HYDROCODONE BITARTRATE AND ACETAMINOPHEN- hydrocodone bitartrate and acetaminophen tablet
Rebel Distributors Corp

Hydrocone Bitartrate and Acetaminophen

DESCRIPTION

DESCRIPTIONHydrocodone 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 affectedby light. The chemical name is 4,5a-Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5). It has the followingstructural formula: Acetaminophen, 4-hydroxyacetanilide, a slightly bitter, white, odorless, crystalline powder, is a non-opiate, non-salicylate analgesicand antipyretic. It has the following structural formula: Hydrocodone Bitartrate and Acetaminophen Tablets USP for oral administration are available in a variety of strengths as described inthe following table. Hydrocodone Strength Bitartrate Acetaminophen 2.5 mg/500mg 2.5 mg 500 mg 5 mg/500 mg 5 mg 500 mg 7.5 mg/325 mg 7.5 mg 325 mg 7.5 mg/500 mg 7.5 mg 500 mg 7.5 mg/650 mg 7.5 mg 650 mg 7.5 mg/750 mg 7.5 mg 750 mg 10 mg/325 mg 10 mg 325 mg 10 mg/500 mg 10 mg 500 mg 10 mg/650 mg 10 mg 650 mg 10 mg/660 mg 10 mg 660 mg 10 mg/750 mg 10 mg 750 mg In addition, each tablet contains the following

INACTIVE INGREDIENT

inactive ingredients: anhydrous lactose, croscarmellose sodium, crospovidone,magnesium stearate, microcrystalline cellulose, povidone, starch and stearic acid; except the 7.5 mg/325 mg, 10 mg/325 mg and 10 page 2 of 7 mg/500 mg tablets do not contain anhydrous lactose. The 7.5 mg/325 mg tablets include FD&C Yellow #6 Aluminum Lake; the 7.5mg/650 mg tablets include FD&C Red #40 Aluminum Lake; the 10 mg/325 mg and 10 mg/750 mg tablets include D&C Yellow #10Aluminum Lake; the 10 mg/500 mg tablets include FD&C Blue #2 Aluminum Lake; and the 10 mg/650 mg tablets include FD&CBlue #1 Aluminum Lake and D&C Yellow #10 Aluminum Lake. Meets USP Dissolution Test 1.

CLINICAL PHARMACOLOGY

CLINICAL PHARMACOLOGYHydrocodone is a semisynthetic narcotic analgesic and antitussive with multiple actions qualitatively similar to those of codeine. Mostof these involve the central nervous system and smooth muscle. The precise

MECHANISM OF ACTION

mechanism of action of hydrocodone and other opiates isnot 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 mechanism is as yet undetermined. Antipyreticactivity is mediated through hypothalamic heat regulating centers. Acetaminophen inhibits prostaglandin synthetase. Therapeuticdoses of acetaminophen have negligible effects on the cardiovascular or respiratory systems; however, toxic doses may causecirculatory failure and rapid, shallow breathing.

PHARMACOKINETICS

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 23.6 261 5.2ng/mL. Maximum serum levels were achieved at 1.3 261 0.3 hours and the half-life was determined to be 3.8 261 0.3 hours. Hydrocodoneexhibits a complex pattern of metabolism including O-demethylation, N-demethylation and 6-ketoreduction to the corresponding 6-aand 6-337 -hydroxymetabolites. See

OVERDOSAGE

OVERDOSAGE for toxicity information.Acetaminophen: Acetaminophen is rapidly absorbed from the gastrointestinal tract and is distributed throughout most body tissues. The plasma half-lifeis 1.25 to 3 hours, but may be increased by liver damage and following overdosage. Elimination of acetaminophen is principally byliver metabolism (conjugation) and subsequent renal excretion of metabolites. Approximately 85% of an oral dose appears in the urinewithin 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 USAGEHydrocodone and acetaminophen tablets are indicated for the relief of moderate to moderately severe pain.

CONTRAINDICATIONS

CONTRAINDICATIONSThis product should not be administered to patients who have previously exhibited Hypersensitivity to hydrocodone oracetaminophen.Patients known to be hypersensitive to other opioids may exhibit cross-sensitivity to hydrocodone.

