CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

86681

DRAFT FINAL PRINTED LABELING

ACETAMINOPHEN AND CODEINE PHOSPHATE TABLETS C III

WARNING: MAY BE HABIT FORMING

DESCRIPTION: Acetaminophen occurs as a white, usually odorless crystalline powder, possessing a slightly bitter taste.

Codeine is an alkaloid obtained from opium or prepared from morphine by methylation. Codeine occurs as colorless or white crystals, effloresces slowly in dry air and is affected by light.

ACTIONS: Acetaminophen is a non-narcotic analgesic and antipyretic agent. Codeine is a narcotic with analgesic and antitussive actions. Codeine retains at least one-half of its analgesic activity when administered orally.

INDICATIONS: For the relief of mild to moderate pain.

CONTRAINDICATIONS: Hypersensitivity to codeine or acetaminophen.

WARNINGS:

Drug Dependence: Codeine 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 this drug and it should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications. Like other narcotic-containing medications, acetaminophen and codeine are subject to the Federal Controlled Substances Act.

Usage in Ambulatory Patients: Codeine 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 drug should be cautioned accordingly.

Interaction with Other Central Nervous System Depressants: Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics or other CNS depressants (including alcohol) concomitantly with acetaminophen and codeine may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in Pregnancy: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, acetaminophen and codeine should not be used in pregnant women unless, in the judgement of the physician, the potential benefits outweigh the possible hazards.

Usage in Children: Acetaminophen and codeine should not be administered to children.

PRECAUTIONS:

Head Injury and Increased Intracranial Pressure: The respiratory depressant effects 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 acetaminophen and codeine or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special Risk Patients: Acetaminophen and codeine should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease and prostatic hypertrophy or urethral stricture.

ADVERSE REACTIONS: The most frequently observed adverse reactions include light headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation, urticaria, skin rash and pruritus.

DOSAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of narcotics. Acetaminophen and codeine is given orally. The usual adult dose is one to two tablets every 4 hours, as needed.

DRUG INTERACTIONS: The CNS depressant effects of this drug may be additive with that of other CNS depressants. See **WARNINGS.**

MANAGEMENT OF OVERDOSAGE:

Signs and Symptoms: Serious overdose with acetaminophen and codeine 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. The ingestion of very large amounts of this drug may, in addition, result in acute hepatic toxicity.

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 is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including codeine. Therefore, an appropriate dose of naloxone (usual initial adult dose: 0.4 mg.) should be administered, preferably by the intravenous route, and simultaneously with efforts at respiratory resuscitation. Since the duration of action of codeine may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric emptying may be useful in removing unabsorbed drug.

Acetaminophen in massive overdosage may cause hepatotoxicity in some patients. Clinical and laboratory evidence of hepatotoxicity may be delayed for up to one week. Close clinical monitoring and serial hepatic enzyme determinations are therefore recommended.

Treatment of acute acetaminophen overdosage is purely symptomatic.

HOW SUPPLIED:

Acetaminophen 300 mg. and Codeine Phosphate 15 mg. Tablets in bottles of 100 and 1000.

Acetaminophen 300 mg. and Codeine Phosphate 30 mg. Tablets in bottles of 100 and 1000.

Acetaminophen 300 mg. and Codeine Phosphate 60 mg. Tablets in bottles of 100 1000.

CAUTION: Federal law prohibits dispensing without prescription.

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NDC 0228-2001-10

PUREPAC

C III

ACETAMINOPHEN with CODEINE PHOSPHATE TABLETS

30 mg.—No. 3

CAUTION: Federal law prohibits dispensing without prescription.

100 TABLETS

EACH TABLET CONTAINS:
Codeine Phosphate ..... 30 mg.
WARNING: May be habit forming.
Acetaminophen ..... 300 mg.

USUAL DOSAGE: See Accompanying Insert.

Lot No.

Store at room temperature 15°-30°C (59°-86°F) in a dry place.

Manufactured by
PUREPAC PHARMACEUTICAL CO.
Division Drug, Inc.
Elizabeth, N.J. 07207 U.S.A.

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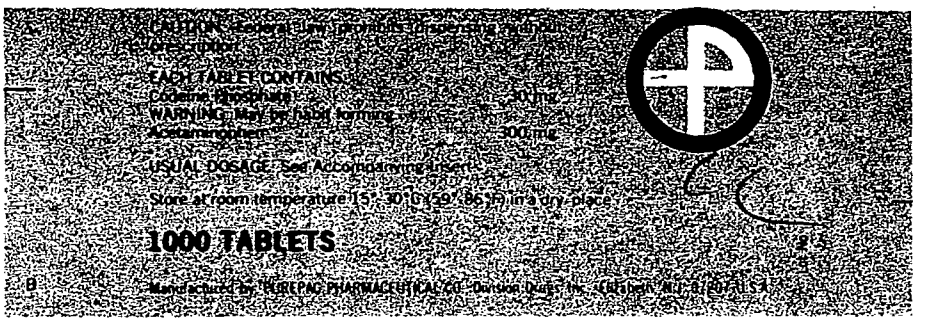
PUREPAC

NDC 0228-2001-96

C III

ACETAMINOPHEN with CODEINE PHOSPHATE TABLETS

30 mg. NO. 3



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