AIRACOF - codeine phosphate, phenylephrine hydrochloride and diphenhydramine hydrochloride  liquid
CENTURION LABS, LLC

Rx Only

DESCRIPTION
A Strawberry-Flavored, clear, alcohol-free, sugar-free, dye-free, liquid for oral administration.

Each 5 mL (teaspoonful) contains:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine phosphate</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>(WARNING: May be habit forming)</td>
<td></td>
</tr>
<tr>
<td>Phenylephrine hydrochloride</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Diphenhydramine hydrochloride</td>
<td>12.5 mg</td>
</tr>
</tbody>
</table>

The phosphate salt of codeine occurs as white, needle-shaped crystals or white crystalline powder. Codeine phosphate is freely soluble in water and slightly soluble in alcohol. The chemical name is Morphinan-6-ol,7,8-didehydroxy-4,5-eposy-3methoxy-17-methyl-, (5α,6α)-, phosphate (1:1) (salt), hemihydrate.

Phenylephrine hydrochloride is a mydriatic and a decongestant and occurs as bitter crystals. The chemical name is: (-)-m-hydroxy-α-[(methyl-amino)methyl] benzyl alcohol hydrochloride.

Diphenhydramine hydrochloride is an antihistaminic. The chemical name is 2-(diphenylmethoxy)-N, N-dimethylethylamine hydrochloride.

Inactive Ingredients: Sodium benzoate, Citric acid, Saccharin sodium, Propylene glycol, Sorbitol, Flavor and Purified water.

CLINICAL PHARMACOLOGY

Codeine Phosphate
Codeine is a narcotic analgesic and antitussive whose effects are due to central action. It is well absorbed via oral administration. Following absorption, codeine is metabolized primarily by enzymes in the liver into morphine and other metabolites. These are excreted primarily in the urine with negligible amounts in the feces.

Phenylephrine Hydrochloride
Phenylephrine is an alpha-adrenergic receptor agonist, and acts predominantly by a direct action on alpha (α) adrenergic receptors. It causes Constriction of blood vessels in the nasal mucosa, which may relieve nasal congestion, after oral ingestion. In therapeutic doses the drug causes little, if any, central nervous system stimulation, and has no significant stimulant effect on the beta (β) adrenergic receptors of the heart.

Diphenhydramine hydrochloride
is an ethanolamine antihistamine with anticholinergic (drying), anti-inflammatory and sedative effects. It does not prevent the release of histamine, but competitively antagonizes histamine at H1, histamine receptors and thus blocks it in the central nervous system and in the periphery. Its antihistaminic effects thus relieve and block such allergic reactions as increased capillary permeability and dilation, edema formation, "flare" and "itch" response, vasoconstriction and vasodilatation, and gastrointestinal and smooth-muscle constriction.

INDICATIONS
AIRACOF™ is an antihistamine, antitussive and decongestant indicated for the symptomatic relief of cough, runny nose, nasal and eustachian tube congestion associated with the common cold, allergy, sinusitis and acute upper respiratory tract infections.

CONTRAINdications
Contraindicated in patients with severe hypertension or severe coronary artery disease, in patients on MAO inhibitor therapy, in patients with narrow-angle glaucoma, urinary retention, or peptic ulcer, during an asthmatic attack, in nursing mothers, and in premature or newborn infants. Contraindicated in patients with hypersensitivity to phenylephrine, codeine, sympathomimetic, amines, diphenhydramine, or other antihistamines of similar chemical structure. Because of its drying effect on lower respiratory secretions, AIRACOF™ is not recommended in the treatment of bronchial asthma.

WARNINGS
Antihistamines may cause drowsiness, dizziness, blurred vision, and otherwise impair mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery.

Sympathomimetic amines should be used cautiously, extremely carefully and sparingly in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, bladder-neck obstruction, hyperthyroidism or prostatic hypertrophy.
Sympathomimetics may produce central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

Products which contain diphenhydramine should not be used in combination with other diphenhydramine formulations; in rare cases toxic psychosis has occurred in children who received combinations of two or more diphenhydramine formulations by any route of administration including topically applied preparations.