WARNINGS

WARNINGSRespiratory 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 center that controls respiratory rhythm, and may produce irregular and periodicbreathing.Head Injury and Increased Intracranial Pressure:The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggeratedin the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcoticsproduce

ADVERSE REACTIONS

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

PRECAUTIONSGeneralSpecial Risk Patients: As with any narcotic analgesic agent, hydrocodone bitartrate and acetaminophen tablets should be used withcaution in elderly or debilitated patients, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison222sdisease, prostatic hypertrophy or urethal stricture. The usual precautions should be observed and the possibility of respiratorydepression should be kept in mind.Cough Reflex : Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when hydrocodonebitartrate and acetaminophen tablets are used postoperatively and in patients with pulmonary disease.

INFORMATION FOR PATIENTS

Information for PatientsHydrocodone, like all narcotics, may impair the mental and/or physical abilities required for the performance of potentially hazardoustasks 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 shouldbe avoided.Hydrocodone may be habit forming. Patients should take the drug only for as long as it is prescribed, in the amounts prescribed, andno more frequently than prescribed.Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when hydrocodone bitartrate andacetaminophen tablets are used postoperatively and in patients with pulmonary disease.

LABORATORY TESTS

Laboratory TestsIn patients with severe hepatic or renal disease, effects of therapy should be monitored with serial liver and/or renal function tests.

DRUG INTERACTIONS

Drug interactionsPatients receiving other narcotic analgesics, antihistamines, antipsychotics, antianxiety agents, or other CNS depressants (includingalcohol) concomitantly with hydrocodone bitartrate and acetaminophen tablets may exhibit an additive CNS depression. Whencombined therapy is contemplated, the dose of one or both agents should be reduced.The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either theantidepressant or hydrocodone.Drug/Laboratory Test InteractionsAcetaminophen may produce false-positive test results for urinary 5-hydroxyindoleacetic acid.Carcinogenesis, Mutagenesis, Impairment of FertilityNo adequate studies have been conducted in animals to determine whether hydrocodone or acetaminophen have a potential forcarcinogenesis, mutagenesis, or impairment of fertility.

PREGNANCY

Pregnancy

TERATOGENIC EFFECTS

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

NONTERATOGENIC EFFECTS

Nonteratogenic effectsBabies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signsinclude 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. There isno consensus on the best method of managing withdrawal.Labor and DeliveryAs with all narcotics, administration of this product to the mother shortly before delivery may result in some degree of respiratorydepression in the newborn, especially if higher doses are used.

NURSING MOTHERS

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

PEDIATRIC USE

Pediatric UseSafety and effectiveness in pediatric patients have not been established.

GERIATRIC USE

Geriatric Use

CLINICAL STUDIES

Clinical studies of hydrocodone bitartrate 5 mg and acetaminophen 500 mg did not include sufficient numbers of subjects aged 65and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identifieddifferences 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, andof 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 toxicreactions may be greater in patients with impaired renal function due to the accumulation of the parent compound and/or metabolites page 4 of 7 in the plasma. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and itmay 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 ofhydrocodone bitartrate and acetaminophen tablets and observed closely.ADVERSE REACTIONSThe most frequently reported adverse reactions are lightheadedness, dizziness, sedation, nausea and vomiting. These effects seem tobe more prominent in ambulatory than in nonambulatory patients, and some of these adverse reactions may be alleviated if the patientlies down.Other adverse reactions include:Central Nervous System: Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear,dysphoria, psychic

DEPENDENCE

dependence, 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 brainstem respiratory centers (see OVERDOSAGE).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 OVERDOSAGE section.

DRUG ABUSE AND DEPENDENCE

DRUG

ABUSE

ABUSE AND DEPENDENCE

CONTROLLED SUBSTANCE

Controlled SubstanceHydrocodone bitartrate and Acetaminophen Tablets are classified as a Schedule lll controlled substance.Abuse and DependencePsychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, thisproduct should be

