PULMADRIN COMPOUND

Syrup

Composition

Each teaspoonful (5 ml) contains:

Codeine phosphate	10 mg
Pseudoephedrine hydrochloride	30 mg
Triprolidine hydrochloride	1.25 mg

Action

Triprolidine provides symptomatic relief in conditions believed to depend wholly, or partly, upon the triggered release of histamine. Triprolidine is a potent, competitive H_1-receptor antagonist of the pyrrolidine class with mild central nervous system depressant properties which may cause drowsiness.

Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory decongestant. Pseudoephedrine is less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and is less potent in causing stimulation of the central nervous system.

After oral administration of a single dose of 2.5 mg Triprolidine to adults the onset of action, as determined by the ability to antagonise histamine-induced weals and flares in the skin, is within 1 to 2 hours. Peak effects occur at about 3 hours, and although activity declines thereafter, significant inhibition of histamine-induced weals and flares still occurs 8 hours after dose. Pseudoephedrine produces its decongestant effect within 30 minutes persisting for at least 4 hours.

Codeine

Narcotic analgesics, including codeine, exert their primary effects on the central nervous system and gastrointestinal tract. The analgesic effects of codeine are due to its central action; however, the precise sites of action have not been determined, and the mechanisms involved appear to be quite complex. Codeine resembles morphine both structurally and pharmacologically, but its actions at the doses of codeine used therapeutically are milder, with less sedation, respiratory depression, and gastrointestinal, urinary, and pupillary effects. Codeine produces an increase in biliary tract pressure, but less than morphine or meperidine. Codeine is less constipating than morphine. Codeine has good antitussive activity, although less than that of morphine at equal doses. It is used in preference to morphine, because side effects are infrequent at the usual antitussive dose of codeine.

Codeine in oral therapeutic dosage does not usually exert major effects on the cardiovascular system.

Narcotic analgesics may cause nausea and vomiting by stimulating the chemoreceptor trigger zone (CTZ); however, they also depress the vomiting center, so that subsequent doses are unlikely to produce vomiting. Nausea is minimal after usual oral doses of codeine.

Narcotic analgesics cause histamine release, which appears to be responsible for wheals or urticaria sometimes seen at the site of injection on parenteral administration. Histamine release may also produce dilation of cutaneous blood vessels, with resultant flushing of the face and neck, pruritus, and sweating.

Codeine and its salts are well absorbed following both oral and parenteral administration. Codeine is about 2/3 as effective orally as parenterally. Codeine is metabolized primarily in the liver by enzymes of the endoplasmic reticulum, where it undergoes O-demethylation, Ndemethylation, and partial conjugation with glucuronic acid. The drug is excreted primarily in the urine, largely as inactive metabolites and small amounts of free and conjugated morphine. Negligible amounts of codeine and its metabolites are found in the feces.

Following oral or subcutaneous administration of codeine, the onset of analgesia occurs within 15 to 30 minutes and lasts for four to six hours.

The cough-depressing action, in animal studies, was observed to occur 15 minutes after oral administration of codeine, peak action at 45 to 60 minutes after ingestion. The duration of action, which is dose-dependent, usually did not exceed 3 hours.

Indications

Pulmadrin Compound provides symptomatic relief of cough (both wet and dry, whether infectious or allergic in origin) and the accompanying nasal and upper respiratory tract congestion associated with the common cold.

Contraindications

- The combination is contraindicated in patients less than 12 years of age, because the combination may cause fatal respiratory depression in this age population
- Known hypersensitivity to any of the components of the preparation or to other drugs of similar chemical structure. Concomitant treatment with monoamine oxidase inhibitors, or within 14 days of their discontinuation.
- Severe hypertension or severe coronary artery disease.
- Patients of any age known to be CYP2D6 ultra-rapid metabolisers. Codeine is converted into morphine by an enzyme called CYP2D6. Some people (known as ultra-rapid metabolisers) convert codeine into morphine faster than others. This results in high morphine levels in the blood, which can cause toxic effects such as breathing difficulties.
- breastfeeding mothers.

