

OBREDON- hydrocodone bitartrate and guaifenesin solution
NOVOTEC PHARMA LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OBREDON (hydrocodone bitartrate and guaifenesin) Oral Solution safely and effectively. See full prescribing information for OBREDON (hydrocodone bitartrate and guaifenesin) Oral Solution.

OBREDON (hydrocodone bitartrate and guaifenesin) Oral Solution for oral administration 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	10/2016
Risks from Concomitant Use with Benzodiazepines or other CNS Depressants (5.1)	10/2016

----- **INDICATIONS AND USAGE** -----

OBREDON Oral Solution is a combination product containing an opioid antitussive and expectorant 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. (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 OBREDON Oral Solution 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 OBREDON Oral Solution. (4)
- Patients receiving monoamine oxidase inhibitor (MAOI) therapy or within 14 days of stopping such therapy. (4)

----- **WARNINGS AND PRECAUTIONS** -----

- 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 OBREDON Oral Solution include: Dizziness, headache, sedation, nausea, and decreased blood pressure. (6)

To report SUSPECTED ADVERSE REACTIONS, contact ABER Pharmaceuticals, LLC. at tel: 1-855-461-5102; www.obredon.com or FDA at 1-800-FDA-1088; www.fda.gov/medwatch.

----- **DRUG INTERACTIONS** -----

- Opioids, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol): Avoid using with OBREDON Oral Solution; 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 Medication Guide.

Revised: 9/2016

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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

OBREDON Oral Solution 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 Pediatric Use (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 OBREDON Oral Solution by the oral route only. Measure OBREDON Oral Solution with an accurate milliliter measuring device. Do not use a household teaspoon to measure the dose [see Dosing (5.10)] .

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

OBREDON Oral Solution is contraindicated in:

- Patients with known hypersensitivity to hydrocodone bitartrate, guaifenesin, or any of the inactive ingredients of OBREDON Oral Solution.
- 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 OBREDON Oral Solution, 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 OBREDON Oral Solution 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 OBREDON Oral Solution, 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 OBREDON Oral Solution 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 OBREDON Oral Solution. Prescribe and administer OBREDON Oral Solution 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 OBREDON Oral Solution should be avoided in these patients.

5.5 Activities Requiring Mental Alertness

Hydrocodone bitartrate, one of the active ingredients in OBREDON Oral Solution, 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 OBREDON Oral Solution. Concurrent use of OBREDON Oral Solution 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

OBREDON Oral Solution 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 OBREDON Oral Solution in patients taking anticholinergic medications [see *DRUG INTERACTIONS (7.3)*].

5.8 Co-administration with MAOIs or Tricyclic Antidepressants

OBREDON Oral Solution should not be used in patients receiving 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

OBREDON Oral Solution 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 OBREDON Oral Solution 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

OBREDON Oral Solution 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

OBREDON Oral Solution should be used with caution in patients with severe renal impairment. [see *Renal Impairment (8.6)*]

5.13 Hepatic Impairment

OBREDON Oral Solution should be used with caution in patients with severe hepatic impairment [see *Hepatic Impairment (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 OBREDON Oral Solution in the clinical setting include the following: Central Nervous System: headache, dizziness, sedation (somnia); Gastrointestinal System: nausea, diarrhea; Cardiovascular System: decreased blood pressure; Vascular System: hot flush.

7 DRUG INTERACTIONS

No specific interaction studies have been conducted with OBREDON Oral Solution.

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 concomitantly with OBREDON Oral Solution 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 OBREDON Oral Solution 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 a 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 OBREDON Oral Solution in pregnant women. Reproductive toxicity studies have not been conducted with OBREDON Oral Solution; 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, OBREDON Oral Solution 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 $\text{mg}/\text{kg}/\text{day}$ 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 $\text{mg}/\text{kg}/\text{day}$, respectively), produced no adverse developmental effects.

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.

8.2 Labor and Delivery

As with all opioids, administration of OBREDON Oral Solution 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 OBREDON Oral Solution 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 OBREDON Oral Solution, 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 OBREDON Oral Solution 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 OBREDON Oral Solution in geriatric populations. Other reported clinical experience with the individual active ingredients of OBREDON Oral Solution 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

OBREDON Oral Solution should be given with caution in patients with severe impairment of renal function.

8.7 Hepatic Impairment

OBREDON Oral Solution should be given with caution in patients with severe impairment of hepatic function.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

OBREDON Oral Solution 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 OBREDON Oral Solution, 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, OBREDON Oral Solution should be prescribed and administered with caution.

