

# THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES

# LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

<b>Vascular Amyloid in the Aging Central Nervous System</b> <i>Joseph Bruni, Juan M. Bilbao and Kenneth P. H. Pritzker</i>	<b>239</b>
<b>Cerebral Hemodynamics in Migraine</b> ..... <i>V. C. Hachinski, J. Olesen, J. W. Norris, B. Larsen, E. Enevoldsen and N. A. Lassen</i>	<b>245</b>
<b>Pure Spastic Paralysis of Corticospinal Origin</b> ..... <i>C. M. Fisher</i>	<b>251</b>
<b>Lumbo-Sacral Radiculopathy Induced by Radiation</b> ..... <i>E. M. Ashenurst, G. R. C. Quartey and A. Starreveld</i>	<b>259</b>
<b>A Community Neurologist's Personal Viewpoint on Neurological Training</b> ..... <i>Charles A. Simpson</i>	<b>265</b>
<b>Central Nervous System Vasculitis in Rheumatoid Arthritis</b> <i>Peter Watson, John Fekete and John Deck</i>	<b>269</b>
<b>Afterdischarge Thresholds and Kindling Rates in Dorsal and Ventral Hippocampus and Dentate Gyrus</b> <i>Ronald Racine, Patty A. Rose and W. M. Burnham</i>	<b>273</b>
<b>Seven Cases of Gilles de la Tourette's Syndrome: Partial Relief with Clonazepam: A Pilot Study</b> ..... <i>M. Gonce and A. Barbeau</i>	<b>279</b>
<b>Platelet Dopamine Uptake in Huntington's Chorea and Gilles de la Tourette's Syndrome: Effect of Haloperidol</b> <i>Roger F. Butterworth, Michel Gonce, and André Barbeau</i>	<b>285</b>
<b>Index to Volume 4</b> .....	<b>(i)</b>

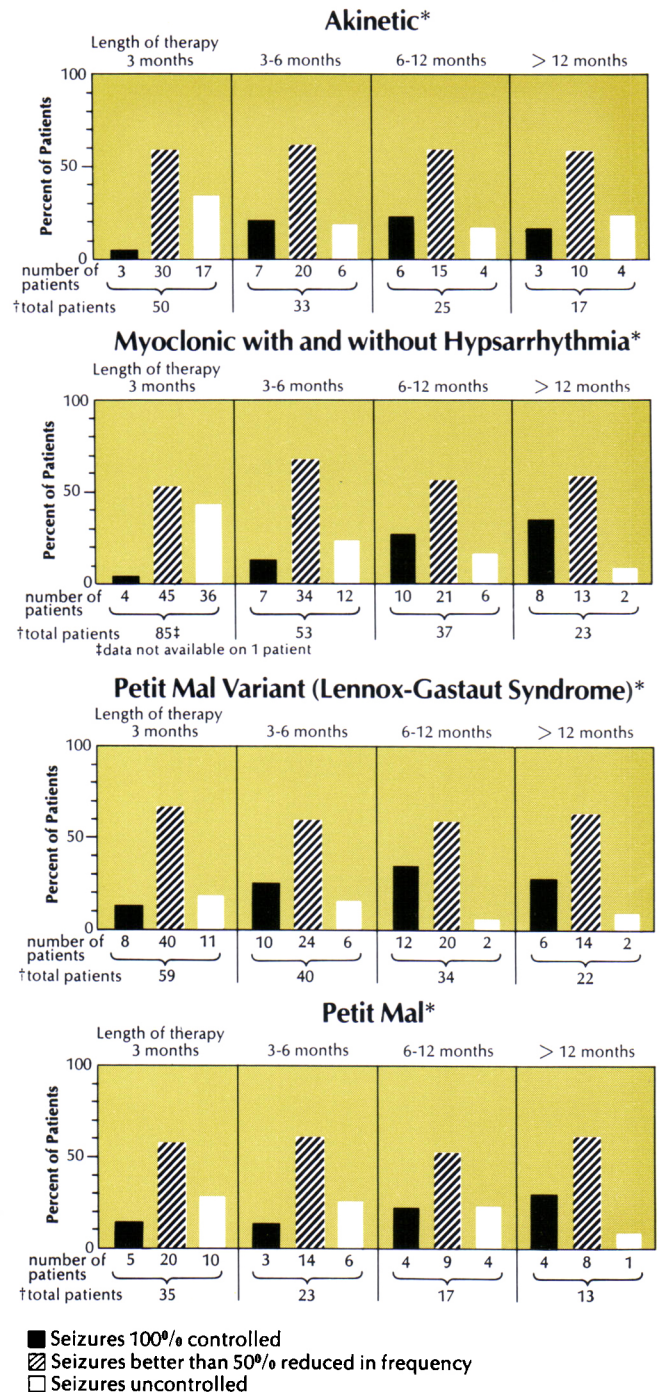
# Rivotril®

## a new oral anticonvulsant from 'Roche' research

RIVOTRIL, with specific and potent anticonvulsant properties, is a new benzodiazepine in the same family as Librium®, Valium® and Dalmane® Roche®. It is therefore characterized by the same high degree of safety and efficacy.

- used alone or as an adjunct, RIVOTRIL can reduce the frequency and/or severity of akinetic, myoclonic and petit mal variant (Lennox-Gastaut syndrome) seizures.
- it may be of value as principal medication in petit mal where succinimide therapy has failed.
- the most frequently noted side effects, drowsiness and ataxia, generally are dose related and can often be controlled by dosage adjustments.

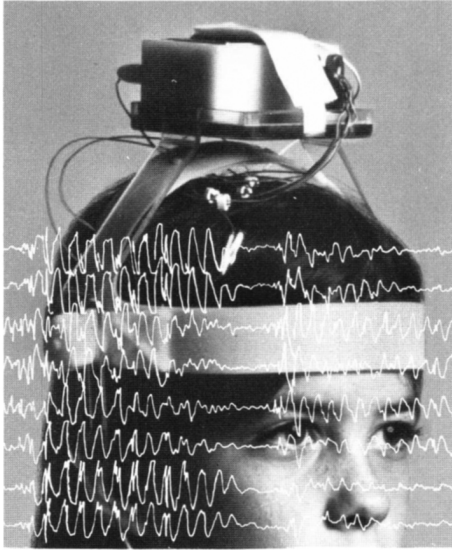
### Effect of RIVOTRIL on seizure frequency



\* Data on file, Hoffmann-La Roche Limited

† Patients dropped from the study for a variety of reasons as well as those treated for less than 12 months account for the decrease in total patient population.

# An important aid in the management of minor seizures



Noninvasive EEG telemetry device used to monitor patients in studies evaluating RIVOTRIL.

## Rivotril® (clonazepam)

### Brief Prescribing Information

#### Action

RIVOTRIL is a benzodiazepine and has sedative, hypnotic, and anticonvulsant properties characteristic of this class of drugs. As an anticonvulsant, it decreases the frequency, amplitude, duration, and spread of discharges in minor motor seizures and suppresses the spike-and-wave discharge in absence seizures.

The maximum blood level of clonazepam after a single oral dose is reached within 1 to 2 hours. The half-life of clonazepam is approximately 18 to 50 hours, and the main route of excretion is in the urine.

#### Indications

RIVOTRIL has been found useful when used alone or as an adjunct in the management of myoclonic and akinetic seizures and petit mal variant (Lennox-Gastaut syndrome).

RIVOTRIL may also be of value in patients with petit mal (absence spells) who have failed to respond satisfactorily to succinimides.

If a loss of anticonvulsant effect occurs, dosage adjustment may re-establish efficacy in some cases.

#### Contraindications

In patients with:

- known hypersensitivity to benzodiazepines
- significant liver disease
- narrow-angle glaucoma

#### Warnings

RIVOTRIL should be used by women of child-bearing potential only when the expected benefits to the patient warrant the possible risks to the fetus. Women who become pregnant should consult their physician promptly with regard to continuing antiepileptic medication.

Mothers receiving RIVOTRIL should not breast feed their infants.

Because adverse effects may possibly become apparent only after years of administration, a risk/benefit consideration of long-term use of RIVOTRIL is important in pediatric patients.

#### Precautions

The use of multiple anticonvulsants may increase CNS-depressant effects and the dosage of each drug may need adjustment to obtain the optimum effect.

To avoid precipitation of status epilepticus, abrupt withdrawal of RIVOTRIL must be avoided. Substitution of another anticonvulsant may be indicated during RIVOTRIL withdrawal.

