

PRODUCT MONOGRAPH

^{Pr}AURO-CYCLOBENZAPRINE

(Cyclobenzaprine Hydrochloride Tablets USP)

10 mg

Skeletal Muscle Relaxant

Auro Pharma Inc.
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Toronto, Ontario
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CANADA

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(Cyclobenzaprine Hydrochloride Tablets USP)

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Oral	Tablet, 10 mg	Lactose <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

INDICATIONS AND CLINICAL USE

AURO-CYCLOBENZAPRINE (cyclobenzaprine hydrochloride) is indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions.

AURO-CYCLOBENZAPRINE should be used only for short periods (up to two or three 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 has 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 the drug. Concomitant use of monoamine oxidase (MAO) inhibitors or within 14 days after their discontinuation. Acute recovery phase of myocardial infarction, and patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure. Hyperthyroidism.

WARNINGS AND PRECAUTIONS

WARNINGS

Cyclobenzaprine hydrochloride is not recommended for periods longer than two or three weeks (see INDICATIONS AND CLINICAL USE).

Cyclobenzaprine hydrochloride 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 more serious central nervous system reactions noted with the tricyclic antidepressants have occurred (see WARNINGS below, and ADVERSE REACTIONS).

Cyclobenzaprine hydrochloride may interact with monoamine oxidase (MAO) inhibitors. Hyperpyretic crises, severe convulsions, and death have occurred in patients receiving tricyclic antidepressants and MAO inhibitors.

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

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

PRECAUTIONS

Cyclobenzaprine hydrochloride may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.

Because of its atropine-like action, Cyclobenzaprine hydrochloride 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.

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

SPECIAL POPULATIONS

Use in Pregnancy: The safe use of Cyclobenzaprine hydrochloride in pregnant women has not been established. Therefore, it should not be administered to women of childbearing potential unless, in the opinion of the treating physician, the anticipated benefits outweigh the possible hazards to the fetus.

Use in Nursing Mothers: Because it is likely that cyclobenzaprine hydrochloride is excreted in milk, Cyclobenzaprine hydrochloride should not be given to nursing mothers.

Use in Children: Safety and effectiveness of Cyclobenzaprine hydrochloride in children below the age of 15 have not been established.

ADVERSE REACTIONS

The following adverse reactions have been reported with cyclobenzaprine hydrochloride tablets:

Most frequent: Drowsiness (39%), dry mouth (27%), dizziness (11%).

Less frequent: Increased heart rate (and several cases of tachycardia), weakness, fatigue, dyspepsia, nausea, paresthesia, unpleasant taste, blurred vision, and insomnia.

Rare: Sweating, myalgia, dyspnea, abdominal pain, constipation, coated tongue, tremors, dysarthria, euphoria, nervousness, disorientation, confusion, headache, urinary retention, decreased bladder tonus, ataxia, depressed mood, hallucinations, and allergic reaction including rash, urticaria, and edema of the face and tongue.

The listing which follows includes other adverse reactions which have been reported with tricyclic compounds, but not with cyclobenzaprine hydrochloride when used in short-term studies in muscle spasm of peripheral origin. Some of these reactions were noted, however, when cyclobenzaprine hydrochloride was studied for other indications, usually in higher dosage. Pharmacologic similarities among the tricyclic drugs require that each of the reactions be considered when cyclobenzaprine hydrochloride is administered.

Cardiovascular: Hypotension, hypertension, palpitation, myocardial infarction, arrhythmias, heart block, stroke.

CNS and Neuromuscular: Confusional states, disturbed concentration, delusions, excitement, anxiety, restlessness, nightmares, numbness and tingling of the extremities, peripheral neuropathy, incoordination, seizures, alteration in EEG patterns, extrapyramidal symptoms, tinnitus, syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Anticholinergic: Disturbance of accommodation, paralytic ileus, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue.

