

The chances  
of one of your patients  
dying suddenly following a  
recent myocardial infarction  
have just been cut  
in half.

# Results of a Recent Post-Myocardial

# ANTURAN REDUCED ANNUAL CARDIAC DEATH RATE BY 48.5% COMPARED WITH PLACEBO.

## The Trial

A prospective, randomized, double-blind, multi-center study analyzing 1,475 patients, comparing the effect of Anturan 200 mg q.i.d. and placebo in the prevention of cardiac mortality in patients with recent myocardial infarction.

Twenty-one U.S. and five Canadian hospitals participated in the trial.

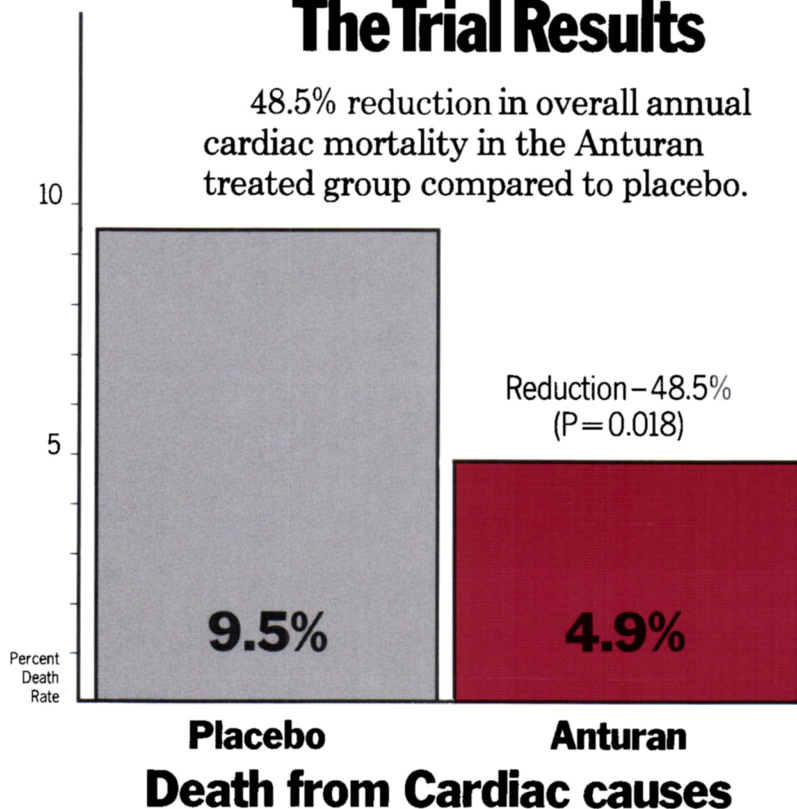
The co-ordinators consisted of representatives of the medical, epidemiological and biostatistical communities of Canada and the U.S.

#### REFERENCE:

1. Sulfapyrazone in the Prevention of Cardiac Death after Myocardial Infarction. The Anturan Reinfarction Trial. The Anturan Reinfarction Trial Research Group. In: *New England Journal of Medicine*, Vol. 298, No. 6, Feb. 9, 1978.

## The Trial Results

48.5% reduction in overall annual cardiac mortality in the Anturan treated group compared to placebo.