In a very few patients, RIVOTRIL may cause a paradoxical increase in seizure activity or new types of seizures. RIVOTRIL may precipitate the onset of grand mal or increase its incidence. The addition of appropriate anticonvulsants or an increase in their dosage may be necessary.

Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness, and should also be warned against the concomitant use of alcohol or other CNS-depressant drugs.

Patients who may be prone to increase drug dosage on their own should be monitored carefully when receiving RIVOTRIL, as benzodiazepines have produced habituation, dependence, and withdrawal symptoms.

RIVOTRIL should be administered with caution to patients with impaired renal function.

Periodic liver function tests and blood counts are recommended during long-term therapy with RIVOTRIL.

Treatment with RIVOTRIL should be instituted with caution in patients with chronic respiratory disease, because of the possibility of hypersecretion in the upper respiratory passages.

#### Adverse reactions

Drowsiness has occurred in 50% and ataxia in 30% of the patients treated with RIVOTRIL. In some cases these effects have diminished with time. Behaviour problems have been noted in approximately 25% and increased salivation in 7% of the patients.

Please see product monograph for a complete list of other possible adverse reactions.

#### Dosage and administration

Dosage of RIVOTRIL must be determined for each patient according to clinical response and tolerance. Dosage depends, above all, on the age of the patient.

The daily requirement should be given in 2 or 3 divided doses. If the doses are not equal, the larger dose should be given before retiring.

*Children up to 10 years or 30 kg:* In order to minimize drowsiness, the initial dosage should usually be between 0.01 and 0.03 mg/kg/day and must not exceed 0.05 mg/kg/day.

The dosage should be increased by 0.25 to 0.5 mg/day every third day, unless seizures are controlled or side effects intervene, until a maintenance dosage of 0.1 to 0.2 mg/kg/day has been reached.

*Adults:* The initial dosage should not exceed 1.5 mg/day.

The dosage should be increased by 0.5 to 1 mg every third day, until seizures are controlled or side effects intervene. The recommended maintenance dosage for adults is 8 to 10 mg/day in 3 divided doses. Dosages in excess of 20 mg/day should be administered with caution.

Whenever RIVOTRIL is added to an anticonvulsant regimen, it should be borne in mind that the use of multiple anticonvulsants may result in increased depressant adverse effects.

#### Supply

Scored tablets, 0.5 and 2 mg. Bottles of 100.

®Reg. Trade Marks

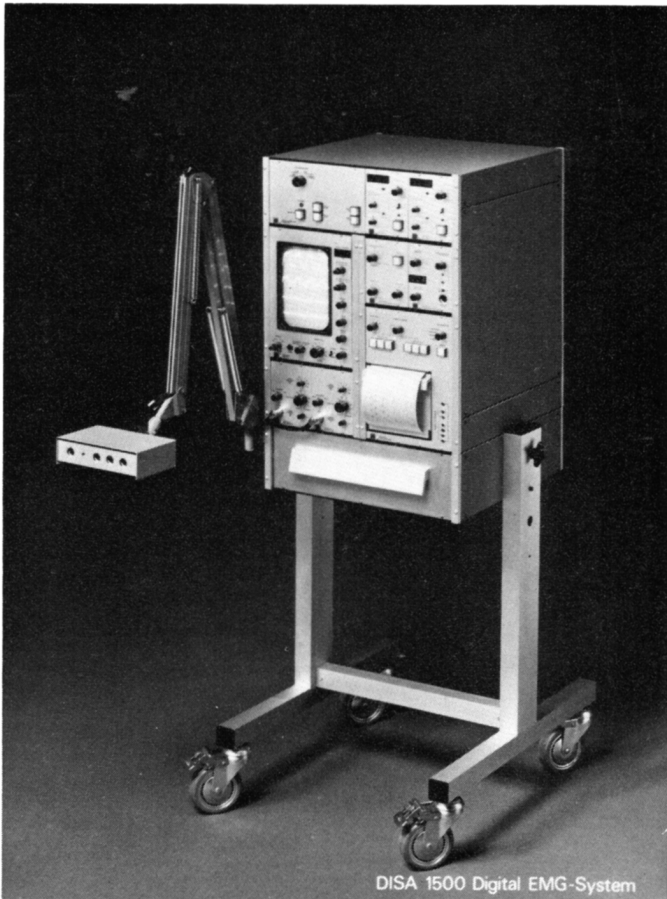
Full prescribing information on request.



Hoffmann-La Roche Limited  
Vaudreuil, Quebec

# DISA

## 1500 DIGITAL EMG SYSTEM



DISA 1500 Digital EMG-System

### FEATURING:

- Ultramodern Modular Design
- High Flexibility
- Hi-Performance EMG Amplifiers
- Digital Storage Monitor
- Instantaneous Full-Bandwidth Recorder
- Constant Current Stimulator
- Digital Signal Averager
- Digital Delay Line
- Delayed Stimulation
- Choice of 1, 2, 3 or 4 Channels
- Mounting in 19" fully Adjustable Rack.

**NOW IN CANADA.  
DISA ELECTRONICS LTD. WITH FULL  
SALES AND SERVICE.**

DISA ELEKTRONIK A/S Denmark, has, as of January 1, 1977, established its own sales and service organization in Canada under the name DISA ELECTRONICS LTD. DISA has carried on electromyography research and development for more than 25 years. The resulting experience and the latest engineering advances are combined in the DISA 1500 Digital Electromyography System.

For further information please call or write to:

**DISA ELECTRONICS LTD., 140 Shorting Road, Scarborough, Ont., M1S 3S6**  
Telephone: (416) 298-2091      Telex: 065-25137

## Editorial Advisory Board

C. Miller Fisher  
Boston

J. C. Richardson  
Toronto

Frank B. Walsh  
Baltimore

Donald B. Tower  
Bethesda

## Editorial Board

Murray L. Barr  
London

Donald W. Baxter  
Montreal

Claude Bertrand  
Montreal

Guy Courtois  
Montreal

John G. Humphrey  
Toronto

Alan J. McComas  
Hamilton

Douglas A. McGreal  
Toronto

George Monckton  
Edmonton

D. G. Montemurro  
London

T. P. Morley  
Toronto

Dwight Parkinson  
Winnipeg

J. W. Phillis  
Saskatoon

Louis J. Poirier  
Quebec

T. B. Rasmussen  
Montreal

Neil B. Rewcastle  
Toronto

J. C. Szerb  
Halifax

Margaret W. Thompson  
Toronto

Juhn A. Wada  
Vancouver

Leonhard S. Wolfe  
Montreal

## Associate Editor

André Barbeau  
Montreal

THE EDITORIAL BOARD wishes to publish original work in the basic and clinical neurosciences on the understanding that it has not been and will not be published elsewhere. Review articles on timely subjects will be accepted. Manuscripts must be in duplicate including illustrations. One of the copies must be the original, ribbon copy. Manuscripts should be typed double spaced, on white paper.

Papers will be accepted in French or English. All papers should be accompanied by a short résumé in both languages. The résumé translation will be done by the editorial board if requested.

Papers should be identified only by the full name of the author, or authors, and the name of the place in which the work was done.

ILLUSTRATIONS: Photographs should be unmounted on glossy paper and show magnification scale. They should be marked on the back with figure number, title of paper and name of author.

Diagrams should be in India ink and large enough to be informative after reduction.

All illustrations should be referred to as figures, numbered consecutively, not included in the body of the text and

## Editor

R. T. Ross  
Winnipeg

all captions should be typed on a separate piece of paper.

Colored illustrations cannot usually be accepted unless the author is prepared to assist with the cost of reproduction.

REFERENCES to authors outside the context of the sentence should read (Name, Year). *i.e.* "However, a recent study (Bird and Iverson, 1975) showed a decreased, etc." Authors mentioned within the context of the sentence should read Name (Year). "*i.e.* . . . twenty years since Ecker and Reimshender (1951) demonstrated, etc." References should be typed in alphabetical order on a separate sheet and include author's name, initials, year, title, publication, volume, first and last page, *i.e.* Isacson, P. (1967). Myxoviruses and autoimmunity. *Progress in Allergy*, 10, 256-292. Abbreviations should be the same as those used in *Cumulated Index Medicus*.

Textbook references should include name of text, author's name, page number, publisher and city.

REPRINTS: Fifty reprints will be supplied free if ordered when the galley proofs are returned. More may be ordered at a nominal charge. Corrections and changes in the galley proofs, apart from printer's errors may be charged to the author.

## Editorial Assistant

Angela B. Ross  
Winnipeg

This journal is indexed by **Index Medicus**, **Excerpta Medica** and **Current Contents — Clinical Practice and Life Science**.

