

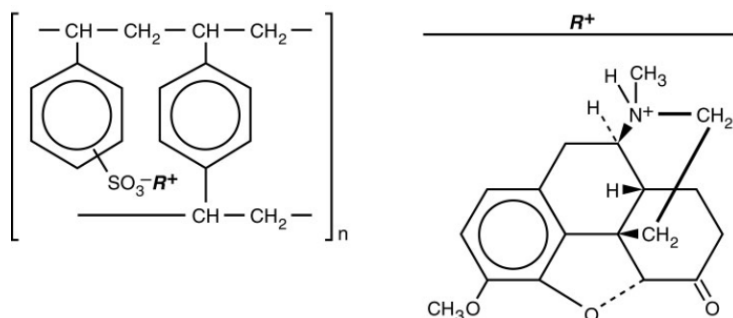
Tussionex[®]
Pennkinetic[®]
(hydrocodone polistirex and chlorpheniramine polistirex)
Extended-Release Suspension CII
 Rx only

DESCRIPTION

Each 5 mL of TUSSIONEX Pennkinetic Extended-Release Suspension contains hydrocodone polistirex equivalent to 10 mg of hydrocodone bitartrate and chlorpheniramine polistirex equivalent to 8 mg of chlorpheniramine maleate. Hydrocodone is a centrally-acting narcotic antitussive. Chlorpheniramine is an antihistamine. TUSSIONEX Pennkinetic Extended-Release Suspension is for oral use only.

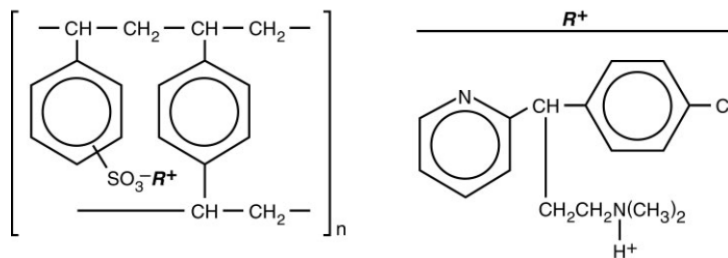
Hydrocodone Polistirex

Sulfonated styrene-divinylbenzene copolymer complex with 4,5 α -epoxy-3-methoxy-17-methylmorphinan-6-one.



Chlorpheniramine Polistirex

Sulfonated styrene-divinylbenzene copolymer complex with 2-[p-chloro- α -[2-(dimethylamino)ethyl]-benzyl]pyridine.



Inactive Ingredients

Ascorbic acid, D&C Yellow No. 10, ethylcellulose, FD&C Yellow No. 6, flavor, high fructose corn syrup, methylparaben, polyethylene glycol 3350, polysorbate 80, pregelatinized starch, propylene glycol, propylparaben, purified water, sucrose, vegetable oil, xanthan gum.

CLINICAL PHARMACOLOGY

Hydrocodone is a semisynthetic narcotic antitussive and analgesic with multiple actions qualitatively similar to those of codeine. The precise mechanism of action of hydrocodone and other opiates is not known; however, hydrocodone is believed to act directly on the cough center. In excessive doses, hydrocodone, like other opium derivatives, will depress respiration. The effects of hydrocodone in therapeutic doses on the cardiovascular system are insignificant. Hydrocodone can produce miosis, euphoria, and physical and psychological dependence.

Chlorpheniramine is an antihistamine drug (H_1 receptor antagonist) that also possesses anticholinergic and sedative activity. It prevents released histamine from dilating capillaries and causing edema of the respiratory mucosa.

Hydrocodone release from TUSSIONEX Pennkinetic Extended-Release Suspension is controlled by the Pennkinetic System, an extended-release drug delivery system, which combines an ion-exchange polymer matrix with a diffusion rate-limiting permeable coating. Chlorpheniramine release is prolonged by use of an ion-exchange polymer system.

Following multiple dosing with TUSSIONEX Pennkinetic Extended-Release Suspension, hydrocodone mean (S.D.) peak plasma concentrations of 22.8 (5.9) ng/mL occurred at 3.4 hours. Chlorpheniramine mean (S.D.) peak plasma concentrations of 58.4 (14.7) ng/mL occurred at 6.3 hours following multiple dosing. Peak plasma levels obtained with an immediate-release syrup occurred at approximately 1.5 hours for hydrocodone and 2.8 hours for chlorpheniramine. The plasma half-lives of hydrocodone and chlorpheniramine have been reported to be approximately 4 and 16 hours, respectively.

