Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup

Analgesic-Antipyretic

Prescribing Information

DESCRIPTION

Each 5 mL of elixir contains 160 mg of acetaminophen and 8 mg of codeine phosphate in a slightly viscous clear red liquid that tastes and smells like cherry.
Non-medicinal ingredients: Alcohol, citric acid, D&C red #33, cherry flavour, polyethylene glycol, sodium benzoate, sodium cyclamate, sorbitol, sucrose and purified water.

CLINICAL PHARMACOLOGY

Acetaminophen and codeine phosphate are analgesic, antipyretic agents. Acetaminophen is distributed throughout most tissues of the body. Acetaminophen is metabolized primarily in the liver. Little unchanged drug is excreted in the urine, but most metabolic products appear in the urine within 24 hours.

Codeine retains at least one-half of its analgesic activity when administered orally. A reduced first-pass metabolism of codeine by the liver accounts for the greater oral potency of codeine when compared to most other morphine-like narcotics. Following absorption, codeine is metabolized by the liver and metabolic products are excreted in the urine. Approximately 10% of the administered codeine is demethylated to morphine, which may account for its analgesic activity.

INDICATIONS AND USAGE

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup is indicated for the relief of minor pains, headaches and fever.

CONTRAINDICATIONS

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup should not be administered to patients who have previously exhibited hypersensitivity to acetaminophen or codeine.

WARNINGS

As with any other analgesic drug, physicians should be cognizant of and supervise the use of acetaminophen in patients with alcoholism, serious kidney or serious liver disease. Chronic heavy alcohol abusers may be at increased risk of liver toxicity from excessive acetaminophen use, although reports of this event are rare. Reports usually involve cases of severe chronic alcoholics and the dosages of acetaminophen most often exceed recommended doses and often involve substantial overdose. Physicians should alert their patients who regularly consume large amounts of alcohol not to exceed the recommended doses of acetaminophen.

Patients should be counseled to consult a physician if redness or swelling is present in area of pain, if symptoms do not improve or if they worsen, or if new symptoms such as high fever, rash, itching, or persistent headache occur, as these may be signs of condition which requires medical attention.

Acetaminophen should not be taken for pain for more than 5 days or for fever for more than 3 days, unless directed by a physician. As with any drug, patients who are pregnant or nursing a baby should consult a physician before taking this product.

Do not use with other products containing acetaminophen, salicylates, or any other pain or fever medicine. Keep out of the reach of children.

PRECAUTIONS

General

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 Elixir with 8 mg Codeine Phosphate Syrup or other narcotics may obscure the diagnosis or clinical course of patients with abdominal conditions.

Special Risk Patients:

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup should be given with caution to certain patients such as elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, and prostatic hypertrophy or urethral stricture.

Occupational Hazards

Codeine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks. Patients using Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup should be cautioned about driving a car or operating potentially hazardous machinery if they become drowsy or show impaired mental or physical abilities while taking this medication.

The patient should understand the single-dose and 24-hour dose limits, and the time interval between doses. Like other narcotic-containing medications, Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup is subject to the Controlled Drugs and Substance Act.

Drug Interactions

Patients receiving other narcotic analgesics, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

The concurrent use of anticholinergics with codeine may produce paralytic ileus.

Patients who concomitantly medicate with warfarin-type anticoagulants and regular doses of acetaminophen have occasionally been reported to have unforeseen elevations in their international normalized ratio [INR]. Physicians should be cognizant of this potential interaction and monitor the INR in such patients closely while therapy is established. Many factors, including diet, medications, and environmental and physical states, may affect how a patient responds to anticoagulant therapy. There have been several reports that suggest that acetaminophen may produce hypoprothrombinemia (elevated INR or prothrombin time) when administered with coumarin derivatives. In other studies, prothrombin time did not change. Reported changes have been generally of limited clinical significance; however, periodic evaluation of prothrombin time should be performed when these agents are administered concurrently.

In the period immediately following discharge from the hospital or whenever other medications are initiated, discontinued, or taken regularly, it is important to monitor patient response to anticoagulation therapy with additional prothrombin time of INR determinations.

Use in Pregnancy

Teratogenic Effects:

Codeine: A study in rats and rabbits reported no teratogenic effect of codeine administered during the period of organogenesis in doses ranging from 5 to 120 mg/kg. In the rat, doses at the 120 mg/kg level, in the toxic range for the adult animal, were associated with an increase in embryo resorption at the time of implantation. In another study, a single 100 mg/kg dose of codeine administered to pregnant mice reportedly resulted in delayed ossification in the offspring.

There are no studies in humans, and the significance of these findings to humans, if any, is not known.

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects:

Dependence and withdrawal signs have been reported in newborns whosemothers took opiates regularly during pregnancy. These signs include irritability, excessive crying, tremors, hyperreflexia, fever, vomiting, and diarrhea. Signs usually appear during the first few days of life.

Labour and Delivery:

Narcotic analgesics cross the placental barrier. The closer to delivery and the larger the dose used, the greater the possibility of respiratory depression in the newborn. Narcotic analgesics should be avoided during labour if delivery of a premature infant is anticipated. If the mother has received narcotic analgesics during labour, newborn infants should be observed closely for signs of respiratory depression. Resuscitation may be required (see OVERDOSAGE). The effects of codeine, if any, on the later growth, development, and functional maturation of the child is unknown.

