

NDC 11584-0476-1

NDC 11584-0476-5

RELAGESIC

Rx only

Each tablet contains:

Acetaminophen

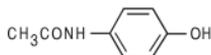
650 mg

Phenyltoloxamine Citrate

50 mg

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

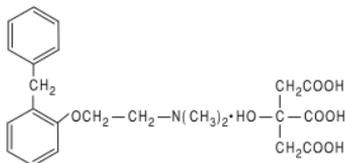
1. Acetaminophen

 $C_8H_9NO_2$

MW=151.17

Phenyltoloxamine citrate is an antihistamine having the chemical name N,N-dimethyl-2-(∞ -phenyl-o-tolyloxy) ethylamine dihydrogen citrate with the following structure:

2. Phenyltoloxamine citrate

 $C_{17}H_{21}NO \cdot C_6H_8O_7$

MW=447.48

Inactive Ingredients: Each tablet contains povidone, microcrystalline cellulose, sodium starch glycolate and magnesium stearate.

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.

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

Acetaminophen: 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: Phenyltoloxamine is an H_1 blocking agent which interferes with the action of histamine primarily in capillaries surrounding mucous tissues and sensory nerves of the nasal and adjacent areas. It has the ability to interfere with certain areas of acetylcholine-inhibiting secretions in the nose, mouth and pharynx. It commonly causes CNS depression.

INDICATIONS AND USAGE: For the temporary relief of minor aches and pains associated with headaches, backache, muscular aches, the menstrual and premenstrual periods, colds, the flu, toothaches, as well as for minor pain from arthritis, and to reduce fever.

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

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.

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Pregnancy: *Teratogenic Effects:* Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. Relagesic 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 the pediatric population have not been established.

Dermatological: skin rash, pruritus.

The following adverse drug events may be borne in mind as potential effects of acetaminophen: allergic reactions, rash, thrombocytopenia, agranulocytosis.

OVERDOSAGE: Following an acute overdosage, toxicity may result from phenyltoloxamine citrate or acetaminophen.

Acetaminophen: In acetaminophen overdosage: 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.

In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10 grams or fatalities with less than 15 grams.

Treatment: A single or multiple overdose with phenyltoloxamine citrate or acetaminophen is a potentially lethal overdose, and consultation with a regional poison control center is recommended. Immediate treatment includes support of cardiorespiratory function and measures to reduce drug absorption. Vomiting should be induced mechanically, or with syrup of ipecac, 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. The toxic dose for adults for acetaminophen is 10 g.

DOSAGE: Adults (12 years and over) - ½ or 1 tablet every 4 - 6 hours.
Maximum daily dose - 5 tablets.
Children (6 to under 12 years) - ½ tablet every 4 - 6 hours.
Maximum daily dose - 2½ tablets
Children under 6 years of age: consult a physician.

WARNINGS: Do not take this product for pain for more than 10 days (adults) or 5 days (children), 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. May cause drowsiness; alcohol, sedatives, and tranquilizers may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Do not take this product if you are taking sedatives or tranquilizers, without first consulting your physician. Use caution when driving a motor vehicle or operating machinery.

Keep this and all drugs out of the reach of children. In case of accidental overdose, seek professional assistance or contact a Poison Control Center immediately. Prompt medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms. As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.

STORE AT ROOM TEMPERATURE 15° - 30°C (59° - 86°F). AVOID EXCESSIVE HEAT.

HOW SUPPLIED: RELAGESIC is available as a white tablet with "RELAGESIC" debossed on one and "IEL/650" debossed and scored on the other side, in bottles of 100 count NDC 11584-0476-1, sample packages and bottles of 500 tablets NDC 11584-0476-5.

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