

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FLOWTUSS® safely and effectively. See full prescribing information for FLOWTUSS.

FLOWTUSS (hydrocodone bitartrate and guaifenesin) oral solution, CII  
Initial U.S. Approval: 2014

**WARNING: RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS**  
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death [see Warnings and Precautions (5.1), Drug Interactions (7.1)]. Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol. See full prescribing information for complete boxed warning.

### RECENT MAJOR CHANGES

Boxed Warning 1/2017  
Warnings and Precautions, Risks from Concomitant use with Benzodiazepines or Other CNS Depressants (5.1) 1/2017

### INDICATIONS AND USAGE

FLOWTUSS is a combination of hydrocodone, an opioid antitussive, and guaifenesin, an expectorant indicated for the symptomatic relief of cough and to loosen mucus associated with the common cold.

#### Important Limitations of Use:

Not indicated for pediatric patients under 18 years of age (8.4)

### DOSAGE AND ADMINISTRATION

- Adults and adolescents 18 years of age and older: 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours (2.1)
- Measure FLOWTUSS with an accurate milliliter measuring device. (5.10)

### DOSAGE FORMS AND STRENGTHS

Oral solution: Each 5 mL contains hydrocodone bitartrate, USP, 2.5 mg; and guaifenesin, USP, 200 mg. (3)

### CONTRAINDICATIONS

- Patients with known hypersensitivity to hydrocodone bitartrate, guaifenesin, or any of the inactive ingredients of FLOWTUSS. (4)
- Patients receiving monoamine oxidase inhibitor (MAOI) therapy or within 14 days of stopping such therapy. (4)

### WARNINGS AND PRECAUTIONS

- Risks from Concomitant Use with Benzodiazepines or other CNS Depressants. (5.1)
- Dose-related respiratory depression: Use with caution. (5.2)
- Drug Dependence: Prescribe with caution that is appropriate to the use of other opioids. (5.3)
- Head injury and increased intracranial pressure: Avoid in patients with head injury, intracranial lesions or increased intracranial pressure. (5.4)
- Activities requiring mental alertness: Avoid engaging in hazardous tasks requiring complete mental alertness such as driving or operating machinery. (5.5)
- Acute abdominal conditions: Use with caution in patients with acute abdominal conditions. (5.6)
- Coexisting conditions: Use with caution in patients with diabetes, thyroid disease, Addison's disease, prostatic hypertrophy, or urethral stricture, or asthma. (5.11)

### ADVERSE REACTIONS

The most common adverse reactions of FLOWTUSS include: Dizziness, headache, sedation, nausea, and decreased blood pressure (6)

To report SUSPECTED ADVERSE REACTIONS, contact Mission Pharmacal Company at 1-800-298-1087 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

- Benzodiazepines, opioids, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol); Avoid using with FLOWTUSS; may exhibit additive CNS depression. (7.1)
- MAO inhibitors (MAOIs) or tricyclic antidepressants: Do not use. May increase the effect of either the antidepressant or hydrocodone. (7.2)
- Anticholinergic drugs: Use with caution in order to avoid paralytic ileus and excessive anticholinergic effects. (7.3)

### USE IN SPECIFIC POPULATIONS

- Renal Impairment: Use with caution in patients with severe renal impairment. (8.6)
- Hepatic Impairment: Use with caution in patients with severe hepatic impairment. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 1/2017

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## FULL PRESCRIBING INFORMATION

### WARNING: RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death [see *Warnings and Precautions (5.1)*, *Drug Interactions (7.1)*]. Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol.

## 1 INDICATIONS AND USAGE

FLOWTUSS is indicated for symptomatic relief of cough and to loosen mucus associated with the common cold.

### Important Limitations of Use:

Not indicated for pediatric patients under 18 years of age [see *Use in Specific Populations (8.4)*].

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Recommended Dosage

Adults and adolescents 18 years of age and older: 10 mL every 4 to 6 hours, not to exceed 6 doses (60 mL) in 24 hours.

Administer FLOWTUSS by the oral route only. Measure FLOWTUSS with an accurate milliliter measuring device. Do not use a household teaspoon to measure the dose [see *Warnings and Precautions (5.9)*].

