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PROTUSS
LIQUID

Rev. 02/01 835A00

Rx only

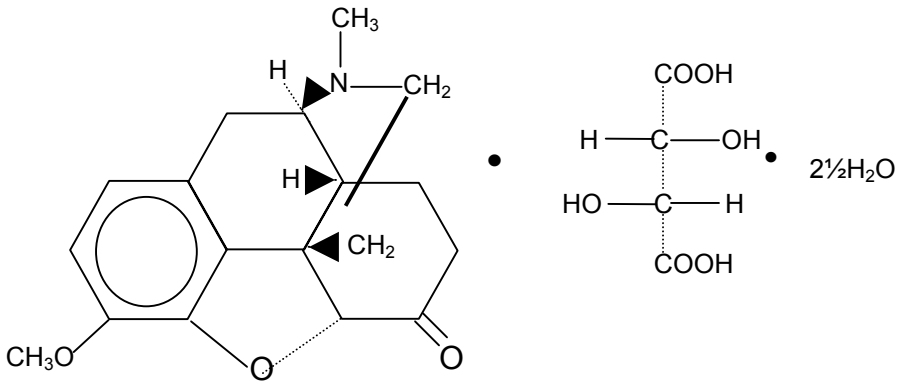
DESCRIPTION:
A purple colored, grape-flavored, sweet-tasting syrup for oral administration, which is ALCOHOL FREE, CORN FREE, TARTRAZINE FREE and SUGAR FREE.

Each teaspoonful (5 mL) contains:
Hydrocodone Bitartrate .....5 mg
WARNING: May be habit forming
Potassium Guaiacolsulfonate .....300 mg

Also contains benzoic acid, citric acid anhydrous, propylene glycol, purified water, saccharin sodium, sorbitol solution, natural and artificial flavor, with FD&C Blue #1 and D&C Red #33 as coloring. May also contain other ingredients.

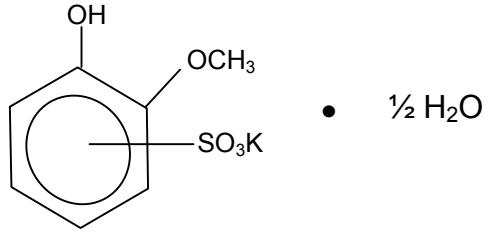
This product contains ingredients of the following therapeutic classes: antitussive and expectorant.

Hydrocodone bitartrate is an opioid analgesic and antitussive which occurs as fine, white crystals or as a crystalline powder. It is affected by light. The chemical name is 4,5 α-epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5). Its structure is as follows:



$C_{18}H_{21}NO_3 \bullet C_4H_6O_6 \bullet 2\ 1/2\ H_2O$
M.W 494.490

Potassium guaiacolsulfonate is an expectorant. The chemical name is benzenesulfonic acid, hydroxy-methoxy-, monopotassium salt, hemihydrate. Its structure is as follows:



$C_7H_7KO_5S \bullet 1/2\ H_2O$
M.W 251.30

CLINICAL PHARMACOLOGY:

Clinical trials have proven hydrocodone bitartrate to be an effective antitussive agent which is pharmacologically 2 to 8 times as potent as codeine. At equi-effective doses, its sedative action is greater than codeine. The precise mechanism of action of hydrocodone and other opiates is not known, however, hydrocodone is believed to act by directly depressing the cough center. In excessive doses hydrocodone, like other opium derivatives, can depress respiration. The effects of hydrocodone in therapeutic doses on the cardiovascular system is insignificant. The constipation effects of hydrocodone are much weaker than those of morphine and no stronger than those of codeine. Hydrocodone can produce miosis, euphoria, physical and psychological dependence. At therapeutic antitussive doses, it does exert analgesic effects. Following a 10 mg oral dose of hydrocodone administered to five male human subjects, the mean peak concentration was 23.6 +/- 5.2 ng/mL. Maximum serum levels were achieved at 1.3 +/- 0.3 hours and 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.

Potassium guaiacolsulfonate has been used empirically for many decades as an expectorant.

INDICATIONS AND USAGE:
For the temporary relief of dry, non-productive cough due to colds, pertussis or influenza.

CONTRAINDICATIONS:
Hypersensitivity to any of the ingredients. Patients known to be hypersensitive to other opioids may exhibit cross-sensitivity to PROTUSS Liquid. Hydrocodone is contraindicated in the presence of an intracranial lesion associated with increased intracranial pressure; and whenever ventilatory function is depressed.