Hematologic: Bone marrow depression including agranulocytosis, leukopenia, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Epigastric distress, vomiting, anorexia, stomatitis, diarrhea, parotid swelling, black tongue. Rarely hepatitis (including altered liver function and jaundice).

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement and galactorrhea in the female. Increased or decreased libido, elevation and lowering of blood sugar levels.

Other: Weight gain or loss, urinary frequency, mydriasis, jaundice, alopecia.

Withdrawal symptoms: Abrupt cessation of treatment after prolonged administration may produce nausea, headache and malaise. These are not indicative of addiction.

DOSAGE AND ADMINISTRATION

The usual dosage of Cyclobenzaprine hydrochloride is 10 mg three times a day with range of 20 to 40 mg a day in divided doses. Dosage should not exceed 60 mg a day. Use of AURO-CYCLOBENZAPRINE is not indicated or recommended for periods longer than two or three weeks.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Manifestations: High doses may cause temporary confusion, disturbed concentration, transient visual hallucinations, agitation, hyperactive reflexes, muscle rigidity, vomiting, or hyperpyrexia, in addition to anything listed under ADVERSE REACTIONS. Based on the known pharmacologic actions of the drug, overdose may cause drowsiness, hypothermia, tachycardia and other cardiac rhythm abnormalities such as bundle branch block, ECG evidence of impaired conduction, and congestive heart failure. Other manifestations may be dilated pupils, convulsions, severe hypotension, stupor, and coma.

Treatment: Treatment is symptomatic and supportive. Empty the stomach as quickly as possible by emesis, followed by gastric lavage. After gastric lavage, activated charcoal may be administered. Twenty to 30 g of the activated charcoal may be given every four to six hours during the first 24 to 48 hours after ingestion. An ECG should be taken and close monitoring of cardiac function must be instituted if there is any evidence of dysrhythmia. Maintenance of an open airway, adequate fluid intake, and regulation of body temperature are necessary.

The slow intravenous administration of one to three mg of physostigmine salicylate is reported to reverse symptoms of poisoning by atropine and other drugs with anticholinergic activity. Physostigmine may be helpful in the treatment of cyclobenzaprine overdose. Because physostigmine is rapidly metabolized, its dosage should be repeated as often as required when life threatening signs such as arrhythmias, convulsions, and deep coma recur or persist.

Standard medical measures should be used to manage circulatory shock and metabolic acidosis. Cardiac arrhythmias may be treated with neostigmine, pyridostigmine, or propranolol. When signs of cardiac failure occur, the use of a short-acting digitalis

preparation should be considered. Close monitoring of cardiac function for not less than five days is advisable.

Anticonvulsants may be given to control seizures.

Dialysis is probably of no value because of low plasma concentrations of the drug.

Since overdosage is often deliberate, patients may attempt suicide by other means during the recovery phase. Deaths by deliberate or accidental overdosage have occurred with this class of drugs.

ACTIONS AND CLINICAL PHARMACOLOGY

Cyclobenzaprine hydrochloride relieves skeletal muscle spasm of local origin without interfering with muscle function. It is not effective in muscle spasm due to central nervous system disease.

Controlled clinical studies show that cyclobenzaprine hydrochloride improves the signs and symptoms of skeletal muscle spasm.

Cyclobenzaprine hydrochloride is well absorbed in man after oral administration, but there is a large intersubject variation in plasma levels. After oral or intravenous doses (10 mg) of ¹⁴C-labelled cyclobenzaprine hydrochloride to human subjects, plasma levels of radioactivity were comparable. In addition, the excretion of radioactivity was similar after both routes (38 to 51 percent in the urine; 14 to 15 percent in the feces), suggesting that oral absorption is almost complete. The half-life varies from one to three days. No effect, on plasma levels or bioavailability was noted in 14 human subjects, when cyclobenzaprine hydrochloride and multiple doses of acetylsalicylic acid was co administered.

