Cyclobenzaprine hydrochloride tablets should be used only for short periods (up to two or three weeks) because adequate evidence of effectiveness for a longer period is not available, and because muscle spasm associated with acute, painful musculoskeletal conditions is generally of short duration and acute pharmacotherapy 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) concurrently with MAO inhibitors.

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

Hyperthyroidism.

WARNINGS

Seizorhin热潮 Syndrome

The development of a potentially life-threatening aseptorhin热潮 syndrome has been reported with cyclobenzaprine hydrochloride when used in combination with other drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin reuptake inhibitors (SNRIs), antidepressant (TCAs), tramadol, lioptamip, mephenytoin, or cyclobenzaprine. The concomitant use of Cyclobenzaprine hydrochloride with MAO inhibitors is contraindicated (see CONTRAINDICATIONS). Seizorhin热潮 syndrome symptoms may include one or more of the following: hyperreflexia, agitation, hallucinations, autonomic instability (e.g., diaphoresis, tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., tremors, akinesia, hyporeflexia, clonus, muscle rigidity), and/or gastrointestinal symptoms (e.g., vomiting, diarrhea). Treatment with Cyclobenzaprine hydrochloride and any concomitant aseptorhin热潮 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 aseptorhin热潮 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., amitryptiline 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 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 anticholinergic signs, 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

Gastrointestinal symptoms

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 intracranial pressure, and in patients taking anticholinergic medication.

Impaired Hepatic Function

The plasma concentration of cyclobenzaprine is increased in patients with hepatic impairment (see PRECAUTIONS). Use in the Elderly and PRECAUTIONS, Impaired Hepatic Function.

Elderly

In a pharmacokinetic study in elderly individuals (65 yr old, mean [SD] 70.5 [8.5] yr; n=10) steady state cyclobenzaprine plasma concentrations of 1.4-fold (1.77 [0.18] ng/mL, range 0.92 to 2.57 [0.38] ng/mL) higher than those seen in a group of eighteen younger adults (101.4 ng/hr/mL, range 36.1-182.9 ng/hr/mL) were observed. Drug accumulation when dosed three times a day, reaching steady state within 3-4 days at plasma concentrations about four-fold higher than those observed in younger adults (see Table). Peak plasma concentration was 25.9 ng/mL, (range, 12.8-46.1 ng/mL) and area under the concentration-time curve (AUC) was 127.3 [95% CI: 111.7-143.8] ng•hr/mL, (range, 84.0-192.7 ng•hr/mL).

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

Hepatic Impairment

In a pharmacokinetic study of sixteen subjects with hepatic impairment (15 mild; 1 moderate per Child-Pugh class), mean [SD] peak plasma concentrations of cyclobenzaprine hydrochloride tablets were 1.7-fold (1.71 [0.19] ng/mL, range 1.0-2.82 [0.29] ng/mL) higher than those seen in a group of eighteen younger adults (101.4 ng/hr/mL, range 36.1-182.9 ng/hr/mL) were observed. Drug accumulation when dosed three times a day, reaching steady state within 3-4 days at plasma concentrations observed in young adults (see Table). Peak plasma concentration was 25.9 ng/mL, (range, 12.8-46.1 ng/mL) and area under the concentration-time curve (AUC) was 127.3 [95% CI: 111.7-143.8] ng•hr/mL, (range, 84.0-192.7 ng•hr/mL).

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 muscle spasm, some of the more serious central nervous system reactions noted with the tricyclic antidepressants have occurred (see WARNINGS, below and ADVERSE REACTIONS).

Cyclobenzaprine hydrochloride tablets in the elderly 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, lioptamip, mephenytoin, venlafaxine, 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 any of the following symptoms (see WARNINGS, and see PRECAUTIONS, Drug Interactions).

Drug Interactions

Cyclobenzaprine may have life threatening interactions with MAO inhibitors (see CONTRAINDICATIONS). Concomitant use of cyclobenzaprine and other drugs, such as SSRIs, SNRIs, TCAs, tramadol, lioptamip, mephenytoin, venlafaxine, or MAO inhibitors. Concomitant use with other 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 aseptorhin热潮 drugs is clinically warranted, careful observation is advised, particularly during treatment initiation or dose increases (see PRECAUTIONS, Drug Interactions).

Cyclobenzaprine may have life threatening interactions with MAO inhibitors (see CONTRAINDICATIONS). Concomitant use of cyclobenzaprine and other drugs, such as SSRIs, SNRIs, TCAs, tramadol, lioptamip, mephenytoin, venlafaxine, or MAO inhibitors. Concomitant use with other 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 aseptorhin热潮 drugs is clinically warranted, careful observation is advised, particularly during treatment initiation or dose increases (see PRECAUTIONS, Drug Interactions).

Cyclobenzaprine may blunt the antipruritic action of guaifenesin and similarly acting agents.

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

ADVERSE REACTIONS

Incidence of most common adverse reactions in the 2 double-blind, placebo-controlled 5 mg studies (incidence of > 3% on cyclobenzaprine hydrochloride tablets 5 mg):

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Cyclobenzaprine Hydrochloride Tablets</th>
<th>Placebo</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclobenzaprine Hydrochloride Tablets 5 mg</td>
<td>N=648</td>
<td>N=249</td>
<td>N=403</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>21%</td>
<td>24%</td>
<td>22%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5%</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Headache</td>
<td>5%</td>
<td>11%</td>
<td>9%</td>
</tr>
</tbody>
</table>
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 435 patients treated with cyclobenzaprine hydrochloride tablets 10 mg in additional controlled clinical studies. 7007 patients in the post-marketing 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 hydrochloride 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.

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

Paralytic ileus; tongue discoloration; stomatitis; parotid swelling.

Ageusia; tinnitus.

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

Liver/Gallbladder: Acute fulminating hepatitis.

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

Bradycardia; atrioventricular (AV) block; first-degree AV block; second-degree AV block (Mobitz I); second-degree AV block (Mobitz II); third-degree AV block; ventricular tachycardia; pulse not palpable; death.

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

Rapidly after cyclobenzaprine overdose; therefore, hospital monitoring is required as soon as possible.

Dizziness 11% 3%

Nervous System and Psychiatric: Tinnitus; carpopedal spasm; dysarthria; ataxia; vertigo; gait disturbance; peripheral neuropathy; nystagmus; ataxia; aphasia; seizures; extrapyramidal symptoms.

Drowsiness 39% 16%

Vomiting; anorexia; diarrhea; gastrointestinal pain; gas; indigestion; nausea; vomiting; abdominal cramps; colic; diarrhea; epigastric distress; flatulence; dyspepsia; abdominal pain; abdominal discomfort; abdominal distention; abdominal distension; indigestion; flatulence.

Dosage and Administration

Use of cyclobenzaprine hydrochloride tablets for periods longer than two or three weeks is not recommended (see INDICATIONS AND USAGE).