Each tablet contains Hydrocodone Bitartrate 2.5 mg, Acetaminophen 325 mg.

Usual adult dosage: One or two tablets every four to six hours, as needed for pain. Total daily dosage should not exceed eight tablets. See insert for full prescribing information.

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

Store at 20° to 25°C (68° to 77°F) [See USP

Controlled Room Temperature].

Keep this and all medication out of the reach of children.

Manufactured by:

Watson Laboratories, Inc.
Corona, CA 92879 USA

Distributed by: Watson Pharma, Inc.
Each tablet contains: Hydrocodone Bitartrate 2.5 mg, Acetaminophen 325 mg

Usual adult dosage: One or two tablets every four to six hours, as needed for pain. Total daily dosage should not exceed eight tablets. See insert for full prescribing information.

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

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

Keep this and all medication out of the reach of children.

Manufactured by Watson Laboratories, Inc.
Corona, CA 92880 USA 220085-1
Each tablet contains: Hydrocodone Bitartrate 7.5 mg, Acetaminophen 325 mg

Usual adult dosage: One tablet every four to six hours, as needed for pain. Total daily dosage should not exceed six tablets. See insert for full prescribing information.

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

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

Keep this and all medications out of the reach of children.

Manufactured by: Watson Laboratories, Inc. Corona, CA 92880 USA

Distributed by: Watson Pharma, Inc.
Each tablet contains: Hydrocodone Bitartrate 10 mg, Acetaminophen 325 mg

Usual adult dosage: One tablet every four to six hours, as needed for pain. Total daily dosage should not exceed six tablets. See insert for full prescribing information.

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

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

Keep this and all medication out of the reach of children.

Manufactured by: Watson Laboratories, Inc. Corona, CA 92880 USA 222107-1

Distributed by: Watson Pharma, Inc.
NORCO® 10/325
Hydrocodone Bitartrate and Acetaminophen Tablets, USP

10 mg/325 mg

Each tablet contains: Hydrocodone bitartrate 10 mg, Acetaminophen 325 mg

Rx only

500 Tablets

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

Usual adult dosage: One tablet every four to six hours, as needed for pain. Total daily dosage should not exceed six tablets.

See insert for full prescribing information.

Keep this and all medication out of the reach of children.

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

Manufactured by:
Watson Laboratories, Inc.
Corona, CA 92880 USA

Distributed by:
Watson Pharma, Inc.
 Parsippany, NJ 07054 USA
NDC 52544-162-05

NORCO® 7.5/325
Hydrocodone Bitartrate and
Acetaminophen Tablets, USP

7.5 mg/325 mg

Each tablet contains: Hydrocodone bitartrate 7.5 mg,
Acetaminophen 325 mg

Rx only

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

Usual adult dosage: One tablet every four to
six hours, as needed for pain. Total daily dosage
should not exceed 16 tablets.

See insert for full prescribing information.

Keep this and all medication out of the reach
of children.

Store at 24° to 25°C (75° to 77°F)
([see USP Controlled Room Temperature]).

Manufactured by:
Watson Laboratories, Inc.
Corona, CA 92880 USA

Distributed by:
Watson Pharma, Inc.
 Parsippany, NJ 07054 USA

500 Tablets
BOXED WARNING
Hepatotoxicity
Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen containing product.

DESCRIPTION
Hydrocodone bitartrate and acetaminophen is supplied in tablet form for oral administration. Hydrocodone bitartrate is an opioid analgesic and antitussive and occurs as fine, white, odorless, crystalline powder. It is affected by light. The chemical name is 4,5a-Epiprocyanofuran-3,8-diol [2R-(2a,3b,4a,5a)] hydrochloride (HCl) hydrate (C20H22NO4·HCl·2H2O). It has the following structural formula:

Acetaminophen, 4'-Hydroxyacetaminophen, a slightly bitter, white, odorless, crystalline powder is a non-ionic, non-salicylate analgesic and antipyretic. It has the following structural formula:

Each hydrocodone bitartrate and Acetaminophen tablet contains:
Hydrocodone Bitartrate, USP 2.5 mg
Acetaminophen, USP 25 mg

CLINICAL PHARMACOLOGY
Hydrocodone is a semisynthetic narcotic analgesic and antitussive with multiple actions qualitatively similar to those of codeine. Most of these involve the central nervous system (CNS) and smooth muscle. The precise mechanism of action of hydrocodone and other opioids is not known, although it is believed to relate to the existence of opiate receptors in the central nervous system. In addition to analgesia, narcotics may produce dysrhythmias, changes in mood and mental clouding.

