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ACAMOLI COLD

SYRUP

Composition

Acamoli Cold Raspberry Flavor
Each teaspoonful (5 ml) contains:

Active Ingredients

Paracetamol (Acetaminophen)	160 mg
Chlorpheniramine maleate	1 mg
Pseudoephedrine hydrochloride	15 mg

Other Ingredients
Glycerin, sorbitol*, povidone, sodium cyclamate, acesulfame potassium, methylparaben, saccharin sodium**, color edicol supra red ponceau, raspberry flavoring CD63904, sodium hydroxide solution, purified water.

Acamoli Cold Strawberry Flavor
Each teaspoonful (5 ml) contains:

Active Ingredients

Paracetamol (Acetaminophen)	160 mg
Chlorpheniramine maleate	1 mg
Pseudoephedrine hydrochloride	15 mg

Other Ingredients
Glycerin, sorbitol*, povidone, sodium cyclamate, acesulfame potassium, methylparaben, saccharin sodium**, flavor strawberry 502301T, color red FDC No.40, sodium hydroxide solution, purified water

* Contains sorbitol 525 mg/5 ml.
** Contains saccharin sodium 2 mg/5 ml
Sodium content: 2.5 mg/5 ml

NOTE: ACAMOLI COLD SYRUP DOES NOT CONTAIN SUGAR.

Mechanism of Action

Paracetamol is a clinically-proven non-salicylate analgesic and antipyretic with rapid absorption and action. It produces analgesia by elevation of the pain threshold, and antipyresis through action on the hypothalamic heat-regulating center.

Paracetamol is particularly suitable for patients with peptic ulcer as it does not cause gastric irritation and also for patients who have salicylate intolerance.

Chlorpheniramine maleate antagonizes most of the pharmacological effects of histamine by competitive antagonism of histamine at the H_1-histamine receptor. It controls rhinorrhea, sneezing and lacrimation associated with elevated histamine levels.

Pseudoephedrine is a sympathomimetic which acts predominantly on α-receptors and has little effect on β-receptors. **Therefore, it is an effective oral nasal decongestant with mild CNS stimulation**.

Indications

For the relief of cold symptoms such as nasal congestion and runny nose, accompanied with pains and fever.

Contraindications

Known hypersensitivity to any ingredient of the preparation.

During lactation.

Newborn and premature infants.

Asthma or other lower respiratory tract conditions, narrow-angle glaucoma, stenosing peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, pyloroduodenal obstruction.

Concomitant use with monoamine oxidase (MAO) inhibitor therapy or within 14 days of discontinuation of such therapy (see Drug Interactions).

Severe hypertension and severe coronary artery disease.

Do not use in children under the age of 2 years.

Warnings

Paracetamol can cause accidental poisoning in toddlers and infants. Paracetamol-containing products should be kept well out of reach of children.

Potentially fatal hepatotoxicity can result from paracetamol overdosage. However, in rare cases, hepatotoxicity has occurred in patients receiving high or excessive doses within therapeutic doses. Certain patients may be more susceptible to paracetamol hepatotoxicity, e.g., chronic alcoholics, patients with liver disease, or those who are malnourished or taking other drugs that induce hepatic enzymes.

Because of the risk of heptotoxicity, patients should be cautioned against the inadvertent administration of excessive doses of paracetamol by using multiple paracetamol-containing product at once, such as cough and cold remedies, analgesics or arthritic formulations, antipyretics or products for relief of menstrual symptoms or muscle spasm. Administration of paracetamol to children may be especially prone to error due to the many concentrations and strengths of products available. To avoid dosing errors, all product labels should be checked carefully to ensure calculation of the amount of paracetamol to be given.

Use in Pregnancy

Safety of use in pregnancy has not been established.

Use in Pediatrics:

Antihistamines may diminish mental alertness; conversely, they may occasionally produce excitation, particularly in young children.

Overdose of antihistamines, particularly in infants and children, may produce hallucinations, central nervous system depression, convulsions and even death.

Adverse Reactions

Adverse Reactions Attributed to Paracetamol

Adverse reactions of paracetamol are rare and usually mild.

Hepatotoxicity: see Warnings.

Hematologic: neutropenia and thrombocytopenia purpura have been reported and rarely agranulocytosis.

