Prescribing Information

^{N}COACTIFED®

Syrup
(Triprolidine HCl – Pseudoephedrine HCl – Codeine phosphate)

Antihistamine – Antitussive Decongestant

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Prescribing Information

^{N}COACTIFED®

Syrup

(Triprolidine HCl – Pseudoephedrine HCl – Codeine Phosphate)

Indications

The temporary relief of coughs associated with allergy or the common cold.

Regardless of the clinical setting, codeine, including COACTIFED®, must not be used in patients below the age of 18 years due to increased safety concerns (See Warnings and Precautions/ Special Populations/Children)

Contraindications

COACTIFED® is contraindicated in:

- Newborn or premature infants.
- Patients under the age of 18 years.
- Women who are breastfeeding (see Lactation)
- Women who are pregnant, or during labor and delivery.
- Patients who are known to be CYP2D6 extensive or ultra-rapid metabolisers for whom there is an increased risk of developing symptoms of opioid toxicity, even at commonly prescribed doses (see Pharmacology). General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression which may be life-threatening and very rarely fatal.

- Individuals with hypersensitivity to codeine phosphate or other opioids; triprolidine hydrochloride, or other antihistamines of similar chemical structure; sympathomimetic amines including pseudoephedrine.

- Individuals with hypersensitivity to any excipient in COACTIFED®. COACTIFED® contains methylparaben. It is contraindicated in patients with hypersensitivity to parabens.

- Patients receiving MAO inhibitors or who have taken any within the preceding 2 weeks. The concomitant use of pseudoephedrine and this type of product may cause a rise in blood pressure. In addition, the concomitant use of a codeine-containing product and monoamine oxidase inhibitors can occasionally result in symptoms such as hyperpyrexia, arrhythmia, myoclonus or coma.

- Patients with lower respiratory tract symptoms, including asthma, bronchitis, bronchiectasis.

- Patients with chronic or persistent cough, such as what occurs with asthma, smoking or emphysema, or where cough is accompanied by excessive secretions.

- Patients receiving any other sympathomimetics, such as decongestants, appetite suppressants, and stimulants used for the treatment of Attention Deficit and Hyperactivity Disorder (ADHD).

- Patients in or at risk of developing respiratory failure.

- Patients with hypertension or coronary artery disease.

- Patients with severe hepatic impairment, as it may precipitate hepatic encephalopathy.

- Patients with moderate to severe renal impairment (glomerular filtration rate less than 60 mL/min).

- Patients with pheochromocytoma.

- Patients with head injury or raised intracranial pressure, since further depression of respiration will increase cerebral edema.

- Patients with ulcerative colitis, since in common with other opioid analgesics, codeine may precipitate toxic dilatation or spasm of the colon.

Warnings and Precautions

General

Before prescribing medication to suppress or modify cough, it is important to ascertain that the underlying cause of the cough is identified, that modification of the cough does not increase the risk of clinical or physiological complications, and that appropriate therapy for the primary disease is provided.

COACTIFED® should not be used in patients with a history of arrhythmia, epilepsy, increased intraocular pressure (narrow angle glaucoma), prostatic hypertrophy, bladder neck obstruction, diabetes mellitus, ischemic heart disease and hyperthyroidism, unless its benefits outweigh its risks in these patients.

COACTIFIED® contains sucrose. COACTIFIED® should be used with considerable caution in patients with diabetes mellitus.

COACTIFED® should be prescribed with caution for certain special at risk patients such as the elderly and debilitated, for those with gallbladder disease or gallstones, history of bronchial asthma, or urethral stricture.

Patients' self-medication should be assessed. COACTIFED® should not be used by patients intolerant to sympathomimetics used for the relief of nasal or sinus congestion. Such drugs include ephedrine, epinephrine, phenylpropanolamine and phenylephrine. Symptoms of intolerance include drowsiness, dizziness, weakness, difficulty in breathing, tenseness, muscle tremors or palpitations.