INDICATIONS AND USAGE

TUSSIONEX Pennkinetic Extended-Release Suspension is indicated for relief of cough and upper respiratory symptoms associated with allergy or a cold in adults and children 6 years of age and older.

CONTRAINDICATIONS

TUSSIONEX Pennkinetic Extended-Release Suspension is contraindicated in patients with a known allergy or sensitivity to hydrocodone or chlorpheniramine.

The use of TUSSIONEX Pennkinetic Extended-Release Suspension is contraindicated in children less than 6 years of age due to the risk of fatal respiratory depression.

WARNINGS

Respiratory Depression

As with all narcotics, TUSSIONEX Pennkinetic Extended-Release Suspension produces dose-related respiratory depression by directly acting on brain stem respiratory centers. Hydrocodone affects the center that controls respiratory rhythm and may produce irregular and periodic breathing. Caution should be exercised when TUSSIONEX Pennkinetic Extended-Release Suspension is used postoperatively and in patients with pulmonary disease, or whenever ventilatory function is depressed. If respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride and other supportive measures when indicated (see OVERDOSAGE).

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 pre-existing 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.

Obstructive Bowel Disease

Chronic use of narcotics may result in obstructive bowel disease especially in patients with underlying intestinal motility disorder.

Pediatric Use

The use of TUSSIONEX Pennkinetic Extended-Release Suspension is contraindicated in children less than 6 years of age (see CONTRAINDICATIONS).

In pediatric patients, as well as adults, the respiratory center is sensitive to the depressant action of narcotic cough suppressants in a dose-dependent manner. Caution should be exercised when administering TUSSIONEX Pennkinetic Extended-Release Suspension to pediatric patients 6 years of age and older. Overdose or concomitant administration of TUSSIONEX Pennkinetic Extended-Release Suspension with other respiratory depressants may increase the risk of respiratory depression in pediatric patients. Benefit to risk ratio should be carefully considered, especially in pediatric patients with respiratory embarrassment (e.g., croup) (see PRECAUTIONS).

PRECAUTIONS

General

Caution is advised when prescribing this drug to patients with narrow-angle glaucoma, asthma, or prostatic hypertrophy.

Special Risk Patients

As with any narcotic agent, TUSSIONEX Pennkinetic Extended-Release Suspension 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.

Information for Patients

Patients should be advised that TUSSIONEX Pennkinetic Extended-Release Suspension may produce marked drowsiness and impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.

TUSSIONEX Pennkinetic Extended-Release Suspension must not be diluted with fluids or mixed with other drugs as this may alter the resin-binding and change the absorption rate, possibly increasing the toxicity.

Patients should be advised to measure TUSSIONEX Pennkinetic Extended-Release Suspension with an accurate measuring device. A household teaspoon is not an accurate measuring device and could lead to overdosage. A pharmacist can recommend an appropriate measuring device and can provide instructions for measuring the correct dose.

A dosing spoon is provided with the 4 oz (115 mL) packaged product. One side of the spoon is for a 2.5 mL dose. The other side of the spoon is for a 5 mL dose. Instruct the patient to fill to level the side of the spoon for the dose that has been prescribed. The spoon should not be overfilled. Rinse the measuring device or dosing spoon after each use.

Shake well before using.

Keep out of the reach of children.

Cough Reflex

Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when TUSSIONEX Pennkinetic Extended-Release Suspension is used postoperatively, and in patients with pulmonary disease.

Drug Interactions

Patients receiving narcotics, antihistaminics, antipsychotics, antianxiety agents, or other CNS depressants (including alcohol) concomitantly with TUSSIONEX Pennkinetic Extended-Release

Suspension may exhibit 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 hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone.

The concurrent use of other anticholinergics with hydrocodone may produce paralytic ileus.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity, and reproductive studies have not been conducted with TUSSIONEX Pennkinetic Extended-Release Suspension.

Pregnancy

Teratogenic Effects – Pregnancy Category C

Hydrocodone 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. TUSSIONEX Pennkinetic Extended-Release Suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects

Babies born to mothers 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.