Hypersensitivity: reactions including skin eruptions, laryngeal edema, bronchospasm, and/or anaphylaxis have occurred rarely. Dose-dependent cross-sensitivity to paracetamol may occur in aspirin-sensitive asthmatics. Low initial doses of paracetamol (less than 1000 mg) are recommended in these patients, with monitoring for about 3 hours following initial doses.

Renal: nephropathy, including papillary renal failure has been reported following consumption of large amounts of paracetamol. Renal tubular necrosis has been associated occasionally with hepatic injury produced by paracetamol overdose.

Adverse Reactions Attributed to Antihistamines, Including Chlorpheniramine Maleate

Adverse reactions which have generally been reported with the use of antihistamines are as follows:

Central Nervous System

Sedation, extrapyramidal reactions, dizziness, drowsiness, disturbed coordination, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, paresthesias, neuritis, convulsions, euphoria, hallucinations, hysteria, faintness.

Special Senses

Acute labyrinthitis, blurred vision, diplopia, vertigo, tinnitus.

Allergic

Peripheral, angioneurotic and laryngeal edema, drug rash, urticaria, photosensitivity, anaphylactic shock.

Gastrointestinal

Epigastric distress, dryness of mouth, anorexia, nausea, vomiting, diarrhea, constipation.

Cardiovascular

Hypotension, headache, palpitations, tachycardia, extrasystoles.

Genitourinary

Urinary frequency, difficult urination, urinary retention, early menses.

Respiratory

Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness, dryness of nose and throat.

Hematological

Hemolytic anemia, thrombocytopenia, leukopenia, agranulocytosis.

Miscellaneous

Fatigue, chills, headache, excessive perspiration, sore throat, fever.

Adverser Reactions attributed to pseudoephedrine component

Cardiovascular stimulation – elevated blood pressure, tachycardia or arrhythmias.
Central nervous system (CNS) stimulation – restlessness, insomnia, anxiety, tremors and (rarely) hallucinations.
Skin rashes and urinary retention

Other

Convulsions , hallucinations , shortness of breath or troubled breathing , nervousness, dizziness or lightheadedness , headache, increased sweating, nausea or vomiting unusual paleness, weakness.

Precautions

For Paracetamol

If a sensitivity reaction occurs, discontinue use.

Paracetamol should be given with care to patients with impaired kidney or liver function.

Risk-benefit ratio should be taken into consideration in the presence of viral hepatitis and alcoholism, since there is an increased risk of hepatotoxicity.

For Chlorpheniarmine Maleate

Since drowsiness may occur, patients should be warned that their ability to perform potentially-hazardous tasks requiring mental alertness or physical coordination such as driving a vehicle or operating machinery, may be impaired. Children should be warned not to participate in activities such as riding a bicycle or playing near traffic.

Antihistamines have an atropine-like action. Therefore, they should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease or hypertension.

Since antihistamines may cause epigastric distress, they should preferably be taken after meals to diminish gastric irritation.

For Pseudoephedrine

Caution should be exercised when administered to patients with diabetes, hypertension, cardiovascular disease, diabetes mellitus, elevated intraocular pressure, prostatic enlargment, hyperthyroidism, and hyperreactivity to ephedrine.

Sympathomimetic amines may cause confusion, hallucinations, or CNS stimulation in geriatric patients.

This preparation contains sorbitol 525 mg/5ml. It has been reported that the maximum allowed daily intake of sorbitol for diabetics is 25 g.

This preparation also contains saccharin sodium 2 mg/5 ml. A quantity of 5 mg/kg body weight/day should not be exceeded.

Drug Interactions

Drug Interactions Involving Paracetamol

Paracetamol/Oral Anticoagulants: Regular administration of paracetamol may enhance the activity of coumarin anticoagulants when given concurrently. Occasional doses have no significant effect.

Paracetamol/Hepatic Enzyme-Inducing Agents (e.g.: Barbiturates, Rifampicin, Phenytoin)/ Carbamazepine, Hepatotoxic Medications/ Alcohol: Concurrent administration of enzyme inducers and paracetamol may decrease the therapeutic effect of paracetamol, probably because of increased metabolism resulting from induction of hepatic microsomal enzyme activity.

The risk of hepatotoxicity with single toxic doses or prolonged use of high doses of paracetamol may be increased in patients consuming alcoholic beverages or in patients taking other hepatotoxic medications.

Paracetamol/ Salicylates/ Other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): Chronic high-dose administration of paracetamol with salicylates and/or other non-steroidal anti-inflammatory drugs increases the risk of analgesic nephropathy.

