



Zgesic Tablets

Rx only

500367 Rev. 07/08

DESCRIPTION:

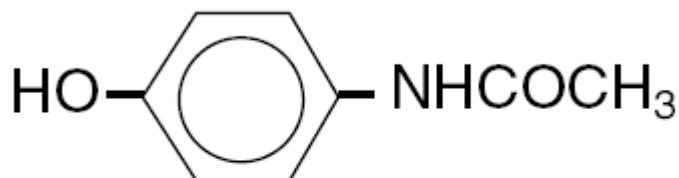
Each tablet contains:

Acetaminophen 600 mg
Phenyltoloxamine Citrate 66 mg

In a specially prepared base to provide a prolonged therapeutic effect.

Inactive ingredients in each tablet are: calcium phosphate dibasic, magnesium stearate, methylcellulose, povidone and silicified microcrystalline cellulose.

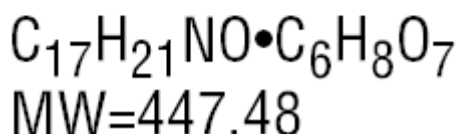
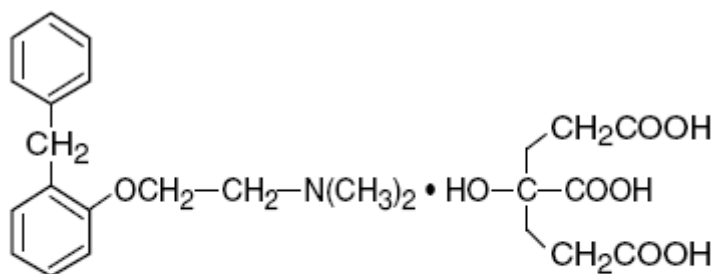
Acetaminophen, 4'-hydroxyacetanilide, a slightly bitter, white, odorless, crystalline powder, is a non-opiate, nonsalicylate analgesic and antipyretic. It has the following structural formula:



$C_8H_9NO_2$

MW=151.17

Phenyltoloxamine Citrate, N, N-dimethyl-2-(α -phenyl-toloxyl) ethylamine dihydrogen citrate, is an antihistamine used to augment analgesia. It occurs as crystals from water or methanol. It is soluble in water. Phenyltoloxamine Citrate has the following structural formula:



CLINICAL PHARMACOLOGY:

The analgesic action of acetaminophen involves peripheral influences, but the specific mechanism is as yet undetermined. Antipyretic activity is mediated through hypothalamic heat regulating centers. Acetaminophen inhibits prostaglandin synthetase. Therapeutic doses of acetaminophen have negligible effects on the cardiovascular or respiratory systems; however, toxic doses may cause circulatory failure and rapid, shallow breathing. Acetaminophen blocks the chemical cyclic AMP, a byproduct of prostaglandins, which cause the nerve endings to be more sensitive to pain impulses. Phenyltoloxamine Citrate is an ethanolamine type antihistamine, that acts as an adjuvant analgesic, which augments the analgesic effect of acetaminophen. It has been suggested that analgesic effects of antihistamines are related to the modulation of histaminergic and serotonergic pathways. More specific mechanisms that have been postulated include interactions with one or more pain mediators such as substance P, bradykinins, prostaglandins and cyclic nucleotides.

Pharmacokinetics: The behavior of the individual components is described below.

Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. The plasma half-life is 1.25 to 3 hours, but may be increased by liver damage and following overdose. Elimination of acetaminophen is principally by liver metabolism (conjugation) and subsequent renal excretion of metabolites. Approximately 85% of an oral dose appears in the urine within 24 hours of administration, most as the glucuronide conjugate, with small amounts of other conjugates and unchanged drug.

See **OVERDOSAGE** for toxicity information.

Phenyltoloxamine Citrate is well absorbed following oral administration. It is metabolized in the liver and excreted in the urine predominately, as its metabolites.

INDICATIONS AND USAGE:

For the temporary relief of mild to moderate pain associated with tension headaches,

musculoskeletal injury, dysmenorrhea, colds and flu, sinus pain, toothaches, as well as for minor pain from arthritis, and to help reduce fever.

CONTRAINDICATIONS:

This product should not be administered to patients who have previously exhibited hypersensitivity to acetaminophen or phenyltoloxamine citrate.

WARNINGS:

Do not take this product for arthritis, and to help reduce fever.

CONTRAINDICATIONS:

This product should not be administered to patients who have previously exhibited hypersensitivity to acetaminophen or phenyltoloxamine citrate.

WARNINGS:

Do not take this product for pain more than 10 days (adults) or 5 days (children) unless directed by a physician, and do not take for fever for more than 3 days unless directed by a physician. If pain or fever persists, if new symptoms occur, or if redness or swelling is present, consult a physician immediately because these could be signs of a serious condition.