Although codeine may be habit forming when used over long periods or in high doses, studies indicate that addiction to codeine is uncommon and requires high parenteral doses. Nevertheless, patients should take the drug only for as long, in the amounts, and as frequently as prescribed.

Large doses of codeine may cause the release of significant quantities of histamine, which may be associated with hypotension, cutaneous vasodilation, urticaria and, more rarely, bronchoconstriction.

Gastrointestinal

COACTIFED® should not be used in patients with obstructive bowel disorder or acute abdominal conditions (i.e. acute appendicitis or pancreatitis), stenosing peptic ulcer or phyloroduodenal obstruction, unless its benefits outweigh its risks in these patients. Codeine may obscure signs on which to judge the diagnosis or clinical course of patients with acute abdominal conditions.

There have been reports of ischemic colitis with pseudoephedrine. COACTIFED® should be discontinued immediately and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischemic colitis develop.

Respiratory
Codeine, including COACTIFIED®, is not recommended for use in any patient in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, lung infections, multiple trauma or extensive surgical procedures.

Ultra-Rapid Metabolizers of Codeine

Some individuals may be ultra-rapid metabolizers due to a specific CYP2D6*2x2 genotype. These individuals convert codeine into its active metabolite, morphine, more rapidly and completely than other people. This rapid conversion results in higher than expected serum morphine levels. Even at labeled dosage regimens, individuals who are ultra-rapid metabolizers may experience overdose symptoms such as extreme sleepiness, confusion, or shallow breathing.

The prevalence of this CYP2D6 phenotype varies widely and has been estimated at 0.5 to 1% in Chinese, Japanese and Hispanics, 1 to 10% in Caucasians, 3% in African Americans, and 16 to 28% in North Africans, Ethiopians, and Arabs. Data are not available for other ethnic groups.

Neurological Symptoms

There have been rare cases of posterior reversible encephalopathy (PRES)/reversible cerebral vasoconstriction syndrome (RCVS) reported with sympathomimetic drugs, including pseudoephedrine. Symptoms reported included sudden onset of severe headache, nausea, vomiting, and visual disturbances. Most cases improved or resolved within a few days following appropriate treatment. Pseudoephedrine should be discontinued immediately and medical advice sought if signs/symptoms of PRES/RCVS develop.

Occupational hazards

COACTIFED® may cause drowsiness and impair performance in tests of auditory vigilance. There is individual variation in response to antihistamines.

Patients should be warned about engaging in activities requiring mental alertness such as driving a car, or operating dangerous machinery or hazardous appliances, until they are reasonably certain the COACTIFED® does not adversely affect their performance.

Drug Interactions
COACTIFED® should not be used with other cough and cold medications with an antihistamine, sympathomimetic, and antitussive.

Because of its pseudoephedrine content, COACTIFED® may interact with drugs acting on the cardiovascular system, including bretylium, guanethidine, methyldopa, and alpha- and beta-adrenergic blocking agents.

Concomitant use of COACTIFED® with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants), or with monoamine oxidase inhibitors (resulting in serotonin syndrome), which interfere with the catabolism of sympathomimetic amines, may cause a rise in blood pressure.

Users of COACTIFED® should avoid the concomitant use of alcohol or other centrally acting sedatives. Patients receiving other opioid analgesics, antipsychotics, tricyclic antidepressants, anxiolytics, hypnotics or other CNS depressants concomitantly with COACTIFED® may exhibit increased sedation and an enhanced effect on respiratory inhibition.

Codeine, like other opioids, may antagonise the effects of metoclopramide and domperidone on gastrointestinal motility.

Special Populations

Pregnancy

COACTIFED® is contraindicated for use in pregnant women.

During the last trimester of pregnancy codeine may cause withdrawal symptoms in the neonate.

Administration of opioids during labour may produce gastric stasis and increase the risk of vomiting and aspiration pneumonia in the mother.