The analgesic action of acetaminophen involves peripheral influence, but the specific mechanism is as yet undetermined. Antipyretic activity is mediated through hypothalamic heat regulating centers. Acetaminophen inhibits prostaglandin synthesis. Therapeutic doses of acetaminophen have negligible effect on the cardiac conduction or respiratory systems; however, toxic doses may cause circulatory failure and papillary muscle dysrhythmias.

Pharmacokinetics: The behavior of the individual components is described below.

Hydrocodone: Following a 10 mg oral dose of hydrocodone administered to five adult male subjects, the mean peak concentration was 25.9 ± 2.9 ng/ml. Maximum serum levels were achieved at 1.3 ± 0.3 hours and the half-life was determined to be 3.9 ± 0.3 hours. Hydrocodone exhibits a complex pattern of metabolism including O-demethylation, N-demethylation and O-oxidation to the corresponding 6-O and 4-O-hydroxy metabolites. See OVERDOSAGE for toxicity information.

Acetaminophen: Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. The plasma half-life is 1.25 to 3 hours, but may be increased by liver damage and following overdosage. Elimination of acetaminophen is principally by liver metabolism (conjugation) and a small amount by excretion of metabolites. Approximately 15% of an oral dose appears in the urine within 24 hours of administration, most as the glucuronide conjugate, with small amounts of other conjugates and unchanged drug. See OVERDOSAGE for toxicity information.

INDICATIONS AND USAGE
Hydrocodone and acetaminophen tablets are indicated for the relief of moderate to severe pain.

CONTRAINDICATIONS
This product should not be administered to patients who have previously exhibited hypersensitivity to hydrocodone or acetaminophen.

Patients known to be hypersensitive to other opioids may exhibit cross-sensitivity to hydrocodone.

WARNINGS
Hepatotoxicity
Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen containing product. The excessive intake of acetaminophen may be intentional in the form of an overdose or unintentional as patients attempting to obtain more pain relief or unknowingly take other acetaminophen containing products.

The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen.

Instruct patients to look for acetaminophen or APAP on package labels and to not use more than one product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

Serious skin reactions
Rarely acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs of serious skin reactions, and the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Hypersensitivity/nephropathy
There have been post-marketing reports of hypersensitivity and nephropathy associated with the use of acetaminophen. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, pruritus, and vomiting. There were infrequent reports of life-threatening anaphylaxis requiring emergency medical attention. Instruct patients to discontinue Hydrocodone Bitartrate and Acetaminophen Tablets, USP immediately and seek medical care if they experience these symptoms. Do not prescribe Hydrocodone Bitartrate and Acetaminophen Tablets, USP for patients with acetaminophen allergy.

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

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

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

PRECAUTIONS
General: Special Risk Patients: As with any narcotic analgesic agent, hydrocodone bitartrate and acetaminophen tablets should be used with caution in elderly or debilitated patients, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostate hyperplasia or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

Drug/Herbal: Hydrocodone may cause the cough reflex, and as with all narcotics, cough should be exercised when hydrocodone bitartrate and acetaminophen tablets are used post-operatively and in patients with pulmonary disease.

Information for Patients/Caregivers
- Do not take Hydrocodone Bitartrate and Acetaminophen Tablets, USP if you are allergic to any of its ingredients.
- If you develop signs of allergy such as a rash or difficulty breathing stop taking Hydrocodone Bitartrate and Acetaminophen Tablets, USP and contact your healthcare provider immediately.
- Do not take more than 4000 milligrams of acetaminophen per day. Call your doctor if you took more than the recommended dose.
- Hydrocodone, like all narcotics, may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery; patients should be cautioned accordingly.
- Alcohol and other CNS depressants may produce an additive CNS depression, when taken with this combination product, and should be avoided.