prescribed and administered with caution. However, psychic dependence is unlikely to develop when hydrocodonebitartrate 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 awithdrawal syndrome, assumes clinically significant proportions only after several weeks of continued narcotic use, although somemild degree of physical dependence may develop after a few days of narcotic therapy. Tolerance, in which increasingly large dosesare required in order to produce the same degree of analgesia, is manifested initially by a shortened duration of analgesic effect, andsubsequently by decreases in the intensity of analgesia. The rate of development of tolerance varies among patients.OVERDOSAGEFollowing an acute overdosage, 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 respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammyskin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death mayoccur.Acetaminophen: In acetaminophen overdosage: dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubularnecrosis, hypoglycemic coma, and thrombocytopenia 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.In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10 grams, or fatalities with less than 15 grams.Treatment:A single or multiple overdose with hydrocodone and acetaminophen is a potentially lethal polydrug overdose, and consultation with aregional poison control center is recommended.Immediate treatment includes support of cardiorespiratory function and measures to reduce drug absorption. Vomiting should beinduced mechanically, or with syrup of ipecac, if the patient is alert (adequate pharyngeal and laryngeal reflexes). Oral activatedcharcoal (1 g/kg) should follow gastric emptying. The first dose should be accompanied by an appropriate cathartic. If repeated dosesare used, the cathartic might be included with alternate doses as required. Hypotension is usually hypovolemic and should respond to page 5 of 7 fluids. Vasopressors and other supportive measures should be employed as indicated. A cuffed endotracheal tube should be insertedbefore gastric lavage of the unconscious patient and, when necessary, to provide assisted respiration.Meticulous attention should be given to maintaining adequate pulmonary ventilation. In severe cases of intoxication, peritonealdialysis, or preferably hemodialysis may be considered. If hypoprothrombinemia occurs due to acetaminophen overdose, vitamin Kshould be administered intravenously.Naloxone, a narcotic antagonist, can reverse respiratory depression and coma associated with opioid overdose. Naloxonehydrochloride 0.4 mg to 2 mg is given parenterally. Since the duration of action of hydrocodone may exceed that of the naloxone,the patient should be kept under continuous surveillance and repeated doses of the antagonist should be administered as needed tomaintain adequate respiration. A narcotic antagonist should not be administered in the absence of clinically significant respiratory orcardiovascular depression.If the dose of acetaminophen may have exceeded 140 mg/kg, acetylcysteine should be administered as early as possible. Serumacetaminophen levels should be obtained, since levels four or more hours following ingestion help predict acetaminophen toxicity. Donot await acetaminophen assay results before initiating treatment. Hepatic enzymes should be obtained initially, and repeated at 24-hour intervals.Methemoglobinemia over 30% should be treated with methylene blue by slow intravenous administration.The toxic dose for adults for acetaminophen is 10 g.DOSAGE AND ADMINISTRATIONDosage should be adjusted according to the severity of the pain and the response of the patient. However, it should be kept in mindthat tolerance to hydrocodone can develop with continued use and that the incidence of untoward effects is dose related. 2.5 mg/500 mg5 mg/500 mg The usual adult dosage is one or two tablets every four to six hours as needed for pain. The totaldaily dosage should not exceed 8 tablets 7.5 mg/325 mg7.5 mg/500 mg7.5 mg/650 mg The usual adult dosage is one tablet every four to six hours as needed for pain. The total dailydosage should not exceed 6 tablets. 7.5 mg/750 mg The usual adult dosage is one tablet every four to six hours as needed for pain. The total dailydosage should not exceed 5 tablets. 10 mg/325 mg10 mg/500 mg10 mg/650 mg10 mg/660 mg The usual adult dosage is one tablet every four to six hours as needed for pain. The total dailydosage should not exceed 6 tablets. 10 mg/750 mg The usual

adult dosage is one tablet every four to six hours as needed for pain. The total dailydosage should not exceed 5 tablets.

HOW SUPPLIED

HOW SUPPLIEDHydrocodone Bitartrate and Acetaminophen Tablets USP are available in10 mg/500 mg 10 mg hydrocodone bitartrate and 500 mg acetaminophen, capsule-shaped, blue tablets bisected on one side anddebossed with WATSON 540 on the other side, supplied in unit dose packages of :