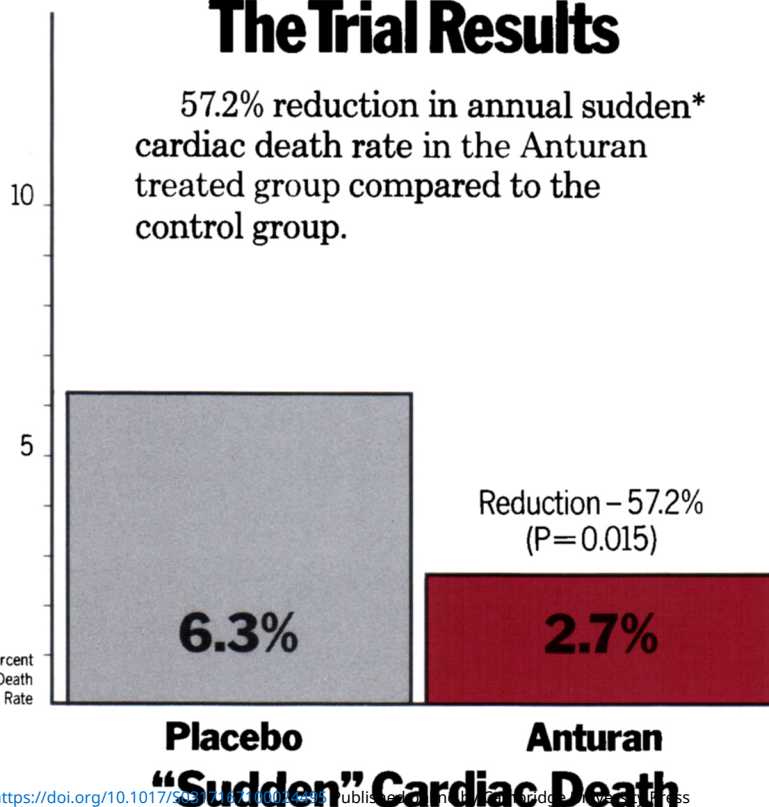


# Infarction Trial:<sup>1</sup>

# ANNUAL SUDDEN\* CARDIAC DEATH RATE BY 57.2% COMPARED WITH PLACEBO.

## The Trial Results

57.2% reduction in annual sudden\* cardiac death rate in the Anturan treated group compared to the control group.



"The data reflect excellent randomization, compliance with therapy and tolerance of the drug."<sup>1</sup>

## Conclusion

"There are approximately 900 deaths per week in the United States among patients who have recently recovered from an acute myocardial infarction. If the benefit of sulfinpyrazone therapy can be shown to be sustained in the later periods of this trial, conservative interpretation of the overall results to date suggest the feasibility of reducing cardiac deaths during the first year after myocardial infarction by 200 to 300 per week."<sup>1</sup>

\*Sudden death - within 60 minutes of onset of symptoms.

It's a matter of life.

**ANTURAN**  
four times  
**200mg** a day



## Abstract<sup>1</sup>

The Anturan Reinfarction Trial is a randomized, double-blind, multicenter clinical trial comparing sulfinpyrazone (200 mg four times a day) and placebo in the prevention of cardiac mortality among patients with a recent documented myocardial infarction. Results represent data accumulated on 1475 eligible patients entered 25 to 35 days after myocardial infarction and followed for an average of 8.4 months. The data reflect excellent randomization, compliance with therapy and tolerance of the drug. All 69 deaths were of a cardio-

vascular nature (68 cardiac and one cerebrovascular). For cardiac deaths, the annual death rate was 9.5 per cent in the placebo group and 4.9 per cent in the sulfinpyrazone group, representing an observed reduction of 48.5 per cent ( $P = 0.018$ ). The annual sudden-cardiac-death rate was 6.3 per cent for the placebo and 2.7 per cent for the sulfinpyrazone group, representing a 57.2 per cent reduction in sudden-cardiac-death rate ( $P = 0.015$ ). Sulfinpyrazone appears to be effective in reducing cardiac deaths during the first year after myocardial infarction.

## Brief Prescribing Information

### INDICATIONS:

**1** Clinical states in which abnormal platelet behavior is a causative or associated factor, as demonstrated by:

- thromboembolism associated with vascular and cardiac prostheses
- recurrent venous thrombosis
- arteriovenous shunt thrombosis

**2** Chronic phases of gout, both the intercritical or silent stage and the gouty arthritis stage.

### DOSAGE AND ADMINISTRATION:

**Thromboembolic conditions:**—Usual daily dosage is 600–800 mg in divided doses. It is recommended not to exceed 1000 mg (20 mg/kg for a 50 kg man) daily.

**Gout:**—Usual daily dosage is 200–400 mg in divided doses. This average dosage may be increased to 800 mg if necessary, or reduced to 200 mg when urate blood level has been satisfactorily controlled. Minimum effective dose should be maintained indefinitely without interruption even during acute attacks, which should be treated concomitantly with either Butazolidin or colchicine.

