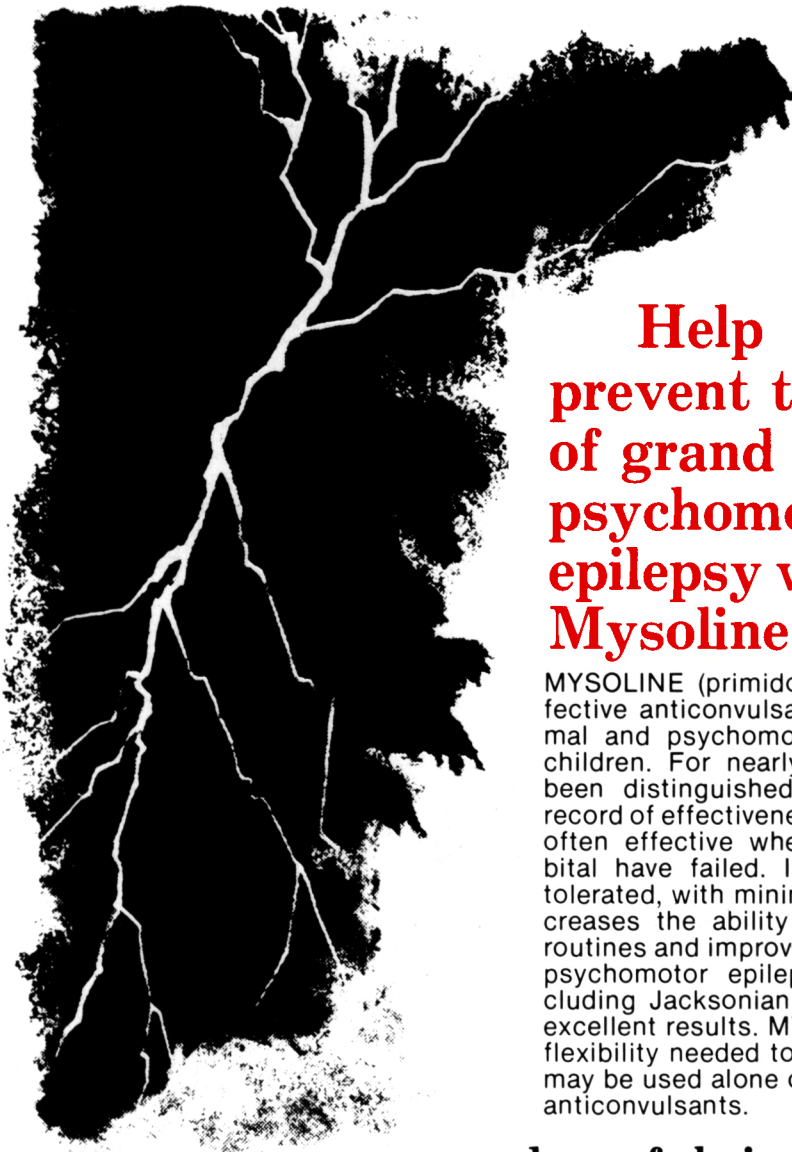


THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

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Scientific Programme of the 11th Canadian Congress of Neurological Sciences
Winnipeg June 23 - 26, 1976.



Help prevent the storm of grand mal and psychomotor epilepsy with Mysoline

MYSOLINE (primidone USP) is a safe and effective anticonvulsant for the control of grand mal and psychomotor epilepsy in adults and children. For nearly 20 years MYSOLINE has been distinguished by its worldwide clinical record of effectiveness and safety. MYSOLINE is often effective where phenytoin or phenobarbital have failed. It is also frequently better tolerated, with minimal sedation. MYSOLINE increases the ability to carry out normal daily routines and improves outlook. In grand mal and psychomotor epilepsy, in focal epilepsy, including Jacksonian seizures, MYSOLINE gives excellent results. MYSOLINE allows the dosage flexibility needed to individualize therapy and it may be used alone or in combination with other anticonvulsants.