Labor and Delivery

As with all narcotics, administration of TUSSIONEX Pennkinetic Extended-Release Suspension 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 reactions in nursing infants from TUSSIONEX Pennkinetic Extended-Release Suspension, 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

The use of TUSSIONEX Pennkinetic Extended-Release Suspension is contraindicated in children less than 6 years of age (see CONTRAINDICATIONS and ADVERSE REACTIONS, Respiratory, Thoracic and Mediastinal Disorders).

TUSSIONEX Pennkinetic Extended-Release Suspension should be used with caution in pediatric patients 6 years of age and older (see WARNINGS, Pediatric Use).

Geriatric Use

Clinical studies of TUSSIONEX did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

Gastrointestinal Disorders

Nausea and vomiting may occur; they are more frequent in ambulatory than in recumbent patients. Prolonged administration of TUSSIONEX Pennkinetic Extended-Release Suspension may produce constipation.

General Disorders and Administration Site Conditions

Death

Nervous System Disorders

Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, euphoria, dizziness, psychic dependence, mood changes.

Renal and Urinary Disorders

Ureteral spasm, spasm of vesical sphincters, and urinary retention have been reported with opiates.

Respiratory, Thoracic and Mediastinal Disorders

Dryness of the pharynx, occasional tightness of the chest, and respiratory depression (see CONTRAINDICATIONS).

TUSSIONEX Pennkinetic Extended-Release Suspension may produce dose-related respiratory depression by acting directly on brain stem respiratory centers (see OVERDOSAGE). Use of TUSSIONEX Pennkinetic Extended-Release Suspension in children less than 6 years of age has been associated with fatal respiratory depression. Overdose with TUSSIONEX Pennkinetic Extended-Release Suspension in children 6 years of age and older, in adolescents, and in adults has been associated with fatal respiratory depression.

Skin and Subcutaneous Tissue Disorders

Rash, pruritus.

DRUG ABUSE AND DEPENDENCE

TUSSIONEX Pennkinetic Extended-Release Suspension is a Schedule II narcotic. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of narcotics; therefore, TUSSIONEX Pennkinetic Extended-Release Suspension should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when TUSSIONEX Pennkinetic Extended-Release Suspension is used for a short time for the treatment of cough. Physical dependence, the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome, assumes clinically significant proportions only after several weeks of continued oral narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic therapy.

OVERDOSAGE

Signs and Symptoms

Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. Although miosis is characteristic of narcotic overdose, mydriasis may occur in terminal narcosis or severe hypoxia. In severe overdose apnea, circulatory collapse, cardiac arrest and death may occur. The manifestations of chlorpheniramine overdose may vary from central nervous system depression to stimulation.

Treatment

Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdose or unusual sensitivity to narcotics including hydrocodone. Therefore,

an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of hydrocodone in this formulation may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. For further information, see full prescribing information for naloxone hydrochloride. An antagonist should not be administered in the absence of clinically significant respiratory depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug.

DOSAGE AND ADMINISTRATION

It is important that TUSSIONEX is measured with an accurate measuring device (see PRECAUTIONS, Information for Patients).

A dosing spoon is provided with the 4 oz (115 mL) packaged product. One side of the spoon is for a 2.5 mL dose. The other side of the spoon is for a 5 mL dose. Fill to level the side of the spoon for the dose that has been prescribed. Do not overfill. Rinse with water after each use.

For prescriptions where a dosing spoon is not provided, a pharmacist can provide an appropriate measuring device and can provide instructions for measuring the correct dose. A household teaspoon is not an accurate measuring device and could lead to overdose.

Each 5 mL of Tussionex Pennkinetic Extended-Release Suspension contains hydrocodone polistirex equivalent to 10 mg hydrocodone bitartrate, and chlorpheniramine polistirex equivalent to 8 mg chlorpheniramine maleate. Shake well before using. Rinse the measuring device with water after each use.

Adults and Children 12 Years and Older

5 mL every 12 hours; do not exceed 10 mL in 24 hours.

Children 6-11 Years of Age

2.5 mL every 12 hours; do not exceed 5 mL in 24 hours.

This medicine is contraindicated in children under 6 years of age (see CONTRAINDICATIONS).

HOW SUPPLIED

TUSSIONEX Pennkinetic (hydrocodone polistirex and chlorpheniramine polistirex) Extended-Release Suspension, equivalent to 10 mg hydrocodone bitartrate and 8 mg chlorpheniramine maleate per 5 mL, is a gold-colored suspension available as:

- NDC 53014-548-01 4 oz amber plastic bottle containing 115 mL of suspension. Each bottle is supplied with a plastic dosing spoon calibrated for measuring 2.5 mL and 5 mL doses.