Newborn and Premature Infants

This preparation should not be used in newborn or premature babies, because of their greater susceptibility to the antimuscarinic effects of the antihistamine component, such as CNS excitation and an increased tendency toward convulsions.

Lower Respiratory Tract Conditions

Antihistamines and codeine are both contraindicated for use in the treatment of lower respiratory tract symptoms, including asthma.

Other Medical Conditions

This preparation is contraindicated in patients with narrow-angle glaucoma, stenosing peptic ulcer, epilepsy, symptomatic prostatic hypertrophy, bladder neck obstruction and pyloroduodenal obstruction.

Warnings

Sympathomimetics may produce CNS stimulation. Because of the codeine component, prolonged use may cause dependence.

Pregnancy

Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers

This preparation is associated with increased risk of undesirable side effects in infants and is contraindicated in nursing mothers.

Paediatric Use

Respiratory Depression in Children

The combination is contraindicated in pediatric patients less than 12 years of age, because the combination may cause fatal respiratory depression in this age population.

Use of antihistamines is not recommended in newborn or premature infants.

Codeine is not recommended for adolescents (12 to 18) who have problems with breathing.

Codeine is converted into morphine by an enzyme called CYP2D6. Some people (known as ultra-rapid metabolisers) convert codeine into morphine faster than others. This results in high morphine levels in the blood, which can cause toxic effects such as breathing difficulties.

Antihistamine-containing preparations may diminish mental alertness; conversely, a paradoxical reaction characterized by hyperexcitability may occur.

Antihistamine overdosage, particularly in infants and children, may produce hallucinations, central nervous system depression, convulsions and even death.

Very young children may be more sensitive to the effects, especially the vasopressor effects, of sympathomimetic amines.

Elderly Use
Dizziness, sedation, hypotension, hyperexcitability, confusion and antimuscarinic side effects such as dryness of the mouth and urinary retention (especially in males), are more likely to occur in geriatric patients taking antihistamines. If the antimuscarinic side effects occur and continue or are severe, treatment should be discontinued.

Hallucinations, seizures, CNS depression and confusion may be more likely to occur in geriatric patients taking sympathomimetics. Geriatric patients may also be more sensitive to the effects, especially to the vasopressor effects, of sympathomimetic amines.
Patients above 60 years of age should therefore be closely monitored.

Adverse Reactions

Central Nervous System
Sedation, sleepiness, extrapyramidal reactions, dizziness, disturbed coordination, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, paraesthesias, neuritis, convulsions, euphoria, hallucinations, hysteria and faintness.

Special Senses
Acute labyrinthitis, blurred vision, diplopia, vertigo and tinnitus.

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

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

Cardiovascular
Hypotension, headache, palpitations, tachycardia and extrasystoles.

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

Respiratory
Tightness of chest and wheezing, nasal stuffiness, dryness of nose and throat and thickening of bronchial secretions.

Hematological
Hemolytic anemia, thrombocytopenia, leukopenia and agranulocytosis.

General
Fatigue, chills, headache and excessive perspiration.

Precautions
This preparation may cause drowsiness. 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. Similarly, children should be warned not to participate in activities such as riding a bicycle or playing near traffic.

Preparations containing 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, this preparation should preferably be taken after meals to diminish gastric irritation.

This preparation should be administered with caution in patients with mild to moderate hypertension, cardiovascular disease (including ischemic heart disease), diabetes mellitus, elevated intraocular pressure, hyperthyroidism, or prostatic enlargement.

Sympathomimetic amines may cause confusion, hallucinations or CNS stimulation in geriatric patients. Because of the codeine component, use with caution in patients with hepatic dysfunction, urinary dysfunction and in patients with head injury.

Drug Interactions
Triprolidine and Codeine/ Alcohol/ CNS Depressants/ Tricyclic Antidepressants
Concurrent use may potentiate the CNS depressant effects of Triprolidine, these agents or codeine.