Do not give this product to children under 12 years of age for the pain of arthritis unless directed by a physician. Caution should be exercised when used in patients with prostatic hypertrophy, urinary retention, bladder neck obstruction, increased ocular pressure, and asthma.

PRECAUTIONS:

Information for Patients: Patient consultation should include the following information regarding the proper use of this product:

- Do not exceed recommended dosage.
- May be taken with food or milk to lessen gastric irritation.
- Do not drive or operate heavy machinery if drowsiness or dizziness occurs.
- Concomitant use of alcohol and other central nervous system depressants (hypnotics, sedatives, tranquilizers and anti-anxiety drugs) while taking this product may have an additive effect on drowsiness.
- If a dose is missed, the medication should be taken as soon as possible unless it is almost time for the next dose. Do not double the dose.

Laboratory Tests: In patients with severe hepatic or renal disease, effects of therapy should be monitored with serial liver and/or renal function tests.

Drug/Laboratory Test Interactions: Acetaminophen may produce false-positive test results for urinary 5-hydroxyindoleacetic acid.

The sedative effects of phenyltoloxamine citrate are additive to the CNS depressant effects of alcohol, hypnotics, sedatives and tranquilizers.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No adequate studies have been conducted in animals to determine whether phenyltoloxamine citrate or

acetaminophen have a potential for carcinogenesis, mutagenesis, or impairment of fertility.

Pregnancy: *Teratogenic Effects:*

Pregnancy Category C: There are no adequate and well controlled studies in pregnant women. Zgesic Tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Acetaminophen is excreted in breast milk in small amounts, but the significance of its effects on nursing infants is not known.

Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from phenyltoloxamine citrate and acetaminophen, 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 under 6 years of age have not been established.

Geriatric Use: Use with caution; antihistamines may cause dizziness, sedation, confusional states and hypotension in the elderly.

Drug Interactions: Monoamine oxidase inhibitors (MAOIs) may prolong and intensify the sedative and anticholinergic effect of antihistamines; additive CNS effects may occur with concomitant use of alcohol and CNS depressants. Hepatotoxicity has occurred in chronic alcoholics following moderate to excessive doses of acetaminophen.

ADVERSE REACTIONS:

Adverse reactions include drowsiness, dizziness, lassitude, nausea, blurred vision, pruritis, skin rash and diaphoresis.

OVERDOSAGE:

In all cases of suspected overdose, immediately call your regional poison control center, and/or contact a physician immediately.

Signs and Symptoms: Following an acute overdose, toxicity may result from acetaminophen or phenyltoloxamine citrate. In acetaminophen overdose: dose dependent, potentially fatal hepatic necrosis effect 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 hepatotoxicity may not be apparent until 48 to 72 hours postingestion. In adults, hepatotoxicity has rarely been reported with acute overdoses of less than 10 grams or fatalities with less than 15 grams.

Recommended Treatment: A single or multiple overdose with acetaminophen or phenyltoloxamine citrate is a potentially lethal overdose, and consultation with a regional poison control center is recommended. Immediate treatment includes support of cardio respiratory function and measures to reduce drug absorption. Vomiting should be induced mechanically if the patient is alert (adequate pharyngeal and laryngeal

reflexes). If the dose of acetaminophen may have exceeded 140 mg/kg, acetylcysteine should be administered as early as possible. Serum acetaminophen levels should be obtained since levels four or more hours following ingestion help predict acetaminophen toxicity. Do not await acetaminophen assay results before initiating treatment. Hepatic enzymes should be obtained initially, and repeated at 24-hour intervals. Methemoglobinemia over 30% should be treated with methylene blue by slow intravenous administration.

DOSAGE AND ADMINISTRATION:

Adults and children over 12 years of age: 1 to 2 tablets every 8 to 12 hours, not to exceed 6 tablets in 24 hours.

Children 6 to 12 years: As prescribed by physician.

Not recommended for children under 6 years of age.

Tablets should not be chewed or crushed prior to swallowing. Do not exceed recommended dosage.

HOW SUPPLIED:

Zgesic Tablets are supplied as white, capsule-shaped tablets debossed "ZGESIC" on one side, the opposite side is plain. Available in bottles of 90 tablets, NDC 64543-400-90.

KEEP THIS AND ALL MEDICATION OUT OF THE REACH OF CHILDREN. IN CASE OF ACCIDENTAL OVERDOSE, CALL A DOCTOR OR CONTACT A POISON CONTROL CENTER IMMEDIATELY.

Dispense in tight, light-resistant containers as defined in the USP/NF, with child resistant closures.

Store at controlled room temperature between 20°-25°C (68°-77°F); see USP Controlled Room Temperature. Avoid exposure to heat.

Manufactured for:
Capellon Pharmaceuticals, Ltd.
Fort Worth, TX 76118

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