120 NDC 21695-273-72

90 NDC 21695-273-90

60 NDC 21695-273-60

45 NDC 21695-273-45

30 NDC 21695-273-30

28 NDC 21695-273-28

12 NDC 21695-273-12

8 NDC 21695-273-08

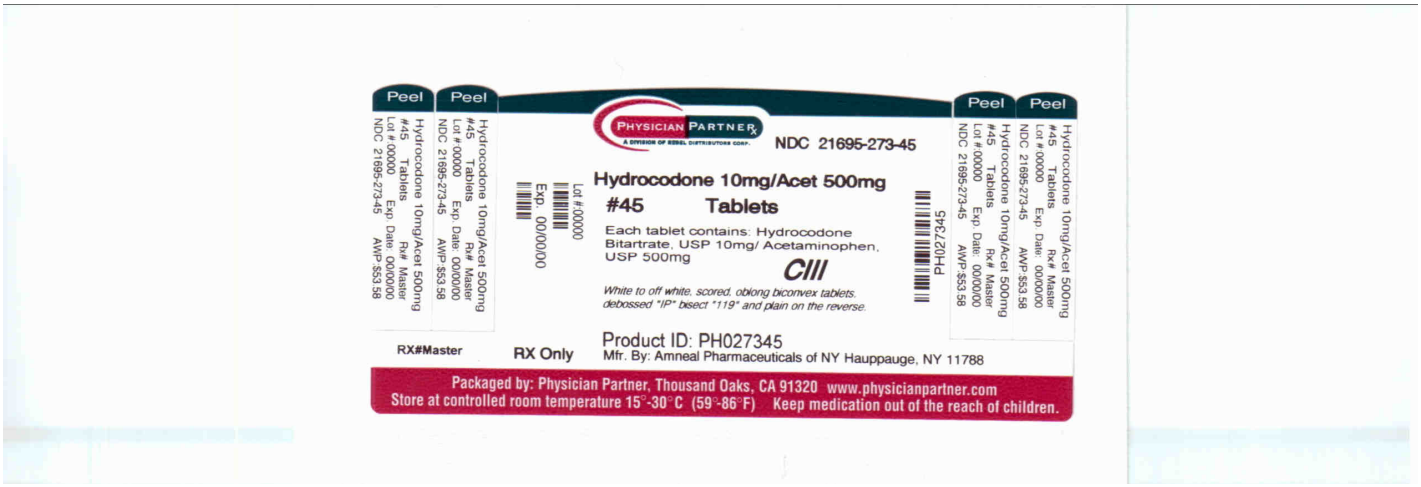
Store at 20260-25260C (68260-77260F). [See USP controlled room temperature].Rx onlyManufactured by:Watson Laboratories, Inc.Corona, CA 92880 USADistributed by:Watson Pharma, Inc.Corona, CA 92880 USA

Repackaged by:

Rebel Distributors Corp

Thousand Oaks, CA 91320

Principal Display Panel



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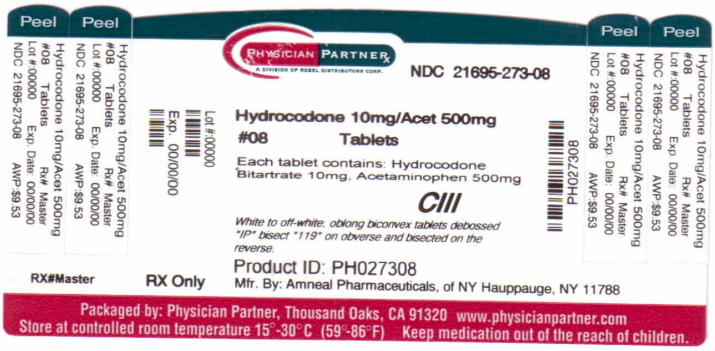

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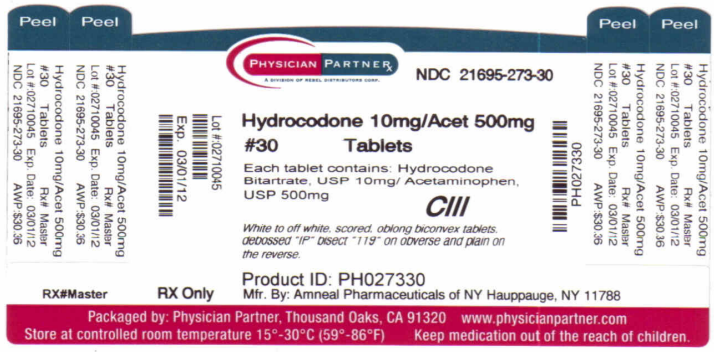

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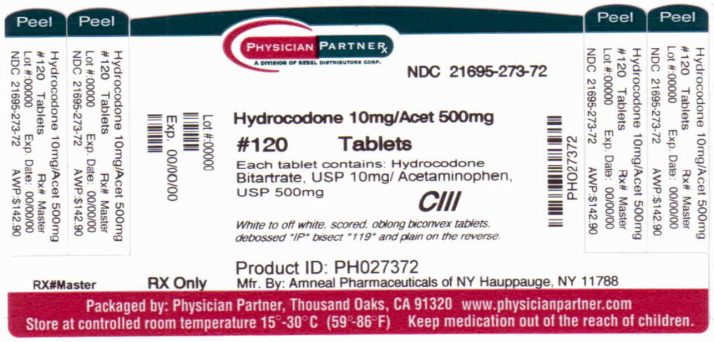