Paracetamol/ Zidovudine: Paracetamol may competitively inhibit the hepatic glucuronidation and decrease the clearance of zidovudine. Zidovudine may also inhibit the hepatic glucuronidation of paracetamol. Concurrent use should be avoided, because the toxicity of either or both medications may be potentiated.

Paracetamol/Cholestyramine: Cholestyramine may reduce the absorption of paracetamol. Oral doses of cholestyramine and paracetamol should be given at least 1 hour apart.

Paracetamol/Metoclopramide/Domperidone: The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.

Drug Interactions Involving Chlorpheniramine Maleate

Antihistamines/Alcohol/CNS Depressants/(including Tricyclic Antidepressants):

Antihistamines may have additive effects when used concurrently with alcohol or other CNS depressants, e.g. hypnotics, sedatives, tranquilizers, antianxiety agents, narcotic analgesics.

Antihistamines/ Monoamine Oxidase Inhibitors: Concurrent administration of antihistamines and monoamine oxidase (MAO) inhibitors may prolong and intensify the anticholinergic (drying) effects of antihistamines. Therefore concurrent use of antihistamines with monoamine oxidase (MAO) inhibitor therapy or within 14 days of discontinuation of such therapy is contraindicated (see Contraindications).
***Antihistamines/ Ototoxic Medications*:** Symptoms of ototoxicity may be masked if antihistamines are used concurrently with ototoxic medications, particularly aminoglycoside antibiotics such as amikacin, dihydrostreptomycin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin, and viomycin.
Antihistamines/Anticholinergic Agents or Other Agents Possessing Anticholinergic Activity: Concurrent use may lead to a potentiation of the anticholinergic effects. Therefore caution should be exercised and patients should be advised to promptly report occurrence of gastrointestinal problems, since paralytic ileus may occur upon concurrent therapy of antihistamines and anticholinergic agents.

Drug Interactions Involving Pseudoephedrine
Pseudoephedrine/MAO Inhibitors: Concurrent use of sympathomimetics (including pseudoephedrine) with MAO inhibitors may prolong and intensify the effects of sympathomimetics. Severe hypertensive reactions may occur when sympathomimetics are administered to patients receiving MAO inhibitors. Concomitant use is therefore contraindicated (see Contraindications).
Pseudoephedrine/β-Blockers: β-Blockers increase the effects of sympathomimetics.
Pseudoephedrine/Methyldopa/Mecamylamine/Reserpine: The antihypertensive effects of these drugs may be reduced by sympathomimetics.
Pseudoephedrine/Inhalation Anesthetics: Administration of pseudoephedrine prior to or shortly after anesthesia may increase the risk of severe ventricular arrhythmias, especially in patients with preexisting heart disease, because these anesthetics generally sensitize the myocardium to the effects of sympathomimetics.
Pseudoephedrine/CNS Stimulation-Producing Medications (Including Appetite Suppressants)/Other Sympathomimetics (Including Cough and Cold Medications): Concurrent use of CNS-producing mediations with pseudoephedrine may result in additive CNS stimulation to excessive levels, which may cause unwanted effects such as nervousness, irritability, insomnia, or possibly convulsions or cardiac arrhythmias. Concurrent administration of pseudoephedrine with other sympathomimetics may, in addition to possibly increasing CNS stimulation, lead to possible increase in the cardiovascular effects of either the other sympathomimetic or pseudoephedrine, with the increased potential for side effects.
Pseudoephedrine/Digitalis Glycosides : Concurrent use with pseudoephedrine may increase the risk of cardiac arrhythmias; caution and electrocardiographic monitoring are very important if concurrent use is necessary.
Pseudoephedrine/Levodopa: Concurrent use with pseudoephedrine may increase the possibility of cardiac arrhythmias; dosage reduction of the sympathomimetic is recommended.
Pseudoephedrine//Cocaine (mucosal-local) In addition to increasing CNS stimulation, concurrent use with pseudoephedrine may increase the cardiovascular effects of either or both medications and the risk of adverse effects.
Pseudoephedrine//Nitrates: Concurrent use with pseudoephedrine may reduce the antianginal effects of these medications.
Pseudoephedrine//Thyroid Hormones: Concurrent use may increase the effects of either these medications or pseudoephedrine; thyroid hormones enhance risk of coronary insufficiency when sympathomimetic agents are administered to patients with coronary artery disease; therefore dosage adjustment is recommended.