## 3 DOSAGE FORMS AND STRENGTHS

Oral solution: Each 5 mL contains hydrocodone bitartrate, USP, 2.5 mg; and guaifenesin, USP, 200 mg [see *Description (11)*].

## 4 CONTRAINDICATIONS

FLOWTUSS is contraindicated in:

- Patients with known hypersensitivity to hydrocodone bitartrate, guaifenesin, or any of the inactive ingredients of FLOWTUSS.
- Patients receiving MAOI therapy or within 14 days of stopping such therapy [see *Drug Interactions (7.2)*].

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Risks from Concomitant Use with Benzodiazepines or other CNS Depressants

Concomitant use of opioids, including FLOWTUSS, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Because

of these risks, avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol [see *Drug Interactions (7.1)*].

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol.

Advise both patients and caregivers about the risks of respiratory depression and sedation if FLOWTUSS is used with benzodiazepines, alcohol, or other CNS depressants [see *Patient Counseling Information (17)*].

## 5.2 Respiratory Depression

Hydrocodone bitartrate, one of the active ingredients in FLOWTUSS, produces dose-related respiratory depression by directly acting on brain stem respiratory centers. Overdose of hydrocodone bitartrate in adults has been associated with fatal respiratory depression, and the use of hydrocodone bitartrate in children less than 6 years of age has been associated with fatal respiratory depression. Exercise caution when administering FLOWTUSS because of the potential for respiratory depression. If respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride and other supportive measures when indicated [see *Overdosage (10)*].

## 5.3 Drug Dependence

Hydrocodone 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 FLOWTUSS. Prescribe and administer FLOWTUSS with the same degree of caution appropriate to the use of other opioid drugs [see *Drug Abuse and Dependence (9.2), (9.3)*].

## 5.4 Head Injury and Increased Intracranial Pressure

The respiratory depression effects of opioids 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, opioids produce adverse reactions which may obscure the clinical course of patients with head injuries. The use of FLOWTUSS should be avoided in these patients.

## 5.5 Activities Requiring Mental Alertness

Hydrocodone bitartrate, one of the active ingredients in FLOWTUSS, 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. Advise patients to avoid engaging in hazardous tasks requiring mental alertness and motor coordination after ingestion of FLOWTUSS. Concurrent use of FLOWTUSS with alcohol or other central nervous system depressants should be avoided because additional impairment of central nervous system performance may occur.

## 5.6 Acute Abdominal Conditions

FLOWTUSS should be used with caution in patients with acute abdominal conditions since the administration of hydrocodone may obscure the diagnosis or clinical course of patients with acute abdominal conditions. The concurrent use of other anticholinergics with hydrocodone may produce paralytic ileus [see *Drug Interactions (7.3)*].

### **5.7 Co-administration with Anticholinergics**

The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus. Exercise caution when using FLOWTUSS in patients taking anticholinergic medications [see *Drug Interactions (7.3)*].

### **5.8 Co-administration with Monoamine Oxidase Inhibitors (MAOIs) or Tricyclic Antidepressants**

FLOWTUSS should not be used in patients receiving monoamine oxidase inhibitor (MAOI) therapy or within 14 days of stopping such therapy. The use of MAOIs or tricyclic antidepressants with hydrocodone bitartrate may increase the effect of either the antidepressant or hydrocodone [see *Contraindications (4)* and *Drug Interactions (7.2)*].

### **5.9 Persistent Cough**

FLOWTUSS should not be used in patients with a persistent or chronic cough such as occurs with smoking, asthma, chronic bronchitis, or emphysema, or where cough is accompanied by excessive phlegm (mucus).

### **5.10 Dosing**

Patients should be advised to measure FLOWTUSS with an accurate milliliter measuring device. Patients should be informed that a household teaspoon is not an accurate measuring device and could lead to overdosage, which can result in serious adverse reactions [see *Overdosage (10)*]. Patients should be advised to ask their pharmacist to recommend an appropriate measuring device and for instructions for measuring the correct dose.

### **5.11 Coexisting Conditions**

FLOWTUSS should be used with caution in patients with diabetes, thyroid disease, Addison's disease, prostatic hypertrophy or urethral stricture, and asthma.

