CYCLOBENZAPRINE HYDROCHLORIDE- cyclobenzaprine hydrochloride tablet, film coated
Advagen Pharma Limited

Cyclobenzaprine hydrochloride, USP

DESCRIPTION

Cyclobenzaprine hydrochloride, USP is a tricyclic amine salt which is white to off white, odourless, crystalline powder with the molecular formula $C_{20}H_{21}N \bullet HCl$ and a molecular weight of 311.9. It has a melting point of 217°C, and a pKa of 8.47 at 25°C. It is freely soluble in water, in alcohol and in methanol, sparingly soluble in isopropanol, slightly soluble in chloroform and in methylene chloride, insoluble in n-hexane. If aqueous solutions are made alkaline, the free base separates. Cyclobenzaprine hydrochloride is designated chemically as 3-(5H -dibenzo[a,d] cyclohepten-5-ylidene)- *N,N*-dimethyl-1-propanamine hydrochloride, and has the following structural formula:

Cyclobenzaprine hydrochloride tablets, USP are available as 5 mg, 7.5 mg and 10 mg tablets for oral administration. Each 5 mg, 7.5 mg and 10 mg tablet contains cyclobenzaprine hydrochloride and the following inactive ingredients: crospovidone, hypromellose, lactose anhydrous, macrogol, magnesium stearate, polysorbate 80, pregelatinized starch, silicified microcrystalline cellulose, titanium dioxide. The tablets of 5 mg and 10 mg also contain D&C Yellow #10 Aluminum Lake and FD&C Yellow #6 Sunset Yellow FCF Aluminum Lake. In addition, the 5 mg tablets contain FD&C Blue #2/INDIGO Carmine Aluminum Lake.

CLINICAL PHARMACOLOGY

Cyclobenzaprine hydrochloride relieves skeletal muscle spasm of local origin without interfering with muscle function. It is ineffective in muscle spasm due to central nervous system disease.

Cyclobenzaprine reduced or abolished skeletal muscle hyperactivity in several animal models. Animal studies indicate that cyclobenzaprine does not act at the neuromuscular junction or directly on skeletal muscle. Such studies show that cyclobenzaprine acts primarily within the central nervous system at brain stem as opposed to spinal cord levels, although its action on the latter may contribute to its overall skeletal muscle relaxant activity. Evidence suggests that the net effect of cyclobenzaprine is a reduction

of tonic somatic motor activity, influencing both gamma (γ) and alpha (α) motor systems.

Pharmacological studies in animals showed a similarity between the effects of cyclobenzaprine and the structurally related tricyclic antidepressants, including reserpine antagonism, norepinephrine potentiation, potent peripheral and central anticholinergic effects, and sedation. Cyclobenzaprine caused slight to moderate increase in heart rate in animals.

Pharmacokinetics

Estimates of mean oral bioavailability of cyclobenzaprine range from 33% to 55%. Cyclobenzaprine exhibits linear pharmacokinetics over the dose range 2.5 mg to 10 mg, and is subject to enterohepatic circulation. It is highly bound to plasma proteins. Drug accumulates when dosed 3 times a day, reaching steady-state within 3 to 4 days at plasma concentrations about 4-fold higher than after a single dose. At steady-state in healthy subjects receiving 10 mg t.i.d. (n = 18), peak plasma concentration was 25.9 ng/mL (range, 12.8 to 46.1 ng/mL), and area under the concentration-time (AUC) curve over an 8-hour dosing interval was 177 ng·hr/mL (range, 80 to 319 ng·hr/mL).

Cyclobenzaprine is extensively metabolized, and is excreted primarily as glucuronides via the kidney. Cytochromes P450 3A4, 1A2, and, to a lesser extent, 2D6, mediate N-demethylation, one of the oxidative pathways for cyclobenzaprine. Cyclobenzaprine is eliminated quite slowly, with an effective half-life of 18 hours (range 8 to 37 hours; n = 18); plasma clearance is 0.7 L/min.

The plasma concentration of cyclobenzaprine is generally higher in the elderly and in patients with hepatic impairment (see PRECAUTIONS: Use in the Elderlyand PRECAUTIONS: Impaired Hepatic Function).

Elderly

In a pharmacokinetic study in elderly individuals (≥ 65 yrs old), mean (n = 10) steady-state cyclobenzaprine AUC values were approximately 1.7-fold (171 ng·hr/mL, range 96.1 to 255.3) higher than those seen in a group of 18 younger adults (101.4 ng·hr/mL, range 36.1 to 182.9) from another study. Elderly male subjects had the highest observed mean increase, approximately 2.4-fold (198.3 ng·hr/mL, range 155.6 to 255.3 vs. 83.2 ng·hr/mL, range 41.1 to 142.5 for younger males) while levels in elderly females were increased to a much lesser extent, approximately 1.2-fold (143.8 ng·hr/mL, range 96.1 to 196.3 vs. 115.9 ng·hr/mL, range 36.1 to 182.9 for younger females).

In light of these findings, therapy with cyclobenzaprine in the elderly should be initiated with a 5 mg dose and titrated slowly upward.