Diagnostic Interference

For Paracetamol

Blood Glucose Determinations

May be falsely decreased when measured by the glucose oxidase/ peroxidase method, but probably not when measured by the hexokinase/ glucose-6-phosphate dehydrogenase (G6PD) method.

Serum Uric Acid Determinations

Falsely increased values may occur when the phosphotungstate uric acid test method is used.

Urine 5-hydroxyindoleacetic Acid (5-HIAA) Determinations

Qualitative screening tests using nitrosonaphthol reagent may produce false-positive test results. The quantitative test is unaffected.

Pancreatic Function Test Using Bentiromide

Administration of paracetamol prior to the bentiromide test will invalidate the test results, because paracetamol is also metabolized to an arylamine and will therefore increase the apparent quantity of para-aminobenzoic acid (PABA) recovered. It is recommended that paracetamol be discontinued at least 3 days prior to administration of bentiromide.

For Chlorpheniramine Maleate

Antihistamines should be discontinued about 4 days prior to skin testing procedures since they may prevent or diminish otherwise positive reactions to dermal reactivity indicators.

Information for Patients

This product should not be taken for more than 5 days when used for pain, and not more than 3 days when used for fever, unless directed by the physician. If pain or fever persists, or gets worse, if new symptoms occur, or if redness or swelling is present, the physician should be consulted because these could be signs of a serious condition. If sore throat is severe, persists for more than 2 days, is accompanied or followed by fever, headache, rash, nausea, or vomiting, the physician should be consulted promptly. ***The recommended dosage must not be exceeded***. If nervousness, dizziness, or sleeplessness occur, the product should be discontinued and the physician consulted.

This product may cause excitability, especially in children. Children who have a breathing problem such as chronic bronchitis, or children who have glaucoma, heart disease, high blood pressure, thyroid disease, or diabetes should not receive this product without first consulting the child's physician.

This product may cause drowsiness. Sedatives and tranquilizers may increase the drowsiness effect. Therefore this product should not be administered to children who are taking sedatives or tranquilizers without first consulting the child's physician. ***The recommended dose must not be exceeded***. Taking more than the recommended dose (overdosage) may not provide more relief and could cause serious health problems.

As with all drugs, this product should be kept out of reach of children. In case of accidental overdosage, the physician should be contacted immediately. Prompt medical attention is critical even if no signs and symptoms are noticed.

This product should not be administered with other products containing paracetamol.

Dosage and Administration

Notes: All doses at all ages may be repeated 3-4 times a day if needed, at intervals of not less than 4 hours between the doses. The product should not be administered more than 4 times in 24 hours.

For children under 6 years of age [under 22 kg (48 lbs.)] the physician should be consulted.

Adults and Children 12 Years of Age and Over
10 ml (2 teaspoonfuls), 3-4 times daily if needed.

Children 6-11 Years of Age [22 – 43 kg (48-95 lbs.)]
5-10 ml (1- 2 teaspoonfuls) 3-4 times daily if needed.

Recommended Dosage of Acamoli Cold Syrup When Prescribed by the Physician

Age	Weight	Dose
12-23 months	Approx. 8-10 kg. (18-23 lbs)	3.75 ml.
2-3 years	Approx. 11-16 kg (24-35 lbs.)	5 ml.
4-5 years	Approx. 16-21 kg (36-47 lbs.)	7.5 ml.
6-8 years	Approx. 22-27 kg (48-59 lbs.)	10 ml .
9-10 years	Approx. 27-32 kg (60-71 lbs.)	12.5 ml
11 years	Approx. 33-43 kg (72-95 lbs.)	15 ml.

Note: 1 lb = 0.4536 kg.

Overdosage

For Paracetamol

Manifestations

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia, and abdominal pain. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

In massive overdosage, paracetamol may cause hepatic toxicity. In adults and adolescents, hepatic toxicity has been rarely reported following ingestion of acute overdose of less than 7.5 –10 g. Fatalities are infrequent (less than 3-4% of untreated cases) and have been rarely reported with overdoses of less than 15 g. Early symptoms following a potentially hepatotoxic overdose may include nausea, vomiting, stomach pain, diaphoresis, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48-72 hours post-ingestion.