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 OBREDON Oral Solution.

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 OBREDON Oral Solution 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

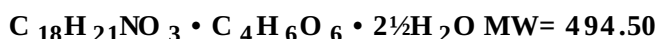
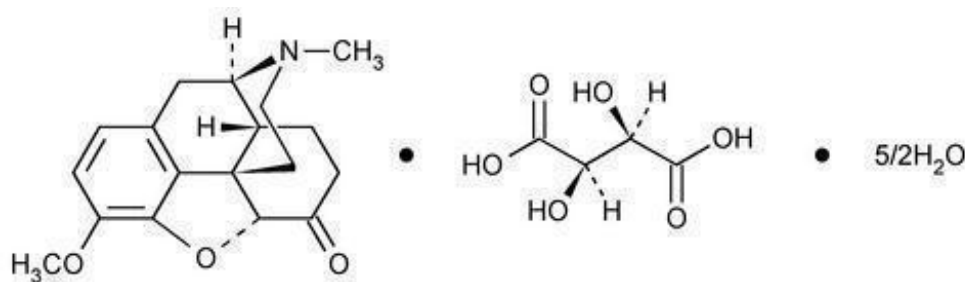
OBREDON Oral Solution contains hydrocodone bitartrate (a centrally-acting opioid antitussive) and guaifenesin (an expectorant).

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

OBREDON Oral Solution also contains: artificial raspberry flavor, citric acid, glycerin, methylparaben, potassium citrate, potassium sorbate, propylene glycol, propylparaben, purified water, and saccharin sodium.

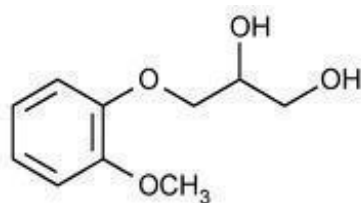
11.1 Hydrocodone Bitartrate

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 α)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate (1:1), hydrate (2:5). It is also known as 4,5 α -Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5); and may be represented by the following structural formula:



11.2 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 single dose administration of 10 mL OBREDON Oral Solution are equivalent to 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 OBREDON Oral Solution administered to 36 healthy adults (19-74 years), the geometric mean C_{max} and AUC_{0-inf} for hydrocodone were 12.6 ng/ml and 80.9 ng·hr/ml, respectively. The median time to maximum concentration for hydrocodone was about 1.25 hours. Food has no significant effect on the extent of absorption of hydrocodone. The mean plasma half-life of hydrocodone is approximately 5 hours.

Guaifenesin: Following a single 10 mL oral dose of OBREDON Oral Solution administered to 57 healthy adults (19-74 years), the geometric mean C_{max} and AUC_{0-inf} for guaifenesin were 3.7 mcg/ml and 4.2 mcg·hr/ml, respectively. The median time to maximum concentration was about 20 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 were 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 OBREDON Oral Solution; 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/m² basis).

Guaifenesin:

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

14 CLINICAL STUDIES

Efficacy studies were not conducted with OBREDON Oral Solution. Efficacy of OBREDON Oral Solution is based on demonstration of bioequivalence to the individual comparator products [see *CLINICAL PHARMACOLOGY (12.3)*].

16 HOW SUPPLIED/STORAGE AND HANDLING

OBREDON Oral Solution is supplied as a clear, 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 69166-523-16 (raspberry flavored)

White HDPE bottles of 4 fl oz. (118 mL): NDC 69166-523-04 (raspberry flavored)

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

[See FDA-Approved Patient Labeling]

Overdosage

Advise patients not to increase the dose or dosing frequency of OBREDON Oral Solution 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 OBREDON Oral Solution 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 OBREDON Oral Solution is used with benzodiazepines or other CNS depressants, including alcohol. Because of this risk, patients should avoid concomitant use of OBREDON Oral Solution with benzodiazepines or other CNS depressants, including alcohol [see WARNINGS AND PRECAUTIONS (5.1), 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 OBREDON Oral Solution may produce marked drowsiness [see WARNINGS AND PRECAUTIONS (5.5)].

Drug Dependence

Caution patients that OBREDON Oral Solution contains hydrocodone bitartrate and can produce drug dependence [see WARNINGS AND PRECAUTIONS (5.3)].

For Medical Information

Contact Medical Affairs Department

Phone: 1-855-461-5102

Manufactured for:

Accelis Pharma

East Windsor, NJ 08520



MEDICATION GUIDE

OBREDON Oral Solution (Oh-brě-don Oral Solution)

(hydrocodone bitartrate and guaifenesin) Each 5 mL contains hydrocodone bitartrate, USP, 2.5 mg; and guaifenesin, USP, 200 mg. C-II

What is the most important information I should know about OBREDON Oral Solution?