WARNINGS:
May be habit forming. Hydrocodone can produce drug dependence of the morphine type and therefore has the potential for being abused. Psychic dependence, physicial dependence and tolerance may develop upon repeated administration of PROTUSS Liquid 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: PROTUSS Liquid produces dose-related respiratory depression by directly acting on the 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 depressant properties of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggeraged 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 PROTUSS Liquid or other opioids may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

PRECAUTIONS:
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 physiologic complications, and that appropriate therapy for the primary disease is provided.

Usage in Ambulatory Patients:
Hydrocodone, like all narcotics, may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery, and patients should be warned accordingly.

Drug Interactions: Patients receiving other narcotics, analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative hypnotics or other CNS depressants (including alcohol) concomitantly with hydrocodone may exhibit an additive CNS depression. When such combined therapy is contemplated the dose of one or both agents should be reduced. (see **WARNINGS**).

Carcinogenesis, Mutagenesis, Impairment of Fertility:
Carcinogenicity, mutagenicity and reproduction studies have not been conducted with PROTUSS Liquid

Usage in Pregnancy:
Teratogenic Effects: Pregnancy Category C. Animal reproduction studies have not been conducted with PROTUSS Liquid. It also not known whether PROTUSS Liquid can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. PROTUSS Liquid 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. There is no consensus on the best method of managing withdrawal. Chlorpromazine 0.7. to 1.0 mg/kg q6h, phenobarbital 2 mg/kg q6h, and paregoric 2 to 4 drops/kg q4h, have been used to treat withdrawal symptoms in infants. The duration of therapy is 4 to 28 days, with the dosages decreased as tolerated.

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 PROTUSS Liquid, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE REACTIONS:
Respiratory System: Hydrocodone causes dose-related respiratory depression by acting directly on brain stem respiratory centers.

Cardiovascular System: Hypertension, postural hypotension and palpitations.

Genitourinary System: Ureteral spasm, spasm of vesical sphincters and urinary retention have been reported with opiates.

Central Nervous System: Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychic dependence, mood changes and blurred vision.

Gastrointestinal System: Nausea and vomiting occur more frequently in ambulatory than in recumbent patients.

DRUG ABUSE AND DEPENDENCE:
PROTUSS Liquid is subject to the Federal Controlled Substances Act (Schedule III). Psychic dependence, physical dependence and tolerance may develop upon repeated administration of narcotics; therefore, PROTUSS Liquid should be prescribed and administered with caution.

Physical dependence is the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome.

Patients physically dependent on opioids will develop an abstinence syndrome upon abrupt discontinuation of an opioid or following the administration of a narcotic antagonist. The character and severity of the withdrawal symptoms are related to the degree of physical dependence. Manifestations of opioid withdrawal are similar to but milder than that of morphine and include lacrimation, rhinorrhea, yawning, sweating, restlessness, dilated pupils, anorexia, gooseflesh, irritability and tremor. In more severe forms, nausea, vomiting, intestinal spasm and diarrhea, increased heart rate and blood pressure, chills, and pains in bones and muscles of the back and extremities may occur. Peak effects will usually be apparent at 48 to 72 hours.

Treatment of withdrawal is usually managed by providing sufficient quantity of an opioid to suppress severe withdrawal symptoms and then gradually reducing the dose of opioid over a period of several days.

OVERDOSAGE:
Signs and Symptoms: Serious overdosage with PROTUSS Liquid is characterized by respiratory depression (a decrease in respiration 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.

Treatment: Primary attention should be given to the establishment 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 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. Activated charcoal may be of benefit.

USUAL DOSAGE:
Adults and older children: 1 to 1 1/2 teaspoonfuls; Children 6 to 12 years of age: 1/2 to 1 teaspoonful; Children 3 to 6 years of age: 1/4 to 1/2 teaspoonful. These doses may be given four times daily as needed. Not recommended for children under 3 years of age.

HOW SUPPLIED:
PROTUSS Liquid, each teaspoonful (5 mL) of which contains hydrocodone bitartrate **(WARNING: May be habit forming)** 5 mg and potassium guaiacolsulfonate 300 mg, is supplied as a purple colored, grape flavored liquid. It is available in bottles of 4 fl oz, NDC 59630-100-04, and in bottles of 16 fl oz, NDC 59630-100-16.

Dispense in a tight, light-resistant container with a child-resistant closure.
Store at controlled room temperature, 15˚C to 30˚C (59˚F to 86˚F).

Rx Only

Manufactured for:
FIRST HORIZON
PHARMACEUTICAL™ CORP.
Roswell, GA 30076

Manufactured by:
MIKART, INC.
Atlanta, GA 30318

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