SUBSCRIPTIONS: This journal is issued four times a year. The annual rate is \$24.00 (Canadian); Internes, Residents, Pre- and Post-Doctoral Students, \$12.00 per annum. Single copies \$10.00 each.

ADVERTISING: Enquiries regarding advertising space and rates should be directed to LEX LTD. VANCO PUBLICATIONS, 2 Tremont Crescent, Don Mills, Ontario M3B 2S1.

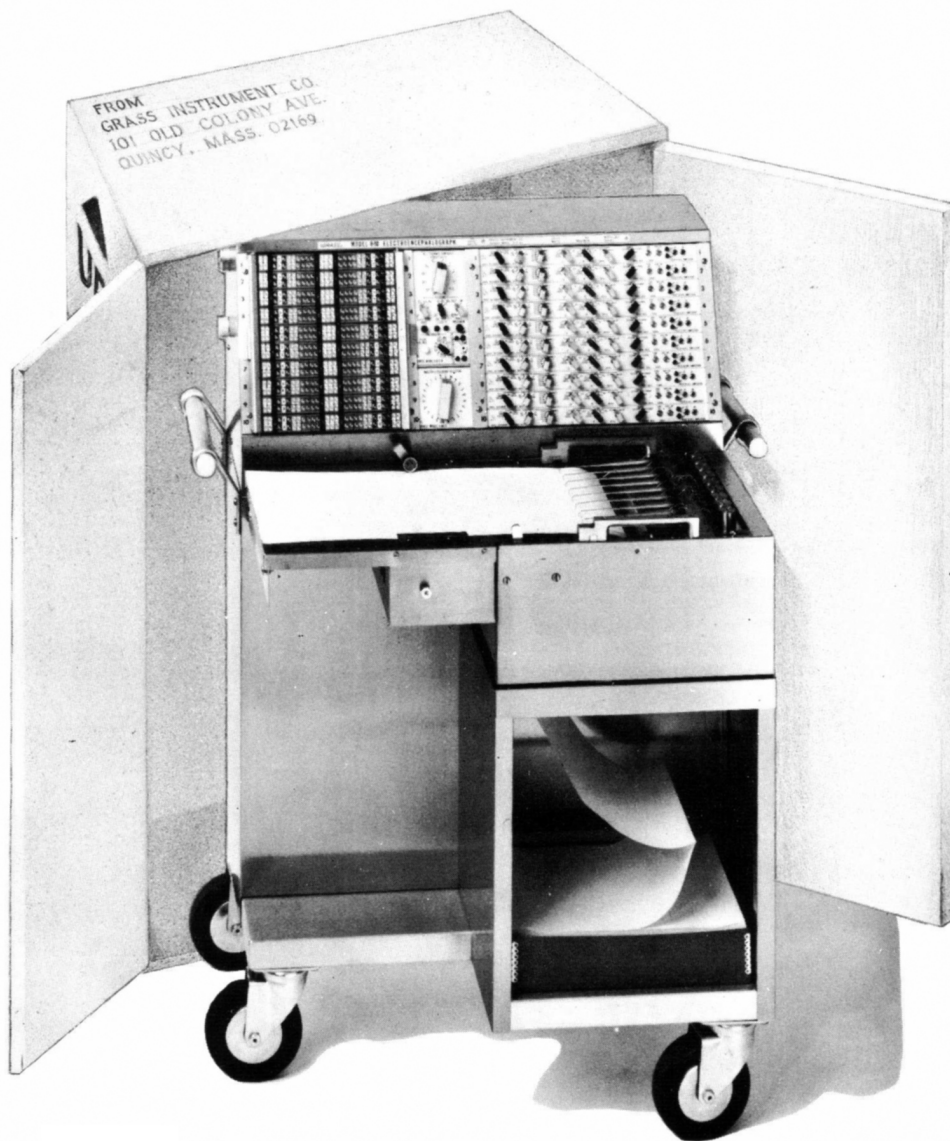
All communications, manuscripts, subscriptions, etc., should be sent to the Editor, at 1516 - 233 Kennedy St., Winnipeg, Canada R3C 3J5.

COPYRIGHT © 1977 by THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES INC. No part of this journal may be reproduced in any form without the prior permission of The Canadian Journal of Neurological Sciences.

Printed by The Public Press Limited, 1760 Ellice Avenue, WINNIPEG, Manitoba R3H 0B6.

Mailed under second class registration number 3307. Postage paid at Winnipeg, Manitoba.

<b>Vascular Amyloid in the Aging Central Nervous System</b> Joseph Bruni, Juan M. Bilbao and Kenneth P. H. Pritzker .....	239
<b>Cerebral Hemodynamics in Migraine</b> V. C. Hachinski, J. Olesen, J. W. Norris, B. Larsen, E. Enevoldsen and N. A. Lassen .....	245
<b>Pure Spastic Paralysis of Corticospinal Origin — C. M. Fisher .....</b>	251
<b>Lumbo-Sacral Radiculopathy Induced by Radiation</b> E. M. Ashenurst, G. R. C. Quartey and A. Starreveld .....	259
<b>A Community Neurologist's Personal Viewpoint on Neurological Training</b> Charles A. Simpson .....	265
<b>Central Nervous System Vasculitis in Rheumatoid Arthritis</b> Peter Watson, John Fekete and John Deck .....	269
<b>Afterdischarge Thresholds and Kindling Rates in Dorsal and Ventral Hippocampus and Dentate Gyrus — Ronald Racine, Patty A. Rose and W. M. Burnham .....</b>	273
<b>Seven Cases of Gilles de la Tourette's Syndrome: Partial Relief with Clonazepam: A Pilot Study — M. Gonce and A. Barbeau .....</b>	279
<b>Platelet Dopamine Uptake In Huntington's Chorea and Gilles de la Tourette's Syndrome: Effect of Haloperidol — Roger F. Butterworth, Michel Gonce and André Barbeau .....</b>	285
<b>Index to Volume 4 .....</b>	(i)



## WHAT TO DO WHEN YOUR EEG ARRIVES-

1. fill inkwells and load paper
2. connect electrodes
3. plug in AC cable and turn on EEG

you are ready to record.

you don't need a service man to get started with a  
**GRASS** EEG.

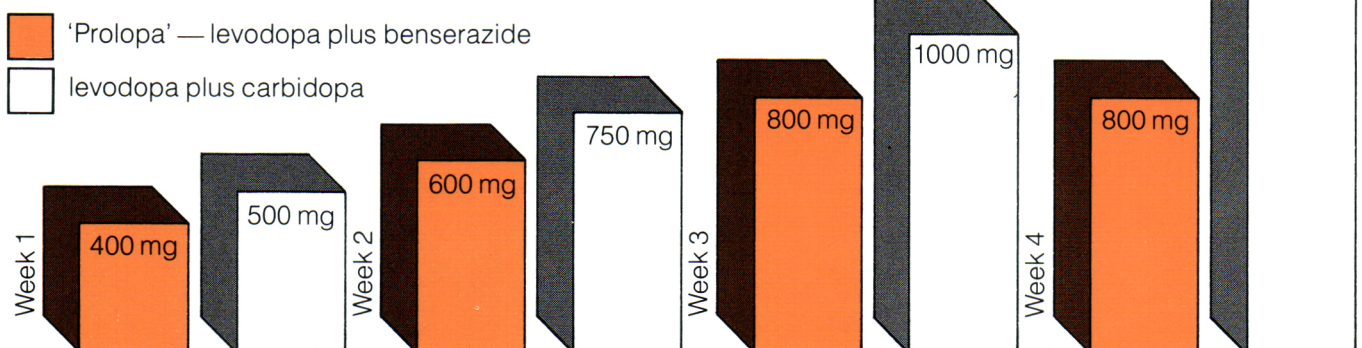
# Progress for the Parkinsonian Patient

# Prolopa<sup>®</sup>



- 1971** Roche was the first to introduce levodopa (Larodopa\*), a drug which could substantially improve the life of the Parkinsonian patient.
- 1977** Continuous research and clinical trials enables Roche to introduce 'Prolopa' (levodopa plus the decarboxylase inhibitor benserazide in a 4:1 ratio). 'Prolopa' provides significant advantages for the patient and physician:
- An equal degree of improvement to that obtained with levodopa alone in the signs and symptoms of Parkinson's disease.<sup>1</sup>
  - A marked reduction (approximately fivefold) in the daily dosage of levodopa needed to obtain a satisfactory response from patients.<sup>2,3</sup>
  - A more rapid clinical response. Maximum benefit achieved in days as opposed to months with levodopa.<sup>4</sup>
  - Less frequent occurrences of the side effects of nausea and vomiting with 'Prolopa' than with levodopa only.<sup>5</sup>
  - A simpler dosage regimen.<sup>2</sup>
  - Within the range of recommended doses, less levodopa is required to reach optimal dosage for most patients than with the combination of L-dopa plus carbidopa.<sup>6</sup>

Levodopa daily intake based on the maximum recommended doses for a patient not receiving levodopa. (Calculated from Manufacturers' Product Monographs.)