The change from other uricosuric agents to Anturan should be made at full dosage.

It is important to distribute the total dose as well as possible over a 24-hour period. It is recommended that Anturan be taken with meals.

### CONTRAINDICATIONS:

The safe use of sulfinpyrazone in pregnancy has not been established. It should not be used during pregnancy unless in the opinion of the treating physician the expected benefits outweigh the potential risks.

Active peptic ulcer.

Known hypersensitivity to sulfinpyrazone and other pyrazolone derivatives. Severe hepatic or renal disease, unless due to platelet aggregates.

### WARNINGS:

Avoid salicylate therapy, unless administered under careful supervision:

- (i) Salicylates and citrates antagonize the uricosuric action of sulfinpyrazone and may therefore interfere with uric acid excretion.
- (ii) Salicylates may cause unpredictable and at times, serious prolongation of the bleeding time and in combination with sulfinpyrazone may cause bleeding episodes. If during Anturan therapy, aspirin or another chemically-related drug must be used, patients should be urged to report immediately any undue bleeding episode.

It should be administered with care to patients with a history of healed peptic ulcer.

### PRECAUTIONS:

As with all pyrazole compounds, patients receiving Anturan should be kept under close medical supervision and periodic blood counts are recommended.

Recent reports have indicated that Anturan potentiates the action of sulfonamides, e.g., sulfadiazine, sulfisoxazole. Other pyrazole compounds e.g., phenylbutazone, potentiate the hypoglycemic effects of sulfonylureas. There have also been reports that phenylbutazone enhances the effects of insulin in diabetics. Therefore, it is recommended that Anturan be used with caution in conjunction with insulin, sulfonamides, the sulfonylurea hypoglycemic agents and, in general, with agents known to displace, or to be displaced by, other substances, such as penicillin, from serum albumin binding sites.

Because Anturan is a potent uricosuric agent, it may precipitate urolithiasis and renal colic, especially in the initial stages of therapy, in hyperuricemic patients. For this reason, an adequate fluid intake and alkalinization of the urine are recommended. In cases with significant renal impairment, periodic assessment of renal function is indicated.

Since Anturan modifies platelet behavior and, therefore, interferes with one of the components of the blood-clotting system, it should be used with care in conjunction with certain vitamin K antagonists which inhibit clotting through a different mechanism. Regular estimations of bleeding time should be performed.

### ADVERSE REACTIONS:

The most frequently reported adverse reactions to Anturan have been gastric complaints or disturbances. Anturan may aggravate or reactivate peptic ulcer. Gastrointestinal bleeding has been reported.

Skin rashes have been reported in rare instances. When they occur, Anturan should be withdrawn.

Anemia, leukopenia, agranulocytosis, thrombocytopenia have rarely been associated with the administration of Anturan.

### DOSAGE FORMS:

**Anturan 100 mg:** Each white, single scored tablet, imprinted Geigy and bearing the identification code FK, contains 100 mg sulfinpyrazone Geigy standard. Supplied in bottles of 100 and 1,000.

**Anturan 200 mg:** Each white, sugar-coated tablet, imprinted Geigy, contains 200 mg sulfinpyrazone Geigy standard. Supplied in bottles of 100 and 500. Product monograph supplied on request.

# Geigy

Dorval, H9S 1B1, Que.

