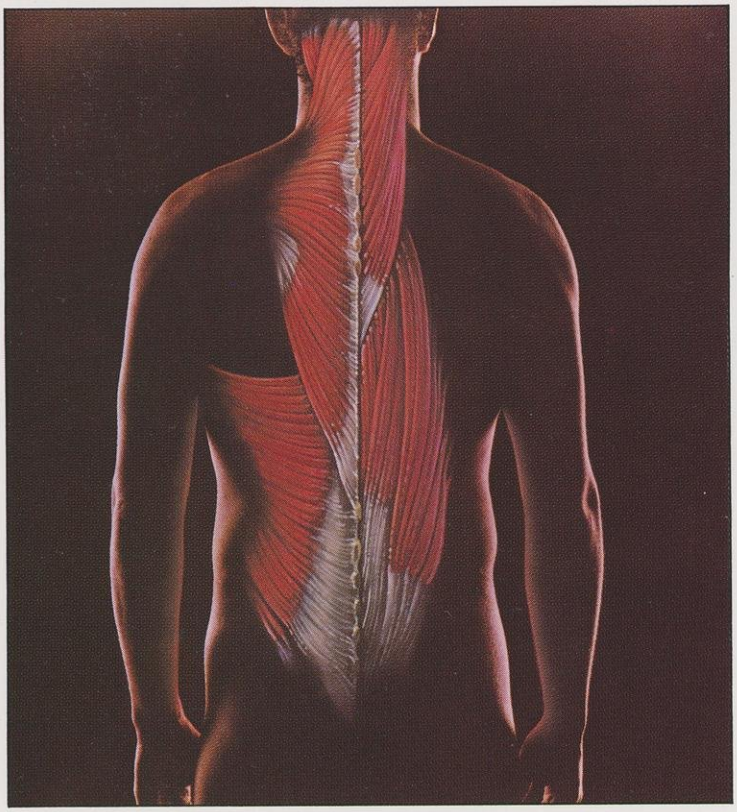
Flexeril advertisement.

[s.l.]: [s.n.], 1974

A significant new agent from Merck Sharp & Dohme



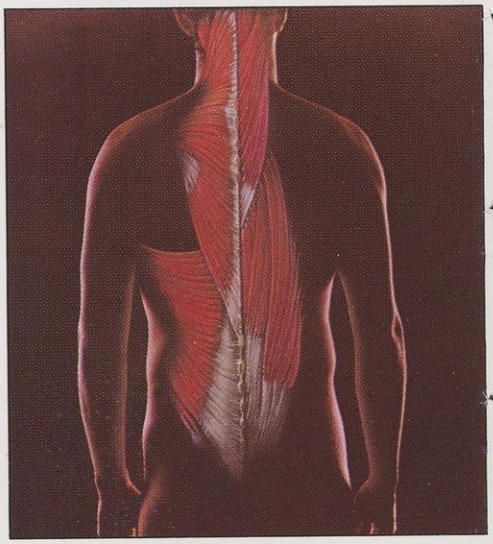
FLEXERIL™
(CYCLOBENZAPRINE HCl|MSD)

an adjunct to rest and physical therapy in the short-term management of **skeletal muscle spasm of local origin**

For a brief summary of prescribing information, please see last page of this advertisement.

MSD
MERCK SHARP & DOHME

Efficacy evaluated in 16 double-blind studies



FLEXERIL™ (Cyclobenzaprine HCl, MSD) is indicated as an adjunct to rest and physical therapy for relief of muscle spasm associated with acute, painful musculoskeletal conditions. FLEXERIL has not been found effective in the treatment of spasticity associated with cerebral or spinal cord disease, or in children with cerebral palsy. **Use of cyclobenzaprine for periods longer than two or three weeks is not recommended because adequate evidence of effectiveness for more prolonged use is not available and the condition being treated is generally of short duration.**

Improvement seen in the basic elements of response

- relief of muscle spasm as determined by palpation
- reduction of local pain
- reduction of tenderness
- increase in range of motion
- improvement in activities of daily living*

*Activities of daily living is the investigator's assessment of the patient's ability to perform essential and customary tasks including dressing, turning, bending, and walking.

Efficacy compared with ■ placebo ■ placebo and diazepam†

In the 16 double-blind controlled studies involving 952 patients, FLEXERIL was compared to placebo in 759 patients. In 12 of the 16 studies improvement with FLEXERIL was significantly greater than with placebo.
In 8 of the 16 double-blind controlled clinical studies, FLEXERIL was also compared to diazepam, a standard active drug. In three of these studies there was a significantly greater improvement with FLEXERIL than with diazepam while in the remaining studies the improvement following both treatments was comparable.
Adverse reactions were comparable with FLEXERIL and diazepam. Dry mouth was observed more frequently with FLEXERIL; dizziness more frequently with diazepam. The incidence of drowsiness, the most frequent adverse reaction, was similar with both drugs.