Hepatic Impairment

In a pharmacokinetic study of 16 subjects with hepatic impairment (15 mild, 1 moderate per Child-Pugh score), both AUC and C_{max}were approximately double the values seen in the healthy control group. Based on the findings, cyclobenzaprine should be used with caution in subjects with mild hepatic impairment starting with the 5 mg dose and titrating slowly upward. Due to the lack of data in subjects with more severe hepatic insufficiency, the use of cyclobenzaprine in subjects with moderate to severe impairment is not recommended.

No significant effect on plasma levels or bioavailability of cyclobenzaprine or aspirin was

noted when single or multiple doses of the two drugs were administered concomitantly. Concomitant administration of cyclobenzaprine and naproxen or diflunisal was well tolerated with no reported unexpected adverse effects. However combination therapy of cyclobenzaprine with naproxen was associated with more side effects than therapy with naproxen alone, primarily in the form of drowsiness. No well controlled studies have been performed to indicate that cyclobenzaprine enhances the clinical effect of aspirin or other analgesics, or whether analgesics enhance the clinical effect of cyclobenzaprine in acute musculoskeletal conditions.

Clinical Studies

Eight double-blind controlled clinical studies were performed in 642 patients comparing cyclobenzaprine hydrochloride 10 mg, diazepam, and placebo. Muscle spasm, local pain and tenderness, limitation of motion, and restriction in activities of daily living were evaluated. In three of these studies there was a significantly greater improvement with cyclobenzaprine than with diazepam, while in the other studies the improvement following both treatments was comparable.

Although the frequency and severity of adverse reactions observed in patients treated with cyclobenzaprine were comparable to those observed in patients treated with diazepam, dry mouth was observed more frequently in patients treated with cyclobenzaprine and dizziness more frequently in those treated with diazepam. The incidence of drowsiness, the most frequent adverse reaction, was similar with both drugs.

The efficacy of cyclobenzaprine hydrochloride 5 mg was demonstrated in two 7-day, double-blind, controlled clinical trials enrolling 1,405 patients. One study compared cyclobenzaprine hydrochloride 5 mg and 10 mg t.i.d. to placebo; and a second study compared cyclobenzaprine hydrochloride 5 mg and 2.5 mg t.i.d. to placebo. Primary endpoints for both trials were determined by patient-generated data and included global impression of change, medication helpfulness, and relief from starting backache. Each endpoint consisted of a score on a 5-point rating scale (from 0 or worst outcome to 4 or best outcome). Secondary endpoints included a physician's evaluation of the presence and extent of palpable muscle spasm.

Comparisons of cyclobenzaprine hydrochloride 5 mg and placebo groups in both trials established the statistically significant superiority of the 5 mg dose for all three primary endpoints at day 8 and, in the study comparing 5 mg and 10 mg, at day 3 or 4 as well. A similar effect was observed with cyclobenzaprine hydrochloride 10 mg (all endpoints). Physician-assessed secondary endpoints also showed that cyclobenzaprine hydrochloride 5 mg was associated with a greater reduction in palpable muscle spasm than placebo.

Analysis of the data from controlled studies shows that cyclobenzaprine produces clinical improvement whether or not sedation occurs.

Surveillance Program

A post-marketing surveillance program was carried out in 7,607 patients with acute musculoskeletal disorders, and included 297 patients treated with cyclobenzaprine hydrochloride 10 mg for 30 days or longer. The overall effectiveness of cyclobenzaprine was similar to that observed in the double-blind controlled studies; the overall incidence of adverse effects was less (see ADVERSE REACTIONS).

INDICATIONS AND USAGE

Cyclobenzaprine hydrochloride tablets, USP are indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions.

Improvement is manifested by relief of muscle spasm and its associated signs and symptoms, namely, pain, tenderness, limitation of motion, and restriction in activities of daily living.

Cyclobenzaprine hydrochloride tablets should be used only for short periods (up to 2 or 3 weeks) because adequate evidence of effectiveness for more prolonged use is not available and because muscle spasm associated with acute, painful musculoskeletal conditions is generally of short duration and specific therapy for longer periods is seldom warranted.

Cyclobenzaprine hydrochloride tablets have not been found effective in the treatment of spasticity associated with cerebral or spinal cord disease, or in children with cerebral palsy.

CONTRAINDICATIONS

Hypersensitivity to any component of this product.

Concomitant use of monoamine oxidase (MAO) inhibitors or within 14 days after their discontinuation. Hyperpyretic crisis seizures and deaths have occurred in patients receiving cyclobenzaprine (or structurally similar tricyclic antidepressants) concomitantly with MAO inhibitor drugs.

Acute recovery phase of myocardial infarction, and patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure.

Hyperthyroidism.

WARNINGS

Serotonin Syndrome

The development of a potentially life-threatening serotonin syndrome has been reported with cyclobenzaprine hydrochloride when used in combination with other drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), tramadol, bupropion, meperidine, verapamil, or (MAO) inhibitors. The concomitant use of cyclobenzaprine hydrochloride with MAO inhibitors is contraindicated (see CONTRAINDICATIONS). Serotonin syndrome symptoms may include mental status changes (e.g., confusion, agitation, hallucinations), autonomic instability (e.g., diaphoresis, tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., tremor, ataxia, hyperreflexia, clonus, muscle rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Treatment with cyclobenzaprine hydrochloride and any concomitant serotonergic agents should be discontinued immediately if the above reactions occur and supportive symptomatic treatment should be initiated. If concomitant treatment with cyclobenzaprine hydrochloride and other serotonergic drugs is clinically warranted,

careful observation is advised, particularly during treatment initiation or dose increases (see PRECAUTIONS: Drug Interactions).