- Taking OBREDON Oral Solution with benzodiazepines, or other central nervous system depressants, including alcohol can cause severe drowsiness, breathing problems (respiratory depression), coma, and death.
- OBREDON Oral Solution can cause you to be drowsy. Do not drive a car or operate machinery until you know how OBREDON Oral Solution affects you. OBREDON Oral Solution can slow your thinking and motor skills, and may affect your vision.
- Women who breastfeed should talk to their healthcare provider before taking OBREDON Oral Solution.
- Call your healthcare provider or get emergency medical help right away if anyone taking OBREDON Oral Solution has any of the symptoms below:
 - increased sleepiness
 - confusion
 - difficulty breathing
 - shallow breathing
 - limpness
 - your baby has difficulty breastfeeding
- Keep OBREDON Oral Solution 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 OBREDON Oral Solution, get emergency medical help right away.
- OBREDON Oral Solution can cause serious side effects, including death.
- Take OBREDON Oral Solution exactly as prescribed by your healthcare provider. If you take the wrong dose of OBREDON Oral Solution, you could overdose and die.
- OBREDON Oral Solution is not for children under 18 years of age.

What is OBREDON Oral Solution?

- OBREDON Oral Solution is a prescription medicine used to treat a cough and to loosen mucus associated with the common cold, in patients 18 years and older. OBREDON Oral Solution contains two medicines, hydrocodone and guaifenesin. Hydrocodone is a narcotic cough suppressant. Guaifenesin is an expectorant.
- **OBREDON Oral Solution is a federal controlled substance (C-II) because it contains hydrocodone that can be abused or lead to dependence.** Keep OBREDON Oral Solution in a safe place to prevent misuse and abuse. Selling or giving away OBREDON Oral Solution 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.
- OBREDON Oral Solution is not for children under 18 years of age. It is not known if OBREDON Oral Solution is safe and effective in children.

Who should not take OBREDON Oral Solution?

- Do not take OBREDON Oral Solution if you are allergic to any of the ingredients in OBREDON Oral Solution. 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 OBREDON Oral Solution if you are allergic to certain other opioid medicines.
- Do not take OBREDON Oral Solution 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 OBREDON Oral Solution.

- **Do not** start OBREDON Oral Solution if you stopped taking an MAOI in the last 14 days.

Before you take OBREDON Oral Solution, tell your healthcare provider about all of your medical conditions, including if you:

- ◦ have a drug dependence
- have lung or breathing problems
- 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)
- plan to have surgery
- drink alcohol
- have kidney or liver problems
- have diabetes
- have thyroid problems, such as hypothyroidism
- are pregnant or plan to become pregnant. It is not known if OBREDON Oral Solution will harm your unborn baby. You and your healthcare provider should decide if you should take OBREDON Oral Solution while you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if OBREDON Oral Solution passes into your breast milk. You and your healthcare provider should decide if you will take OBREDON Oral Solution or breastfeed. You should not do both.

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

Taking OBREDON Oral Solution with certain other medicines can cause side effects or affect how well OBREDON Oral Solution 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
- The use of MAOIs or tricyclic antidepressants with hydrocodone bitartrate may increase the effect of either the antidepressant or hydrocodone.

How should I take OBREDON Oral Solution?

- Take OBREDON Oral Solution exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much OBREDON Oral Solution to take and when to take it. Do not change your dose without talking to your healthcare provider.
- Administer OBREDON Oral Solution by the oral route only.
- Ask your pharmacist to give you a measuring device to help you measure the correct amount of OBREDON Oral Solution. Do not use a household teaspoon to measure your medicine. You may accidentally take too much.
- If you take too much OBREDON Oral Solution, call your healthcare provider or go to the nearest hospital emergency room right away.

What should I avoid while taking OBREDON Oral Solution?

- OBREDON Oral Solution can cause you to be drowsy. Do not drive a car or operate machinery while you take OBREDON Oral Solution until you know how it affects you.
- Avoid drinking alcohol while taking OBREDON Oral Solution. Drinking alcohol can increase your

chances of having serious side effects.

What are the possible side effects of OBREDON Oral Solution?