G-8033

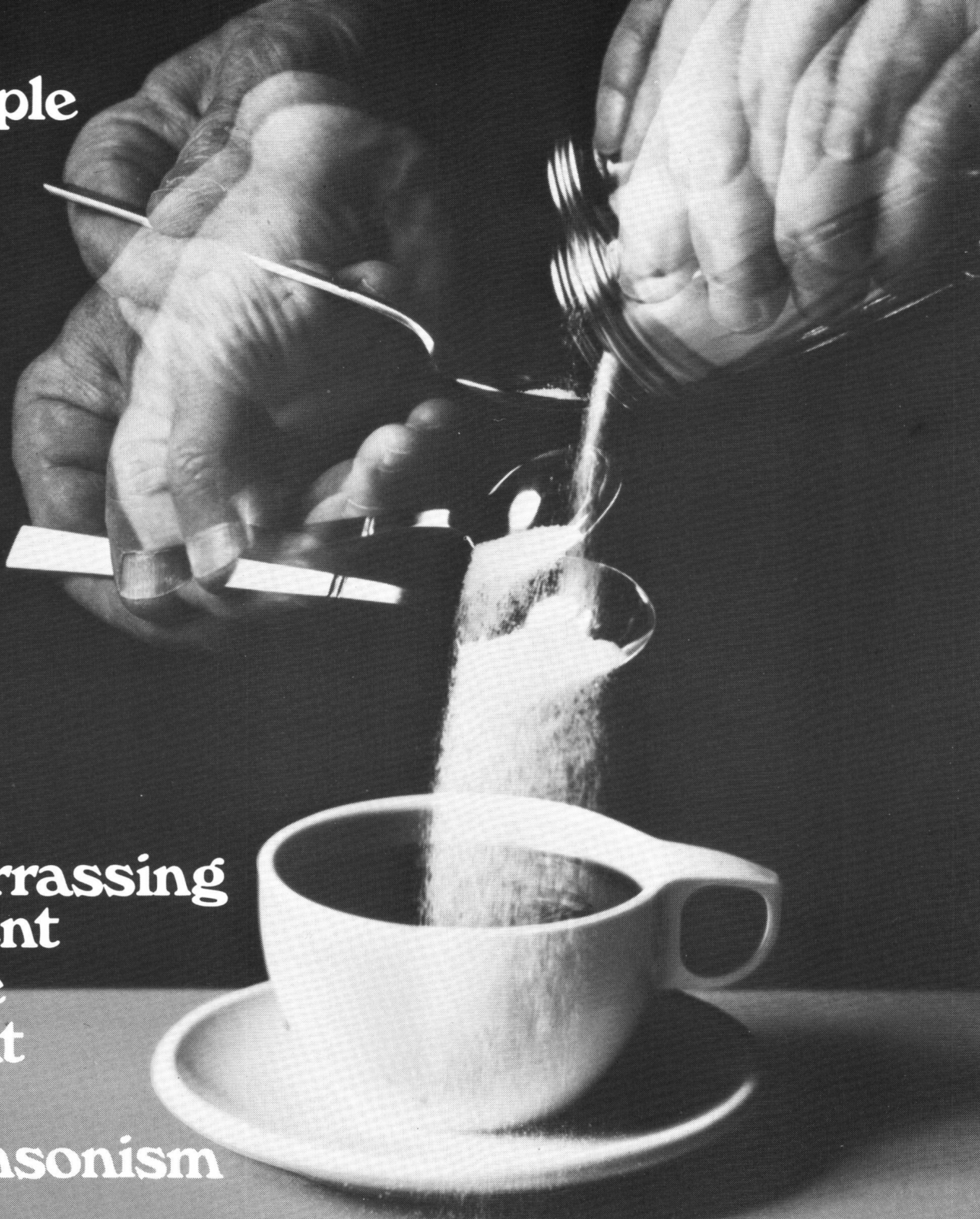
It's a matter of life.

# ANTURAN<sup>®</sup>

## 200 mg four times a day



**A simple  
task**



**but an  
embarrassing  
moment  
for the  
patient  
with  
parkinsonism**

**Cogentin<sup>\*</sup>**

(bentropine mesylate, MSD Std.)

**Antiparkinsonian agent**



**MERCK  
SHARP  
& DOHME** CANADA LIMITED  
POINTE CLAIRE, QUEBEC H9R 4P7

\*Trademark CGT-8-481-JA

FULL PRESCRIBING INFORMATION AVAILABLE ON REQUEST



# Symmetrel<sup>®</sup> Capsules 100 mg (amantadine HCl)

## for the management of Parkinson's syndrome

 **Chemically distinct**

(Not related to levodopa or anticholinergic antiparkinson drugs.)

 **Fast onset of action**

(Usually effective within 1 week in contrast to the slower response from levodopa.)