Cyclobenzaprine is closely related to the tricyclic antidepressants, e.g., amitriptyline and imipramine. In short term studies for indications other than muscle spasm associated with acute musculoskeletal conditions, and usually at doses somewhat greater than those recommended for skeletal muscle spasm, some of the more serious central nervous system reactions noted with the tricyclic antidepressants have occurred (see WARNINGS, below, and ADVERSE REACTIONS).

Tricyclic antidepressants have been reported to produce arrhythmias, sinus tachycardia, prolongation of the conduction time leading to myocardial infarction and stroke.

Cyclobenzaprine may enhance the effects of alcohol, barbiturates, and other CNS depressants.

PRECAUTIONS

General

Because of its atropine-like action, cyclobenzaprine should be used with caution in patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and in patients taking anticholinergic medication.

Impaired Hepatic Function

The plasma concentration of cyclobenzaprine is increased in patients with hepatic impairment (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Hepatic Impairment). These patients are generally more susceptible to drugs with potentially sedating effects, including cyclobenzaprine. Cyclobenzaprine hydrochloride should be used with caution in subjects with mild hepatic impairment starting with a 5 mg dose and titrating slowly upward. Due to the lack of data in subjects with more severe hepatic insufficiency, the use of cyclobenzaprine in subjects with moderate to severe impairment is not recommended.

Information for Patients

Cyclobenzaprine, especially when used with alcohol or other CNS depressants, may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle. In the elderly, the frequency and severity of adverse events associated with the use of cyclobenzaprine, with or without concomitant medications, is increased. In elderly patients, cyclobenzaprine hydrochloride should be initiated with a 5 mg dose and titrated slowly upward.

Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of cyclobenzaprine hydrochloride and other drugs, such as SSRIs, SNRIs, TCAs, tramadol, bupropion, meperidine, verapamil or MAO inhibitors. Patients should be advised of the signs and symptoms of serotonin syndrome, and be instructed to seek medical care immediately if they experience these symptoms (see WARNINGSand PRECAUTIONS: Drug Interactions).

Drug Interactions

Cyclobenzaprine may have life-threatening interactions with MAO inhibitors (see CONTRAINDICATIONS). Postmarketing cases of serotonin syndrome have been

reported during combined use of cyclobenzaprine hydrochloride and other drugs, such as SSRIs, SNRIs, TCAs, tramadol, bupropion, meperidine, verapamil or MAO inhibitors. If concomitant treatment with cyclobenzaprine hydrochloride and other serotonergic drugs is clinically warranted, careful observation is advised, particularly during treatment initiation or dose increases (see WARNINGS).

Cyclobenzaprine may enhance the effects of alcohol, barbiturates, and other CNS depressants.

Tricyclic antidepressants may block the antihypertensive action of guanethidine and similarly acting compounds.

Tricyclic antidepressants may enhance the seizure risk in patients taking tramadol.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In rats treated with cyclobenzaprine for up to 67 weeks at doses of approximately 5 to 40 times the maximum recommended human dose, pale, sometimes enlarged, livers were noted and there was a dose-related hepatocyte vacuolation with lipidosis. In the higher dose groups this microscopic change was seen after 26 weeks and even earlier in rats which died prior to 26 weeks; at lower doses, the change was not seen until after 26 weeks.

Cyclobenzaprine did not affect the onset, incidence or distribution of neoplasia in an 81-week study in the mouse or in a 105-week study in the rat.

At oral doses of up to 10 times the human dose, cyclobenzaprine did not adversely affect the reproductive performance or fertility of male or female rats. Cyclobenzaprine did not demonstrate mutagenic activity in the male mouse at dose levels of up to 20 times the human dose.

Pregnancy

Teratogenic Effects. Pregnancy Category B

Reproduction studies have been performed in rats, mice and rabbits at doses up to 20 times the human dose, and have revealed no evidence of impaired fertility or harm to the fetus due to cyclobenzaprine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because cyclobenzaprine is closely related to the tricyclic antidepressants, some of which are known to be excreted in human milk, caution should be exercised when cyclobenzaprine hydrochloride is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of cyclobenzaprine in pediatric patients below 15 years of age have not been established.

Use in the Elderly

The plasma concentration of cyclobenzaprine is increased in the elderly (see CLINICAL PHARMACOLOGY: Pharmacokinetics: Elderly). The elderly may also be more at risk for

CNS adverse events such as hallucinations and confusion, cardiac events resulting in falls or other sequelae, drug-drug and drug-disease interactions. For these reasons, in the elderly, cyclobenzaprine should be used only if clearly needed. In such patients cyclobenzaprine hydrochloride should be initiated with a 5 mg dose and titrated slowly upward.