Cyclobenzaprine hydrochloride is extensively metabolized in man. In the study with ¹⁴C-labelled drug, about 1 percent of the dose was excreted in the urine as unchanged cyclobenzaprine hydrochloride. The metabolites (probably glucuronides) were excreted as water-soluble conjugates. After oral or intravenous administration of 40 mg of unlabelled cyclobenzaprine hydrochloride to two subjects, only 0.2 to 1.5 percent of the dose was excreted as unchanged drug in the urine within 24 hours.

STORAGE AND STABILITY

Store in well-closed containers at room temperature (15° - 30°C).

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms	Tablets
Description	Tablets are butterscotch yellow, biconvex, 5-sided D-shaped film-coated tablets, debossed with 'D' and '32' on one side and plain on other side.
Composition	Medicinal ingredient: Cyclobenzaprine Hydrochloride USP Nonmedicinal ingredients: Lactose monohydrate USNF, Pregelatinized starch USNF, Crosscarmellose Sodium USNF, Magnesium stearate USNF, Hypromellose USP, titanium dioxide USP, Macrogol USNF & Iron oxide yellow USNF.
Packaging	HDPE bottles of 100's, 500's & 1000's count

PART II: SCIENTIFIC INFORMATION

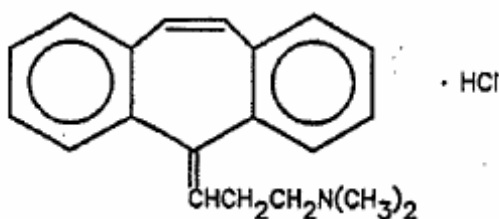
PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Cyclobenzaprine hydrochloride

Chemical Names: 1) 1-Propanamine, 3-5H-dibenzo-[a,d] cyclohepten-5-ylidene)-N,N-dimethyl-, hydrochloride
2) N,N-Dimethyl-5H-dibenzo [a,d]cycloheptene- Δ^5 , γ -propylamine hydrochloride

Structural Formula:



Molecular Formula: C₂₀H₂₁N · HCl

Molecular Weight: 311.85

Physicochemical properties:

Description: Cyclobenzaprine hydrochloride is a white to off-white odourless crystalline powder. It is freely soluble in water, alcohol and methanol; sparingly soluble in isopropyl alcohol; slightly soluble in chloroform and methylene chloride; practically insoluble in hydrocarbon solvents.

Cyclobenzaprine hydrochloride has a melting range between 215° and 219°, and a pKa of 8.47 at 25°C.

CLINICAL TRAILS

Comparative Bioavailability data for Cyclobenzaprine hydrochloride 10 mg Tablets

An Open Label, Randomized, Two Treatment, Two Sequence, Two Period, Cross-Over, Single-Dose Comparative Oral Bioavailability Study of AURO-CYCLOBENZAPRINE Tablets 10 mg (Test) of Aurobindo Pharma Ltd., India and APO-CYCLOBENZAPRINE Tablets 10 mg (Reference) of Apotex Inc., Canada in 48 Healthy, Adult, Male, Human Subjects under fasting conditions.

Cyclobenzaprine Hydrochloride Tablets (1 x 10 mg) From measured data Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test*	Reference†	% Ratio of Geometric Means	90% Confidence Interval
AUC₀₋₇₂ (hr.ng/mL)	156.18 166.35 (34.96)	155.65 170.22 (40.99)	100.34	93.94–107.18
AUC₁ (hr. ng/mL)	192.39 212.54 (45.62)	187.31 211.04 (49.95)	102.71	95.62-110.33
C_{max} (ng/mL)	7.32 7.80 (36.88)	7.48 8.12 (39.58)	97.87	90.24-106.13
T_{max} § (h)	4.00 (2.00-7.50)	4.50 (2.00-8.00)		
T_{1/2} § (h)	32.36 (43.78)	31.17 (53.44)		

*AURO-CYCLOBENZAPRINE 10 mg Tablets, manufactured by Aurobindo Pharma Ltd, India for Auro Pharma Inc.