### **5.12 Renal Impairment**

FLOWTUSS should be used with caution in patients with severe renal impairment [see *Use in Specific Populations (8.6)*].

### **5.13 Hepatic Impairment**

FLOWTUSS should be used with caution in patients with severe hepatic impairment [see *Use in Specific Populations (8.7)*].

## **6 ADVERSE REACTIONS**

Use of hydrocodone bitartrate is associated with the following:

- Respiratory depression [see *Warnings and Precautions (5.1)* and *Overdosage (10)*]
- Drug dependence [see *Warnings and Precautions (5.2)* and *Drug Abuse and Dependence (9.3)*]
- Increased intracranial pressure [see *Warnings and Precautions (5.3)*]
- Decreased mental alertness with impaired mental and/or physical abilities [see *Warnings and Precautions (5.4)*]
- Paralytic ileus [see *Warnings and Precautions (5.5)*]

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The most common adverse reactions experienced by subjects taking a single dose of FLOWTUSS in the clinical setting include the following: Central Nervous System: headache, dizziness, sedation (somnolence); Gastrointestinal System: nausea, diarrhea; Cardiovascular System: decreased blood pressure; Vascular System: hot flush.

## 7 DRUG INTERACTIONS

No specific interaction studies have been conducted with HYCOFENIX.

### 7.1 Benzodiazepines, Opioids, Antihistamines, Antipsychotics, Anti-anxiety Agents, or Other CNS Depressants (Including Alcohol)

The use of benzodiazepines, opioids, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with FLOWTUSS may cause an additive CNS depressant effect, profound sedation, respiratory depression, coma, and death and should be avoided [see *Warnings and Precautions* (5.1)].

### 7.2 MAO Inhibitors or Tricyclic Antidepressants

Do not prescribe FLOWTUSS if the patient is taking a prescription MAOI (i.e., certain drugs used for depression, psychiatric or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping an MAOI drug. The use of MAOIs or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone [see *Warnings and Precautions* (5.8)].

### 7.3 Anticholinergic Drugs

Hydrocodone should be administered cautiously to persons receiving anticholinergic drugs in order to avoid paralytic ileus and excessive anticholinergic effects [see *Warnings and Precautions* (5.7)].

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Teratogenic Effects

#### *Pregnancy Category C*

There are no adequate and well controlled studies of FLOWTUSS in pregnant women. Reproductive toxicity studies have not been conducted with FLOWTUSS; however, studies are available with an individual active ingredient or related active ingredient. Hydrocodone was teratogenic in hamsters. Codeine, an opiate related to hydrocodone, increased resorptions and decreased fetal weight in rats. Because animal reproduction studies are not always predictive of human response, FLOWTUSS should be used during pregnancy only if the benefit justifies the potential risk to the fetus.

#### *Hydrocodone*

Hydrocodone has been shown to be teratogenic in hamsters when given in a dose approximately 27 times the maximum recommended human daily dose (MRHDD) (on a mg/m<sup>2</sup> basis at a single subcutaneous dose of 102 mg/kg on gestation day 8). Reproductive toxicology studies were also conducted with codeine, an opiate related to hydrocodone. In a study in which pregnant rats were dosed throughout organogenesis, a dose of codeine approximately 40 times the MRHDD of

hydrocodone (on a mg/m<sup>2</sup> basis at an oral dose of 120 mg/kg/day of codeine) increased resorptions and decreased fetal weight; however, these effects occurred in the presence of maternal toxicity. In studies in which rabbits and mice were dosed throughout organogenesis, doses of codeine up to approximately 20 and 100 times, respectively, the MRHDD of hydrocodone (on a mg/m<sup>2</sup> basis at oral doses of 30 and 600 mg/kg/day, respectively), produced no adverse developmental effects.

### Non-teratogenic 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.

## **8.2 Labor and Delivery**

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

## **8.3 Nursing Mothers**

Caution should be exercised when FLOWTUSS is administered to nursing mothers. Hydrocodone is known to be excreted in human milk. No studies have been performed to determine if guaifenesin is excreted into breastmilk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from FLOWTUSS, 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.