OBREDON Oral Solution may cause serious side effects, including:

- **See “What is the most important information I should know about OBREDON Oral Solution?”**
- **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 OBREDON Oral Solution exactly as your healthcare provider tells you to take it. Stopping OBREDON Oral Solution suddenly could cause withdrawal symptoms.
- **Bowel problems including constipation or stomach pain.**

The most common side effects of OBREDON Oral Solution include:

- Sleepiness
- Confusion
- nausea and vomiting
- difficulty urinating
- trouble breathing

These are not all the possible side effects of OBREDON Oral Solution.

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 OBREDON Oral Solution?

- Store OBREDON Oral Solution at room temperature between 68°F to 77°F (20°C to 25°C).
- Safely throw away medicine that is out of date or no longer needed.
- **Keep OBREDON Oral Solution and all medicines out of the reach of children.**

General information about the safe and effective use of OBREDON Oral Solution.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use OBREDON Oral Solution for a condition for which it was not prescribed. Do not give OBREDON Oral Solution 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 OBREDON Oral Solution that is written for health professionals.

What are the ingredients in OBREDON Oral Solution?

Active ingredients: Hydrocodone Bitartrate and Guaifenesin

Inactive ingredients: artificial raspberry flavor, citric acid, glycerin, methylparaben, potassium citrate, potassium sorbate, propylene glycol, propylparaben, purified water, and saccharin sodium

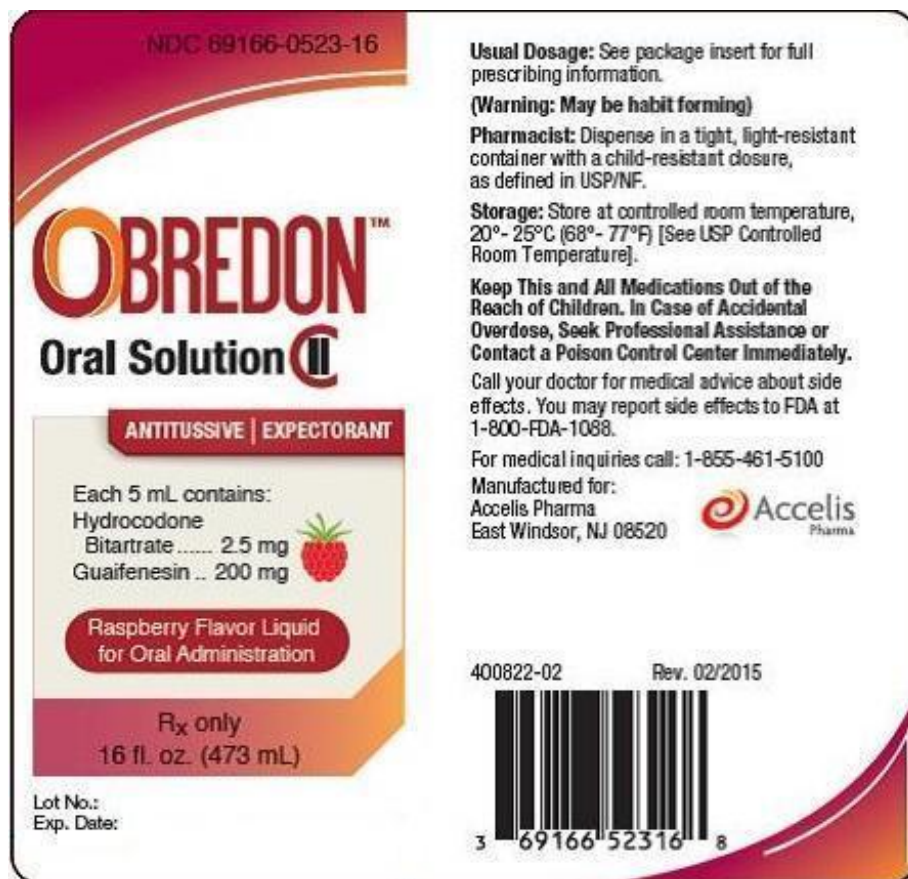
Manufactured for:

Accelis Pharma, East Windsor, NJ 08520

For more information, go to www.obredon.com or call 1-855-461-5102.

This Medication Guide has been approved by the U.S. Food and Drug Administration Issued: 09/2016

Principal Display Panel-16 fl oz. Bottle



16 fl oz. Bottle Label

NDC 69166-523-16

OBREDON (hydrocodone bitartrate and guaifenesin) Oral Solution CII

2.5 mg/ 200 mg per 5 mL

Contains:

Hydrocodone Bitartrate ... 2.5 mg/5 mL

WARNING: May be habit forming.