†APO-CYCLOBENZAPRINE 10 mg Tablets, Apotex Canada Inc. were purchased in Canada

§ Expressed as the Median (Range) instead of Arithmetic Mean (%CV)

§ Expressed as arithmetic mean (%CV) only

PHARMACOLOGY

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.

Cyclobenzaprine hydrochloride has skeletal muscle spasmolytic activity in a number of experimental situations, including tetanus toxin hyperactivity in rabbits, supraspinal rigidity and ischemic cord (spinal) rigidity in cats, and muscle spasm in mice.

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 and alpha motor systems.

Studies in several species of laboratory test animals showed that cyclobenzaprine hydrochloride also possesses psychotropic activity (evidenced by tetrabenazine and reserpine antagonism in mice and rats, potentiation of norepinephrine pressor response in

anesthetized dogs, typical ataraxic drug taming action in monkeys), significant anticholinergic and antihistaminic activity, weak adrenergic blocking and antiserotonin activity, and minor local anesthetic action. In dogs with Heidenhain gastric pouches, cyclobenzaprine did not stimulate gastric secretion.

Following either oral or intravenous doses of ^{14}C -labelled drug, peak plasma levels of radioactivity appeared in half an hour in rats, in two hours in dogs, and in two to four hours in monkeys. Radioactivity was excreted mainly in the feces in rats (59 percent of the dose vs 13 percent in the urine), mainly in the urine in dogs (55 percent vs 28 percent in the feces), and mostly in the urine in monkeys (81 percent vs 14 percent in the feces). Rats excreted 25 percent of an intravenous dose in the bile in six hours. Urinary radioactivity was present almost entirely as water-soluble conjugates, but some species differences were observed in preliminary extraction experiments. The excretion pattern was similar after oral and intravenous doses, suggesting that the drug is extensively absorbed. In rats, all tissues except red blood cells contained higher levels of radioactivity than did plasma two hours after an intravenous dose of labelled drug. Levels were particularly high in small intestine, lung, kidney, and liver. After 48 hours all levels had declined, but activity persisted in liver, kidney and red blood cells.

TOXICOLOGY

Acute Toxicity

Oral LD_{50} values were approximately 338 mg/kg in mice and 425 mg/kg in rats. Signs of drug effects were similar in both species and included ataxia, decreased respiratory rate, sedation, flaccid hind legs, loss of the ear flick reflex, loss of righting reflex with swimming movements, and intermittent clonic convulsions. Death occurred 30 minutes to seven days following administration and was preceded by weight loss and lethargy. Dogs given single oral doses of 180 mg/kg or more by gavage developed ptyalism, emesis, tremors, convulsions, and increased respiratory rate, and died within an hour. When the same dose was given in a capsule, dogs developed similar physical signs, followed by sedation, but recovered after three days, suggesting that the oral dosage form may influence the toxicity. The drug was more toxic to infant and weanling rats than to young adults.

Subacute and Chronic Toxicity: Signs of drug effect in subacute and chronic toxicity studies in rats, dogs, and monkeys were primarily related to the pharmacologic activity of the compound.

Dose (mg/kg/day)	Duration	Physical Signs	Postmortem Findings
RATS			
5 mg	56 weeks	ptyalism	low incidence of midzonal hepatocytic vacuolation with lipidosis.
10 mg	67 weeks	ptyalism, decreased activity, chromorhinorrhea, rales, frequent micturition, flaccidity, resistance to dosing, irritability	midzonal hepatocytic vacuolation with lipidosis, enlarged hepatocytes, centrilobular necrosis
20 or 40 mg	67 weeks	depressed body wt. gain, increased mortality	same as above. More frequent in males
60 mg	2 weeks	decreased physical activity and growth rate	no postmortem examinations
120 or 240 mg	2 - 8 doses	severe wt. loss, collapse, convulsions, death	no postmortem examinations
DOGS			
2 mg	53 weeks	minimal ptyalism, vomiting, dry nose, dry gums	no treatment-related changes
4 or 8 mg	53 weeks	same as above but more pronounced	small foci of gastric mucosal necrosis, hemorrhage, or inflammation in 3/16 dogs
10 mg	28 weeks	slight weight loss, slightly prominent P & T waves in ECG recordings	small focus of unilateral renal papillary edema in 1 of 4 dogs
60 or 120 mg	28 doses	tachycardia, sedation, ataxia, convulsions, death	no postmortem examination
MONKEYS			
2.5 mg	26 weeks	none observed	no treatment related changes
5 or 10 mg	26 weeks	sleepiness (rare)	no treatment related changes
20 mg	26 weeks	general debilitation (1/6 monkeys), sleepiness	chronic pancreatitis, cholecystitis, cholangitis, focal peritonitis (1/6 monkeys)