'Prolopa': Initially, one capsule b.i.d., increasing by one capsule every three days to a maximum of eight capsules. Combination of levodopa plus carbidopa: Initially ½ tablet b.i.d., increasing by ½ tablet every three days to a maximum of five tablets.



## Brief Prescribing Information

### Classification

Antiparkinsonism agent

### Indications

The treatment of Parkinson's syndrome with the exception of drug-induced parkinsonism.

### Contraindications

Patients with a known sensitivity to levodopa or benserazide. In patients in whom sympathomimetic amines are contraindicated; in conjunction with monoamine oxidase inhibitors or within two weeks of their withdrawal. Clinical or laboratory evidence of uncompensated cardiovascular, endocrine, renal, hepatic, hematologic or pulmonary disease; in narrow angle glaucoma (may be used in wide-angle glaucoma provided that the intra-ocular pressure remains under control). History of melanoma or with suspicious undiagnosed skin lesions.

### Warnings

Discontinue levodopa therapy at least twelve hours before initiation of 'Prolopa' therapy. To avoid inducing central nervous system side effects (abnormal movements) dosage of 'Prolopa' 100-25 should be increased gradually. Observe patients for signs of depression with suicidal tendencies or other serious behavioural changes. Exercise caution in patients with a history of psychotic disorders or who are receiving psychotherapeutic agents such as reserpine, pheno-thiazines or tricycle anti-depressants.

Administer with care to patients with a history of myocardial infarction or who have atrial, nodal or ventricular arrhythmias. The safety of 'Prolopa' in patients under 18 years has not been established. In women of childbearing potential who are or who may become pregnant the anticipated benefits of the drug should be weighed against the possible hazards to mother and fetus. 'Prolopa' should not be given to nursing mothers.

### Precautions

Patients with a history of convulsive disorders should be treated cautiously with 'Prolopa'. Upper gastrointestinal hemorrhage may occur in patient with a history of peptic ulcer.

Patients who improve on 'Prolopa' therapy should be advised to resume normal activities gradually as rapid mobilization may increase the risk of injury. 'Prolopa' should be administered with caution to patients on antihypertensive medication.

### Adverse Reactions

Abnormal involuntary movements are the most common adverse reactions with 'Prolopa'. These are usually dose-dependent and may disappear or become tolerable after dose reduction. Periodic oscillations in performance, end-of-dose akinesia, on-off phenomenon and akinesia paradoxa constitute the most serious problems encountered after prolonged 'Prolopa' therapy.

Side effects such as nausea and vomiting, which are frequently observed during the initial stages of levodopa therapy, are much less common in patients treated with 'Prolopa'. Cardiovascular disturbances such as arrhythmias and orthostatic hypotension are less frequent than in patients treated with levodopa alone. Psychiatric disturbances including mild elation, depression, anxiety, agitation, aggression, hallucinations and delusions are also encountered.

### Dosage

Recommended initial dose is one capsule of 'Prolopa' 100-25 once or twice a day. This dose may be carefully increased by one capsule every third or fourth day until an optimal therapeutic effect is obtained without dyskinesias. Near the upper limits of dosage, the increments should be made slowly, at 2-4 week intervals.

Optimal dosage for most patients is 4-8 capsules of 'Prolopa' 100-25 daily (400-800 mg levodopa), divided into 4-6 doses. Most patients require no more than 6 capsules of 'Prolopa' 100-25 (600 mg levodopa), per day.

'Prolopa' 200-50 capsules are intended only for maintenance therapy once the optimal dosage has been determined using 'Prolopa' 100-25 capsules. No patient should receive more than 5-6 capsules of 'Prolopa' 200-50 daily (1000-1250 mg levodopa in combined therapy), during the first year of treatment.

### Supply

'Prolopa' 100-25 capsules containing 100 mg levodopa and 25 mg benserazide and 'Prolopa' 200-50 capsules containing 200 mg levodopa and 50 mg benserazide, in bottles of 100.

### References

1. Fazio, C. et al.: Treatment of Parkinson's Disease with L-dopa and Association L-dopa plus a DOPA Decarboxylase Inhibitor. *Z. Neuro.*, 202:347. (1972).
2. Barbeau, A.: Treatment of Parkinson's Disease with L-dopa and Ro 4-4602: Review and Present Status. *Advance in Neurology*, Ed.: D.B. Clane, Raven Press, New York, 2:173. (1973).
3. Rinne, U.K. et al.: Treatment of Parkinson's Disease with L-dopa and Decarboxylase Inhibitor. *Neuro.*, 202:1. (1972).
4. Schneider, E. et al.: Wirkungsvergleich von L-dopa und der Kombination L-dopa Decarboxylasehemmer beim Parkinson-Syndrom. *Arch. Psychiat. Nervenkr.*, 217:95. (1973).
5. Steinhausl, H.: Erfahrungsbericht über die Behandlung des Parkinson-Syndroms mit dem Kombinationspräparat L-dopa Dekarboxylasehemmer (Ro-8-0576). *Wien. med. Wschr.*, 123:433. (1973).
6. Manufacturers' Product Monographs.


# Prolopa<sup>®</sup>

## a choice after comparisons

Product monograph available upon request

®Registered Trade Mark for levodopa plus benserazide

\*Registered Trade Mark for levodopa

 Hoffmann-La Roche Limited  
Vaudreuil, Québec

 FAAB  
CCPP

# FROM TECA: A UNIQUE NEW DIRECT RECORDING ELECTROMYOGRAPH

Multiple, single sweep and continuous records appear rapidly on inexpensive 100 mm wide recording paper—without chemical processing—on the TECA Model TE-4 Direct Recording EMG—using a new inertialess recording method.

The new **TECA TE-4** permits, through modular plug-in design, one to four EMG channels. ■ Four traces of information are displayed on a large 7" cathode ray tube and may be automatically recorded simultaneously on 100 mm wide recording paper. ■ An electronic time ruler, a direct reading latency indicator, a delayed stimulus nerve stimulator with dual pulse capability, and a stabilized current muscle stimulator, permit a wide range of accurate rapid tests. ■ A two channel magnetic tape recorder is integrated into the System. ■ The TE-4 is of solid state design, making extensive use of integrated circuits. Modular plug-in construction simplifies service and permits easy expansion of capabilities by addition of modules listed. ■ Many of the above standard EMG features pioneered by TECA are further detailed in the TE-4 Specifications. Also included are new amplifier, stimulator, and System features and extended performance ranges offered. ■ Optional plug-ins: Evoked Potential Averager, Dual Pulse Train Stimulator, Signal Delay Unit (Delay Line), Integrator, Strain Gauge Amplifier.

