

Lorcet® 10/650

Each tablet contains: 10 mg hydrocodone bitartrate (Warning: May be habit-forming) and 650 mg acetaminophen.

Reference:

1. Data on file, Forest Laboratories, New York, NY.

INDICATIONS AND USAGE: For the relief of moderate to moderately severe pain.

CONTRAINDICATIONS: Hypersensitivity to acetaminophen or hydrocodone.

WARNINGS: Respiratory Depression: At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing.

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 preexisting 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 narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

PRECAUTIONS: Special Risk Patients: As with any narcotic analgesic agent, Lorcet® 10/650 should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

Cough Reflex: Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when Lorcet® 10/650 is used postoperatively and in patients with pulmonary disease.

Drug Interactions: Patients receiving other narcotic analgesics, antipsychotics, antiemetic agents, or other CNS depressants (including alcohol) concomitantly with Lorcet® 10/650 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. The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus.

Use in Pregnancy: Teratogenic Effects: Pregnancy Category C. Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. Lorcet® 10/650 should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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 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 dosage decreased as tolerated.

Labor and Delivery: As with all narcotics, administration of Lorcet® 10/650 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 Lorcet® 10/650, 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 have not been established.

ADVERSE REACTIONS: The most frequently observed adverse reactions include lightheadedness, 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:

Central Nervous System: Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence, mood changes.

Gastrointestinal System: The antiemetic phenothiazines are useful in suppressing the nausea and vomiting which may occur (see above); however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia. Prolonged administration of Lorcet® 10/650 may produce constipation.

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

Respiratory Depression: Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. Apply other supportive measures when indicated.

DRUG ABUSE AND DEPENDENCE: Lorcet® 10/650 is subject to the Federal Controlled Substances Act (Schedule III). Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, Lorcet® 10/650 should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when Lorcet® 10/650 is used for a short time for the treatment of pain.

OVERDOSAGE: Acetaminophen: Signs and Symptoms: In acute acetaminophen overdose, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Hydrocodone: Signs and Symptoms: Serious overdose 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 overdose, apnea, circulatory collapse, cardiac arrest and death may occur.

DOSEAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related. The usual adult dosage is one tablet every four to six hours as needed for pain. The total 24 hour dose should not exceed 6 tablets.

CAUTION: Federal law prohibits dispensing without prescription. A Schedule CIII Controlled Substance. Manufactured by: MIKART, INC. ATLANTA, GA 30318 Manufactured for: UAD Laboratories Division of Forest Pharmaceuticals, Inc. St. Louis, MO 63045 Rev. 6/94 Code 558A00

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trol families consumed an unrestricted diet. Food records were collected every day at ages 8 and 13 months. Growth was carefully monitored.

The results of the trial showed that between 7 and 13 months, serum cholesterol and non-high-density-lipoprotein cholesterol concentrations did not change significantly in the intervention group but increased substantially in the group with unrestricted diet.

Daily intakes of energy and saturated fat were lower in the intervention than in the control group at 13 months, and intake of polyunsaturated fat was higher.

Growth did not differ between the groups and was as expected for children at this age. Serum cholesterol concentrations fell significantly in parents of intervention-group infants.

The findings indicate that the increases in serum cholesterol and non-high-density lipoprotein cholesterol that occur in infants between the ages of 7 and 13 months can be avoided by individualized diets, with no effect on the children's growth.

Lapinleimu H, Viikari J, Jokinen E, et al: Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. *Lancet* 1995;345:471-476.

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editorial comments

Filters from cigarettes may pose a health threat to smokers, according to a study conducted by researchers at Roswell Park Cancer Institute in New York.

Led by immunologist John Pauly, MD, the researchers implanted in mice microscopic cellulose acetate fibers from six popular cigarette brands. Six months later, the fibers remained intact with their tar coating. The researchers also found microscopic fibers in lung tissue taken from human smokers with pulmonary cancer. Although no direct link was established between the filters and the development of pulmonary cancer in humans in this study, further investigations will likely examine this possibility.

Complete results are published in the January 15 issue of the *Journal of Cancer Research*.

Children, adolescents, and older minority women are more likely to be homicide victims than other segments of the population in the United States. Such was the conclusion of a report compiled by the Population Reference Bureau, a nongovernment agency.

"Homicide in the United States: Who's at Risk," includes data from 50 years of statistics from the Federal Bureau of Investigation and the National Center for Health Statistics.

In 1990, among minority children aged 4 years and younger, the murder rates were 8.9 per 100,000 boys and 8.6 per 100,000 girls. Comparatively, 1950 homicide rates indicated 2.4 homicides per 100,000 children for both sexes in this group.

Statistics compiled for white children also showed an increase during this period: for boys, the



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