**a drug of choice for control and
maintenance in epilepsy.**

Mysoline*

Dosage: Adults and children over 8 years—week I: 250 mg h.s.; week II: 250 mg b.i.d.; week III: 250 mg t.i.d.; week IV: 250 mg q.i.d. Dosage may be increased until seizures are controlled but should not exceed 2 gm daily. Children under 8 years—half the adult dosage. In patients already receiving other anticonvulsants, dosage is gradually increased while the dosage of the other drug(s) is gradually decreased. **Adverse Effects:** Drowsiness, ataxia, vertigo, anorexia, irritability, general malaise, nausea and vomiting. These reactions are usually minor and transitory tending to disappear as therapy is continued or dosage is adjusted. No serious irreversible toxic reactions have been observed. (Occasionally, megaloblastic anemia has been reported, which is reversible by folic acid, 15 mg daily, while MYSOLINE is continued). As with any drug used over prolonged periods, routine laboratory studies at regular intervals are recommended. **Supplied:** Tablets—250 mg and 125 mg Suspension—250 mg/5ml. Complete prescribing information available on request.



* T. M. Reg.

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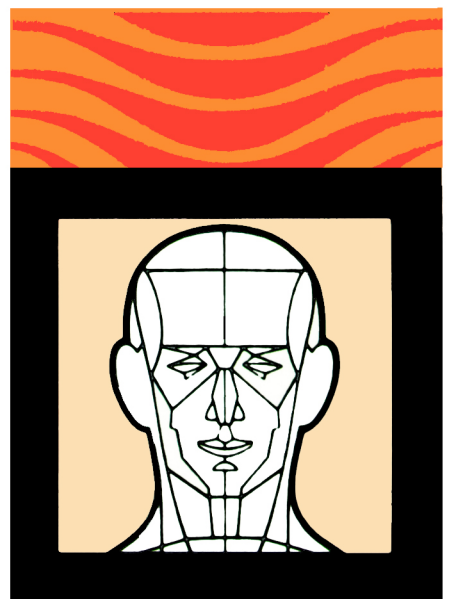
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Quality has
no substitute

A long awaited,
much needed and
significantly **safer**
preparation for
the **prophylactic**
treatment of
migraine

NEW
Sandomigran[®]
FROM SANDOZ PIZOTYLIN



Sandomigran or reduces its frequency significant

Prophylaxis of migraine: the problem.

The prophylactic treatment of vascular headaches has been hampered sometimes by the fact that the most effective agent (methysergide) for the prevention of migraine is associated with certain undesirable side effects. Because of this, the prophylactic therapy of migraine has been confined to a relatively small, select group of patients.

Overcoming the problem.

Extensive research and wide clinical experience have shown that Sandomigran is a highly effective agent against migraine. *Chemically unrelated to methysergide*, Sandomigran is free of the undesirable side effects which have sometimes interfered with or precluded the prophylactic treatment of vascular headaches.

The pharmacological properties of Sandomigran.

Migraine or vascular headache is not, according to many investigators, purely of vascular origin. Many researchers believe that the biogenic amines play an important role in the pathogenesis of migraine.

Chemically unrelated to methysergide, Sandomigran (pizotyline) is a benzocycloheptathiophene derivative possessing strong antagonistic action against certain biogenic amines such as serotonin and histamine and, to a lesser degree, tryptamine, acetylcholine and the catecholamines.

Sandomigran is indicated in the prophylactic – not the symptomatic – treatment of vascular headaches.

Patient selection.

Sandomigran should be considered primarily for the more serious cases of migraine; patients who suffer two or more severe headaches every month.

Sandomigran should also be considered for patients whose headaches do not respond to symptomatic treatment.

7 of every 10 migraine patients may benefit from Sandomigran.

An analysis of 10 controlled studies¹⁻¹⁰ (392 patients) shows the following gratifying results:

Excellent results (Complete disappearance of headaches)	} 65%
Good results (Reduction in frequency and severity of headaches by at least 50%)	



prevents migraine, and severity, without side effects.