ADVERSE REACTIONS

Incidence of most common adverse reactions in the two double-blind*, placebo-controlled 5 mg studies (incidence of > 3% on cyclobenzaprine hydrochloride 5 mg):

	Cyclobenzaprine Hydrochloride 5 mg N = 464	Cyclobenzaprine Hydrochloride 10 mg N = 249	Placebo N = 469
Drowsiness	29%	38%	10%
Dry Mouth	21%	32%	7%
Fatigue	6%	6%	3%
Headache	5%	5%	8%

*Note: Cyclobenzaprine hydrochloride 10 mg data are from one clinical trial. Cyclobenzaprine hydrochloride 5 mg and placebo data are from two studies.

Adverse reactions which were reported in 1% to 3% of the patients were: abdominal pain, acid regurgitation, constipation, diarrhea, dizziness, nausea, irritability, mental acuity decreased, nervousness, upper respiratory infection, and pharyngitis.

The following list of adverse reactions is based on the experience in 473 patients treated with cyclobenzaprine hydrochloride 10 mg in additional controlled clinical studies, 7,607 patients in the postmarketing surveillance program, and reports received since the drug was marketed. The overall incidence of adverse reactions among patients in the surveillance program was less than the incidence in the controlled clinical studies.

The adverse reactions reported most frequently with cyclobenzaprine were drowsiness, dry mouth and dizziness. The incidence of these common adverse reactions was lower in the surveillance program than in the controlled clinical studies:

	Clinical Studies with Cyclobenzaprine hydrochloride 10 mg	Surveillance Program with Cyclobenzaprine hydrochloride 10 mg
Drowsiness	39%	16%
Dry Mouth	27%	7%
Dizziness	11%	3%

Among the less frequent adverse reactions, there was no appreciable difference in incidence in controlled clinical studies or in the surveillance program. Adverse reactions which were reported in 1% to 3% of the patients were: fatigue/tiredness, asthenia, nausea, constipation, dyspepsia, unpleasant taste, blurred vision, headache, nervousness, and confusion.

The following adverse reactions have been reported in postmarketing experience or with an incidence of less than 1% of patients in clinical trials with the 10 mg tablet:

Body as a Whole:Syncope; malaise.

Cardiovascular:Tachycardia; arrhythmia; vasodilatation; palpitation; hypotension.

Digestive:Vomiting; anorexia; diarrhea; gastrointestinal pain; gastritis; thirst; flatulence; edema of the tongue; abnormal liver function and rare reports of hepatitis, jaundice and cholestasis.

Hypersensitivity:Anaphylaxis; angioedema; pruritus; facial edema; urticaria; rash.

Musculoskeletal:Local weakness.

Nervous System and Psychiatric:Seizures; ataxia; vertigo; dysarthria; tremors; hypertonia; convulsions; muscle twitching; disorientation; insomnia; depressed mood; abnormal sensations; anxiety; agitation; psychosis; abnormal thinking and dreaming; hallucinations; excitement; paresthesia; diplopia, serotonin syndrome.

Skin:Sweating.

Special Senses:Ageusia; tinnitus.

Urogenital:Urinary frequency and/or retention.

Causal Relationship Unknown

Other reactions, reported rarely for cyclobenzaprine under circumstances where a causal relationship could not be established or reported for other tricyclic drugs, are listed to serve as alerting information to physicians:

Body as a Whole:Chest pain; edema.

Cardiovascular:Hypertension; myocardial infarction; heart block; stroke.

Digestive:Paralytic ileus; tongue discoloration; stomatitis; parotid swelling.

Endocrine:Inappropriate ADH syndrome.

Hematic and Lymphatic:Purpura; bone marrow depression; leukopenia; eosinophilia; thrombocytopenia.

Metabolic, Nutritional and Immune:Elevation and lowering of blood sugar levels; weight gain or loss.

Musculoskeletal:Myalgia.

Nervous System and Psychiatric:Decreased or increased libido; abnormal gait; delusions; aggressive behavior; paranoia; peripheral neuropathy; Bell's palsy; alteration in EEG patterns; extrapyramidal symptoms.

Respiratory:Dyspnea.

Skin:Photosensitization; alopecia.

Urogenital:Impaired urination; dilatation of urinary tract; impotence; testicular swelling; gynecomastia; breast enlargement; galactorrhea.

DRUG ABUSE AND DEPENDENCE

Pharmacologic similarities among the tricyclic drugs require that certain withdrawal symptoms be considered when cyclobenzaprine is administered, even though they have not been reported to occur with this drug. Abrupt cessation of treatment after prolonged administration rarely may produce nausea, headache, and malaise. These are not indicative of addiction.

OVERDOSAGE

Although rare, deaths may occur from overdosage with cyclobenzaprine. Multiple drug ingestion (including alcohol) is common in deliberate cyclobenzaprine overdose. **As management of overdose is complex and changing, it is recommended that the physician contact a poison control center for current information on treatment**. Signs and symptoms of toxicity may develop rapidly after cyclobenzaprine overdose; therefore, hospital monitoring is required as soon as possible. The acute oral LD_{50} of cyclobenzaprine is approximately 338 and 425 mg/kg in mice and rats, respectively.

Manifestations

The most common effects associated with cyclobenzaprine overdose are drowsiness and tachycardia. Less frequent manifestations include tremor, agitation, coma, ataxia, hypertension, slurred speech, confusion, dizziness, nausea, vomiting, and hallucinations. Rare but potentially critical manifestations of overdose are cardiac arrest, chest pain, cardiac dysrhythmias, severe hypotension, seizures, and neuroleptic malignant syndrome.