No clinical data on exposed pregnancies are available for COACTIFED®. Animal studies with pseudoephedrine and triprolidine do not indicate direct or indirect harmful effects on embryofetal development (see Toxicology section).

Lactation

COACTIFED® is contraindicated in women who are breast-feeding (see Contraindications). Codeine is secreted into human milk. In women with normal codeine metabolism (normal CYP2D6 activity), the amount of codeine secreted into human milk is low and dose-dependent. **However, some women are ultra-rapid metabolisers of codeine (**see **Contraindications, Ultra-Rapid Metabolisers of Codeine). These women achieve higher-than-expected serum levels of codeine's active metabolite, morphine, leading to higher-than-expected levels of morphine in breast milk and potentially dangerously high serum morphine levels in their breast-fed infants. Mothers using codeine should be informed about when to seek immediate medical care and how to identify the signs and symptoms of neonatal toxicity, such as drowsiness or sedation, difficulty breast-feeding, breathing**

difficulties, and decreased tone, in their baby. Therefore, maternal use of codeine can potentially lead to serious adverse reactions, including death in nursing infants.

Since there is a risk of infant exposure to codeine and morphine through breast milk, COACTIFED® is contraindicated in breast-feeding. Prescribers should closely monitor mother-infant pairs and notify treating paediatricians about any use of codeine during breast-feeding.

Elderly

Although there have been no specific studies of COACTIFED® in this group of patients, it may be anticipated that the elderly may be more susceptible to adverse effects. Therefore, reduced dosage and careful monitoring are advised, particularly in cases where there is impairment of renal, hepatic or mental status (see Contraindications, and Dosage and Administration sections).

The elderly are more likely to experience neurological anticholinergic effects and paradoxical excitation.

Children

COACTIFED® must not be used in patients under 18 years of age (see Contraindications).

In young children the respiratory centre is especially susceptible to the depressant action of opioid cough suppressants. Furthermore, some children may be ultra-rapid metabolisers of codeine (see Contraindications - Ultra-Rapid Metabolisers of Codeine).

Hepatic insufficiency

Experience with the use of the product suggests that normal adult dosage is appropriate in the presence of mild to moderate hepatic impairment, although it may be prudent to exercise caution. (See Dosage and Administration section; for severe hepatic impairment, see Contraindications section.)

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in hepatic impairment.

Renal insufficiency

Caution should be exercised when administering COACTIFED® to patients with mild renal impairment, particularly if accompanied by cardiovascular disease (see Contraindications section).

There have been no specific studies of COACTIFED®, triprolidine or codeine in renally impaired patients.

Adverse Reactions

In some patients, drowsiness, dizziness, dry mouth, nausea, and vomiting or mild stimulation may occur (See also Use in Children section).

Triprolidine

Triprolidine may cause sedation, drowsiness, dizziness, disturbance in attention and abnormal coordination. Skin rashes, with or without irritation, have occasionally been reported. Dryness of the mouth, nose and throat may occur. Tachycardia, paradoxical excitation, confusion, nightmares, hallucinations, blurred vision, thickening of bronchial secretions, urinary retention, rash, urticaria and gastrointestinal disturbance including nausea and vomiting may also occur.

Pseudoephedrine

Dizziness, dry mouth, nausea, and vomiting may occur.

Symptoms of central nervous system excitation may occur, including nervousness, agitation, restlessness, sleep disturbance and rarely, hallucinations. Skin rashes, with or without irritation, have occasionally been reported with pseudoephedrine. Urinary retention has been reported occasionally in men receiving pseudoephedrine; prostatic enlargement could have been an important predisposing factor. Dysuria, increased blood pressure, allergic dermatitis, tachycardia and palpitations may also occur.

Codeine

In some patients, dizziness, worsening of headache with prolonged use, drowsiness, pruritis and sweating may occur.

