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.

RECENT MAJOR CHANGES

Boxed Warning	09/2016
Warnings and Precautions, Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants (5.1)	09/2016

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*.

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: 09/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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 inhibitors (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 (5.2)* and *Overdosage (10)*]
- Drug dependence [*see Warnings and Precautions (5.3)* and *Drug Abuse and Dependence (9.3)*]
- Increased intracranial pressure [*see Warnings and Precautions (5.4)*]
- Decreased mental alertness with impaired mental and/or physical abilities [*see Warnings and Precautions (5.5)*]
- Paralytic ileus [*see Warnings and Precautions (5.6)*]

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 FLOWTUSS.

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^2 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^2 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^2 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 β-(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

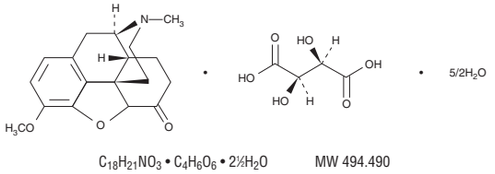
FLOWTUSS (hydrocodone bitartrate and guaifenesin) oral solution contains hydrocodone bitartrate (a centrally-acting opioid antitussive) and guaifenesin (an expectorant).

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

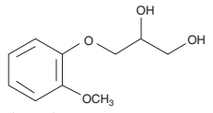
Hydrocodone bitartrate is a centrally-acting opioid antitussive and analgesic. It is affected by light and occurs as fine white crystals or crystalline powder which is derived from the opium alkaloid, thebaine. Its chemical name is morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl-, (5α)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate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



$C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2½H_2O$ MW 494.490

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:



$C_{10}H_{14}O_4$ MW 198.22

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 $AUC_{0\text{-}inf}$ 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 $AUC_{0\text{-}inf}$ 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^2 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** 0178-3482-16

White HDPE bottles of 4 fl. oz. (118 mL): **NDC** 0178-3482-04

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

Please see accompanying Medication Guide. Instruct patients to read the Medication Guide before starting therapy with FLOWTUSS and to reread it each time the prescription is renewed.

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)*].

Mission® PHARMACAL

Manufactured for:
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