Changes in the electrocardiogram, particularly in QRS axis or width, are clinically significant indicators of cyclobenzaprine toxicity. Other potential effects of overdosage include any of the symptoms listed under ADVERSE REACTIONS.

Management

General

As management of overdose is complex and changing, it is recommended that the physician contact a poison control center for current information on treatment.

In order to protect against the rare but potentially critical manifestations described above, obtain an ECG and immediately initiate cardiac monitoring. Protect the patient's airway, establish an intravenous line and initiate gastric decontamination. Observation with cardiac monitoring and observation for signs of CNS or respiratory depression, hypotension, cardiac dysrhythmias and/or conduction blocks, and seizures is necessary. If signs of toxicity occur at any time during this period, extended monitoring is required. Monitoring of plasma drug levels should not guide management of the patient. Dialysis is probably of no value because of low plasma concentrations of the drug.

Gastrointestinal Decontamination

All patients suspected of an overdose with cyclobenzaprine should receive gastrointestinal decontamination. This should include large volume gastric lavage followed by activated charcoal. If consciousness is impaired, the airway should be

secured prior to lavage and emesis is contraindicated.

Cardiovascular

A maximal limb-lead QRS duration of ≥ 0.10 seconds may be the best indication of the severity of the overdose. Serum alkalinization, to a pH of 7.45 to 7.55, using intravenous sodium bicarbonate and hyperventilation (as needed), should be instituted for patients with dysrhythmias and/or QRS widening. A pH > 7.60 or a pCO_2 < 20 mmHg is undesirable. Dysrhythmias unresponsive to sodium bicarbonate therapy/hyperventilation may respond to lidocaine, bretylium or phenytoin. Type 1A and 1C antiarrhythmics are generally contraindicated (e.g., quinidine, disopyramide, and procainamide).

CNS

In patients with CNS depression, early intubation is advised because of the potential for abrupt deterioration. Seizures should be controlled with benzodiazepines or, if these are ineffective, other anticonvulsants (e.g., phenobarbital, phenytoin). Physostigmine is not recommended except to treat life-threatening symptoms that have been unresponsive to other therapies, and then only in close consultation with a poison control center.

Psychiatric Follow-up

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Psychiatric referral may be appropriate.

Pediatric Management

The principles of management of child and adult overdosages are similar. It is strongly recommended that the physician contact the local poison control center for specific pediatric treatment.

DOSAGE AND ADMINISTRATION

For most patients, the recommended dose of cyclobenzaprine hydrochloride tablets is 5 mg three times a day. Based on individual patient response, the dose may be increased to 10 mg three times a day. Use of cyclobenzaprine hydrochloride tablets for periods longer than 2 or 3 weeks is not recommended (see INDICATIONS AND USAGE).

Less frequent dosing should be considered for hepatically impaired or elderly patients (see PRECAUTIONS: Impaired Hepatic Function, and Use in the Elderly).

HOW SUPPLIED

Cyclobenzaprine Hydrochloride Tablets, USP are available containing 5 mg, 7.5 mg or 10 mg of cyclobenzaprine hydrochloride, USP.

The 5 mg tablets are butter scotch yellow film-coated, round tablets debossed with 020 on one side and plain on other side. They are available as follows:

NDC 72888-012-01

bottles of 100 tablets

NDC 72888-012-05

bottles of 500 tablets

NDC 72888-012-00

bottles of 1000 tablets

The 7.5 mg tablets are white to off-white film-coated, round tablets debossed with 021 on one side and plain on other side. They are available as follows:

NDC 72888-013-01

bottles of 100 tablets

The 10 mg tablets are orange-yellow film-coated, round tablets debossed with 022 on one side and plain on other side. They are available as follows:

NDC 72888-014-01

bottles of 100 tablets

NDC 72888-014-05

bottles of 500 tablets

NDC 72888-014-00

bottles of 1000 tablets

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

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

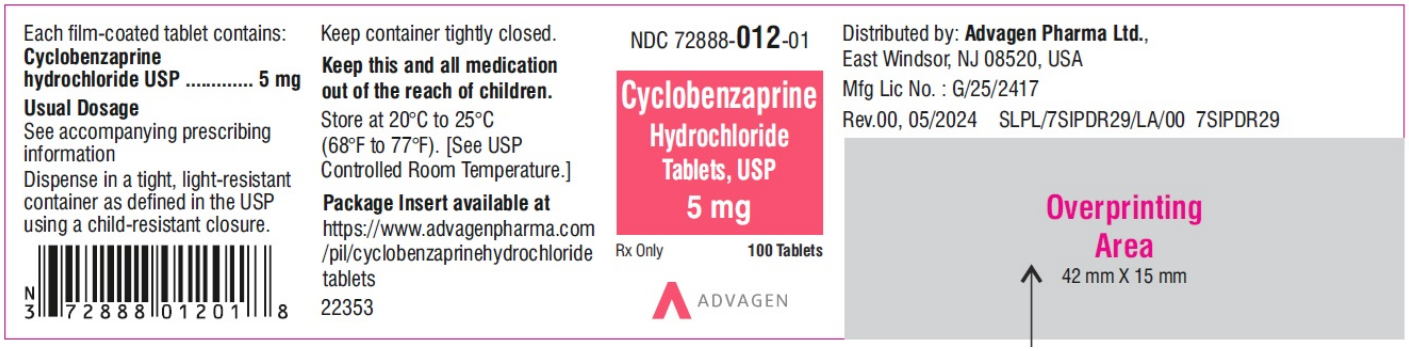
Distributed by:
Advagen Pharma Ltd
East Windsor, NJ 08520, USA.