## **8.4 Pediatric Use**

Safety and effectiveness of FLOWTUSS in pediatric patients under 18 years of age has not been established. The use of hydrocodone in children less than 6 years of age is associated with fatal respiratory depression [see *Warnings and Precautions* (5.2)].

## **8.5 Geriatric Use**

Clinical studies have not been conducted with FLOWTUSS in geriatric populations. Other reported clinical experience with the individual active ingredients of FLOWTUSS has not identified differences in responses between the elderly and patients younger than 65 years of age. In general, dose selection for an elderly patient should be made with caution, 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.

## **8.6 Renal Impairment**

FLOWTUSS should be given with caution in patients with severe impairment of renal function.

## **8.7 Hepatic Impairment**

FLOWTUSS should be given with caution in patients with severe impairment of hepatic function.

# **9 DRUG ABUSE AND DEPENDENCE**

## **9.1 Controlled Substance**

FLOWTUSS is a Schedule II controlled prescription containing hydrocodone bitartrate and should be prescribed and administered with caution.

## 9.2 Abuse

Hydrocodone 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 FLOWTUSS, and it should be prescribed and administered with the same degree of caution appropriate to the use of other opioid drugs.

Abuse of guaifenesin has been linked to the formation of kidney stones composed of the major metabolite  $\beta$ -(2-methoxyphenoxy) lactic acid.

## 9.3 Dependence

Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of opioids; therefore, FLOWTUSS should be prescribed and administered with caution [see *Warnings and Precautions* (5.3)].

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 opioid use, although some mild degree of physical dependence may develop after a few days of opioid therapy.

## 10 OVERDOSAGE

No human overdosage data are available for FLOWTUSS.

### Hydrocodone

Overdosage 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, dizziness, ringing in the ears, confusion, blurred vision, eye problems, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur.

### Guaifenesin

Overdosage with guaifenesin can cause depression of the central nervous system. While present in polypharmacy overdoses, one case of overdose with only significant levels of guaifenesin has been reported. Symptoms included slurred speech, shallow respirations, reduced heart rate with rhythm sinus bradycardia, followed by asystole.

Treatment of overdosage consists of discontinuation of FLOWTUSS together with institution of appropriate therapy. 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 opioid antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdosage or unusual sensitivity to opioids including hydrocodone. Therefore, an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. 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.

## 11 DESCRIPTION

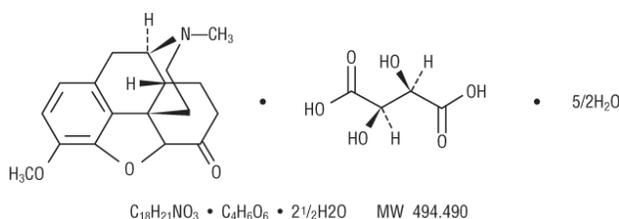
FLOWTUSS (hydrocodone bitartrate and guaifenesin) oral solution contains hydrocodone bitartrate (a centrally-acting opioid antitussive) and guaifenesin (an expectorant).

Each 5 mL dose of FLOWTUSS contains: hydrocodone bitartrate, USP, 2.5 mg; and guaifenesin, USP, 200 mg.

FLOWTUSS also contains: black raspberry flavor, citric acid, D&C Red #33, FD&C Blue #1, glycerin, methylparaben, polyethylene glycol, propylparaben, purified water, saccharin sodium, sodium citrate, and sorbitol.

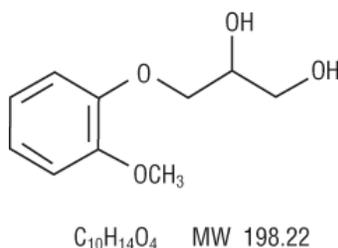
### Hydrocodone Bitartrate

Hydrocodone bitartrate is a centrally-acting opioid antitussive and analgesic. It is affected by light and occurs as fine white crystals or crystalline powder which is derived from the opium alkaloid, thebaine. Its chemical name is morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-, (5 $\alpha$ )-, [R-(R\*,R\*)]-2,3-dihydroxybutanedioate (1:1), hydrate (2:5). It is also known as 4,5 $\alpha$ -Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5); and may be represented by the following structural formula:



### Guaifenesin

Guaifenesin is an expectorant and occurs as a white powder. Its chemical name is 3-(2-methoxyphenoxy)-1,2-propanediol, and may be represented by the following structural formula:



## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

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 will depress respiration. Hydrocodone can produce miosis, euphoria, and physical and physiological dependence.