**Respiratory Depression**
At high doses or in sensitive patients, codeine may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Codeine also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing.

**Head Injury and Increased Intracranial Pressure**
The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a preexisting increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

**Acute Abdominal Conditions**
The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

**Infants and Children**
Diphenhydramine should not be administered to premature or full-term neonates. Infants may have greater susceptibility than adults to the toxic effects of diphenhydramine. Adults who administer diphenhydramine to children should be aware that children may be at increased risk for excitability and central nervous system stimulation. Antihistamine may impair mental alertness in children.

**PRECAUTIONS**

**Information for Patients**
This product may cause drowsiness or dizziness like other antihistamines and narcotic drug products, and accordingly do not drive, operate machinery, or perform other similar activities due to potential impairment, until your reaction to this medicine is known, or after consultation with your physician.

**Special Risk Patients**
Do not use concomitantly with other CNS depressants, including alcohol, or sleep aids, or appetite suppressants, which may increase or otherwise potentiate the sedative effects of diphenhydramine. As with any narcotic analgesic agent, AIRACOF™ should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind. Use diphenhydramine hydrochloride with precaution in patients with narrow-angle glaucoma, stenosing peptic ulcer disease, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, or bladderneck obstruction, history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension. Elderly are more susceptible to the side effects of diphenhydramine.

**Cough Reflex**
Codeine suppresses the cough reflex. As with all narcotics, caution should be exercised when AIRACOF™ is used postoperatively and in patients with pulmonary disease.

**Drug Interactions**
Use of this product with other narcotic analgesics, antipsychotics, antianxiety agents, or other CNS depressants (including alcohol), sleep aids, appetite suppressants and other such products. AIRACOF™ may result in an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced.

The use of MAO inhibitors or tricyclic antidepressants with codeine preparations may increase the effect of either the antidepressant or hydrocodone. The concurrent use of anticholinergics with codeine may produce paralyticileus.

Concomitant use of antihistamines with alcohol, tricyclic antidepressants, barbiturates and other CNS depressants may have an additive effect.

MAO inhibitors and beta adrenergic blockers increase the effect of sympathomimetics. Sympathomimetics may reduce the antihypertensive effects of methyldopa, mecamylamine, reserpine and veratrum alkaloids.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**
Long-term studies in animals to determine mutagenic and carcinogenic potential have not been performed.
Usage in Pregnancy

Teratogenic Effects

Pregnancy Category C
Animal reproduction studies have not been conducted with AIRACOF™. It is also not known whether AIRACOF™ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. AIRACOF™ should be given to a pregnant woman only if clearly needed. Codeine has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. AIRACOF™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects

Babies born to mother who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose. There is no consensus on the best method of managing withdrawal.

Chlorpromazine 0.7 to 1mg/kg q6h, and paregoric 2 to 4 drops kg q4h, have been used to treat withdrawal symptoms in infants. The duration of therapy is 4 to 28 days, with the dosage decreased as tolerated.

Labor and Delivery

As with all narcotics, administration of AIRACOF™ to the mother shortly before delivery may result in some degree of respiratory depression in the newborn especially if higher doses are used.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reaction in nursing infants from AIRACOF™, 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 have not been established, and should not be used in children under 6 years old. Children may be more sensitive to the effects of this product, and may exhibit, in particular, excitability, in addition to the potential adverse events noted above.

Surgery and Hospital Care

Inform your physician of the use of this product before undergoing any medical procedures, including surgery, any hospital, medical or emergency care.

ADVERSE REACTIONS

Antitussives: may include drowsiness, dizziness, nausea or vomiting, constipation, dry mouth, headache, nervousness or restlessness, feeling of well-being, confusion, urinary disturbances, increased sweating, skin rash, hives, itching, swelling of face, flushing, weakness, visual disturbances, change in heart rate, difficulty breathing, loss of appetite, or general feeling of illness or discomfort. Possible allergic reaction to material if inhaled, ingested, or contacts with skin.

Sympathomimetic Amines: Hyperactive individuals may display ephedrine-like reactions such as tachycardia, palpitations, headache, dizziness, or nausea. Sympathomimetics have been associated with certain untoward reactions including restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucinations, convulsions, CNS depression, arrhythmias and cardiovascular collapse with hypotension.