Manufactured by:
Rubicon Research Limited,
Thane 421506, India

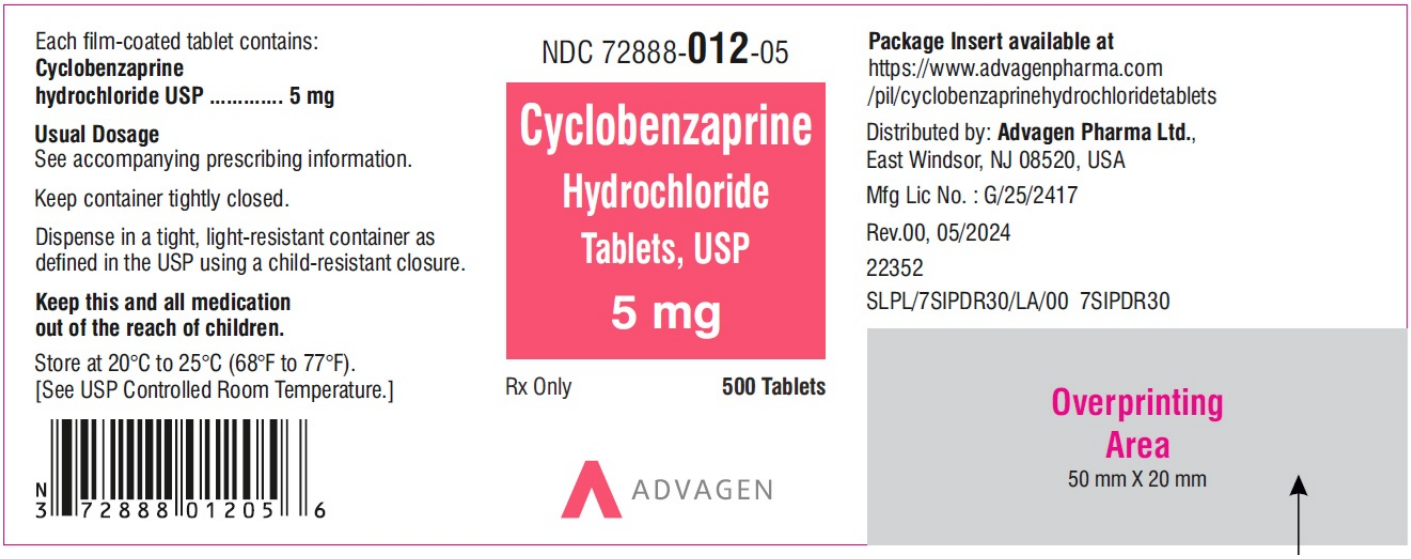
Rev: 01/2026

PRINCIPAL DISPLAY PANEL: Cyclobenzaprine Hydrochloride Tablets, USP 5 MG

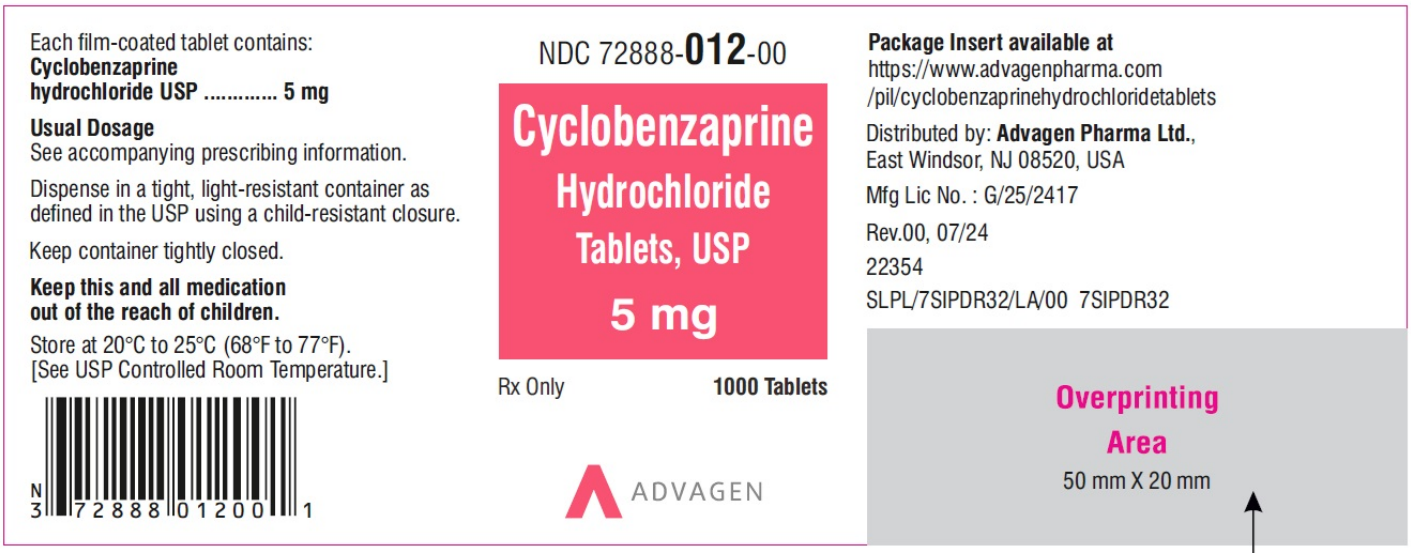
NDC 72888-012-01 bottles of 100 tablets