Drug/Laboratory: When the plasma levels of hydrocodone are high (e.g. 1000 ng/ml or above) the plasma protein binding of other drugs may be decreased.

Drug/ Laboratory Test Interactions: Acetaminophen may produce false-positive test results for urinary 5-hydroxyindoleacetic acid.

Carbohydrase, Hemoglobin, Impairment of Fertility: No adverse effects have been documented in animals to determine whether hydrocodone or acetaminophen has a potential for carcinogenesis, mutagenesis, or impairment of fertility.

Pregnancy: Teratogenic Effects: Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. Hydrocodone bitartrate and acetaminophen tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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

Labor and Delivery: As with all narcotics, administration of this product to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.
Serious overdose with hydrocodone is characterized by respiratory depression, potentially lethal polydrug overdose, and consultation with a regional poison control center is recommended. Immediate treatment includes supporting of cardiorespiratory function and measures to reduce drug absorption. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered.

For hydrocodone overdose, primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including hydrocodone. Since the duration of action of hydrocodone may exceed that of the antagonist, the patient should be kept under continued surveillance, and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. A narcotic antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Gastric decontamination with activated charcoal should be administered just prior to N-acetylcysteine (NAC) to decrease systemic absorption if acetaminophen ingestion is known or suspected to have occurred within a few hours of presentation. Serum acetaminophen levels should be obtained immediately if the patient presents 4 hours or more after ingestion to assess potential risk of hepatotoxicity; acetaminophen levels drawn less than 4 hours post-ingestion may be misleading. To obtain the best possible outcome, NAC should be administered as soon as possible where impending or evolving liver injury is suspected. Intravenous NAC may be administered when circumstances preclude oral administration.

Vigorous supportive therapy is required in severe intoxication. Procedures to limit the continuing absorption of the drug must be readily performed since the hepatic injury is dose dependent and occurs early in the course of intoxication.

**Dosage and Administration**

Dosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related.

**How Supplied**

Hydrocodone Bitartrate and Acetaminophen Tablets USP are available as:

2.5 mg/325 mg 2.5 mg hydrocodone bitartrate and 325 mg acetaminophen, capsule-shaped, white tablets, debossed with 2171 on one side, supplied in bottles of 100 and 500.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light-resistant container with a child-resistant closure.

Manufactured by: Watson Laboratories, Inc., Corona, CA 92880 USA

Distributed by: Watson Pharma, Inc., Parsippany, NJ 07054 USA

Revised: August 2014
Acetaminophen, 3-Isopropylphenylacetamide, a slightly bitter, white, odorless, crystalline powder, is non-toxic, non-sensitizing, and antipyretic. It has the following structural formula:

**Acetaminophen**: 

```
  +-----+     +-----+     +-----+     +-----+     +-----+
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  +-----+     +-----+     +-----+     +-----+     +-----+ 
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  |     |     |     |     |     |     |     |
  +-----+     +-----+     +-----+     +-----+     +-----+ 

CH3
CH3
CH3
```

Hydrocodone Bitartrate and Acetaminophen Tablets USP for oral administration are available in a variety of strengths as described in the following table.

<table>
<thead>
<tr>
<th>Strength</th>
<th>Bitartrate</th>
<th>Acetaminophen</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5 mg/100 mg</td>
<td>7.5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>15 mg/200 mg</td>
<td>15 mg</td>
<td>20 mg</td>
</tr>
</tbody>
</table>

In addition, each tablet contains the following inactive ingredients: microcrystalline cellulose, croscarmellose sodium and magnesium stearate. Meets USP Dissolution Test 1.

**CLINICAL PHARMACOLOGY**

Hydrocodone is a semisynthetic narcotic analgesic and antitussive with multiple actions qualitatively similar to those of codeine. Most of these involve the central nervous system and smooth muscle. The precise mechanism of action of hydrocodone and other opiates is not known, although it is believed to relate to the existence of opiate receptors in the central nervous system. In addition to analgesics, narcotics may produce drowsiness, changes in mood and mental clouding.