Guaifenesin is an expectorant the action of which promotes or facilitates the removal of secretions from the respiratory tract. The precise mechanism of action of guaifenesin is not known; however, it is

thought to act as an expectorant by increasing the volume and reducing the viscosity of secretions in the trachea and bronchi. In turn, this may increase the efficiency of the cough reflex and facilitate removal of the secretions.

### 12.3 Pharmacokinetics

Systemic exposure (in terms of peak plasma concentrations and area under plasma concentration versus time curve) of hydrocodone bitartrate and guaifenesin after a single 10 mL oral dose administration of 5 mg hydrocodone bitartrate and 400 mg guaifenesin are equivalent to the respective reference solutions of 5 mL hydrocodone bitartrate (5 mg/5 mL), and 10 mL guaifenesin (200 mg/5 mL).

#### Hydrocodone

Following a single 10 mL oral dose of 5 mg hydrocodone bitartrate and 400 mg guaifenesin administered to 37 healthy adults, the geometric mean  $C_{max}$  and  $AUC_{0-inf}$  for hydrocodone were 9.0 ng/mL and 61.2 ng•hr/mL, respectively. The median time to maximum concentration for hydrocodone was about 1.67 hours. Food has no significant effect on the extent of absorption of hydrocodone. The mean plasma half-life of hydrocodone is approximately 4 hours.

#### Guaifenesin

Following a single 10 mL oral dose of 5 mg hydrocodone bitartrate and 400 mg guaifenesin administered to 36 healthy adults, the geometric mean  $C_{max}$  and  $AUC_{0-inf}$  for guaifenesin were 2.0 mcg/mL and 2.6 mcg•hr/mL, respectively. The median time to maximum concentration was about 25 minutes. The effect of food on guaifenesin systemic exposure is not considered to be clinically meaningful. The mean plasma half-life of guaifenesin is approximately 1 hour.

#### Drug interactions

When guaifenesin and hydrocodone were administered in combination, the pharmacokinetics for each component was similar to those observed when each component was administered separately.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity, and reproductive studies have not been conducted with FLOWTUSS; however, published information is available for the individual active ingredients or related active ingredients.

#### Hydrocodone

Carcinogenicity studies were conducted with codeine, an opiate related to hydrocodone. In 2 year studies in F344/N rats and B6C3F1 mice, codeine showed no evidence of tumorigenicity at dietary doses up to 70 and 400 mg/kg/day, respectively (approximately 23 and 65 times, respectively, the MRHDD of hydrocodone on a mg/m<sup>2</sup> basis).

#### Guaifenesin

Carcinogenicity, genotoxicity, or reproductive toxicology studies have not been conducted with guaifenesin.

## 14 CLINICAL STUDIES

Efficacy studies were not conducted with FLOWTUSS. Efficacy of FLOWTUSS is based on demonstration of bioequivalence to the individual comparator products [see *Clinical Pharmacology* (12.3)].

## 16 HOW SUPPLIED/STORAGE AND HANDLING

FLOWTUSS (hydrocodone bitartrate and guaifenesin) oral solution is supplied as a violet-colored, black raspberry flavored liquid containing 2.5 mg hydrocodone bitartrate and 200 mg guaifenesin in each 5 mL. It is available in:

White HDPE bottles of 16 fl. oz. (473 mL): NDC 24470-916-16

White HDPE bottles of 4 fl. oz. (118 mL): NDC 24470-916-04

Store solution at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Dispense in a tight, light-resistant container, as defined in the USP, with a child-resistant closure.

## 17 PATIENT COUNSELING INFORMATION

### Overdosage

Advise patients not to increase the dose or dosing frequency of FLOWTUSS because serious adverse events such as respiratory depression may occur with overdosage [see *Warnings and Precautions* (5.2) and *Overdosage* (10)].