NDC 72888-012-05 bottles of 500 tablets

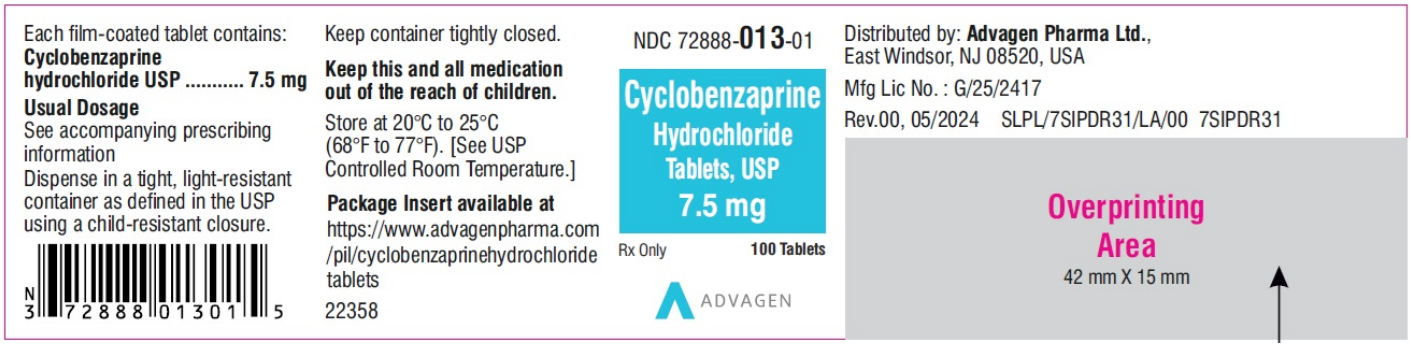


NDC 72888-012-00 bottles of 1000 tablets



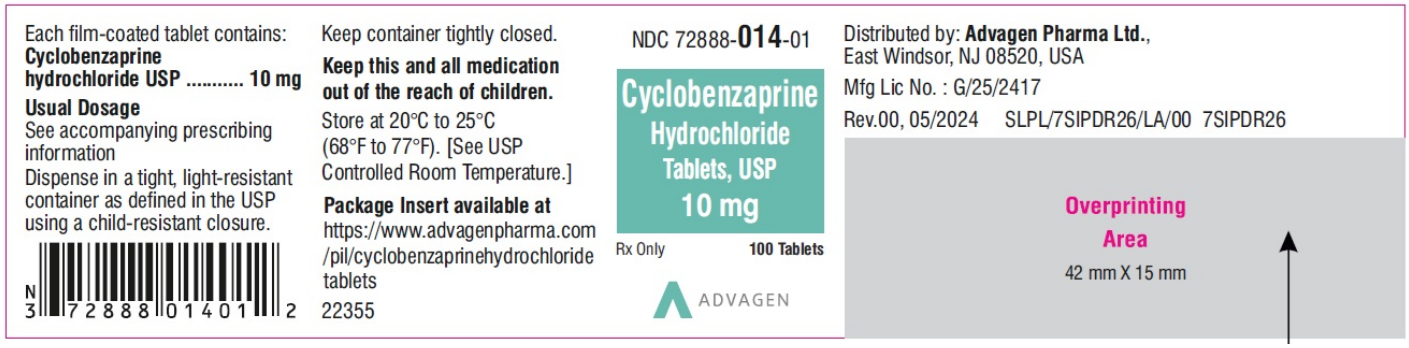
PRINCIPAL DISPLAY PANEL: Cyclobenzaprine Hydrochloride Tablets, USP 7.5 MG