The analgesic action of acetaminophen involves peripheral influences, but the specific mechanism is as yet undetermined. Antipyretic activity is mediated through hypothalamic heat regulating centers. Acetaminophen inhibits prostaglandin synthesis. Therapeutic doses of acetaminophen have negligible effects on the cardiovascular or respiratory systems; however, toxic doses may cause circulatory failure and rapid, shallow breathing.

**Pharmacokinetics:**

Hydrocodone: Following a 10 mg oral dose of hydrocodone administered to five adult male subjects, the mean peak concentration was 22.6 ± 5.2 mg/L. Maximum serum levels were achieved at 1.3 ± 0.2 hours and the half-life was determined to be 5.8 ± 0.2 hours. Hydrocodone exhibits a complex pattern of metabolism including O-dealkylation, N-demethylation and 4-hydroxylation to the corresponding 4a- and 6a-hydroxy metabolites. See OVERDOSAGE for toxicity information.

Acetaminophen: Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. The plasma half-life is 1.5 to 3 hours, but may be increased by liver damage and following overdosage. Elimination of acetaminophen is principally by liver metabolism (conjugation) and subsequent renal excretion of metabolites. Approximately 85% of an oral dose appears in the urine within 24 hours of administration, most as the glucuronide conjugate, with small amounts of other conjugates and unchanged drug. See OVERDOSAGE for toxicity information.

**INDICATIONS AND USAGE**

Hydrocodone and acetaminophen tablets are indicated for the relief of moderate to moderately severe pain.

**CONTRAINdications**

This product should not be administered to patients who have previously exhibited hypersensitivity to hydrocodone or acetaminophen.

Patients known to be hypersensitive to other opioids may exhibit cross-sensitivity to hydrocodone.

**WARNINGS**

Hepatotoxicity

Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product. The excess intake of acetaminophen may be intentional to cause self-harm or unintentional as patients attempt to obtain more pain relief or unknowingly take other acetaminophen-containing products.

The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen.

Instruct patients to look for acetaminophen or APAP on package labels and to not use more than one product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

Serious skin reactions

Rarely, acetaminophen may cause serious skin reactions such as severe generalized urticaria or parotitis (AEUG). Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

**PRECAUTIONS**

**General:** Special Risk Patients: As with any narcotic analgesic agent, hydrocodone bitartrate and acetaminophen tablets should be used with caution in elderly or debilitated patients, and those with a history of depressive illness, diverticular disease, peptic ulcer or biliary tract disease. Patients with seizure disorders may experience exacerbation of their condition.

Cough: Excessive hydrocodone may suppress the cough reflex; as with all narcotics, caution should be exercised when hydrocodone bitartrate and acetaminophen tablets are used postoperatively in patients with pulmonary disease.

**NURSING MOTHERS:**

Acetaminophen is excreted in breast milk in small amounts, but the significance of its effects on nursing infants is not known. It is not known whether hydrocodone is excreted in human milk. Because many drugs are excreted in human milk...
and because of the potential for serious adverse reactions in nursing infants from hydrocodone and acetaminophen, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use:** Safety and effectiveness in pediatric patients have not been established.

**Genetic Use:** Clinical studies of hydrocodone bitartrate 5 mg and acetaminophen 500 mg did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Hydrocodone and the major metabolites of acetaminophen are known to be substantially excreted by the kidney. Thus the risk of toxic reactions may be greater in patients with impaired renal function due to the accumulation of the parent compound and/or metabolites in the plasma. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Hydrocodone may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of hydrocodone bitartrate and acetaminophen tablets and observed closely.

**ADVERSE REACTIONS**

The most frequently reported adverse reactions are lightheadedness, dizziness, sedation, nausea, and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include:

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

- **Gastrointestinal System:** Prolonged administration of hydrocodone bitartrate and acetaminophen tablets may produce constipation.

- **Genitourinary System:** Ureteral spasm, spasm of vesical sphincters, and urinary retention have been reported with opiates.

**Respiratory Depression:** Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brain stem respiratory center (see OVERDOSE).

**Special Senses:** Cases of hearing impairment or permanent loss have been reported predominantly in patients with chronic overdose.

- **Dermatological:** Skin rash, pruritus.

The following adverse drug events may be borne in mind as potential effects of acetaminophen: allergic reactions, rash, thrombocytopenia, agranulocytosis.