PHOTOCOPY OF ACTUAL TRACING

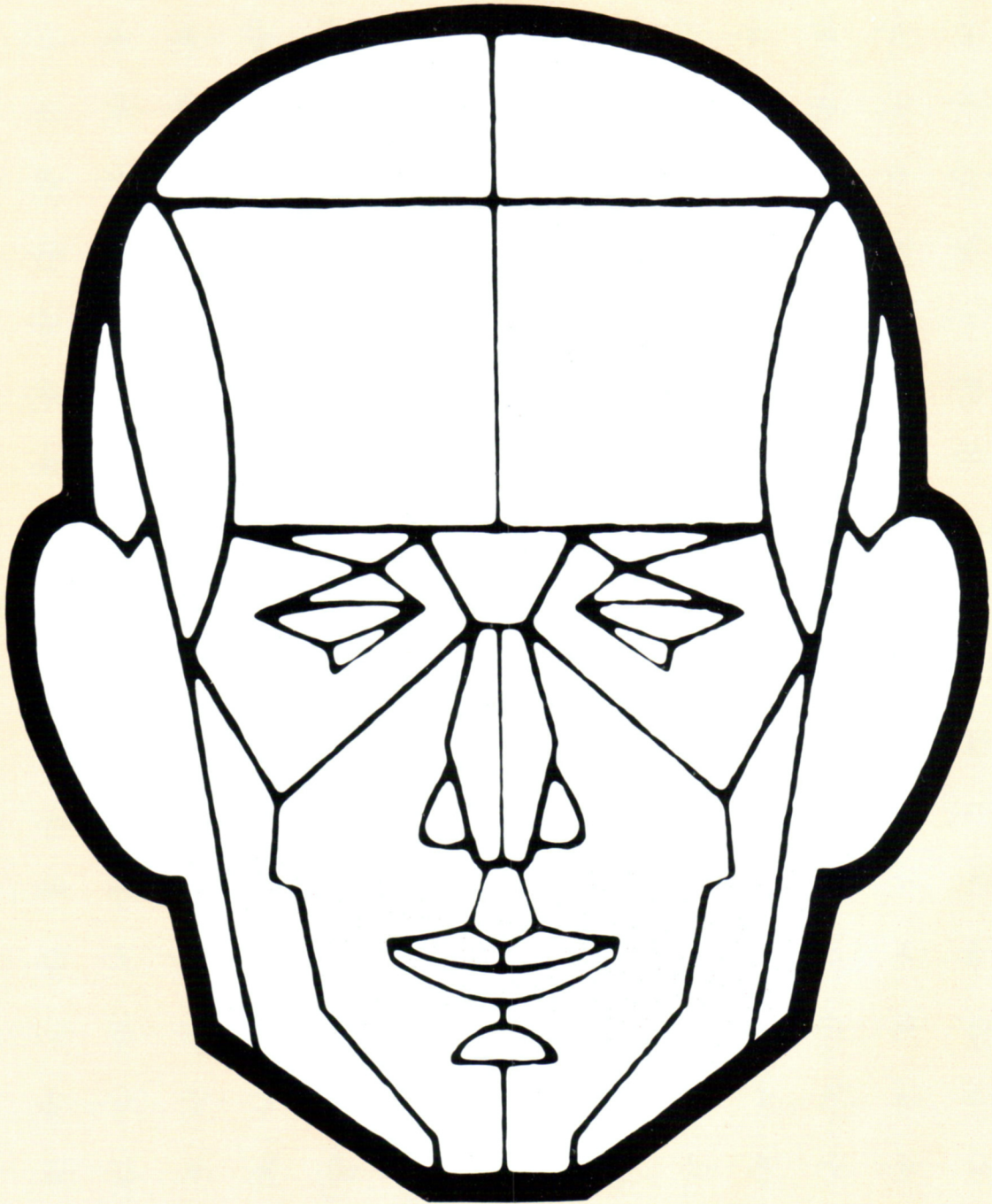
**TECA** is an independent company concerned for the past 15 years with the development, production and maintenance of neuromuscular instrumentation and electrodes for clinical and research studies. TECA also offers a complete range of autoclavable electrodes.

**GENIE AUDIO inc.**

ELECTRO MEDICAL & ACOUSTIC INSTRUMENTS  
9670 PELOQUIN, MONTREAL, CANADA H2C 2J4  
PHONE: (514) 388-9212 CABLE: GENIODIO

**TECA**  
CORPORATION

220 FERRIS AVE., WHITE PLAINS, N.Y.



**There is  
a time to**

**HEAD·OFF  
headache**

**and a  
time to meet**

**headache  
HEAD·ON**

# Symptomatic treatment of vascular headaches

## The time to meet

# headache HEAD-ON

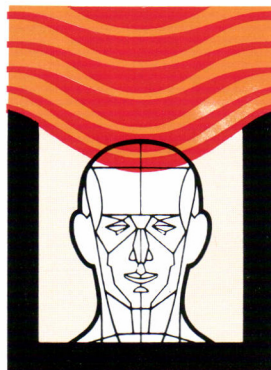
When a patient has vascular headaches that are severe and intense but infrequent, that occur irregularly and are more or less predictable in their onset, that are painful and distressing but, nevertheless, can be controlled once the attack begins, what should be done about them? Meet the headache head-on. Initiate symptomatic therapy. Prescribe Cafergot-PB, to be taken by the patient at the very first sign of the attack.

Cafergot-PB tablets or suppositories relieve the pain and simultaneously relieve the gastrointestinal distress and the nervous tension which many patients experience in association with their migraine attacks.

Cafergot-PB treats the entire migraine syndrome: the headache, the nausea and vomiting, and the nervous tension. The Cafergot-PB suppository works almost as fast and is almost as effective as an injection of ergotamine.

© **Cafergot<sup>®</sup>·PB**  
FROM SANDOZ

stops migraine



after it attacks

# Prophylactic treatment of vascular headaches

## The time to

# HEAD-OFF headache

When a patient has frequently recurring vascular headaches, that are very severe and intense, that occur two or more times a month, that interfere with his or her work and home life, that may not respond adequately to symptomatic treatment, what should be done about them? Don't let the attacks begin. Head-off the headaches. Initiate prophylactic therapy.

Prescribe Sandomigran.

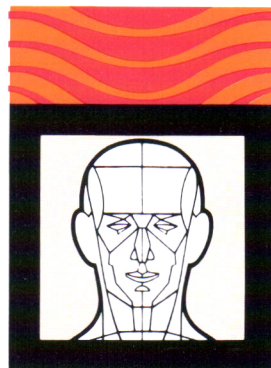
Sandomigran has lifted the restrictions sometimes associated with the prophylactic treatment of migraine. Totally different from methysergide (Sansert), Sandomigran is free of the undesirable side effects which have been associated at times with methysergide therapy.

Sandomigran prevents migraine, or reduces its frequency and severity, without significant side effects.

Now, anyone who suffers from frequent and severe migraine attacks is likely to benefit from Sandomigran therapy.

 **Sandomigran**   
FROM SANDOZ PIZOTYLINÉ

stops migraine



before it attacks

# MIGRAINE

## Sandomigran prescribing information

**Dosage** – The average maintenance dosage is 1 tablet (0.5 mg) t.i.d. A progressive dosage is recommended until the fifth day of therapy.

Treatment should begin with 1 (0.5 mg) tablet at bedtime (first two days), 1 tablet at noon, and at bedtime (next two days), and 1 tablet in the morning, at noon, and at bedtime (from the fifth day onward). The dosage range is 2 to 12 tablets (1 to 6 mg) per day.

Since vascular headache is a paroxysmal but basically chronic disorder, treatment must extend over an adequate period of time in order to obtain maximal benefit. While some patients have responded rather quickly, most investigators agree that a four-week trial period should be instituted to determine the true efficacy of pizotiline in specific cases. The periodic nature of the disorder will have to be considered in determining when and for how long therapy should be maintained. Since some investigators have observed a change in headache pattern after several months of therapy, a drug-free interval is advisable to reassess the necessity of continuing treatment. The dosage should be reduced gradually during the last two weeks of each treatment course to avoid a "headache rebound."

**Composition** – Each ivory-coloured, sugar-coated tablet contains 0.5 mg of pizotiline as the hydrogen malate.

**Side effects** – Increased appetite, weight gain, and drowsiness are the most frequent side effects. An appropriate diet should be recommended by the physician for patients benefiting from the drug but gaining excessive weight. A gradual increase in the dosage of pizotiline is recommended to minimize or reduce the incidence of drowsiness. The following adverse effects have been observed less frequently in relation to the aforementioned reactions: fatigue, nausea, dizziness, headache, confusion, edema, hypotension, depression, weakness, epigastric distress, dry mouth, nervousness, impotence and muscle pain.

**Warnings and precautions** – Since drowsiness may occur with pizotiline, sensitive patients should be cautioned against activities requiring rapid and precise response (i.e. driving an automobile or operating dangerous machinery) until their response to the drug has been determined. Since the effects of antihistamines can potentiate those of other drugs affecting the central nervous system, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, psychotherapeutic agents or other drugs with CNS depressant effects during pizotiline therapy.

Since it is desirable to keep drug administration to a minimum during pregnancy, pizotiline should be given only when the benefits derived from treatment exceed the possible risks to mother and fetus.

Some patients developed tolerance to pizotiline with prolonged use of the drug. An increase in dosage may overcome this tolerance.

After prolonged use, hepatotoxic effects may occur and patients should be advised to report for adequate laboratory evaluation.

Patients with diabetes, cardiovascular disease and known or suspected impaired renal or hepatic function should be given pizotiline with caution, and appropriate laboratory tests should be done at regular intervals.

Lens opacities occurred in two cases but did not appear to be drug-related. However, it is recommended that any impairment in vision be reported to the attending physician for further investigation.