 **Effective with levodopa**

(Either initiated concurrently or added to levodopa. Additional benefit may result — such as smoothing out of fluctuations in performance which sometimes occur when levodopa is administered alone. When the levodopa dose must be reduced because of side effects, the addition of Symmetrel may result in better control of Parkinson's syndrome than is possible with levodopa alone.)

 **Effective with other anticholinergic antiparkinson drugs**

(When these drugs, e.g. benzotropine mesylate, provide only marginal benefits, Symmetrel used concomitantly may provide the same degree of control of Parkinson's syndrome, often with a lower dose of anticholinergic medication, and a possible reduction in anticholinergic side effects.)

 **Effective alone**

(Lessening of Parkinsonian symptomatology usually evident within one week in responsive patients.)

**CONTRAINDICATIONS** "Symmetrel" is contraindicated in patients with known hypersensitivity to the drug

**WARNINGS** Patients with a history of epilepsy or other "seizures" should be observed closely for possible untoward central nervous system effects.

Patients with a history of congestive heart failure or peripheral edema should be followed closely as there are patients who developed congestive heart failure while receiving "Symmetrel" (amantadine HCl).

Safety of use in pregnancy has not been established. Therefore, "Symmetrel" should not be used in women with childbearing potential, unless in the opinion of the physician, the expected benefit to the patient outweighs the possible risks to the fetus (see Toxicology/Effects on Reproduction).

Since the drug is secreted in the milk, "Symmetrel" should not be administered to nursing mothers.

**PRECAUTIONS** The dose of "Symmetrel" may need careful adjustment in patients with renal impairment, congestive heart failure, peripheral edema, or orthostatic hypotension. Since "Symmetrel" is not metabolized and is mainly excreted in the urine, it may accumulate when renal function is inadequate.

Care should be exercised when administering "Symmetrel" to patients with liver disease, a history of recurrent eczematoid rash, or to patients with psychosis or severe psychoneurosis not controlled by chemotherapeutic agents. Careful observation is required when "Symmetrel" is administered concurrently with central nervous system stimulants.

Patients with Parkinson's syndrome improving on "Symmetrel" should resume normal activities gradually and cautiously, consistent with other medical considerations, such as the presence of osteoporosis or phlebotrombosis.

Patients receiving "Symmetrel" (amantadine HCl) who note central nervous system effects of blurring of vision should be cautioned against driving or working in situations where alertness is important.

"Symmetrel" (amantadine HCl) should not be discontinued abruptly since a few patients with Parkinson's syndrome experienced a Parkinsonian crisis, i.e., sudden marked clinical deterioration, when this medication was suddenly stopped.

The dose of anticholinergic drugs or of "Symmetrel" should be reduced if atropine-like effects appear when these drugs are used concurrently.

**ADVERSE REACTIONS** Adverse reactions reported below have occurred in patients while receiving "Symmetrel" (amantadine HCl) alone or in combination

with anticholinergic antiparkinson drugs and/or levodopa

The more important adverse reactions are orthostatic hypotensive episodes, congestive heart failure, depression, psychosis and urinary retention, and rarely confusion, reversible leukopenia and neutropenia, and abnormal liver function test results. Other adverse reactions of less importance which have been observed are, anorexia, anxiety, ataxia, confusion, hallucinations, constipation, dizziness (lightheadedness), dry mouth, headache, insomnia, livedo reticularis, nausea, peripheral edema, drowsiness, dyspnea, fatigue, hyperkinesia, irritability, nightmares, rash, slurred speech, visual disturbance, vomiting and weakness, and very rarely eczematoid dermatitis and oculogyric episodes.

Some side effects were transient and disappeared even with continued administration of the drug.

**DOSAGE AND ADMINISTRATION** The initial dose of "Symmetrel" is 100 mg daily for patients with serious associated medical illnesses or who are receiving high doses of other antiparkinson drugs. After one to several weeks at 100 mg once daily, the dose may be increased to 100 mg twice daily. When "Symmetrel" and levodopa are initiated concurrently, "Symmetrel" should be held constant at 100 mg daily or twice daily while the daily dose of levodopa is gradually increased to optimal dose. When used alone, the usual dose of "Symmetrel" is 100 mg twice a day.