Potential effects of high dosage are listed in the OVERDOSE section.

**DRUG ABUSE AND DEPENDENCE**

Controllable Substance: Hydrocodone Bitartrate and Acetaminophen Tablets are classified as a Schedule II controlled substance.

**Abuse and Dependence:** Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, this product should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when hydrocodone bitartrate and acetaminophen tablets are used for a short time for the treatment of pain.

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 narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic therapy. Tolerance, in which increasingly large doses are required in order to produce the same degree of analgesia, is manifested initially by a shortened duration of analgesic effect, and subsequently by decreases in the intensity of analgesia. The rate of development of tolerance varies among patients.

**OVERDOSE**

Following an acute overdose, toxicity may result from hydrocodone or acetaminophen.

**Signs and Symptoms**

Hydrocodone: Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respirations, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, agenesia, circulatory collapse, cardiac arrest and death may occur.

Acetaminophen: In acetaminophen overdose: dose-dependent, potentially fatal hepatic necrosis. The most serious adverse effect. Renal tubular necrosis, hypoglycemic coma and coagulation defects may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

**Treatment:** A single or multiple drug overdose with hydrocodone and acetaminophen is a potentially lethal polydrug overdose, and consultation with a regional poison control center is recommended. Immediate treatment includes support of cardiopulmonary and measures to reduce drug absorption. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered.

For hydrocodone overdose, primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including hydrocodone. Since the duration of action of hydrocodone may exceed that of the antagonist, the patient should be kept under continued surveillance, and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. A narcotic antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

**Gastric decontamination** with activated charcoal should be administered just prior to N-acetylcysteine (NAC) to decrease systemic absorption if acetaminophen ingestion is known or suspected to have occurred within a few hours of presentation. Serum acetaminophen levels should be obtained immediately if the patient presents 4 hours or more after ingestion to assess potential risk of hepatotoxicity; acetaminophen levels drawn less than 4 hours post-ingestion may be misleading. To obtain the best possible outcome, NAC should be administered as soon as possible where impending or evolving liver injury is suspected. Intravenous NAC may be administered when circumstances preclude oral administration.

Vigorous supportive therapy is required in severe intoxication. Procedures to limit the continuing absorption of the drug must be readily performed since the hepatic injury is dose dependent and occurs early in the course of intoxication.

**DOSE AND ADMINISTRATION**

Dosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related.

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5 mg/325 mg</td>
<td>The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should not exceed 6 tablets.</td>
</tr>
<tr>
<td>10 mg/325 mg</td>
<td>The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dosage should not exceed 6 tablets.</td>
</tr>
</tbody>
</table>

**HOW SUPPLIED**

Hydrocodone Bitartrate and Acetaminophen Tablets USP are available in the following strengths:

- 7.5 mg hydrocodone bitartrate and 325 mg acetaminophen, capsule-shaped, while tablets bisected on one side and debossed with WATSON 3203 on the other side, supplied in bottles of 100 and 500.
- 10 mg hydrocodone bitartrate and 325 mg acetaminophen, capsule-shaped, while tablets bisected on one side and debossed with WATSON 653 on the other side, supplied in bottles of 100 and 500.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light-resistant container with a child-resistant closure.

Manufactured by:
Watson Laboratories, Inc.
Corona, CA 92880 USA

Distributed by:
Watson Pharma, Inc.
Parispany, NJ 07054 USA

Revised: August 2014
**BOXED WARNING**

Hepatotoxicity

Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product.

**DESCRIPTION**

**NORCO® (Hydrocodone bitartrate and acetaminophen)** is supplied in tablet form for oral administration.

Hydrocodone bitartrate is an opioid analgesic and antitussive and occurs as fine, white crystals or as a crystalline powder. It is affected by light. The chemical name is 4,5a-epoxy-3-ethylaminol-7-methylmorphinan-6-one bitartrate (1:1) hydrate (C21H22NO4). It has the following structural formula:

\[
\text{CH}_3\text{CH}_2\text{CN} + \text{H}_2\text{NCH}_2\text{CH}_2\text{OH} \rightarrow \text{C}_2\text{H}_2\text{NCH}_2\text{CH}_2\text{COOH}
\]