In therapeutic doses, codeine is less likely than morphine to produce adverse effects. The most common adverse effects noted with codeine include nausea, vomiting and constipation. Micturition may be difficult. Dry mouth, vertigo, light-headedness, tachycardia, rash and urticaria also occur. These effects occur more commonly in ambulant patients than those at rest in bed. Therapeutic doses of codeine occasionally induce hallucinations. Acute pancreatitis and symptoms of central nervous system depression may also occur.

Symptoms and Treatment of Overdosage

For management of a suspected overdose, contact your regional Poison Control Centre.

Symptoms

In children, the ingredients, in overdosage, may produce hallucinations, convulsions and death. Symptoms of toxicity in children may include fixed dilated pupils, flushed face, dry

mouth, fever, excitation, hallucinations, ataxia, incoordination, athetosis, tonic clonic convulsions, and postictal depression.

In addition to the undesirable effects seen with recommended doses, overdosage with codeine can cause transient euphoria, drowsiness, dizziness, weariness, diminution of sensibility, loss of sensation, vomiting, transient excitement in children and occasionally in adults, miosis progressing to nonreactive pinpoint pupils, itching sometimes with skin rashes and urticaria, and clammy skin with mottled cyanosis. In more severe cases, muscular relaxation with depressed or absent superficial and deep reflexes and a positive Babinski sign may appear. Marked slowing of the respiratory rate with inadequate pulmonary ventilation and consequent cyanosis may occur. Terminal signs include shock, pulmonary edema, hypostatic or aspiration pneumonia and respiratory arrest, with death occurring within 6 to 12 hours following ingestion.

Overdoses of antihistamines may cause hallucinations, convulsions or possibly death, especially in children. Antihistamines are more likely to cause dizziness, sedation and hypotension in elderly patients. Overdosage with triprolidine may produce reactions varying from depression to stimulation of the CNS; the latter is particularly likely in children. Atropine-like signs and symptoms (dry mouth, fixed dilated pupils, flushing, tachycardia, hallucinations, convulsions, urinary retention, cardiac arrhythmias and coma) may occur.

Overdosage with pseudoephedrine can cause excessive CNS stimulation resulting in excitement, nervousness, anxiety, tremor, restlessness and insomnia. Other effects include tachycardia, hypertension, pallor, mydriasis, hyperglycemia and urinary retention. Severe overdosage may cause tachypnea or hyperpnea, hallucinations, hypertensive crisis, convulsions or delirium, but in some individuals there may be CNS depression with somnolence, stupor or respiratory depression. Arrhythmias (including ventricular fibrillation) may lead to hypotension and circulatory collapse. Severe hypokalemia can occur, probably due to compartment shift rather than depletion of potassium. No organ damage or significant metabolic derangement is associated with pseudoephedrine overdosage.

Treatment

Therapy, if instituted within 4 hours of overdosage, is aimed at reducing further absorption of the drug. In the conscious patient, vomiting should be induced even though it may have occurred spontaneously. If vomiting cannot be induced, gastric lavage is indicated. Adequate precautions must be taken to protect against aspiration, especially in children. Charcoal slurry or other suitable agents should be instilled into the stomach after vomiting or lavage. Saline cathartics or milk of magnesia may be of additional benefit.

In the unconscious patient, 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. If breathing is significantly impaired, maintenance of an adequate airway and mechanical support of respiration is the most effective means of providing adequate oxygenation.

Hypotension is an early sign of impending cardiovascular collapse and should be treated vigorously.

Do not use CNS stimulants. Convulsion should be controlled by careful administration of diazepam or short-acting barbiturate, repeated as necessary. Physostigmine may be also considered for use in controlling centrally-mediated convulsions.

Ice packs and cooling sponge baths, not alcohol, can aid in reducing the fever commonly seen in children.

For codeine, continuous stimulation that arouses, but does not exhaust, the patient is useful in preventing coma. Continuous or intermittent oxygen therapy is usually indicated, while naloxone is useful as a codeine antidote. Close nursing care is essential.