Antihistamines: Patients sensitive to antihistamines may experience mild sedation. Possible side effects of antihistamines are drowsiness, restlessness, dizziness, weakness, dry mouth, anorexia, nausea, vomiting, headache, nervousness, blurring of vision, polyuria, heartburn, dysuria and, very rarely, dermatitis.

Other adverse reactions include

Central Nervous System: Drowsiness, metal clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence, mood changes.

Gastrointestinal System: The antiemetic phenothiazines are useful in suppressing the nausea and vomiting which may occur (see above); however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia.

Genitourinary System: Ureteral spasms, spasm of vesical sphincters and urinary retention have been reported.

Respiratory Depression: Codeine may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Codeine also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. If
significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. Apply other supportive measures when indicated.

DRUG ABUSE AND DEPENDENCE
AIRACOF™ is subject to the Federal Controlled Substance ACT (Schedule V).
May be habit forming. Codeine can produce drug dependence of the morphine type and, therefore, has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of AIRACOF™, and it should be prescribed and administered with the same degree of caution appropriate to the use of other narcotic drugs.

OVERDOSAGE
Overdose effects of Codeine phosphate may include cold, clammy skin; confusion; convulsions; severe dizziness; drowsiness; nervousness or restlessness; heartbeat; slow or troubled breathing; and unconsciousness. Antihistamine overdose reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms, dry mouth; fixed, dilated pupils; flushing and gastrointestinal symptoms may also occur.

TREATMENT
Recommended treatment of opioid analgesic overdose may consist of the following: Induced vomiting or perform gastric lavage (if the opioid was taken orally). Administer naloxone (an opioid antagonist) as a single dose of between 400 micrograms and 2 mg, preferably by intravenous infusion. Administer intravenous fluids and/or vasopressors and use of he supportive measures as needed. Continuously monitor patient (mandatory because the duration of action of the opioid may exceed naloxone as needed. Alternatively, initial treatment may be followed by continuous intravenous infusion of naloxone.
Gastric emptying may be useful in removing unabsorbed drug.
Diphenhydramine Hydrochloride Mild overdose of diphenhydramine leads to sedation. Moderate to severe diphenhydramine overdose produces predictable anticholinergic effects: agitated delirium, mydriasis, dry mouth, decreased gastrointestinal motility, urinary retention, and erythema. Rarely, diphenhydramine overdose may cause rhabdomyolysis. Life-threatening overdose is characterized by hyperthermia (from a combination of musculoskeletal action in an agitated patient who is unable to lose heat because of an inability to sweat), seizures, and ventricular tachycardia. Mild to moderate overdoses can be treated supportively. Sedation for severe agitation can be accomplished by intravenous benzodiazepines or physostigmine. Ventricular arrhythmia is treated with intravenous sodium bicarbonate or hypertonic saline.

DOSAGE AND ADMINISTRATION

Individuals 12 years of age and over
2 teaspoonfuls (10 mL) every 4 hours, not to exceed 8 teaspoonfuls in 24 hours.
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.

HOW SUPPLIED
16 fluid ounce bottles.
NDC# 23359-019-16

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°). [see USP Controlled Room Temperature.] Dispense in a tight, light-resistant container as defined in the USP/NF with child-resistance closure.
Tamper evident by foil seal under cap. Do not use if foil seal is broken or missing.

Manufactured for:
CENTURION LABS, LLC
Birmingham, AL 35243
REV. 10/09

PRINCIPAL DISPLAY PANEL - 473 ML BOTTLE LABEL
NDC 23359-019-16
AIRACOF™
LIQUID
Antitussive/Decongestant/
Antihistamine

Each 5 mL (teaspoonful) contains:
Codeine phosphate 7.5 mg
(WARNING: May be habit forming)
Phenylephrine hydrochloride 7.5 mg
Diphenhydramine hydrochloride

CV
Rx Only
16 fl. oz (473 mL)
CENTURION Labs, LLC
LEADING PHARMACEUTICALS