**Contraindications** – Glaucoma, pyloroduodenal obstruction, stenosing pyloric ulcer and predisposition to urinary retention. Pizotiline is also contraindicated in patients taking monoamine oxidase inhibitors and for patients who have a known sensitivity to the drug. Until further studies are completed, the drug is not recommended for children under the age of twelve.

**Supply** – Bottles of 100 tablets.

## Cafergot-PB prescribing information

**Tablets. Dosage** – 2 tablets at the first sign of the attack. One additional tablet every ½ hour, if needed.

Early administration gives the best results. Maximum daily dose is 6 tablets. Maximum weekly dose is 10 tablets. Cafergot-PB is not intended for nor should it be prescribed in the prophylactic treatment of vascular headaches.

**Composition** – Each green-coloured, sugar-coated tablet contains 1 mg of ergotamine tartrate, 100 mg of caffeine, 0.125 mg of the total l-alkaloids of belladonna and 30 mg of sodium pentobarbital.

**Supply** – Bottles of 100 tablets.

**Suppositories. Dosage** – 1 suppository at the first sign of the attack.

One additional suppository in 1 hour, if needed. Maximum dose per attack is 2 suppositories.

Maximum weekly dose is 4 suppositories.

**Composition** – Each suppository contains 2 mg of ergotamine tartrate, 100 mg of caffeine, 0.25 mg of the total l-alkaloids of belladonna and 60 mg of sodium pentobarbital.

**Supply** – Boxes of 12 suppositories.

**Side effects** – Nausea, vomiting, weakness in the legs, muscle pains in the extremities, numbness and tingling in the fingers and toes, precordial distress and pain, and transient tachycardia or bradycardia. Localized edema and itching may occur rarely.

**Precautions** – Although signs and symptoms of ergotism rarely develop – even after long-term intermittent use of the tablets or the suppositories – care should be exercised to remain within the limits of the recommended dosages.

Excessive dryness of the mouth and visual disturbances are signs of overdose or sensitivity to the belladonna alkaloids. A reduction in dosage may be necessary in such cases. Sensitive patients should be cautioned against activities requiring rapid and precise response (i.e. driving an automobile or operating dangerous machinery) until their response to the drug has been determined. This drug may be habit forming due to the presence of a barbiturate in its composition. Cafergot-PB should be kept out of the reach of children.

**Contraindications** – Glaucoma, elevated intraocular pressure, peripheral vascular disease, hypertension, pregnancy, porphyria, coronary heart disease, sepsis, impaired renal or hepatic function. Hypersensitivity to any of the components.

prophylactic treatment

**Sandomigran**<sup>®</sup>  
FROM SANDOZ PIZOTILINE

symptomatic treatment

**Cafergot·PB**<sup>®</sup>  
FROM SANDOZ

Full product information, including references, is available upon request.

**SANDOZ**

SANDOZ (CANADA) LIMITED, DORVAL, QUEBEC

# Tegretol<sup>®</sup>

Carbamazepine

## Brief prescribing information Tegretol<sup>®</sup> 200 mg Carbamazepine

### Indications and clinical use

#### A. Trigeminal Neuralgia:

Tegretol is indicated for the symptomatic relief of pain of trigeminal neuralgia only during periods of exacerbation of true or primary trigeminal neuralgia (tic douloureux). It should not be used preventively during periods of remission. In some patients, Tegretol has relieved glossopharyngeal neuralgia. For patients who fail to respond to Tegretol, or who are sensitive to the drug, recourse to other accepted measures must be considered.

Tegretol is not a simple analgesic and should not be used to relieve trivial facial pains or headaches.

#### B. Tegretol has been found useful in:

- 1) the management of psychomotor (temporal lobe) epilepsy and,
- 2) as an adjunct, in some patients with secondary or partial epilepsy with complex

symptomatology or secondarily generalized seizures, when administered in combination with other antiepileptic medication.

Tegretol is essentially ineffective in controlling petit mal, minor motor, myoclonic and predominantly unilateral seizures, and does not prevent the generalization of epileptic discharge.

### Contraindications

Tegretol should not be administered to patients with a history of hepatic disease or serious blood disorder.

Tegretol should not be administered immediately before, in conjunction with, or immediately after a monoamine oxidase inhibitor. When it seems desirable to administer Tegretol to a patient who has been receiving an MAO inhibitor, there should be as long a drug-free interval as the clinical condition allows, but in no case should this be less than 14 days. Then the dosage of Tegretol should be low initially, and increased very gradually.

Safe use in pregnancy has not been established. Therefore, Tegretol should not be administered during the first three months of pregnancy.

Tegretol should not be given to women of childbearing potential unless, in the opinion of the physician, the expected benefits to the patient outweigh the possible risk to the foetus (See Reproductive Studies). Because of demonstrated toxicity in nursing animals Tegretol should not be administered to nursing mothers.

Because of the similarity of chemical structure, Tegretol should not be administered to patients with known hypersensitivity to any of the tricyclic compounds, such as amitriptyline, trimipramine, imipramine, or their analogues or metabolites.

### Warnings

Although reported infrequently, serious adverse effects have been observed during the use of Tegretol. Agranulocytosis and aplastic anemia have occurred in a few instances with a fatal outcome. Leucopenia, thrombocytopenia and hepatocellular and cholestatic jaundice have also been reported. It is, therefore, important that Tegretol should be used carefully and close clinical and frequent laboratory supervision should be maintained throughout treatment in order to detect as early as possible signs and symptoms of a possible blood dyscrasia.

### Precautions

#### Monitoring of Haematological and Other Adverse Reactions:

Complete blood studies, including platelet counts, and evaluation of hepatic and renal function and urinalysis should be carried out

before treatment is instituted. Careful clinical and laboratory supervision should be maintained throughout treatment, including frequent performance of complete blood counts, in order to detect any early signs or symptoms of blood dyscrasia. Should any signs or symptoms or abnormal laboratory findings suggestive of blood dyscrasia or liver disorder occur, Tegretol should be immediately discontinued until the case is carefully reassessed.

#### Urinary Retention and Increased Intraocular Pressure:

Because of its anticholinergic action, Tegretol should be given cautiously, if at all, to patients with increased intraocular pressure or urinary retention. Such patients should be followed closely while taking the drug.

#### Occurrence of Behavioural Disorders:

Because it is closely related to the other tricyclic drugs, there is some possibility that Tegretol might activate a latent psychosis, or, in elderly patients, produce agitation or confusion, especially when combined with other drugs. Caution should also be exercised in alcoholics.

#### Use in Patients with Cardiovascular Disorders:

Tegretol should be used cautiously in patients with a history of coronary artery disease, organic heart disease, or congestive failure.

#### Driving and Operating Hazardous Machinery:

Because dizziness and drowsiness are possible side effects of Tegretol, patients should be warned about the possible hazards of operating machinery or driving automobiles.

### Adverse reactions:

The reactions which have been most frequently reported with Tegretol are drowsiness, unsteadiness on the feet, vertigo, dizziness, gastrointestinal disturbances, and nausea. These reactions usually occur only during the initial phase of therapy. They have rarely necessitated discontinuing Tegretol therapy, and can be minimized by initiating treatment at a low dosage.

The more serious adverse reactions observed are the haematologic, hepatic, cardiovascular and dermatologic reactions, which require discontinuation of therapy.

The following adverse reactions have been reported:

#### Haematological reactions:

Transitory leucopenia, eosinophilia, leucocytosis, thrombocytopenic purpura, agranulocytosis, macrocytic anemia and aplastic anemia. In a few instances, deaths have occurred.

#### Hepatic disturbances:

During the long-term administration of Tegretol, abnormalities in liver function tests and cholestatic or hepatocellular jaundice have been observed.

#### Dermatological reactions:

The following reactions occurred during treatment with Tegretol: skin sensitivity reactions and rashes, erythematous rashes, pruritic eruptions, urticaria, photosensitivity, pigmentary changes, neurodermatitis and in rare cases Stevens-Johnson syndrome, exfoliative dermatitis, alopecia, diaphoresis, erythema multiforme, erythema nodosum, and aggravation of disseminated lupus erythematosus.

#### Neurological reactions:

The reactions reported as occurring during treatment with Tegretol include vertigo, somnolence, disturbances of coordination, confusion, headache, fatigue, blurred vision, transient diplopia and oculomotor disturbances, speech disturbances, abnormal involuntary movements and increase in motor seizures. In addition, peripheral neuritis and paresthesia, depression with agitation, talkativeness, nystagmus, and tinnitus have been reported but only very rarely. There have been some reports of paralysis and other symptoms of cerebral arterial insufficiency but no conclusive relationship to the administration of Tegretol could be established.

