

References: 1. Laska EM, Sushin A, Meller F et al. Aspirin as an analgesic adjuvant. *JAMA* 1984; 251: 1771-18. 2. Benson GD. Hepatotoxicity following the therapeutic use of antipyretic analgesics. *Am J Med* 1983; 75(suppl 5A): 85-93. 3. Jick H. Effects of aspirin and acetaminophen in gastrointestinal hemorrhage. *Arch Intern Med* 1981; 141: 316-321. 4. Mielke CH Jr. Comparative effects of aspirin and acetaminophen on hemostasis. *Arch Intern Med* 1981; 305-310. 5. Hansten PD. *Drug Interactions*. ed 5. Philadelphia: Lea & Febiger, 1985, p. 95.

ESGIC-PLUS™

Tablets (Butalbital, Acetaminophen and Caffeine Tablets, USP)
50mg/500mg/40mg

Brief Prescribing Information: (Please see package insert for full prescribing information)

DESCRIPTION: Each ESGIC-PLUS™ tablet for oral administration contains:
Butalbital 50 mg
*WARNING: May be habit forming
Acetaminophen 500 mg
Caffeine 40 mg

CLINICAL PHARMACOLOGY: Pharmacologically, ESGIC-PLUS™ combines the analgesic properties of acetaminophen-caffeine with the anxiolytic and muscle relaxant properties of butalbital.

CONTRAINDICATIONS: Hypersensitivity to acetaminophen, caffeine, or barbiturates. Patients with porphyria.

PRECAUTIONS: General: Barbiturates should be administered with caution, if at all, to patients who are mentally depressed, have suicidal tendencies, or a history of drug abuse.

Elderly or debilitated patients may react to barbiturates with marked excitement, depression, and confusion. In some persons, barbiturates repeatedly produce excitement rather than depression.

Drug Interactions: Patients receiving narcotic analgesics, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with ESGIC-PLUS™ (Butalbital, Acetaminophen, and Caffeine) may exhibit additive CNS depressant effects.

Drugs
Butalbital with coumarin anticoagulants

Effect
Decreased effect of anticoagulant because of increased metabolism resulting from enzyme induction.
Decreased blood levels of the antidepressant.

Butalbital with tricyclic antidepressants

Usage in Pregnancy: Adequate studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential or has other adverse effects on the fetus. There are no well-controlled studies in pregnant women. Although there is no clearly defined risk, one cannot exclude the possibility of infrequent or subtle damage to the human fetus. ESGIC-PLUS™ should be used in pregnant women only when clearly needed.

Nursing Mothers: The effects of ESGIC-PLUS™ on infants of nursing mothers are not known. Barbiturates are excreted in the breast milk of nursing mothers. The serum levels in infants are believed to be insignificant with therapeutic doses.

Pediatric Use: Safety and effectiveness in children below the age of 12 have not been established.

ADVERSE REACTIONS: The most frequent adverse reactions are drowsiness and dizziness. Less frequent adverse reactions are lightheadedness and gastrointestinal disturbances including nausea, vomiting and flatulence. Mental confusion or depression can occur due to intolerance or overdosage of butalbital.

Several cases of dermatological reactions including toxic epidermal necrolysis and erythema multiforme have been reported.

DRUG ABUSE & DEPENDENCE: Prolonged use of barbiturates can produce drug dependence, characterized by psychic dependence and tolerance. The abuse liability of ESGIC-PLUS™ is similar to that of other barbiturate-containing drug combinations. Caution should be exercised when prescribing medication for patients with a known propensity for taking excessive quantities of drugs, which is not uncommon in patients with chronic tension headache.

OVERDOSAGE: The toxic effects of acute overdosage of ESGIC-PLUS™ are attributable mainly to its barbiturate component, and, to a lesser extent, acetaminophen. Because toxic effects of caffeine occur in very high dosages only, the possibility of significant caffeine toxicity from ESGIC-PLUS™ overdosage is unlikely.

Barbiturate: Signs and Symptoms: Drowsiness, confusion, coma; respiratory depression; hypotension; shock.

Treatment:

1. Maintenance of an adequate airway, with assisted respiration and oxygen administration as necessary.
2. Monitoring of vital signs and fluid balance.
3. If the patient is conscious and has not lost the gag reflex, emesis may be induced with ipecac. Care should be taken to prevent pulmonary aspiration of vomitus. After completion of vomiting, 30 grams of activated charcoal in a glass of water may be administered.
4. If emesis is contraindicated, gastric lavage may be performed with a cuffed endotracheal tube in place with the patient in the left-down position. Activated charcoal may be left in the emptied stomach and a saline cathartic administered.
5. Fluid therapy and other standard treatment for shock, if needed.
6. If renal function is normal, forced diuresis may aid in the elimination of the barbiturate. Alkalinization of the urine increases renal excretion of some barbiturates, especially phenobarbital.
7. Although not recommended as a routine procedure, hemodialysis may be used in severe barbiturate intoxication or if the patient is anuric or in shock.