Saline cathartics, such as milk of magnesia, help to dilute the concentration of the drugs in the bowel by draining water into the gut, thereby hastening drug elimination.

Adrenergic receptor blocking agents are antidotes to pseudoephedrine. In practice, the most useful is the beta-blocker propranolol, which is indicated when there are signs of cardiac toxicity.

There are no specific antidotes to triprolidine. Histamine should not be given.

Pseudoephedrine and codeine are theoretically dialysable, but the procedures have not been clinically established.

In severe cases of overdosage, it is essential to monitor both the heart by ECG and plasma electrolytes and to give i.v. potassium as indicated by these continuous controls. Vasopressors may be used to treat hypotension, and excessive CNS stimulation may be counteracted with parenteral diazepam. Stimulants should not be used.

Dosage and Administration

Dosing Considerations:

COACTIFED® should be avoided in patients known or suspected to be ultrarapid CYP2D6 metabolizers. If the symptoms do not improve, do not increase the dose or the frequency of dosing.

Adults

Take 10 mL of syrup every 8 hours or every 6 hours. Do not exceed 4 doses in a day (24 hours).

COACTIFED® is contraindicated in patients less than 18 years old.

Codeine, including COACTIFED®, should be prescribed at the lowest effective dose for the shortest period of time. Dosing should be as needed and not on scheduled intervals.

Missed Dose:
As there is no scheduled dosing, take COACTIFED® as needed for cough. Do not exceed 4 doses in a day (24 hours).

Use in the Elderly
Although there have been no specific studies of COACTIFED® in this group of patients, it may be anticipated that the elderly may be more susceptible to adverse effects. Therefore, reduced dosage and careful monitoring is advised, particularly in cases where there is impairment of renal, hepatic or mental status (see Contraindications, and Dosage and Administration sections).

Patients with Special Diseases and Conditions

Hepatic insufficiency

Experience with the use of the product suggests that normal adult dosage is appropriate in the presence of mild to moderate hepatic impairment, although it may be prudent to exercise caution (see Dosage and Administration section; for severe hepatic impairment, see Contraindications section.)

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in hepatic impairment.

Renal insufficiency

Caution should be exercised when administering COACTIFED® to patients with mild to moderate renal impairment, particularly if accompanied by cardiovascular disease (see Contraindications section).

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in renally impaired patients.

Availability of Dosage Forms

Each 5 mL of clear, dark red syrupy liquid contains: triprolidine HCl 2 mg, pseudoephedrine HCl 30 mg and codeine phosphate 10 mg. Also contains methylparaben, sucrose, glycerine, sodium benzoate, red colourant and flavour. Alcohol-free. Bottles of 100 mL. Store between 15°C and 30°C. Protect from light.

Pharmacology

Pharmacodynamic Properties

Pseudoephedrine

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 also less potent in causing stimulation of the central nervous system. Pseudoephedrine produces its decongestant effect within 30 minutes, persisting for at least 4 hours.

Triprolidine

Triprolidine is a potent, competitive histamine H_1-receptor antagonist. Being an alkylamine, the drug possesses minimal anticholinergic activity. Triprolidine provides symptomatic relief in conditions believed to depend wholly, or partly, upon the triggered release of histamine. 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 wheals and flares in the skin, was within 1 to 2 hours. Peak effects occurred at about 3 hours, and although activity declined thereafter, significant inhibition of histamine-induced wheals and flares still occurred 8 hours after a single dose.

Codeine

Codeine is metabolised by the liver enzyme CYP2D6 into morphine, its active metabolite, which is an agonist of opiate receptors and possesses analgesic, antitussive, and antidiarrheal actions.

Pharmacokinetic Properties

Absorption

Pseudoephedrine, triprolidine and codeine are well absorbed from the gut following oral administration.