### Dosing

Advise patients to measure FLOWTUSS with an accurate milliliter measuring device. Patients should be informed that a household teaspoon is not an accurate measuring device and could lead to overdosage, especially when half a teaspoon is measured. Patients should be advised to ask their pharmacist to recommend an appropriate measuring device and for instructions for measuring the correct dose [see *Dosage and Administration* (2) and *Warnings and Precautions* (5.10)].

### Interactions with Benzodiazepines and Other Central Nervous System Depressants

Inform patients and caregivers that potentially fatal additive effects may occur if FLOWTUSS is used with benzodiazepines or other CNS depressants, including alcohol. Because of this risk, patients should avoid concomitant use of FLOWTUSS with benzodiazepines or other CNS depressants, including alcohol [see *Warnings and Precautions* (5.1) and *Drug Interactions* (7.1)].

### Activities Requiring Mental Alertness

Advise patients to avoid engaging in hazardous tasks that require mental alertness and motor coordination such as operating machinery or driving a motor vehicle as FLOWTUSS may produce marked drowsiness [see *Warnings and Precautions* (5.5)].

### Drug Dependence

Caution patients that FLOWTUSS contains hydrocodone bitartrate and can produce drug dependence [see *Warnings and Precautions* (5.3)].

Manufactured for:

MISSION PHARMACAL COMPANY  
San Antonio, TX 78230 1355



1120A00 R0916

**MEDICATION GUIDE**  
**FLOWTUSS® (floh-tus)**  
**(hydrocodone bitartrate and guaifenesin) oral solution, C-II**

**What is the most important information I should know about FLOWTUSS?**

- Taking FLOWTUSS with benzodiazepines, or other central nervous system depressants, including alcohol can cause severe drowsiness, breathing problems (respiratory depression), coma, and death.
- FLOWTUSS can cause you to be drowsy. Avoid driving a car or operating machinery during treatment with FLOWTUSS.
- Women who breastfeed should talk to their healthcare provider before taking FLOWTUSS.
- Call your healthcare provider or get emergency medical help right away if anyone taking FLOWTUSS has any of the symptoms below:
  - increased sleepiness
  - confusion
  - difficulty breathing
  - shallow breathing
  - limpness
  - your baby has difficulty breastfeeding
- Keep FLOWTUSS in a safe place away from children. Accidental use by a child is a medical emergency and can cause death. If a child accidentally takes FLOWTUSS, get emergency medical help right away.
- FLOWTUSS can cause serious side effects, including death.
- Take FLOWTUSS exactly as prescribed by your healthcare provider. If you take the wrong dose of FLOWTUSS, you could overdose and die.
- FLOWTUSS is not for children under 18 years of age.

**What is FLOWTUSS?**

- FLOWTUSS is a prescription medicine used to treat cough and loosen mucus that you can have with the common cold in adults. FLOWTUSS contains 2 medicines, hydrocodone and guaifenesin. Hydrocodone is a narcotic cough suppressant. Guaifenesin is an expectorant.
- **FLOWTUSS is a federal controlled substance (C-II) because it contains hydrocodone that can be abused or lead to dependence.** Keep FLOWTUSS in a safe place to prevent misuse and abuse. Selling or giving away FLOWTUSS may harm others, and is against the law. Tell your healthcare provider if you have abused or been dependent on alcohol, prescription medicines or street drugs.
- FLOWTUSS is not for children under 18 years of age. It is not known if FLOWTUSS is safe and effective in children.

**Who should not take FLOWTUSS?**

- **Do not** take FLOWTUSS if you are allergic to any of the ingredients in FLOWTUSS. See the end of this Medication Guide for a complete list of ingredients. You may have an increased risk of having an allergic reaction to FLOWTUSS if you are allergic to certain other opioid medicines.
- **Do not** take FLOWTUSS if you take a medicine for depression called a Monoamine Oxidase Inhibitor (MAOI)
  - **Do not** take an MAOI within 14 days after you stop taking FLOWTUSS.
  - **Do not** start FLOWTUSS if you stopped taking an MAOI in the last 14 days.