For Medical Information

Contact: Medical Affairs Department

Phone: (866) 822-0068

Fax: (770) 970-8859

Storage:

Store at 20 to 25°C (68 to 77°F); excursions permitted to 15 to 30°C (59 to 86°F)
[see USP Controlled Room Temperature].

TUSSIONEX Pennkinetic Extended-Release Suspension

Manufactured for:

UCB, Inc.

Smyrna, GA 30080



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Rev. 04/2015

PATIENT INFORMATION
TUSSIONEX[®] Pennkinetic[®]
(hydrocodone polistirex and chlorpheniramine polistirex)
Extended-Release Suspension CII

Read this Patient Information before you start taking TUSSIONEX Pennkinetic Extended-Release Suspension and each time you get a refill. There may be new information. This information does not take the place of talking to your doctor about your medical condition or your treatment.

What is TUSSIONEX Pennkinetic Extended-Release Suspension?

TUSSIONEX Pennkinetic Extended-Release Suspension is a prescription medicine used to treat cough and upper respiratory symptoms you can have with allergies or a cold. TUSSIONEX Pennkinetic Extended-Release Suspension is for adults and children age 6 years and older.

TUSSIONEX Pennkinetic Extended-Release Suspension contains two medicines, hydrocodone and chlorpheniramine. Hydrocodone is a narcotic cough suppressant. Chlorpheniramine is an antihistamine.

TUSSIONEX Pennkinetic Extended-Release Suspension is a controlled substance (CII) because it contains hydrocodone that can be a target for people who abuse prescription medicines or street drugs. Keep your TUSSIONEX Pennkinetic Extended-Release Suspension in a safe place, to protect it from theft. Never give your TUSSIONEX Pennkinetic Extended-Release Suspension to anyone else, because it may cause death or harm them. Selling or giving away this medicine is against the law.

Who should not take TUSSIONEX Pennkinetic Extended-Release Suspension?

Do not take TUSSIONEX Pennkinetic Extended-Release Suspension if you:

- are allergic to any of the ingredients in TUSSIONEX Pennkinetic Extended-Release Suspension. See the end of this leaflet for a complete list of ingredients in TUSSIONEX Pennkinetic Extended-Release Suspension.
- are a child under 6 years old. TUSSIONEX Pennkinetic Extended-Release Suspension can cause a decreased rate of breathing (respiratory depression) which can lead to death.

What should I tell my doctor before taking TUSSIONEX Pennkinetic Extended-Release Suspension?

Before you take TUSSIONEX Pennkinetic Extended-Release Suspension, tell your doctor if you:

- have lung or breathing problems
- have had a head injury
- have pain in your belly (abdomen)
- have eye problems, such as glaucoma
- have prostate problems
- have problems with your urinary tract (urethral stricture)

- plan to have surgery
- abuse alcohol
- have kidney or liver problems
- have thyroid problems, such as hypothyroidism
- are pregnant or plan to become pregnant. If you take TUSSIONEX regularly before your baby is born, your newborn baby may have withdrawal symptoms because their body has become use to the medicine. **Symptoms of withdrawal in a newborn baby may include:**
 - irritability
 - crying more than usual
 - shaking (tremors)
 - jitteriness
 - breathing faster than normal
 - diarrhea or more stools than normal
 - sneezing
 - yawning
 - vomiting
 - fever

If you take TUSSIONEX regularly before your baby is born, your baby could have breathing problems.

- are breastfeeding or plan to breastfeed. You and your doctor should decide if you will take TUSSIONEX Pennkinetic Extended-Release Suspension or breastfeed. You should not do both.

Tell your doctor about all of the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal supplements.

Using TUSSIONEX Pennkinetic Extended-Release Suspension with certain other medicines may affect each other. Using TUSSIONEX Pennkinetic Extended-Release Suspension with other medicines can cause serious side effects.

Especially tell your doctor if you:

- take pain medicines such as narcotics
- take cold or allergy medicines that contain antihistamines or cough suppressants
- take medicines for mental illness (anti-psychotics, anti-anxiety)
- drink alcohol
- take medicines for depression including monoamine oxidase inhibitors (MAOIs)
- take medicines for stomach or intestine problems

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take TUSSIONEX Pennkinetic Extended-Release Suspension?