Teratogenicity: Studies in mice and rabbits did not reveal any evidence of embryo lethality or teratogenicity at oral doses of 5, 10 or 20 mg/kg/day. In rats, doses of 5 mg or 10 mg/kg/day did not adversely affect the reproduction performance or fertility of males or females, or the growth and survival of their offspring. At doses of 20 mg/kg/day there was decrease in litter size, decrease in size and survival of the pups, and reduced weight gain of mothers.

Carcinogenicity: Cyclobenzaprine hydrochloride did not have any effect on the onset, incidence or distribution of neoplasms when given in oral doses of 2, 5, and 10 mg/kg/day to mice for 81 weeks or to rats for 105 weeks.

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PART III: CONSUMER INFORMATION

Pr AURO-CYCLOBENZAPRINE
(Cyclobenzaprine Hydrochloride)

This leaflet is part III of a three-part "Product Monograph" published when AURO-CYCLOBENZAPRINE was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary designed specifically for you to read. It will NOT tell you everything about AURO-CYCLOBENZAPRINE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

AURO-CYCLOBENZAPRINE (cyclobenzaprine hydrochloride) is used as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions.

What it does:

AURO-CYCLOBENZAPRINE relieves skeletal muscle spasm of local origin without interfering with muscle function. Your doctor may choose to use this medication for other conditions not listed here. If you're unsure why you are taking this medication, contact your doctor.

When it should not be used:

AURO-CYCLOBENZAPRINE should not be used by anyone who:

- is hypersensitive to the drug cyclobenzaprine or any components of the drug (See section titled **What the nonmedicinal ingredients are**).
- is taking monoamine oxidase inhibitors or has taken them in the past 14 days.
- is in the acute recovery phase of heart attack.
- has arrhythmias, heart block or conduction disturbances, or congestive heart failure.
- has an hyperthyroidism.

What the medicinal ingredient is:

Cyclobenzaprine Hydrochloride.

What the nonmedicinal ingredients are:

Lactose Monohydrate USNF, Pregelatinized Starch USNF, Croscarmellose Sodium USNF, Magnesium Stearate USNF, Hypromellose USP, titanium dioxide USP, Macrogol USNF & Iron oxide yellow USNF.

What dosage forms it comes in:

AURO-CYCLOBENZAPRINE comes as a tablet containing 10 mg of cyclobenzaprine hydrochloride.

WARNINGS AND PRECAUTIONS

BEFORE you use **AURO-CYCLOBENZAPRINE** talk to your doctor or Pharmacist ABOUT:

- Use of **AURO-CYCLOBENZAPRINE** tablets for periods longer than two or three weeks is not recommended.
- **AURO-CYCLOBENZAPRINE** may interact with monoamine oxidase (MAO) inhibitors.
- Hyperpyretic crises, severe convulsions, and deaths have occurred in patients receiving tricyclic antidepressants and MAO inhibitors.
- **AURO-CYCLOBENZAPRINE** may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.
- **AURO-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.
- The safe use of Cyclobenzaprine hydrochloride in pregnant women has not been established. Therefore it should not be administered to women of child bearing potential unless, in the opinion of the doctor, the anticipated benefits outweigh the possible hazards to the fetus.