Guaifenesin 200 mg/5 mL

Rx Only

16 fl oz. (473 mL)

USUAL DOSAGE: See Package Insert for Complete Dosage Recommendations.

Dispense in a tight, light-resistant container with a child-resistant closure.

WARNING: KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

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

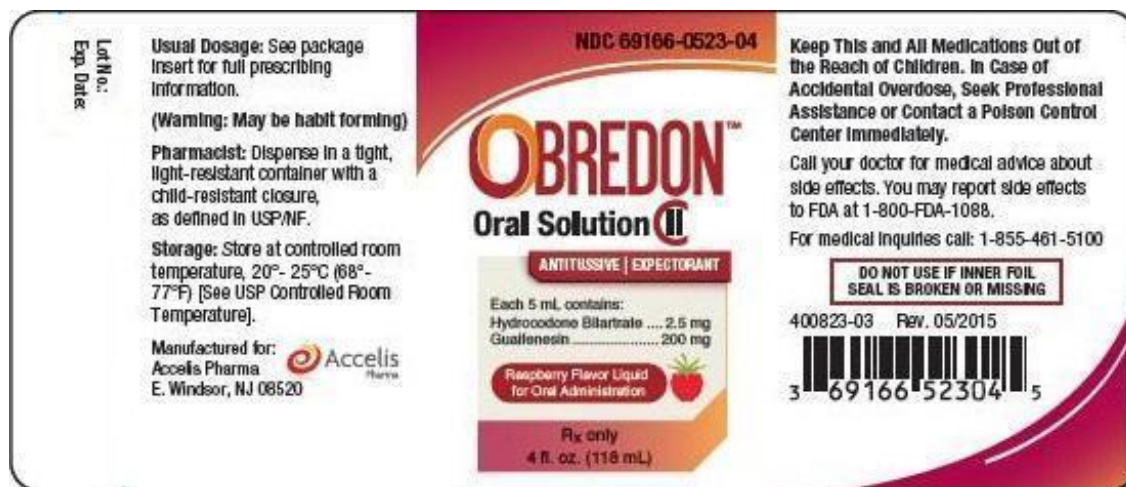
Tamper evident by foil seal under cap. Do not use if foil seal is broken or missing.

Manufactured for:
Accelis Pharma
East Windsor, NJ 08520



400822 05/2015

Principal Display Panel-4 fl oz. Bottle



4 fl oz. Bottle Label

NDC 69166-523-04

OBREDON (hydrocodone bitartrate and guaifenesin) Oral Solution CII

2.5 mg/ 200 mg per 5 mL

Contains:

Hydrocodone Bitartrate ... 2.5 mg/5 mL

WARNING: May be habit forming.

Guaifenesin 200 mg/5 mL

Rx Only

4 fl oz. (118 mL)

USUAL DOSAGE: See Package Insert for Complete Dosage Recommendations.

Dispense in a tight, light-resistant container with a child-resistant closure.

WARNING: KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

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

Tamper evident by foil seal under cap. Do not use if foil seal is broken or missing.

Manufactured for:

Accelis Pharma
East Windsor, NJ 08520



400823 05/2015

OBREDON

hydrocodone bitartrate and guaifenesin solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69166-523
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDROCODONE BITARTRATE (UNII: NO70W886KK) (HYDROCODONE - UNII:6YKS4Y3WQ7)	HYDROCODONE BITARTRATE	2.5 mg in 5 mL
GUAIFENESIN (UNII: 495W7451VQ) (GUAIFENESIN - UNII:495W7451VQ)	GUAIFENESIN	200 mg in 5 mL

Inactive Ingredients

Ingredient Name	Strength
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
GLYCERIN (UNII: PDC6A3C0OX)	
METHYL PARABEN (UNII: A2I8C7HI9T)	
POTASSIUM CITRATE (UNII: EE90ONI6FF)	
POTASSIUM SORBATE (UNII: 1VPU26JZZ4)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
PROPYL PARABEN (UNII: Z8IX2SC1OH)	
WATER (UNII: 059QF0K00R)	
SACCHARIN SODIUM (UNII: SB8ZUX40TY)	

Product Characteristics

Color		Score	
Shape		Size	
Flavor	RASPBERRY	Imprint Code	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69166-523-16	473 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/30/2014	06/30/2018
2	NDC:69166-523-04	118 mL in 1 BOTTLE; Type 0: Not a Combination Product	12/30/2014	06/30/2018

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA205474	12/30/2014	06/30/2018

Labeler - NOVOTEC PHARMA LLC (079460110)