#### Cardiovascular systems:

Recurrence of thrombophlebitis in patients with a prior history of thrombophlebitis, congestive heart failure, aggravation of hypertension, hypotension, syncope and collapse, edema, aggravation of coronary artery disease. Some of these complications have resulted in fatalities.

Other cardiovascular complications (including myocardial infarction and arrhythmia) have been associated with other tricyclic compounds. Whether all these complications are drug-related is not known at this time.

#### Genitourinary reactions:

Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, and impotence. Elevation of BUN, albuminuria and glycosuria also have been observed.

#### Digestive tract:

Disturbances associated with Tegretol therapy have included nausea, vomiting, gastric or abdominal discomfort, diarrhoea, anorexia and dryness of the mouth and throat, glossitis and stomatitis.

#### Eyes:

There is no conclusive evidence that Tegretol produces pathological changes in the cornea, lens or retina. However, it should be recognized that many phenothiazines and related drugs have been shown to cause eye changes. By analogy, periodic eye examinations, including slit-lamp funduscopy and tonometry, are recommended.

Other reactions reported during treatment with Tegretol include fever and chills, lymphadenopathy, aching joints and muscles, leg cramps and conjunctivitis.

### Dosage and administration

#### Use in psychomotor and other secondary or partial seizures:

A low initial daily dosage with a gradual increase in dosage is advised. Dosage should be adjusted to the needs of the individual patient.

#### Initially:

100 to 200 mg once or twice a day depending on the severity of the case and previous therapeutic history. The initial dosage is progressively increased, until the best response is obtained, up to 600 mg daily. The usual optimal dosage is 600 mg daily, but occasionally dosages up to 800 to 1000 mg have been used for short periods. As soon as disappearance of seizures has been obtained and maintained, dosage should be reduced very gradually until a minimum effective dose is reached.


#### Use in trigeminal neuralgia:

The initial daily dosage should be small; 200 mg, taken in two doses of 100 mg each is recommended. The total daily dosage can be increased by 200 mg per day until relief of pain is obtained. This is usually achieved at a dosage between 200 and 800 mg daily, but occasionally up to 1200 mg per day may be necessary. As soon as relief of pain has been obtained and maintained, progressive reduction in dosage should be attempted until a minimum effective dosage is reached. Because trigeminal neuralgia is characterized by periods of remission, attempts should be made to reduce or discontinue the use of Tegretol at intervals of not more than 3 months, depending upon the individual clinical course.

Prophylactic use of the drug in trigeminal neuralgia is not recommended.

Tegretol should be taken in two or three divided doses daily, with meals whenever possible.

#### Dosage forms

Tegretol is available as a 200 mg white, round, single-scored tablet, engraved with  signet.

#### Availability

Bottles of 50 and 500 tablets. Protect from moisture.

#### References

1. Livingston, S.: "Comprehensive Management of Epilepsy in Infancy, Childhood and Adolescence". Springfield, Charles C. Thomas, 1972
  2. Braunhofer, J.: Med Klin. 60: 343-348, 1965
  3. Lerman, P., and Kivity-Ephraim, S.: Carbamazepine, Sole Anticonvulsant for Focal Epilepsy of Childhood. Epilepsia, 15: 229-234, 1974. New York
- Full information is available on request.

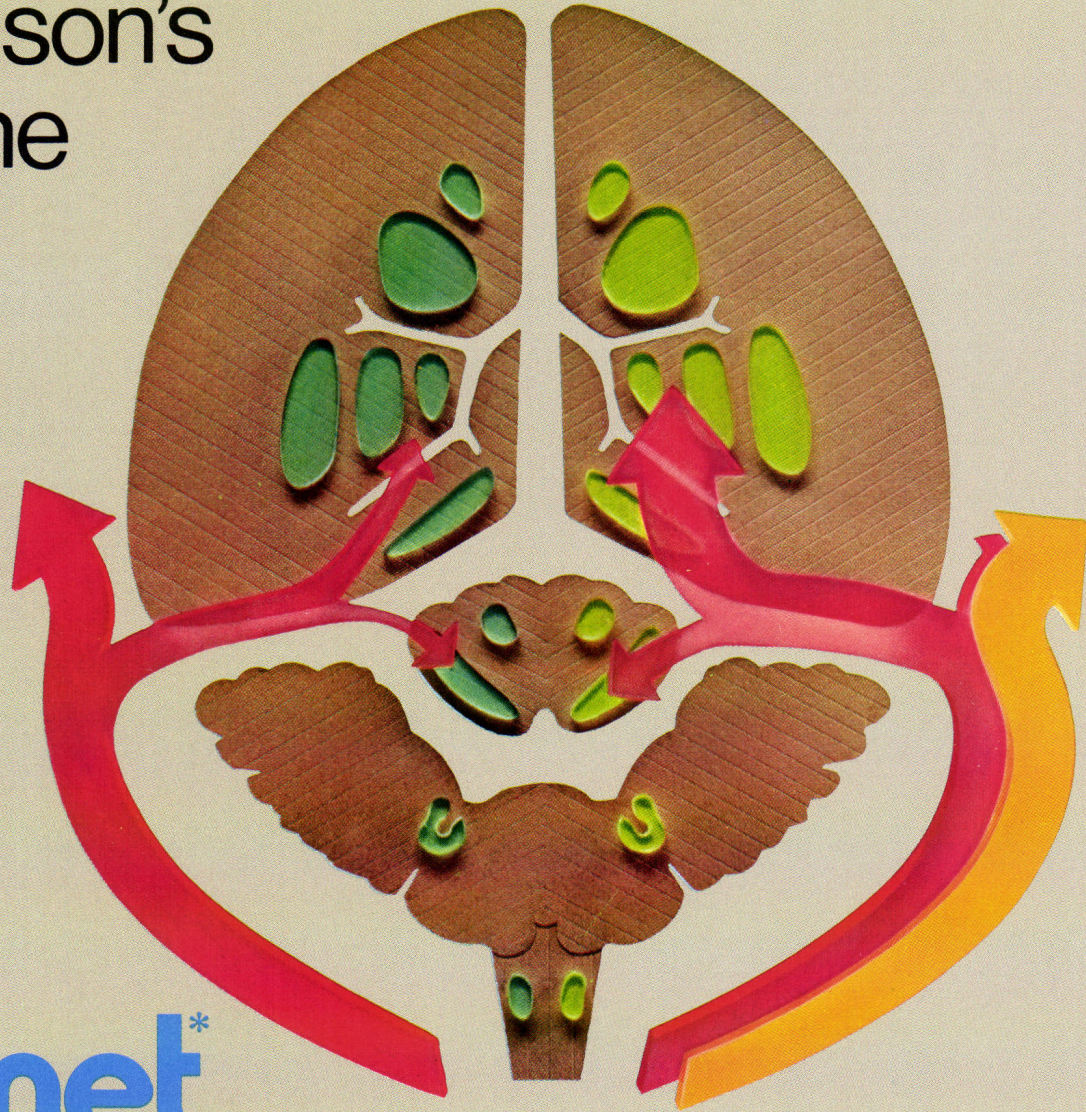
# Geigy

Dorval, P.Q., H9S 1B1

SEE OUTSIDE BACK COVER

**sinemet\***  
(levodopa and carbidopa combination)

the emerging standard of therapy  
in Parkinson's  
syndrome



**sinemet\***

by efficiently increasing the cerebral supply of dopamine

- permits control of the major symptoms particularly rigidity and bradykinesia
- enables patients to lead more normal lives

Common adverse reactions that can occur with SINEMET\* are abnormal involuntary movements and, less frequently, mental changes. These usually can be diminished by dosage reduction.

\*Trademark



# sinemet\*

(levodopa and carbidopa combination)

## INDICATIONS

Treatment of Parkinson's syndrome with exception of drug induced parkinsonism.

## CONTRAINDICATIONS

When a sympathomimetic amine is contraindicated; with monoamine oxidase inhibitors, which should be discontinued two weeks prior to starting SINEMET\*; in uncompensated cardiovascular, endocrine, hematologic, hepatic, pulmonary or renal disease; in narrow-angle glaucoma; in patients with suspicious, undiagnosed skin lesions or a history of melanoma.

## WARNINGS

When given to patients receiving levodopa alone, discontinue levodopa at least 12 hours before initiating SINEMET\* at a dosage that provides approximately 20% of previous levodopa.

Not recommended in drug-induced extrapyramidal reactions; contraindicated in management of intention tremor and Huntington's chorea.