IMPORTANT: PLEASE READ

- Because it is likely that Cyclobenzaprine hydrochloride is excreted in milk, it should not be given to nursing mothers.
- The Safety and effectiveness of Cyclobenzaprine hydrochloride in children below the age of 15 have not been established.

In the event of an overdose, you should **IMMEDIATELY** contact either your doctor, the nearest hospital emergency department or poison control centre.

Missed Dose:

Talk to your doctor if you miss a dose.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with AURO-CYCLOBENZAPRINE include:

- alcohol, barbiturates and other medications that cause sedation
- MAO inhibitors (e.g., phenelzine, tranylcypromine)
- tricyclic antidepressants (e.g., amitriptyline, doxepin, imipramine, nortriptyline)

If you are taking any of these drugs, speak with your doctor or pharmacist

PROPER USE OF THIS MEDICATION

Usual dose:

The usual dosage of AURO-CYCLOBENZAPRINE tablets is 10 mg three times a day; with a range of 20 to 40 mg a day in divided doses. Dosage should not exceed 60 mg a day.

Over Dosage:

High doses may cause temporary confusion, disturbed concentration, transient visual hallucinations, agitation, hyperactive reflexes, muscle rigidity, vomiting, or hyperpyrexia. Based on the known pharmacological actions of the drug, over dosage may cause drowsiness, hypothermia, tachycardia and other cardiac rhythm abnormalities such as bundle branch block, ECG evidence of impaired conduction, and congestive heart failure. Other manifestations may be dilated pupils, convulsions, severe hypotension, stupor, and coma.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

You may experience some side effects such as

- Cardiovascular: Hypotension, hypertension, palpitation, myocardial infarction, arrhythmias, heart block, stroke.
- CNS and Neuromuscular: Confusional states, disturbed concentration, delusions, excitement, anxiety, restlessness, nightmares, numbness and tingling of the extremities, peripheral neuropathy, incoordination, seizures, alteration in EEG patterns, extrapyramidal symptoms, tinnitus, syndrome of inappropriate ADH (antidiuretic hormone) secretion.
- Gastrointestinal: Epigastric distress, vomiting, anorexia, stomatitis, diarrhea, parotid swelling, black tongue. Rarely hepatitis (including altered liver function and jaundice).
- Anticholinergic: Disturbance of accommodation, paralytic ileus, dilatation of urinary tract.
- Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue.
- Hematologic: Bone marrow depression including agranulocytosis, leukopenia, eosinophilia, purpura, and thrombocytopenia.
- Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement and galactorrhea in the female. Increased or decreased libido,

IMPORTANT: PLEASE READ

elevation and lowering of blood sugar levels.

- Other: Weight gain or loss, urinary frequency, mydriasis, jaundice, alopecia.
- Withdrawal symptoms: Abrupt cessation of treatment after prolonged administration may produce nausea, headache, and malaise. These are not indicative of addiction.

provider or pharmacist immediately, so that these effects may be properly addressed.

HOW TO STORE IT

Store at room temperature between 15° - 30°C in tightly sealed containers.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Most frequent	Drowsiness (39%), dry mouth (27%), dizziness (11%).		√	
Less common	Increased heart rate (and several cases or tachycardia), weakness, fatigue, dyspepsia, nausea, paresthesia, unpleasant taste, blurred vision, and insomnia.		√	
Rare or Uncommon	Sweating, myalgia, dyspnea, abdominal pain, constipation, coated tongue, tremors, dysarthria, euphoria, nervousness, disorientation, confusion, headache, urinary retention, decreased bladder tonus, ataxia, depressed mood, hallucinations, and allergic reaction including rash, urticaria, and edema of the face and tongue.			√

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reaction associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

Auro Pharma Inc.,
1170, Sheppard Ave. West, Unit #16
Toronto, Ontario
Canada – M3K 2A3

Revised on: April 20, 2010.

This is NOT a complete list of side effects. For any unexpected effects while taking AURO-CYCLOBENZAPRINE, contact your health care