Lactation

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup is not recommended during lactation because safety in nursing mothers has not been established. Acetaminophen passes into breast milk but is not likely to have an adverse effect on the infant at therapeutic doses.

Some studies, but not others, have reported detectable amounts of codeine in breast milk. The levels are probably not clinically significant after usual therapeutic dosage. The possibility of clinically important amounts being excreted in breast milk in individuals abusing codeine should be considered.

Children

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup should not be administered to children except on the advice of a physician. Safe dosage of this product has not been established in infants below the age of 2 years.

Drug Abuse and 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 Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup. This medication should be prescribed and administered with the same degree of caution appropriate to the use of other oral narcotic-containing medications.

ADVERSE REACTIONS

The most frequently observed adverse effects include lightheadedness, dizziness, sedation, shortness of breath, nausea, and vomiting. These effects seem to be more prominent in ambulatory patients than in non-ambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include allergic reactions, euphoria, dysphoria, constipation, abdominal pain, and pruritus. The incidence and severity of gastrointestinal upset is less than after salicylate administration.

The classic gastrointestinal irritation associated with non-steroidal anti-inflammatory drugs, including acetylsalicylic acid (ASA), does not occur with acetaminophen. Sensitivity reactions

are rare and may manifest as rash or urticaria. Cross-reactivity in ASA-sensitive persons has been rarely reported. If sensitivity is suspected, discontinue use of the medication.

Patients who concomitantly medicate with warfarin-type anticoagulants and regular doses of acetaminophen have occasionally been reported to have unforeseen elevations in their INR. Physicians should be cognisant of this potential interaction and monitor the INR in such patients closely while therapy is established (see WARNINGS AND PRECAUTIONS, Drug Interactions).

At higher doses, codeine has most of the disadvantages of morphine, including respiratory depression.

OVERDOSAGE

Acetaminophen

Typical Toxidrome: Significant overdoses of acetaminophen may result in potentially fatal hepatotoxicity. The physician should be mindful that there is no early presentation that is pathognomonic for the overdose. A high degree of clinical suspicion must always be maintained.

Due to the wide availability of acetaminophen, it is commonly involved in single and mixed drug overdose situations and the practitioner should have a low threshold for screening for its presence in a patient's serum. Acute toxicity after single dose overdoses of acetaminophen can be anticipated when the overdose exceeds 150 mg/kg. Chronic alcohol abusers, cachectic individuals, and persons taking pharmacologic inducers of the hepatic P450 microsomal enzyme system may be at risk with lower exposures. Chronic intoxication has rarely been reported in persons consuming in excess of 150 mg/kg of acetaminophen daily for several days.

Specific Antidote: NAC (N-acetylcysteine) administered by either the intravenous or the oral route is known to be a highly effective antidote for acetaminophen poisoning. It is most effective when administered within 8 hours of a significant overdose but reports have indicated benefits to treatment initiated well beyond this time period. It is imperative to administer the antidote as early as possible in the time course of acute intoxication to reap the full benefits of the antidote's protective effects.

General Management: When the possibility of acetaminophen overdose exists, treatment should begin immediately and include appropriate decontamination of the GI tract, proper supportive care, careful assessment of appropriately timed serum acetaminophen estimations evaluated against the Matthew-Rumack nomogram, timely administration of NAC as required and appropriate follow-up care. Physicians unfamiliar with the current management of acetaminophen overdose should consult with a poison control centre immediately. Telephone numbers for local poison control centres are available in the local phone directory. Delays in initiation of appropriate therapy may jeopardize the patient's chances for full recovery.

Codeine

Typical Toxidrome: Narcotic/Opiate

Treatment: Stabilize the patient (A,B,C's), undertake appropriate gastrointestinal tract decontamination procedures, initiate supportive care, administer antidote as needed (see manufacturer's product monograph), consult with a Regional Poison Control Centre regarding ongoing management, and arrange for appropriate follow-up care.

Specific antidote: Naloxone HCl

DOSAGE AND ADMINISTRATION

Dosage should be adjusted according to severity of pain and response of the patient. However, it should be kept in mind that tolerance to codeine can develop with continued use and that the incidence of untoward effects is dose related. Adult doses of codeine, higher than 60 mg, fail to give commensurate relief of pain but merely prolong analgesia, and are associated with an appreciably increased incidence of undesirable side effects. Equivalently high doses in children would have similar effects.

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup is given orally. As an analgesic-antipyretic, the dose is given every 4 to 6 hours as required. Not to exceed 5 doses in a 24-hour period.

Adults:	10-20 mL every 4 to 6 hours as required.
Children (12 years and older):	10-20 mL every 4 to 6 hours as required.

HOW SUPPLIED

Acetaminophen Elixir with 8 mg Codeine Phosphate Syrup: viscous clear red liquid in a 500 mL bottle.

JAMP Pharma Corporation
Boucherville, Québec
J4B 5H2

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