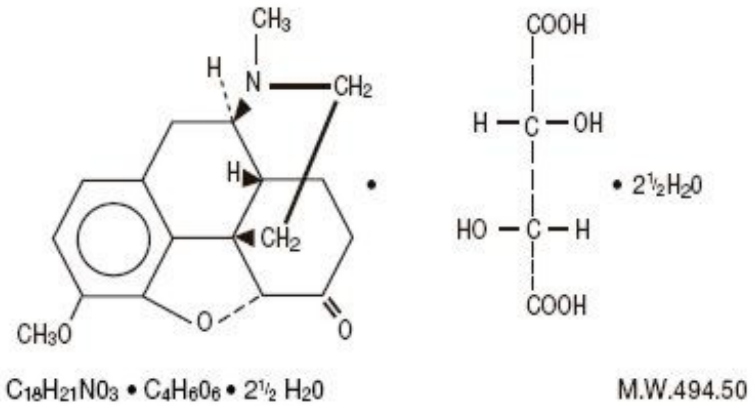
DESCRIPTION

This product contains hydrocodone (dihydrocodeinone) bitartrate, a semisynthetic centrally-acting narcotic antitussive. Homatropine Methylbromide is included in a subtherapeutic amount to discourage deliberate overdosage.

Each 5 mL (teaspoonful) contains:
Hydrocodone Bitartrate, USP . . . . . 5 mg
Homatropine Methylbromide, USP . . . . 1.5 mg
Alcohol . . . . . less than 0.1%
(contributed by flavorings)

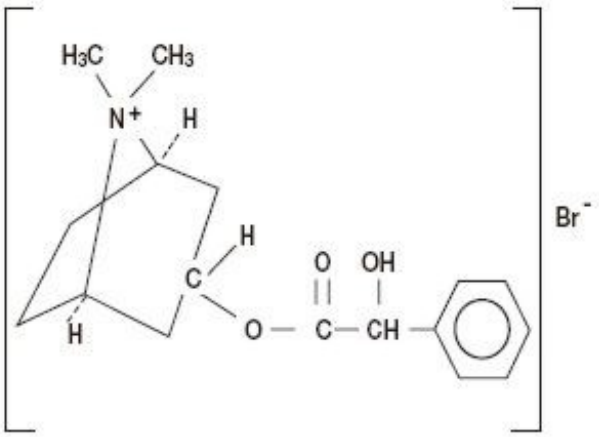
Also contains: Caramel, NF; Cherry Flavor; D&C Red No. 33; Glycerin, USP; Liquid Sugar; Methylparaben, NF; Propylene Glycol, USP; Propylparaben, NF and Sorbitol Solution, USP. Citric Acid, USP or Sodium Citrate, USP may be added for pH adjustment.

The hydrocodone component is 4,5α-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, and has the following structural formula:



HYDROCODONE BITARTRATE

Homatropine Methylbromide is 8-Azoniabicyclo[3.2.1]octane,3-[(hydroxyphenylacetyl)-oxy]-8,8-dimethyl-, bromide,endo-; a white crystal or fine white crystalline powder, and has the following structural formula:



$C_{17}H_{24}BrNO_3$ M.W. 370.29

HOMATROPINE METHYLBROMIDE

CLINICAL PHARMACOLOGY

Hydrocodone is a semisynthetic narcotic 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

This product is indicated for the symptomatic relief of cough.

CONTRAINDICATIONS

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

WARNINGS

May be habit forming. 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 and it should be prescribed and administered with the same degree of caution appropriate to the use of other narcotic drugs (See **DRUG ABUSE AND DEPENDENCE**).

Respiratory Depression

This product 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 narcotics 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, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions

The administration of this product or other narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Pediatric Use

In young children, as well as adults, the respiratory center is sensitive to the depressant action of narcotic cough suppressants in a dose-dependent manner. Benefit to risk ratio should be carefully considered especially in children with respiratory embarrassment (e.g., croup).

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 complication, and that appropriate therapy for the primary disease is provided.

Special Risk Patients

This product 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

Hydrocodone may 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 this product should be cautioned accordingly.

Drug Interactions

Patients receiving narcotics, antihistamines, antipsychotics, antianxiety agents or other Central Nervous System (CNS) depressants (including alcohol) concomitantly with this product may exhibit an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced. 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 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. It is also not known whether it can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. It 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 narcotics, administration of this product 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, 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 in children under six years of age have not been established.

ADVERSE REACTIONS

CNS

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 may produce constipation.

Genitourinary System

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

Respiratory Depression

This product may produce dose-related respiratory depression by acting directly on brain stem respiratory centers (See **OVERDOSAGE**).

Dermatological

Skin rash, pruritus.

DRUG ABUSE AND DEPENDENCE

This product is a Schedule III narcotic. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of narcotics; therefore, it should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when 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 narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic 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 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 narcotic antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdosage or unusual sensitivity to narcotics 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

Adults and children 12 years of age and over: 5 mL (teaspoonful) of the syrup every four to six hours as needed; do not exceed 6 teaspoonfuls in 24 hours.

Children 6 to 12 years of age: 2.5 mL (½ teaspoonful) of the syrup every four to six hours as needed; do not exceed 3 teaspoonfuls in 24 hours.

HOW SUPPLIED

This product is a red-colored, cherry-flavored syrup in 16 fl oz (473 mL) and gallon (3785 mL) bottles.

RECOMMENDED STORAGE

Store at controlled room temperature, 15 °–30 °C (59 °–86 °F) [see USP].

AVOID FREEZING

Dispense in a tight, light-resistant container as defined in the USP.

Rx Only

Oral prescription where permitted by state law.

Product No.: 8455

Manufactured By:
Morton Grove Pharmaceuticals, Inc.
Morton Grove, IL 60053

A50-8455-16
REV. 7-04

PRINCIPAL DISPLAY PANEL - 473 mL Bottle Label

MGP

NDC 60432-455-16

**HYDROCODONE
AND HOMATROPINE
SYRUP**

**(Hydrocodone Bitartrate and
Homatropine Methylbromide Syrup)**

CIII

DO NOT USE IF INNER FOIL SEAL PRINTED "SEALED
FOR YOUR PROTECTION" IS BROKEN OR MISSING.

**BULK CONTAINER —
NOT FOR HOUSEHOLD USE**

Oral prescription where permitted by state law.

Rx Only

NET: 1 Pint (473 mL)

HYDROCODONE BITARTRATE AND HOMATROPINE METHYLBROMIDE

hydrocodone bitartrate and homatropine methylbromide syrup

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:60432-455
Route of Administration	ORAL	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Hydrocodone Bitartrate (HYDROCODONE)	Hydrocodone Bitartrate	5 mg in 5 mL
Homatropine Methylbromide (METHYLHOMATROPINE)	Homatropine Methylbromide	1.5 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
Water	
SUCROSE	
GLYCERIN	
PROPYLENE GLYCOL	
METHYLPARABEN	
PROPYLPARABEN	
Sorbitol	
D&C RED NO. 33	
CARAMEL	
ANHYDROUS CITRIC ACID	
TRISODIUM CITRATE DIHYDRATE	

Product Characteristics

Color	RED	**Score**	
Shape		**Size**	
Flavor	CHERRY	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60432-455-16	473 mL in 1 BOTTLE, PLASTIC		
2	NDC:60432-455-28	3785 mL in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA088008	03/03/1983	

Labeler - Morton Grove Pharmaceuticals, Inc. (801897505)

Revised: 9/2012 Morton Grove Pharmaceuticals, Inc.