Acetaminophen, 4-hydroxyacetanilide, a slightly bitter, white, odorless, crystalline powder is a non-narcotic, non-sedative analgesic and antipyretic. It has the following structural formula:

\[
\text{CH}_2\text{OH} + \text{H}_3\text{CCH}_2\text{COOH} \rightarrow \text{CH}_2\text{OH} + \text{H}_3\text{CCH}_2\text{COOH}
\]

**NORCO®,** for oral administration is available in the following strengths:

**Hydrocodone Bitartrate Acetaminophen**

**NORCO® 7.5/325**
7.5 mg  325 mg

**NORCO® 10/325**
10 mg  325 mg

In addition, each tablet contains the following inactive ingredients: croscarmellose sodium, crospovidone, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid.

Meets USP Dissolution Test 1.

**CLINICAL PHARMACOLOGY**

Hydrocodone is a synthetic narcotic analgesic and antitussive with multiple actions qualitatively similar to those of codeine. Most of these involve the central nervous system and smooth muscle. The precise mechanism of action of hydrocodone and other opiates is not known, although it is believed to relate to the existence of opiate receptors in the central nervous system. In addition to analgesia, narcotics may produce drowsiness, changes in mood and mental clouding.

The analgesic action of acetaminophen involves peripheral influences, but the specific mechanisms are not yet understood. Antipyretic activity is mediated through hypothalamic heat regulating centers. Acetaminophen inhibits prostaglandin synthesis. Therapeutic doses of acetaminophen may have negligible effects on the cardiovascular or respiratory systems; however, toxic doses may cause circulatory failure and rapid, shallow breathing.

**Pharmacokinetics:** The behavior of the individual components is described below.

**Hydrocodone:** Following a 10 mg oral dose of hydrocodone administered to five adult male subjects, the mean peak concentration was 22.6 ± 5.2 ng/mL. Maximum serum levels were achieved at 1.5 ± 0.3 hours and the half-life was determined to be 3.8 ± 0.3 hours. Hydrocodone exhibits a complex pattern of metabolism including O-demethylation, N-demethylation and 6-dehydroxylation to the corresponding 6- and 6-beta-hydroxymetabolites. See OVERDOSAGE for toxicity information.

**Acetaminophen:** Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. The plasma half-life is 1.2 to 3 hours, but may be increased by liver damage and following overdose. Elimination of acetaminophen is principally by liver metabolism (conjugation) and subsequent renal excretion of metabolites. Approximately 85% of an oral dose appears in the urine within 24 hours of administration, mostly as the glucuronide conjugate, with small amounts of other conjugates and unchanged drug. See OVERDOSAGE for toxicity information.

**INDICATIONS AND USAGE**

**NORCO®** is indicated for the relief of moderate to moderately severe pain.

**CONTRAINDICATIONS**

**NORCO®** should not be administered to patients who have previously exhibited hypersensitivity to hydrocodone or acetaminophen.

Patients known to be hypersensitive to other opioids may exhibit cross-sensitivity to hydrocodone.

**WARNINGS**

Hepatotoxicity

Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen containing product. The excessive intake of acetaminophen may be intentional to cause self-harm or unintentional as patients attempt to obtain more pain relief or to unwarily take other acetaminophen-containing products.

The risk of acute liver failure is higher in individuals with underlying liver disease and in individuals who ingest alcohol while taking acetaminophen.

Instruct patients to look for acetaminophen or APAP on package labels and not to use more than one acetaminophen product that contains acetaminophen. Instruct patients to seek medical attention immediately upon ingestion of more than 4000 milligrams of acetaminophen per day, even if they feel well.

Serious skin reactions

Rashes, acniform eruptions, exfoliative dermatitis, erythematous rash, pustular rash, and angioedema. These skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

**Hypersensitivity/anaphylaxis**

There have been post-marketing reports of hypersensitivity and anaphylaxis associated with use of acetaminophen. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, pruritus, and vomiting. There were infrequent reports of life-threatening anaphylaxis requiring emergency medical attention. Instruct patients to discontinue NORCO® tablets immediately and seek medical care if they experience these symptoms. Do not prescribe NORCO® tablets to patients with acetaminophen allergy.