Levodopa related central effects such as involuntary movements may occur at lower dosages and sooner, and the 'on and off' phenomenon may appear earlier with combination therapy.

Monitor carefully all patients for the development of mental changes, depression with suicidal tendencies, or other serious antisocial behaviour.

Cardiac function should be monitored continuously during period of initial dosage adjustment in patients with arrhythmias.

Upper gastrointestinal hemorrhage is possible in patients with history of peptic ulcer.

Safety of SINEMET\* in patients under 18 years of age not established.

**Pregnancy and lactation:** In women of child-bearing potential, weigh benefits against risks. Should not be given to nursing mothers. Effects on human pregnancy and lactation unknown.

## PRECAUTIONS

**General:** Periodic evaluations of hepatic, hematopoietic, cardiovascular and renal function recommended in extended therapy. Treat patients with history of convulsions cautiously. **Physical Activity:** Advise patients improved on SINEMET\* to increase physical activities gradually, with caution consistent with other medical considerations. **In Glaucoma:** May be given cautiously to patients with wide angle glaucoma, provided intraocular pressure is well controlled and can be carefully monitored during therapy. **With Anti-hypertensive Therapy:** Asymptomatic postural hypotension has been reported occasionally, give cautiously to patients on antihypertensive drugs, checking carefully for changes in pulse rate and blood pressure. Dosage adjustment of antihypertensive drug may be required. **With Psychoactive Drugs:** If concomitant administration is necessary, administer psychoactive drugs with great caution and observe patients for unusual adverse reactions. **With Anesthetics:** Discontinue SINEMET\* the night before general anesthesia and reinstitute as soon as patient can take medication orally.

## ADVERSE REACTIONS

**Most Common: Abnormal Involuntary Movements**—usually diminished by dosage reduction—choreiform, dystonic and other involuntary movements. Muscle twitching and blepharospasm may be early signs of excessive dosage. **Other Serious Reactions:** Oscillations in performance: diurnal variations, independent oscillations in akinesia with stereotyped dyskinesias, sudden akinetic crises related to dyskinesias, akinesia paradoxa (hypotonic freezing) and 'on and off' phenomenon. **Psychiatric:** paranoid ideation, psychotic episodes, depression with or without development of suicidal tendencies and dementia. Levodopa may produce hypomania when given regularly to bipolar depressed patients. Rarely convulsions (causal relationship not established). Cardiac irregularities and/or palpitations, orthostatic hypotensive episodes, anorexia, nausea, vomiting and dizziness.

## Other adverse reactions that may occur:

**Psychiatric:** increased libido with serious antisocial behaviour, euphoria, lethargy, sedation, stimulation, fatigue and malaise, confusion, insomnia, nightmares, hallucinations and delusions, agitation and anxiety. **Neurologic:** ataxia, faintness, impairment of gait, headache, increased hand tremor, akinetic episodes, "akinesia paradoxa", increase in the frequency and duration of the oscillations in performance, torticollis, trismus, tightness of the mouth, lips or tongue, oculogyric crisis, weakness, numbness, bruxism, priapism. **Gastrointestinal:** constipation, diarrhea, epigastric and abdominal distress and pain, flatulence; eructation, hiccups, sialorrhea; difficulty in swallowing, bitter taste, dry mouth; duodenal ulcer; gastrointestinal bleeding; burning sensation of the tongue. **Cardiovascular:** arrhythmias, hypotension, non-specific ECG changes, flushing, phlebitis. **Hematologic:** hemolytic anemia, leukopenia, agranulocytosis. **Dermatologic:** sweating, edema, hair loss, pallor, rash, bad odor, dark sweat. **Musculoskeletal:** low back pain, muscle spasm and twitching, musculoskeletal pain. **Respiratory:** feeling of pressure in the chest, cough, hoarseness, bizarre breathing pattern, postnasal drip, **Urogenital:** urinary frequency, retention, incontinence, hematuria, dark urine, nocturia, and one report of interstitial nephritis. **Special Senses:** blurred vision, diplopia, dilated pupils, activation of latent Horner's syndrome. **Miscellaneous:** hot flashes, weight gain or loss. **Abnormalities in laboratory tests reported with levodopa alone, which may occur with SINEMET\*:** Elevations of blood urea nitrogen, SGOT, SGPT, LDH, bilirubin, alkaline phosphatase or protein bound iodine. Occasional reduction in WBC, hemoglobin and hematocrit. Elevations of uric acid with colorimetric method. Positive Coombs tests reported both with SINEMET\* and with levodopa alone, but hemolytic anemia extremely rare.

## DOSAGE SUMMARY

**In order to reduce the incidence of adverse reactions and achieve maximal benefit, therapy with SINEMET\* must be individualized and drug administration continuously matched to the needs and tolerance of the patient. Combined therapy with SINEMET\* has a narrower therapeutic range than with levodopa alone because of its greater milligram potency. Therefore, titration and adjustment of dosage should be made in small steps and recommended dosage ranges not be exceeded. Appearance of involuntary movements should be regarded as a sign of levodopa toxicity and an indication of overdosage, requiring dose reduction. Treatment should, therefore, aim at maximal benefit without dyskinesias.**

### Therapy in Patients not receiving Levodopa:

Initially ½ tablet once or twice a day, increase by ½ tablet every three days if desirable. An optimum dose of 3 to 5 tablets a day divided into 4 to 6 doses.

### Therapy in Patients receiving Levodopa:

Discontinue levodopa for at least 12 hours, then give approximately 20% of the previous levodopa dose in 4 to 6 divided doses.

FOR COMPLETE PRESCRIBING INFORMATION, PARTICULARLY DETAILS OF DOSAGE AND ADMINISTRATION, PLEASE CONSULT PRODUCT MONOGRAPH WHICH IS AVAILABLE ON REQUEST.

## HOW SUPPLIED

Ca8804—Tablets SINEMET\* 250, dapple-blue, oval, biconvex, scored, compressed tablets coded MSD 654, each containing 25 mg of carbidopa and 250 mg of levodopa. Available in bottles of 100 and 500.

\*Trademark

SNM-7-487a-JA



**MERCK  
SHARP  
& DOHME** CANADA LIMITED  
POINTE CLAIRE, QUEBEC

# MOVING?

PLEASE NOTIFY US OF YOUR  
CHANGE OF ADDRESS IN  
ADVANCE.

PASTE OLD  
ADDRESS LABEL  
HERE

## NEW ADDRESS:

### NAME:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

(LAST) (FIRST) (MIDDLE INITIAL)

### STREET ADDRESS:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

### CITY:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

### PROVINCE/STATE:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

### COUNTRY:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

### POSTAL/ZIP CODE:

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

## MAIL TO:

C.J.N.S.

1516 - 233 Kennedy St.

Winnipeg, Canada R3C 3J5



# Headcuffed

by tension headache

**DOSAGE:** 2 tablets or capsules at once, followed by 1 tablet or capsule in a ½ hour and 1 tablet or capsule every 3 to 4 hours if required.

**SIDE EFFECTS:** In rare instances, drowsiness, nausea, constipation, skin rash or dizziness may occur.

**PRECAUTIONS:** Due to presence of butalbital, may be habit-forming. Sensitive patients should be cautioned against activities requiring rapid or precise response (i.e. driving an automobile or operating dangerous machinery) until their response to the drug has been determined.

◇ **ANALGESIC plus SEDATIVE**  
**Fiorinal**®

Tablets or Capsules — without phenacetin

Let Fiorinal help release the patient from the aching, pressing, painfully tight feeling of tension headache. Its analgesic component helps relieve pain while its sedative component helps relax the patient.

**CONTRAINDICATIONS:** Porphyria, hypersensitivity to any of the components.

**COMPOSITION:** Each tablet or capsule contains: 330 mg acetylsalicylic acid, 40 mg caffeine, 50 mg Sandoptal (butalbital).

**SUPPLY:** Bottles of 100 and 500 tablets or capsules.

Full prescribing information is available upon request.

**SANDOZ**®  
W W W

# <sup>®</sup>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.

MEMBER  
PMAC  
LABORATORIES MONTREAL  
DU PONT  
Subsidiary of E.I. du Pont de Nemours & Co. (Inc.)

# Anturan<sup>®</sup> 200mg

a product for  
serious consideration  
in many patients with  
arterial  
thromboembolic  
disorders



**an effective  
platelet inhibiting agent**

**exerting an anti-thrombotic effect**

**well tolerated over long periods  
of continuous administration**

A major Canadian advance

**Geigy**

Dorval, Qué. H9S 1B1

G-5081 R