- Take TUSSIONEX Pennkinetic Extended-Release Suspension exactly as your doctor tells you.
- Shake the TUSSIONEX Pennkinetic Extended-Release Suspension bottle well before you use it.

- **Do not** mix TUSSIONEX Pennkinetic Extended-Release Suspension with other fluids or medicines. Mixing may change how TUSSIONEX Pennkinetic Extended-Release Suspension works.
- TUSSIONEX Pennkinetic Extended-Release Suspension can be taken with or without food.
- **Only measure TUSSIONEX Pennkinetic Extended-Release Suspension with the dosing spoon that comes with your prescription. See Figure A.** If you do not have a dosing spoon for your medicine, ask your pharmacist to give you a measuring device to help you measure the correct amount of TUSSIONEX Pennkinetic Extended-Release Suspension. **Do not use a household teaspoon to measure your medicine. You may accidentally take too much.**
 - One side of the dosing spoon is marked for a 2.5 mL dose. The other side of the spoon is marked for a 5 mL dose. Find the side of the spoon that has the dose you are taking.
 - Fill that side of the spoon so the medicine is level with the rim of the spoon. **Do not** overfill the spoon.
 - Rinse the spoon with water after each use.

Figure A



- If you take too much TUSSIONEX Pennkinetic Extended-Release Suspension, call your doctor or go to the nearest hospital emergency room right away.

What should I avoid while taking TUSSIONEX Pennkinetic Extended-Release Suspension?

- TUSSIONEX Pennkinetic Extended-Release Suspension can cause you to be drowsy. Do not drive a car or use machinery while you take TUSSIONEX Pennkinetic Extended-Release Suspension until you know how it affects you.
- Do not drink alcohol while taking TUSSIONEX Pennkinetic Extended-Release Suspension. Drinking alcohol can increase your chances of having serious side effects.

What are the possible side effects of TUSSIONEX Pennkinetic Extended-Release Suspension?

TUSSIONEX Pennkinetic Extended-Release Suspension may cause serious side effects, including:

- Decreased breathing (respiratory depression) which can lead to death. Call your doctor or get emergency treatment right away if you have:
 - shallow or slow breathing
 - confusion
 - excessive sleepiness
- drowsiness leading to inability to think clearly or do normal physical activities
- bowel problems, including constipation and bowel obstruction

The most common side effects of TUSSIONEX Pennkinetic Extended-Release Suspension are:

- nausea and vomiting
- constipation
- nervous system problems (anxiety, fear, dizziness, mood changes)
- urinary tract problems
- dry throat
- chest tightness

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of TUSSIONEX Pennkinetic Extended-Release Suspension. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store TUSSIONEX Pennkinetic Extended-Release Suspension?

- Store TUSSIONEX Pennkinetic Extended-Release Suspension in a safe place at 68°F to 77°F (20°C to 25°C).
- Safely throw away medicine that is out of date or no longer needed.
- **Keep TUSSIONEX Pennkinetic Extended-Release Suspension and all medicines out of the reach of children.**

General information about TUSSIONEX Pennkinetic Extended-Release Suspension

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use TUSSIONEX Pennkinetic Extended-Release Suspension for a condition for which it was not prescribed. Do not give TUSSIONEX Pennkinetic Extended-Release Suspension to other people, even if they have the same condition. It may harm them and it is against the law.

This Patient Information Leaflet summarizes the most important information about TUSSIONEX Pennkinetic Extended-Release Suspension. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about TUSSIONEX Pennkinetic Extended-Release Suspension that is written for healthcare professionals.

For more information about TUSSIONEX Pennkinetic Extended-Release Suspension call 1-866-822-0068 or go to www.tussionex.com.

What are the ingredients in TUSSIONEX Pennkinetic Extended-Release Suspension?

Active Ingredient: hydrocodone polistirex and chlorpheniramine polistirex

Inactive Ingredients: Ascorbic acid, D&C Yellow No. 10, ethylcellulose, FD&C Yellow No. 6, flavor, high fructose corn syrup, methylparaben, polyethylene glycol 3350, polysorbate 80, pregelatinized starch, propylene glycol, propylparaben, purified water, sucrose, vegetable oil, xanthan gum.

TUSSIONEX Pennkinetic Extended-Release Suspension

Manufactured for:

UCB, Inc.

Smyrna, GA 30080

This patient information has been approved by the U.S. Food and Drug Administration.

Issued: 04/2015