Moderate results
(Reduction in frequency and severity of
headaches by an appreciable degree, but
not reaching the aforementioned standards) } 10%

Long-term effectiveness and safety of Sandomigran.

Sandomigran may be prescribed confidently for more migraine patients than ever before. A continuum of international data, based on up to 5 years of clinical experience in 60 countries, provides convincing evidence of the sustained effectiveness and extraordinary safety of Sandomigran.

Remarkably free of undesirable side effects.

Apart from two frequently observed side effects – moderate weight gain and mild sedation in the initial phase of treatment (neither of which is totally undesirable in some migraine patients who might be characteristically underweight or apprehensive) – other side effects such as dry mouth, drowsiness, dizziness, and nausea are not only mild but rare.

Appetite stimulation and weight gain in some patients.

Studies have shown that increased weight may occur in some patients during the first months of treatment with Sandomigran. A weight gain of about 2 to 5 kg may be observed but any increase in weight usually stabilizes in the course of 2 or 3 months of therapy. Some patients are able to reduce their weight while still on the drug. An appropriate diet is suggested for those patients who benefit from the drug but who may gain excessive weight.

Sandomigran dosage.

The average maintenance dosage is 1 tablet (0.5 mg) t.i.d. Treatment should begin with 1 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).

Most investigators agree that a four week-trial period is required to determine the true efficacy of the drug in any given patient.

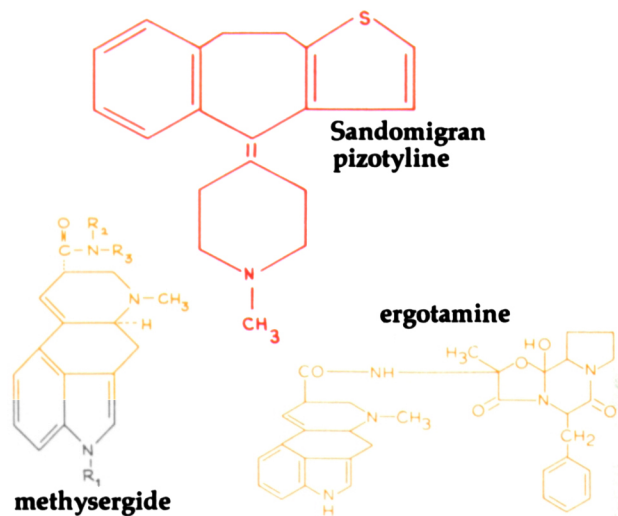
NEW
Sandomigran[®]
stops migraine before it attacks

NEW Sandomigran®

PIZOTYLINE

Chemistry

The chemical structure of pizotyline (Sandomigran) is totally different to the chemical structure of either methysergide (Sansert) or ergotamine.



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 pizotyline 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 pizotyline 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 pizotyline 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 pizotyline, sensitive patients should be cautioned against activities requiring rapid and precise responses (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 pizotyline therapy. Since it is desirable to keep drug administration to a minimum during pregnancy, pizotyline should be given only when the benefits derived from treatment exceed the possible risks to mother and fetus.

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

After prolonged use hepatotoxic effects might 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 pizotyline 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. Pizotyline 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.

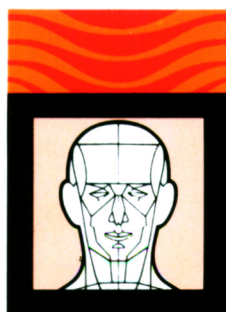
Supply – Bottles of 100 tablets.