†Valium® (diazepam, Roche)

Efficacy independent of sedation

Clinical improvement occurs regardless of any sedative action. **However, drowsiness, the most frequent adverse reaction, occurred in approximately 40 percent of patients studied.**

Relieves spasm without interfering with muscle function

Relieves skeletal muscle spasm of local origin without interfering with muscle function. Not recommended for muscle spasm due to central nervous system disease. FLEXERIL is often effective in relieving local pain secondary to skeletal muscle spasm. However, it will not relieve pain unrelated to spasm.

Prompt onset of action

Clinical improvement has been observed as early as the first day of therapy in some patients. The full therapeutic response often can be expected during the first week of therapy.

Simple dosage regimen

Usual dosage: one 10-mg tablet t.i.d., with a range of 20 to 40 mg per day in divided doses. Dosage should not exceed 60 mg per day. Use for periods longer than two or three weeks is not recommended.

NEW

Tablets, 10 mg

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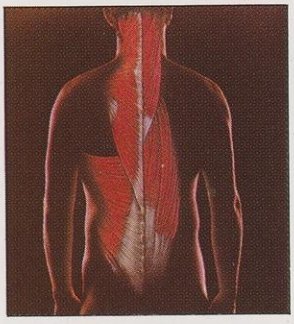
Understanding the limitations of FLEXERIL™ (CYCLOBENZAPRINE HCl|MSD) is important in evaluating its clinical benefits.



CAUTIONARY INFORMATION

Note: FLEXERIL has not been found effective in the treatment of spasticity associated with cerebral or spinal cord disease, or in children with cerebral palsy.

Contraindicated in hypersensitivity to the drug, in those who have received an MAOI within two weeks, or in hyperthyroidism; during the acute recovery phase of myocardial infarction and in patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure.

FLEXERIL is closely related to the tricyclic antidepressants. 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 tricyclic antidepressants have occurred. Tricyclic antidepressants have been reported to produce arrhythmias, sinus tachycardia, prolongation of the conduction time leading to myocardial infarction and stroke.

May enhance effects of alcohol, barbiturates, and other CNS depressants. Caution patients about performance of hazardous tasks or driving. Use with caution in patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and in patients taking anticholinergic medications. Tricyclic antidepressants may block the antihypertensive action of guanethidine and similarly acting compounds.

FLEXERIL is not recommended in pregnant women, nursing mothers, or children below the age of 15.

NEW

FLEXERIL™

(CYCLOBENZAPRINE HCl|MSD)

an adjunct to rest and physical therapy in the short-term management of **skeletal muscle spasm of local origin**

Note: FLEXERIL 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 MAO inhibitors or within 14 days after their discontinuation; acute recovery phase of myocardial infarction; arrhythmias, heart block or conduction disturbances, or congestive heart failure; hyperthyroidism.

Warnings: *Use of FLEXERIL (Cyclobenzaprine HCl, MSD) for periods longer than two or three weeks is not recommended.* FLEXERIL 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**). FLEXERIL may interact with monoamine oxidase (MAO) inhibitors. Hyperpyretic crisis, severe convulsions, and deaths have occurred in patients receiving tricyclic antidepressants and MAO inhibitor drugs. Tricyclic antidepressants have been reported to produce arrhythmias, sinus tachycardia, prolongation of the conduction time leading to myocardial infarction and stroke. FLEXERIL may enhance the effects of alcohol, barbiturates, and other CNS depressants.

Precautions: May impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle. 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.

In rats treated with FLEXERIL for up to 67 weeks at doses of 5 to 50 mg/kg, 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. In clinical trials with FLEXERIL, most of which were short term, no liver function abnormalities were noted.

Use in Pregnancy: Safe use in pregnant women has not been established; anticipated benefits must be weighed against possible hazards to mother and child.

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

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

Adverse Reactions: *Most frequent:* Drowsiness (40%), dry mouth (28%), dizziness (11%). *Less frequent:* Increased heart rate (and several cases of tachycardia), weakness, dyspepsia, 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, and ataxia.

In the listing which follows are other adverse reactions which have been reported with tricyclic compounds, but not with FLEXERIL when used in short-term studies in muscle spasm of peripheral origin. Some of these reactions (e.g., hallucinations) were noted, however, when FLEXERIL 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 is administered: *Cardiovascular:* Hypotension, hypertension, palpitation, myocardial infarction, arrhythmias, heart block, stroke. *CNS and Neuromuscular:* Confusional states, disturbed concentration, delusions, hallucinations, 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:* Nausea, 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:* Fatigue, 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.

Overdosage: Treatment is symptomatic and supportive. Empty the stomach as quickly as possible by emesis, followed by gastric lavage. 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. In addition, the intravenous administration of 1 to 3 mg physostigmine salicylate, which is reported to reverse symptoms of poisoning by atropine and other drugs with anticholinergic activity, 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.

How Supplied: Tablets containing 10 mg cyclobenzaprine HCl, in bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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