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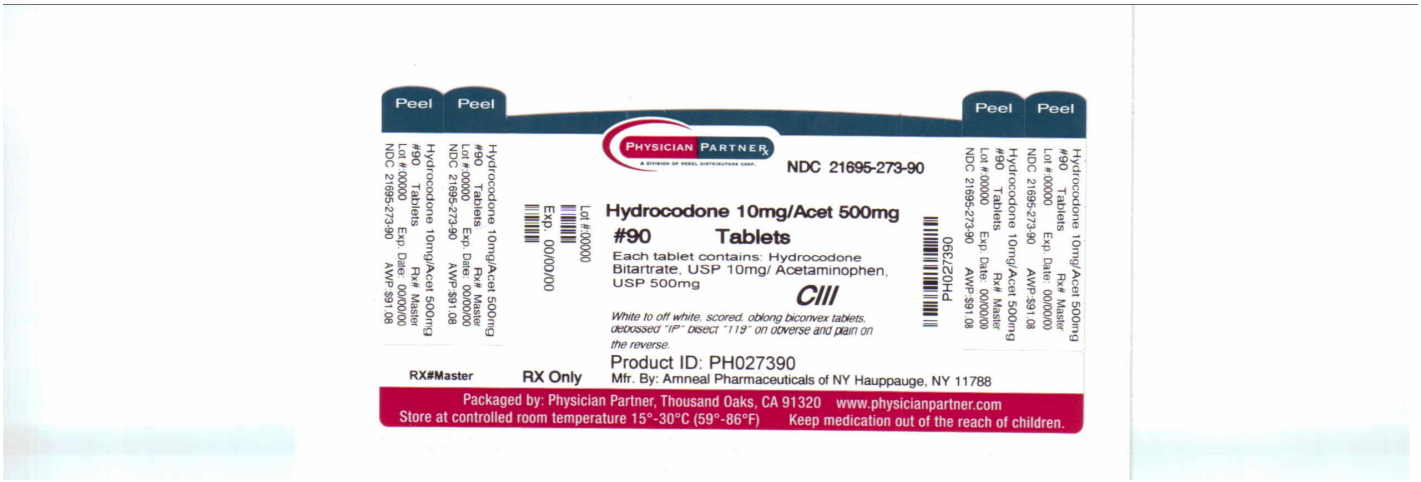

HYDROCODONE BITARTRATE AND ACETAMINOPHEN

hydrocodone bitartrate and acetaminophen tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:21695-273(NDC:53746-119)
Route of Administration	ORAL	**DEA Schedule**	CIII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDROCODONE BITARTRATE (UNII: NO70W886KK) (HYDROCODONE - UNII:6YKS4Y3WQ7)	HYDROCODONE BITARTRATE	10 mg
ACETAMINOPHEN (UNII: 362O9ITL9D) (ACETAMINOPHEN - UNII:362O9ITL9D)	ACETAMINOPHEN	500 mg

Inactive Ingredients

Ingredient Name	Strength
HYDRATED SILICA (UNII: Y6O7T4G8P9)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
CROSPOVIDONE (UNII: 68401960MK)	
D&C RED NO. 27 (UNII: 2LRS185U6K)	
D&C RED NO. 30 (UNII: 2S42T2808B)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
COPOVIDONE (UNII: D9C330MD8B)	
STARCH, CORN (UNII: O8232NY3SJ)	
STEARIC ACID (UNII: 4ELV7Z65AP)	

Product Characteristics

Color	white	**Score**	2 pieces
Shape	CAPSULE (TABLET)	**Size**	15mm
Flavor		**Imprint Code**	IP;119
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:21695-273-72	120 in 1 BOTTLE		
2	NDC:21695-273-90	90 in 1 BOTTLE		
3	NDC:21695-273-60	60 in 1 BOTTLE		
4	NDC:21695-273-45	45 in 1 BOTTLE		
5	NDC:21695-273-30	30 in 1 BOTTLE		
6	NDC:21695-273-28	28 in 1 BOTTLE		
7	NDC:21695-273-12	12 in 1 BOTTLE		
8	NDC:21695-273-08	8 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA075659	07/30/2010	

Labeler - Rebel Distributors Corp (118802834)

Establishment

Name	Address	ID/FEI	Business Operations
Rebel Distributors Corp		118802834	RELABEL, REPACK

Revised: 12/2010 Rebel Distributors Corp