Triprolidine and Pseudoephedrine
After the administration of 10 mL ACTIFED syrup (containing 2.5 mg triprolidine hydrochloride and 60 mg pseudoephedrine hydrochloride) to healthy adult volunteers,

- the peak plasma concentration (C_{max}) of triprolidine was 6.0 ng/mL, occurring at about 1.5 hours after drug administration

- the C_{max} of pseudoephedrine was approximately 180 ng/mL, with T_{max} occurring at approximately 1.5 hours after drug administration

Codeine
Following oral administration, peak plasma concentrations occur in approximately 1 hour. Maximum plasma concentrations of codeine are in the range of 100 to 300 ng/mL following normal therapeutic doses.

Distribution

The apparent volumes of distribution (Vd/F) are approximately:

- 7.5 L/kg for triprolidine
- 2.8 L/kg for pseudoephedrine
- 3.6 L/kg for codeine

Metabolism and Elimination

Triprolidine

The plasma half-life (t½) of triprolidine was approximately 3.2 hours. Animal hepatic microsomal enzyme studies have revealed the presence of several triprolidine metabolites with an oxidized product of the toluene methyl group predominating. In man, it has been reported that only about 1% of an administered dose is eliminated as unchanged triprolidine over a 24-hour period. The apparent total body clearance of triprolidine (Cl/F) was approximately 30 to 37 mL/min/kg. The elimination rate constant (Kcl) was approximately 0.26 hr^{-1}.

Pseudoephedrine

The plasma half-life (t½) was approximately 5.5 hours. Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite. Pseudoephedrine and its metabolite are excreted in the urine; 55% to 90% of a dose is excreted unchanged. The apparent total body clearance of pseudoephedrine (Cl/F) was approximately 7.5 mL/min/kg. The elimination rate constant (Kcl) was approximately 0.13 hr^{-1}. The rate of urinary elimination is accelerated when the urine is acidified. Conversely, as the urine pH increases, the rate of urinary excretion is slowed.

Codeine

The plasma half-life (t½) of codeine was approximately 3 to 4 hours.

Codeine is metabolised by the liver enzyme CYP2D6 via O-demethylation to form morphine, and via N-demethylation to form norcodeine. Codeine and its metabolites are also glucuronidated and sulphated in the liver.

Individuals who are heterozygous for the CYP2D6*2A allele are classified as ultra-rapid metabolisers of codeine. In these patients CYP2D6 enzyme is induced and O-demethylation of codeine to morphine is increased. If the patient is an extensive or ultra-rapid metaboliser,

there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. (see Contraindications).

After an oral dose, about 86% is excreted in the urine in 24 hours as free drug and metabolites, the majority as metabolites. Trace amounts of codeine are found in the feces. Unchanged drug accounts for 6 to 8% of the dose in urine in 24 hours, which may be increased to about 10% when the urinary pH is decreased.

Pharmacokinetics in Renal Insufficiency

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in renally impaired patients.

Pharmacokinetics in Hepatic Insufficiency

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in hepatic impairment.

Pharmacokinetics in the Elderly

There have been no specific studies of COACTIFED®, triprolidine, pseudoephedrine or codeine in the elderly.

Toxicology

Mutagenicity

Triprolidine was not mutagenic in bacterial cells in an Ames test.

Pseudoephedrine is not genotoxic in a battery of *in vivo* and *in vitro* tests in bacterial and mammalian assay systems.

Codeine was not mutagenic in bacterial cells *in vitro*, or in an *in vivo* mouse micronucleus test.

Carcinogenicity

Triprolidine and codeine were not carcinogenic in assays performed in mice and rats.

There is insufficient information available to determine whether pseudoephedrine has carcinogenic potential.

Teratogenicity

Triprolidine did not produce teratogenic effects at oral doses of up to 125 mg/kg/day in the rat, or 100 mg/kg/day in the rabbit.

Pseudoephedrine did not produce teratogenic effects at oral doses of up to 432 mg/kg/day in the rat, or 200 mg/kg/day in the rabbit.