Serious toxicity or fatalities are extremely infrequent in children, possibly due to differences in the way they metabolize paracetamol. An acute overdosage of less than 150 mg/kg bodyweight in children has not been associated with hepatic toxicity.

Treatment
Adults and Adolescents

Regardless of the quantity of paracetamol reported or assumed to have been ingested, N-acetylcysteine should be administered immediately, if 24 hours or less have elapsed from the time of ingestion.

An initial dose of 150 mg N-acetylcysteine/kg body weight is infused I.V. in 200 ml of 5% Dextrose Injection over 15 minutes. This is followed by I.V infusion of 50 mg N-acetylcysteine/kg body weight in 500 ml of 5% Dextrose Injection over the next 4 hours, and 100 mg N-acetylcysteine/kg body weight in 1 liter of 5% Dextrose Injection over the next 16 hours (providing a total dose of 300 mg/kg body weight of N-acetylcysteine over 20 hours).

In addition to N-acetylcysteine administration, it is recommended that the stomach be emptied promptly by lavage, or by induction of emesis with syrup of ipecac.

A serum paracetamol assay should be obtained as early as possible, but not less than 4 hours following ingestion. If plasma level falls above the lower treatment line on the paracetamol overdose nomogram, acetylcycteine therapy should be continued.

Liver function tests should be performed initially, and repeated at 24-hour intervals.

Children

Induce emesis using syrup of ipecac.

A serum paracetamol assay should be obtained as soon as possible, but not less than 4 hours following ingestion.

If more than 150 mg/kg body weight or an unknown amount was ingested, plasma paracetamol level should be obtained. The plasma paracetamol level should be obtained as soon as possible, but no sooner than 4 hours following ingestion. If plasma level falls above the lower treatment line on the paracetamol overdose nomogram, the acetylcysteine therapy should be initiated and continued for a full course of therapy. If a paracetamol assay is not available and the paracetamol ingestion exceeds 150 mg/kg body weight, N-acetylcysteine therapy should be initiated and continued for a full course.

The dosage and administration of N-acetylcysteine in children is the same as recommended for adults and adolescents. However, the quantity of I.V. fluid used in children should be modified, taking into account both age and weight.

For Chlorpheniramine Maleate
Manifestations

Antihistamine overdosage reactions may vary from central nervous system depression to stimulation, especially in children. Atropine-like signs and symptoms such as dry mouth, fixed dilated pupils and flushing, as well as gastrointestinal symptoms, may occur.

Treatment

There is no specific therapy for acute overdosage with antihistamines. General symptomatic and supportive measures should be instituted promptly and maintained for as long as necessary.

Conscious Patients

Vomiting should be induced even though it may have occurred spontaneously. If the patient is unable to vomit, gastric lavage is indicated. Isotonic saline is the lavage of choice. Adequate precautions must be taken to protect against aspiration, especially in infants and children.

Charcoal slurry or another suitable agent should be instilled into the stomach after vomiting or lavage. Saline cathartics or milk of magnesia may be of additional benefit.

Unconscious Patients

The airway should be secured with a cuffed endotracheal tube before attempting to evacuate the gastric contents. Intensive supportive and nursing care are indicated, as for any comatose patient.

Do not administer CNS stimulants.

Hypotension is an early sign of impending cardiovascular collapse. If a vasopressor agent is needed, noradrenaline, phenylephrine or dopamine is indicated. Use of adrenaline should be avoided since it may worsen hypertension. In case of convulsions, diazepam may be used and repeated as necessary.

When life-threatening CNS signs and symptoms are present, intravenous physostigmine salicylate may be considered.

Ice packs and cooling sponge baths, but not alcohol, can help in reducing the fever commonly observed in children.

Hemoperfusion may be used in severe cases.

For Pseudoephedrine

Manifestations

As with other sympathomimetic agents, symptoms of overdosage include: mild anxiety, irritability, restlessness, tremor, convulsions, palpitations, hypertension, and difficulty in micturition. Symptoms usually appear within 4-8 hours of ingestion and are transient, usually requiring no treatment.

Treatment

Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed if indicated. Catheterization of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

Storage

Store in a cool place. Do not refrigerate.

Registration Numbers:

Acamoli Cold Strawberry Flavor: 118 76 29879 00
Acamoli Cold Raspberry Flavor: 118 77 29880 00.

Presentation

Bottles of 100 ml.

Manufacturer

Teva Industries Pharmaceuticals Ltd
P.O.Box 3190, Petach Tikva.