Patients whose responses are not optimal with "Symmetrel" (amantadine HCl) at 200 mg daily may benefit from an increase to 300 mg daily in divided doses. Patients who experience a fall-off of effectiveness may regain benefit by increasing the dose to 300 mg daily, such patients should be supervised closely by their physicians.

**DOSAGE FORMS** CAPSULES: (bottles of 100) — each red, soft gelatin capsule contains 100 mg of amantadine HCl

Product monograph, with complete references, available upon request.

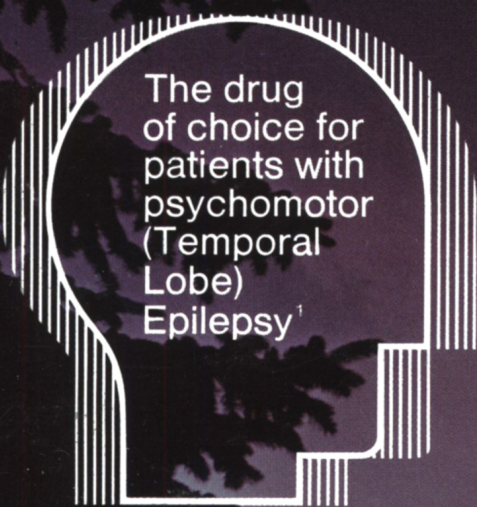
Subsidiary of E.I. du Pont de Nemours & Co. (Inc.)




In epilepsy\*

# Tegretol<sup>®</sup>


provides control of seizures  
and alleviation of personality  
disorders.



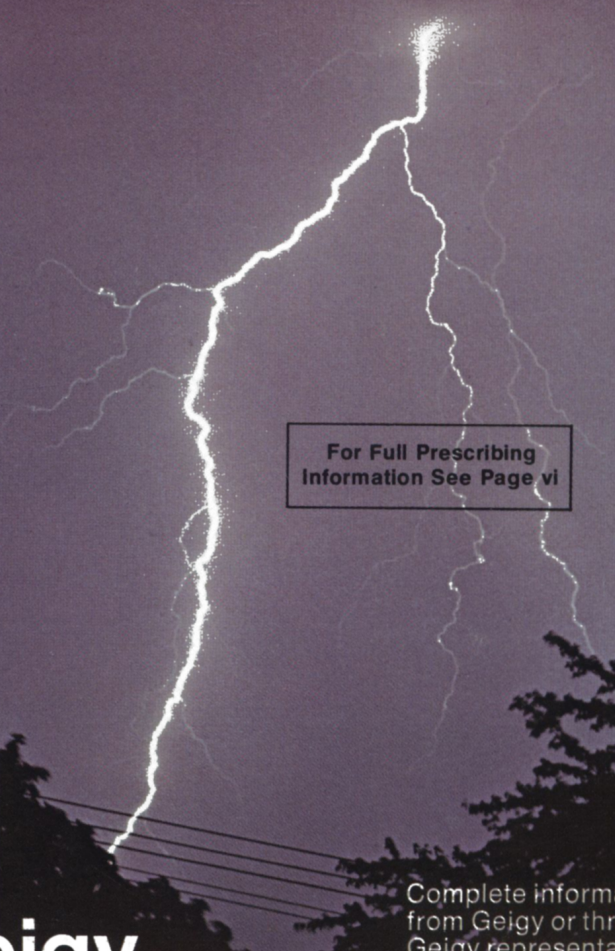
The drug  
of choice for  
patients with  
psychomotor  
(Temporal  
Lobe)  
Epilepsy<sup>1</sup>



Reliable  
control for  
patients who  
are refractory  
to treatment  
with other  
anticonvul-  
sants<sup>2</sup>



Improved  
compatibility  
for patients  
with excessive  
sedation or  
Hyperplasia  
of Gingival  
Mucosa due  
to other  
agents<sup>3</sup>



For Full Prescribing  
Information See Page vi

**Geigy**

Dover, P.O. H9S 1B1

Complete information available  
from Geigy or through your  
Geigy representative

\*See indications, brief prescribing  
information