Codeine did not produce teratogenic effects at oral doses of up to 120 mg/kg/day in the rat, or 30 mg/kg/day in the rabbit. However, at 120 mg/kg/day there was an increase in mortality in rat embryos near the period of implantation.

Fertility

There is no information on the effect of COACTIFED® on human fertility. Oral administration of pseudoephedrine to rats, at doses of 100 mg/kg/day in males and 20 mg/kg/day in females, did not impair fertility or alter morphological development and survival.

No studies have been conducted in animals to determine whether triprolidine or codeine have the potential to impair fertility.

PART III: CONSUMER INFORMATION

[N]COACTIFED®

Syrup
(Triprolidine HCl – Pseudoephedrine HCl – Codeine phosphate)

This leaflet is part III of "Prescribing Information" published when COACTIFED® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about COACTIFED®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
COACTIFED® is used for the temporary relief of coughs associated with allergy or the common cold. For adults 18 years or older.

What it does:
Triprolidine is an antihistamine. Pseudoephedrine is a decongestant. Codeine is a cough suppressant.

When it should not be used:
COACTIFED® must not be used in children.

Do not use COACTIFED® if you:

- are under 18 years
- **are pregnant, or in labor or delivery**
- are breast-feeding. The use of codeine-containing products while breast-feeding may harm your baby. If you breastfeed and take COACTIFED®, seek immediate medical care for your baby if they are overly drowsy, sedated, have difficulty breast-feeding, have breathing difficulties, and are floppy (have decreased muscle tone). This is very serious for the baby and can lead to death. Tell the baby's doctor that you are breastfeeding and took COACTIFED®.
- have been told by your doctor that you break down codeine rapidly. This can lead to codeine overdose even at the usual adult dose.
- have a chronic cough that occurs with asthma, smoking or emphysema, or when there is an unusually large amount of mucus or phlegm with the cough
- have a head injury or increased pressure in your head
- are currently taking or have recently taken (within 2 weeks) monoamine oxidase (MAO) inhibitors (which may be used for depression, psychiatric or emotional conditions, or Parkinson's disease) (e.g. phenelzine sulphate, moclobemide)
- have severe high blood pressure or heart condition
- have severe liver or kidney problems
- have pheochromocytoma (adrenal gland tumour)
- have ulcerative colitits
- suffer from seizures
- are allergic to this drug, other opioids or other antihistamines, to parabens (product contains methylparaben) or to any ingredient in the formulation (see "What the nonmedicinal ingredients are")
- have asthma, bronchitis, emphysema or other breathing problems
- are taking medicines for cough and cold, Attention Deficit and Hyperactivity Disorder (ADHD) or to decrease appetite

What the medicinal ingredients are:
Triprolidine hydrochloride, pseudoephedrine hydrochloride and codeine phosphate.

What the nonmedicinal ingredients are:
Red colourant, flavour, glycerine, methylparaben, sodium benzoate and sucrose. Alcohol-free.

What dosage forms it comes in:
2 mg triprolidine, 30 mg pseudoephedrine, 10 mg codeine in 5 mL of syrup.

WARNINGS AND PRECAUTIONS

BEFORE you use COACTIFED® talk to your doctor or pharmacist if you:

- have high blood pressure, heart disease or a heart condition, liver or kidney problems, diabetes, glaucoma, thyroid disease, gallbladder disease including gallstones, enlarged prostate or difficulty in urinating, ulcers, bowel obstruction or abdominal pain or infections (such as an inflamed appendix or pancreas), or epilepsy.
- are older than 65 years old, or suffer from a long-term illness.
- have asthma, a persistent or chronic cough or any other respiratory complications (i.e., difficulty breathing).
- are planning on becoming pregnant.
- are taking tranquilizers, sedatives, sedating antihistamines or other depressants, or 3 or more alcoholic beverages per day.
- are taking any other drug including over the counter drugs.
- have diabetes, as COACTIFIED® contains sucrose.