Acetaminophen: Signs and Symptoms: In acute acetaminophen overdosage, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur.

In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10 grams and fatalities with less than 15 grams. Importantly, young children seem to be more resistant than adults to the hepatotoxic effect of an acetaminophen overdose.

Early symptoms following a potentially hepatotoxic overdosage may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may be apparent until 48 to 72 hours post-ingestion.

Treatment: The stomach should be emptied promptly by lavage or by induction of emesis with syrup of ipecac. Patients' estimates of the quantity of a drug ingested are notoriously unreliable. Therefore, if an acetaminophen overdose is suspected, a serum acetaminophen assay should be obtained as early as possible, but no sooner than four hours following ingestion. Liver function studies should be obtained initially and repeated at 24-hour intervals.

The antidote, N-acetylcysteine, should be administered as early as possible, preferably within 16 hours of the overdose ingestion for optimal results, but in any case, within 24 hours. Following recovery, there are no residual, structural or functional hepatic abnormalities.

DOSAGE AND ADMINISTRATION: Oral: One ESGIC-PLUS™ tablet every four hours as needed. Do not exceed six tablets or capsules per day.

HOW SUPPLIED: ESGIC-PLUS™ (Butalbital) 50 mg [*WARNING: May be habit forming], Acetaminophen 500 mg and Caffeine 40 mg Tablets are white, capsule-shaped, single-scored, and are debossed "FOREST" on the upper side, "678" on one side of the score on the lower side. They are supplied as: Bottles of 100—NDC 0456-0678-01.

Storage: Store at controlled room temperature 15°-30°C (59°-86°F). Protect from moisture.

Dispense in a tight, light-resistant container with a child-resistant closure.

CAUTION: Federal law prohibits dispensing without prescription.

Manufactured by: MIKART, INC., Atlanta, GA 30318

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Low-dose aspirin for the prevention and treatment of preeclampsia

Low-dose aspirin (60-150 mg/d) is a widely used and well-tolerated antiplatelet treatment. This mode of therapy has the effect of irreversibly inhibiting almost all platelet cyclo-oxygenase activity, thereby blocking synthesis of the vasoconstrictor and platelet-aggregating agent thromboxane.

In preeclampsia, aspirin helps to rectify the intravascular imbalance between thromboxane and prostacyclin.

In this multicenter study, 9364 women were randomly given 60 mg of aspirin daily or matching placebo. Seventy-four percent were entered for prophylaxis of preeclampsia; 12%, for prophylaxis of intrauterine growth retardation (IUGR); 12%, for treatment of preeclampsia; and 3%, for treatment of IUGR.

Overall, the use of aspirin reduced the incidence of proteinuric preeclampsia by only 12%, which was not significant. Also, aspirin use did not have any significant effect on the incidence of IUGR or of stillbirth and neonatal death. Aspirin did, however, significantly reduce the likelihood of preterm delivery. There was a significant trend toward progressively greater reductions in proteinuric preeclampsia the more preterm the delivery.

Aspirin was not associated with a significant increase in placental hemorrhages or in bleeding during preparation for epidural anesthesia, but there was a slight increase in the use of blood trans-

fusion after delivery. Low-dose aspirin was generally safe for the fetus and newborn infant, with no evidence of an increased likelihood of bleeding.

The study findings do not support routine prophylactic or therapeutic administration of antiplatelet therapy in pregnancy to all women at increased risk of preeclampsia or IUGR. Low-dose aspirin may be justified in women judged to be especially liable to early-onset preeclampsia severe enough to need very preterm delivery. In such women, it seems appropriate to start low-dose aspirin prophylactically early in the second trimester.

CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group: CLASP: A randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. *Lancet* 1994;343:619-629.

Effect of cranberry juice intake on bacteriuria and pyuria

To determine the effect of regular intake of cranberry juice on bacteriuria and pyuria in elderly women, the researchers conducted a trial with 153 elderly women (mean age, 78.5 years).

The subjects were randomly assigned to consume 300 mL/d of a commercially available standard cranberry beverage or of a specially prepared synthetic placebo drink that was indistinguishable in taste, appearance, and vitamin C content but lacked cranberry content.

A baseline urine sample and six clean-voided study urine sam-