**Respiratory Depression:** At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression by acting directly on the brainstem respiratory center. Hydrocodone also affects the cerebellar control that regulates the respiratory rhythm, and may produce irregular and periodic breathing.

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

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

**PRECAUTIONS**

**General:** Special Risk Patients: As with any narcotic analgesic agent, NORCO® should be used with caution in elderly or debilitated patients and those with impaired hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

**Cough Reflex:** Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when NORCO® is used postoperatively in patients with pulmonary disease.

**Information for Patients/Caregivers:**

- Do not take NORCO® Tablets if you are allergic to any of its ingredients.
- If you develop signs of allergy such as a rash or difficulty breathing stop taking NORCO® Tablets and contact your healthcare provider immediately.
- Do not take more than 4000 milligrams of acetaminophen per day. Call your doctor if you take more than the recommended dose.

Hydrocodone, like all narcotics, may impair the mental and physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery; patients should be cautioned accordingly.

Alcohol and other CNS depressants may produce an additive CNS depression, when taken with this combination product, and should be avoided.

Hydrocodone may be habit-forming. Patients should take the drug only for as long as it is prescribed, and no more frequently, and in no larger amounts, than prescribed. The risk of addiction increases with the duration of treatment. Laboratory Tests: In patients with severe hepatic or renal disease, effects of therapy should be monitored with serial liver and renal function tests.

**Drug Interactions:** Patients receiving other narcotics, antidepressants, antipsychotics, anxiolytics, or other CNS depressants (including alcohol) concomitantly with NORCO® may exhibit an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced.

The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of the antidepressant or hydrocodone.

**Drug/Laboratory Test Interactions:** Acetaminophen may produce false-positive test results for urinary 5-hydroxyindoleacetic acid.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** No adequate studies have been conducted in animals to determine whether hydrocodone or acetaminophen have a potential for carcinogenesis, mutagenesis, or impairment of fertility.

**Pregnancy: Teratogenic Effects:** Studies done in rodents to which were being taking opioids regularly prior to mating or which will be physically challenged during pregnancy. The withdrawing signs include tremors and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The incidence of the syndrome does not always correlate with the duration of maternal opioid use or dose. There is no consensus on the best method of managing withdrawal.

**Labor and Delivery:** As with all narcotics, administration of this product to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

**Nursing Mothers:** Acetaminophen is excreted in breast milk in small amounts, but the significance of its effects on nursing infants is not known. It is not known whether hydrocodone is excreted in human milk. Because many drugs are excreted in human milk and because the potential for serious adverse reactions in nursing infants from hydrocodone and acetaminophen 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.
known or suspected to have occurred within a few hours of presentation. Serum acetaminophen levels should be obtained immediately if the patient presents 4 hours or more after ingestion to assess potential risk of hepatotoxicity; acetaminophen levels drawn less than 4 hours post-ingestion may be misleading. To obtain the best possible outcome, NAC should be administered as soon as possible where impending or evolving liver injury is suspected. Intravenous NAC may be administered when circumstances preclude oral administration.

Vigorous supportive therapy is required in severe intoxication. Procedures to limit the continuing absorption of the drug must be readily performed since the hepatic injury is dose dependent and occurs early in the course of intoxication.

**DOSEAGE AND ADMINISTRATION**

Doseage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mind that tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related.

**NORCO® 7.5/325 and NORCO® 10/325** - The usual adult dosage is one tablet every four to six hours as needed for pain. The total daily dose should not exceed 6 tablets.

**HOW SUPPLIED**

NORCO® 7.5/325 is available as capsule-shaped, white tablets bisected on one side and debossed with “NORCO 729” on the other side. Each tablet contains 7.5 mg hydrocodone bitartrate and 325 mg acetaminophen. They are supplied in bottles of 100 and 500.

**NORCO® 10/325 is available as capsule-shaped, white tablets bisected on one side and debossed with “NORCO 539” on the other side. Each tablet contains 10 mg hydrocodone bitartrate and 325 mg acetaminophen. They are supplied in bottles of 100 and 500.**

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light-resistant container with a child-resistant closure.

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