**Before you take FLOWTUSS, tell your healthcare provider about all of your medical conditions, including if you:**

- have lung or breathing problems
- have a drug dependence
- have had a head injury
- have pain in your stomach-area (abdomen)
- have a history of severe or persistent cough
- have prostate problems
- have problems with your urinary tract (urethral stricture)
- are pregnant or plan to become pregnant. It is not known if FLOWTUSS will harm your unborn baby. You and your healthcare provider should decide if you should take FLOWTUSS while you are pregnant.
- are breastfeeding or plan to breastfeed. Hydrocodone passes into your breast milk and may harm your baby. You and your healthcare provider should decide if you will take FLOWTUSS or breastfeed. You should not do both.
- plan to have surgery
- drink alcohol
- have kidney or liver problems
- have diabetes
- have thyroid problems, such as hypothyroidism
- have Addison's disease

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins and herbal supplements.

Taking FLOWTUSS with certain other medicines can cause side effects or affect how well FLOWTUSS or the other medicines work. Do not start or stop other medicines without talking to your healthcare provider.

Especially tell your healthcare provider 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) and tricyclics
- take medicines for asthma, stomach or intestine problems.

Ask your healthcare provider if you are not sure if you take one of these medicines.

### How should I take FLOWTUSS?

- Take FLOWTUSS exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much FLOWTUSS to take and when to take it. Do not change your dose without talking to your healthcare provider.
- Take FLOWTUSS by mouth only.
- FLOWTUSS should be taken using an accurate milliliter measuring device.
- Ask your pharmacist to give you a measuring device to help you measure the correct amount of FLOWTUSS. **Do not use a household teaspoon to measure your medicine. You may accidentally take too much.**
- If you take too much FLOWTUSS, call your healthcare provider or go to the nearest hospital emergency room right away.

### What should I avoid while taking FLOWTUSS?

- FLOWTUSS can cause you to be drowsy. Avoid driving a car or operating machinery during treatment with FLOWTUSS.
- Avoid drinking alcohol during treatment with FLOWTUSS. Drinking alcohol can increase your chances of having serious side effects.

### What are the possible side effects of FLOWTUSS?

**FLOWTUSS may cause serious side effects, including:**

**See “What is the most important information I should know about FLOWTUSS?”**

- **Breathing problems (respiratory depression) which can lead to death.** Call your healthcare provider or get emergency treatment right away if you are sleeping more than usual, have shallow or slow breathing, or confusion.
- **Physical dependence or abuse.** Take FLOWTUSS exactly as your healthcare provider tells you to take it. Stopping FLOWTUSS suddenly could cause withdrawal symptoms.
- **Bowel problems including constipation or stomach pain.**
- **Increased intracranial pressure.**

The most common side effects of FLOWTUSS include:

- |                        |                            |
|------------------------|----------------------------|
| • sleepiness           | • dizziness                |
| • confusion            | • headache                 |
| • nausea and vomiting  | • decreased blood pressure |
| • difficulty urinating | • diarrhea                 |
| • trouble breathing    | • hot flush                |

These are not all the possible side effects of FLOWTUSS.

**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 FLOWTUSS?

- Store FLOWTUSS at room temperature between 20° to 25°C (68° to 77°F).
- Keep FLOWTUSS in a tightly closed, child-resistant container and out of the light.
- Safely throw away medicine that is out of date or no longer needed.
- **Keep FLOWTUSS and all medicines out of the reach of children.**

### General information about the safe and effective use of FLOWTUSS.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FLOWTUSS for a condition for which it was not prescribed. Do not give FLOWTUSS to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about FLOWTUSS that is written for health professionals.

### What are the ingredients in FLOWTUSS?

**Active Ingredients:** hydrocodone bitartrate and guaifenesin.

**Inactive Ingredients:** black raspberry flavor, citric acid, D&C Red #33, FD&C Blue #1, glycerin, methylparaben, polyethylene glycol, propylparaben, purified water, saccharin sodium, sodium citrate, and sorbitol.

Manufactured for: MISSION PHARMACAL COMPANY San Antonio, TX 78230 1355  
For more information, go to [www.flowtuss.com](http://www.flowtuss.com) or call 1-800-298-1087.

This Medication Guide has been approved by the U.S. Food and Drug Administration.



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