Triprolidine/ Monoamine Oxidase Inhibitors
Concurrent use may prolong and intensify the antimuscarinic effects and CNS depressant effects of Triprolidine. Because of the Pseudoephedrine component, concurrent use is contraindicated (see Pseudoephedrine/Monoamine Oxidase Inhibitors).

Triprolidine/ Ototoxic Medications
Symptoms of ototoxicity may be masked if Triprolidine is used concurrently with ototoxic drugs, particularly aminoglycoside antibiotics such as amikacin, dihydrostreptomycin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin and viomycin.

Pseudoephedrine/ Monoamine Oxidase Inhibitors
Concomitant treatment with monoamine oxidase inhibitors, or within 14 days of their discontinuation, is contraindicated.

Concurrent use may prolong and intensify cardiac stimulant and vasopressor effects (including headache, cardiac arrhythmias, and vomiting, sudden and severe hypertensive and hyperpyretic crises) because of release of catecholamines, which accumulate in intraneuronal storage sites during monoamine oxidase inhibitor therapy.

Pseudoephedrine/ ß-Adrenergic Blocking Agents
Concomitant use may result in unopposed alpha-adrenergic activity of Pseudoephedrine with a risk of hypertension, excessive bradycardia and possible heart block. The therapeutic effect of the ß-adrenergic blocking agents may be inhibited.

Pseudoephedrine/ Antihypertensive Drugs
Concomitant use may cause a reduced antihypertensive effect.

Pseudoephedrine/ Digitalis Glycosides/ Anesthetics (hydrocarbon inhalation)
Cardiac arrhythmias may occur when Pseudoephedrine is used prior to anesthesia or concurrently with digitalis glycosides, because of sensitization of the myocardium to the effects of Pseudoephedrine.

Pseudoephedrine/ Other Sympathomimetics
In addition to possibly increasing CNS stimulation, concurrent use may increase the effects of either the other sympathomimetics or Pseudoephedrine and the potential for side effects.

Codeine/ Narcotic Analgesics/ Phenothiazines/ Other Tranquilizers
Use with caution as concurrent use may cause respiratory depression and hypotension.

Diagnostic Interference
Antihistamine-containing preparations should be discontinued about 4 days prior to skin testing procedures, since they may prevent or diminish otherwise positive reactions to dermal reactivity indicators.

Dosage and Administration
The combination is contraindicated in pediatric patients less than 12 years of age.

Adults (12 years of age and over)	5 mL (1 teaspoonful) every 4 to 6 hours, not to exceed 30.0 mL in 24 hours.

Over Dosage
Manifestations
The typical symptoms which may be observed following an overdose with an antihistamine-decongestant preparation include clumsiness or unsteadiness, severe dryness of the mouth, nose or throat, flushing or redness of the face, shortness of breath or troubled breathing (antimuscarinic effects, especially in children), convulsions, hallucinations (CNS stimulation, especially in children), severe drowsiness, continuing headache, unusually slow or fast heartbeat (sympathomimetic effects may indicate hypertension).
The effects of codeine over dosage include cold clammy skin, severe dizziness, and pinpoint pupils of eyes or severe weakness.

Treatment
General symptomatic and supportive measures should be instituted promptly and maintained for as long as necessary.

In conscious patients, vomiting should be induced even though it may have occurred spontaneously. Adequate precautions must be taken to protect against aspiration, especially in infants and children. If vomiting cannot be induced, gastric lavage is indicated, using isotonic saline. Because Pseudoephedrine is rapidly absorbed from the gut, these measures should be instituted within 4 hours of the overdose in order to be effective.
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.

In unconscious patients, the airway should be secured with a cuffed endotracheal tube before attempting to evacuate the gastric contents. Intensive supportive and nursing care is 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 or phenylephrine should be used. Adrenaline should not be used since it may lower blood pressure further.

Ice packs and cooling sponge baths can aid in reducing the fever commonly observed in children.

Intravenous diazepam may be administered for delirium or convulsions.
Naloxone may be used to treat codeine toxicity

Presentation

Pulmadrin Compound
Bottle of 120 ml.