NDC 72888-013-01 bottles of 100 tablets

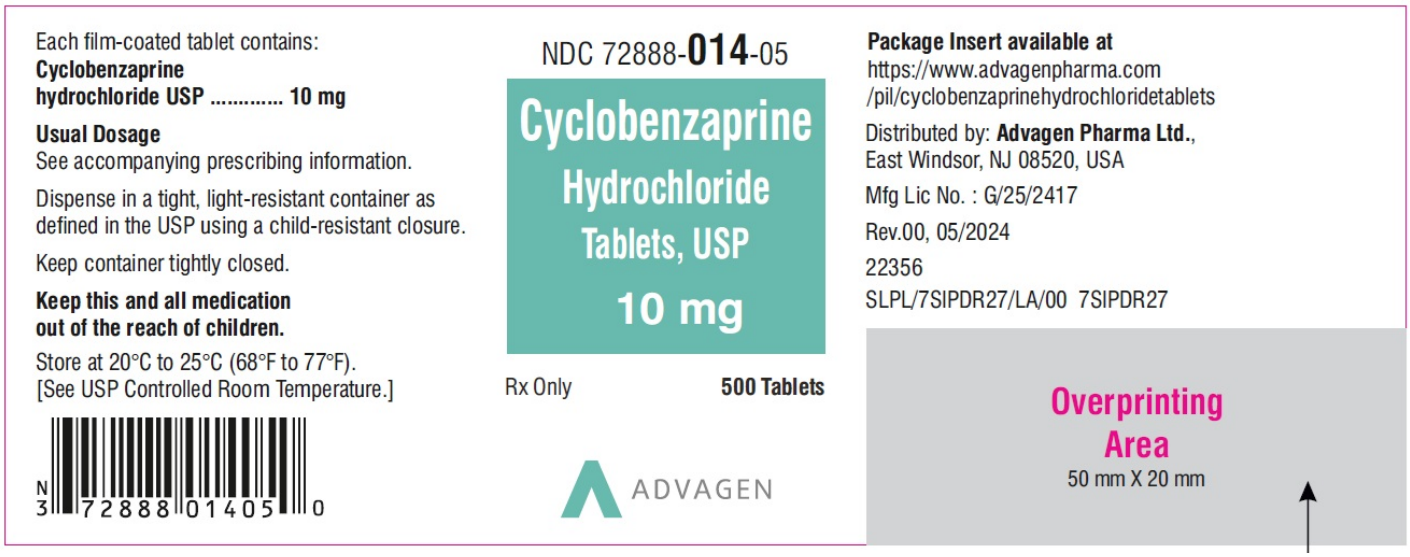


PRINCIPAL DISPLAY PANEL: Cyclobenzaprine Hydrochloride Tablets, USP 10 MG

NDC 72888-014-01 bottles of 100 tablets



NDC 72888-014-05 bottles of 500 tablets



NDC 72888-014-00 bottles of 1000 tablets

Each film-coated tablet contains:
Cyclobenzaprine hydrochloride USP ..... 10 mg

Usual Dosage
See accompanying prescribing information

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.
Keep container tightly closed.

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

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

NDC 72888-**014**-00

Cyclobenzaprine Hydrochloride Tablets, USP 10 mg

Rx Only **1000 Tablets**

ADVAGEN

Package Insert available at
https://www.advagenpharma.com/pil/cyclobenzaprinehydrochloridetablets

Distributed by:
Advagen Pharma Ltd.,
East Windsor, NJ 08520, USA

Mfg Lic No. : G/25/2417

Rev.00, 05/2024

22357

SLPL/7SIPDR28/LA/00 7SIPDR28

Overprinting Area
55 mm X 20 mm

CYCLOBENZAPRINE HYDROCHLORIDE

cyclobenzaprine hydrochloride tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:72888-012
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYCLOBENZAPRINE HYDROCHLORIDE (UNII: 0VE05JYS2P) (CYCLOBENZAPRINE - UNII:69O5WQQ5TI)	CYCLOBENZAPRINE HYDROCHLORIDE	5 mg

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
STARCH, CORN (UNII: O8232NY3SJ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	yellow (butter scotch)	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	020
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72888-012-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	
2	NDC:72888-012-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	
3	NDC:72888-012-00	1000 in 1 BOTTLE; Type 0: Not a Combination Product	11/01/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA208170	05/31/2017	

CYCLOBENZAPRINE HYDROCHLORIDE

cyclobenzaprine hydrochloride tablet, film coated

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:72888-013
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYCLOBENZAPRINE HYDROCHLORIDE (UNII: 0VE05JYS2P) (CYCLOBENZAPRINE - UNII:69O5WQQ5TI)	CYCLOBENZAPRINE HYDROCHLORIDE	7.5 mg

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	

SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
STARCH, CORN (UNII: O8232NY3SJ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics			
Color	white (white to off-white)	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	021
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72888-013-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA208170	05/31/2017	

CYCLOBENZAPRINE HYDROCHLORIDE

cyclobenzaprine hydrochloride tablet, film coated

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:72888-014
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CYCLOBENZAPRINE HYDROCHLORIDE (UNII: 0VE05JYS2P) (CYCLOBENZAPRINE - UNII:69O5WQQ5TI)	CYCLOBENZAPRINE HYDROCHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
CROSPOVIDONE (15 MPA.S AT 5%) (UNII: 68401960MK)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	

SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
STARCH, CORN (UNII: O8232NY3SJ)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	

Product Characteristics

Color	orange (Orange-yellow)	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	022
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72888-014-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	
2	NDC:72888-014-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	
3	NDC:72888-014-00	1000 in 1 BOTTLE; Type 0: Not a Combination Product	05/31/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA208170	05/31/2017	

Labeler - Advagen Pharma Limited (051627256)

Registrant - Rubicon Research Limited (918629544)

Establishment

Name	Address	ID/FEI	Business Operations
Rubicon Research Limited		677604197	manufacture(72888-012, 72888-013, 72888-014) , analysis(72888-012, 72888-013, 72888-014) , label(72888-012, 72888-013, 72888-014) , pack(72888-012, 72888-013, 72888-014)

Revised: 1/2026 Advagen Pharma Limited