COACTIFED may cause drowsiness. Do not drive or operate machinery requiring mental alertness until you know how this medication affects you.

Codeine may be habit forming. Do not exceed the dose prescribed by your doctor.

COACTIFED® is not recommended for anyone who has or is at risk for breathing problems such as:

- lung infections, or respiratory conditions
- neuromuscular disorders
- severe heart problems
- recent multiple traumas or extensive surgical procedures

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with COACTIFED® include:

- other cough suppressants (antitussives), antihistamines or decongestant medications
- certain antidepressants (tricyclic and MAO inhibitors)
- certain medications for anxiety or psychosis
- medications for high blood pressure or heart conditions
- alcohol
- tranquilizers or other sedatives
- Domperidone and metoclopramide often used for nausea and vomiting and to help food move through digestion.

PROPER USE OF THIS MEDICATION

Always take COACTIFED® exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor should prescribe COACTIFED® at the lowest effective dose for the shortest period of time. It should only be used **as needed**. Do not take a dose unless you currently need it for cough.

Usual Adult dose
Do not exceed 4 doses in 24 hours.
Adults: 10 mL syrup three or four times a day

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

The most important sign of overdose is decreased breathing (abnormally slow or weak breathing).

Other signs include: feeling tired or sleeping for longer than usual, confusion, feeling sick, vomiting, constipation, decreased or lack of appetite.

Missed Dose:
As there is no scheduled dosing, take COACTIFED as needed for cough. Do not exceed 4 doses in 24 hours.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

- Some people may experience: headache, dizziness, abnormal coordination, vertigo, lightheadedness
- sleeplessness, nightmares, disturbance in attention
- nervousness, agitation, restlessness, mild stimulation
- shortness of breath
- nausea, vomiting, bloating
- dry mouth, nose and/or throat
- skin rash, itching or hives
- sweating

Consult your doctor if you feel sedated or drowsy, confused, have shallow breathing or have severe constipation.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate help
		Only if severe	In all cases	
Common	Drowsiness		✓	
	Depression: feeling sad, unexplained weight change, sleep disturbances, lack of interest in usual activities, confused		✓	
	Hallucinations: see or hear things that are not there		✓	
	Fast or irregular heartbeat		✓	

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate help
		Only if severe	In all cases	
Common	**Low Blood Pressure:** dizziness, fainting, lightheadedness		✓	
	Severe constipation		✓	
	Difficult or painful urination, urine retention		✓	
	Visions Changes: blurred vision, glaucoma or other eye disorder		✓	
	Thickening of secretions (phlegm) from the lungs		✓	
	Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
	Inflammation of the Pancreas: abdominal pain that lasts and gets worse when you lie down, nausea, vomiting		✓	
	Sedated or drowsy		✓	
	Shallow breathing		✓	
Rare	**Encephalopathy** (brain injury) : altered mental state, confusion, inability to concentrate, lethargy			✓
	Cerebral vasoconstriction syndrome: sudden, severe headache, Nausea, vomiting, visual disturbances			✓

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate help
		Only if severe	In all cases	
Rare	**Codeine Overdose:** shallow breathing, feeling tired or sleeping for longer than usual, extreme sleepiness, confusion, feeling sick, vomiting, constipation, decreased or lack of appetite.			✓
	Ischemic colitis: sudden abdominal pain, rectal bleeding or bloody stools			✓

This is not a complete list of side effects. For any unexpected effects while taking COACTIFED®, contact your doctor or pharmacist.

HOW TO STORE IT

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Store between 15°C and 30°C. Protect from light.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:
By toll-free telephone: 866-234-2345
By toll-free fax: 866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: CanadaVigilance@hc-sc.gc.ca
By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety and Effectiveness Information Bureau
Marketed Health Products Directorate
Tunney's Pasture, AL 0701E
Ottawa ON K1A 0K9
NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: http://www.gsk.ca or by contacting the sponsor,
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Mississauga, Ontario
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1-800-387-7374

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