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Full prescribing information is available upon request.

stops migraine



before it attacks

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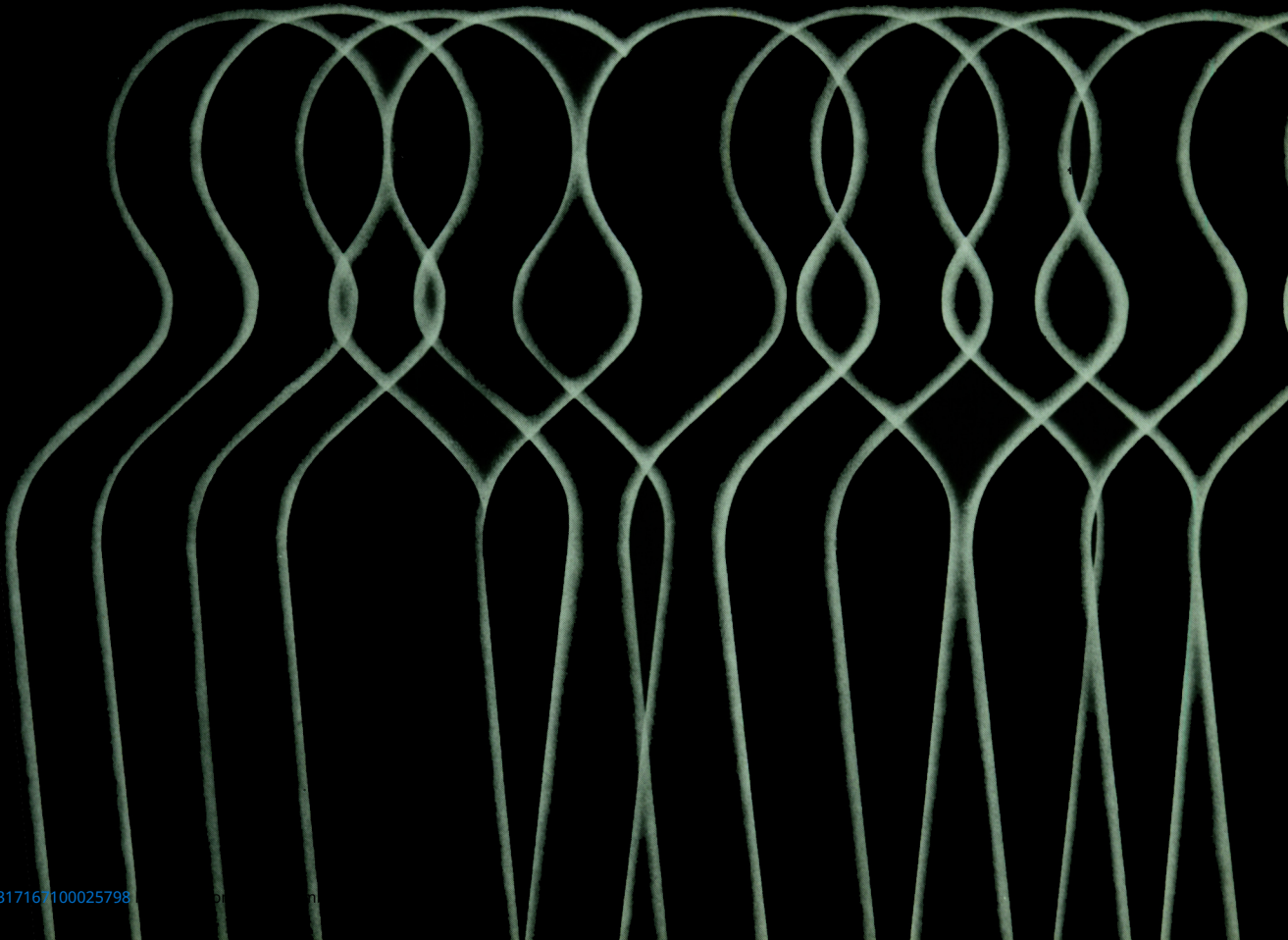
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new **sinemet**^{*}
(levodopa and carbidopa combination)

**a most significant
advance in the treatment
of Parkinson's syndrome**



new **SINEMET***

Improves Quality of Life

SINEMET* permits control of many of the symptoms of Parkinson's syndrome, particularly rigidity and bradykinesia.

Highly Effective

SINEMET* therapy provides symptomatic relief, with levodopa dose requirements reduced by 75-80%.

Significantly Improved Tolerance

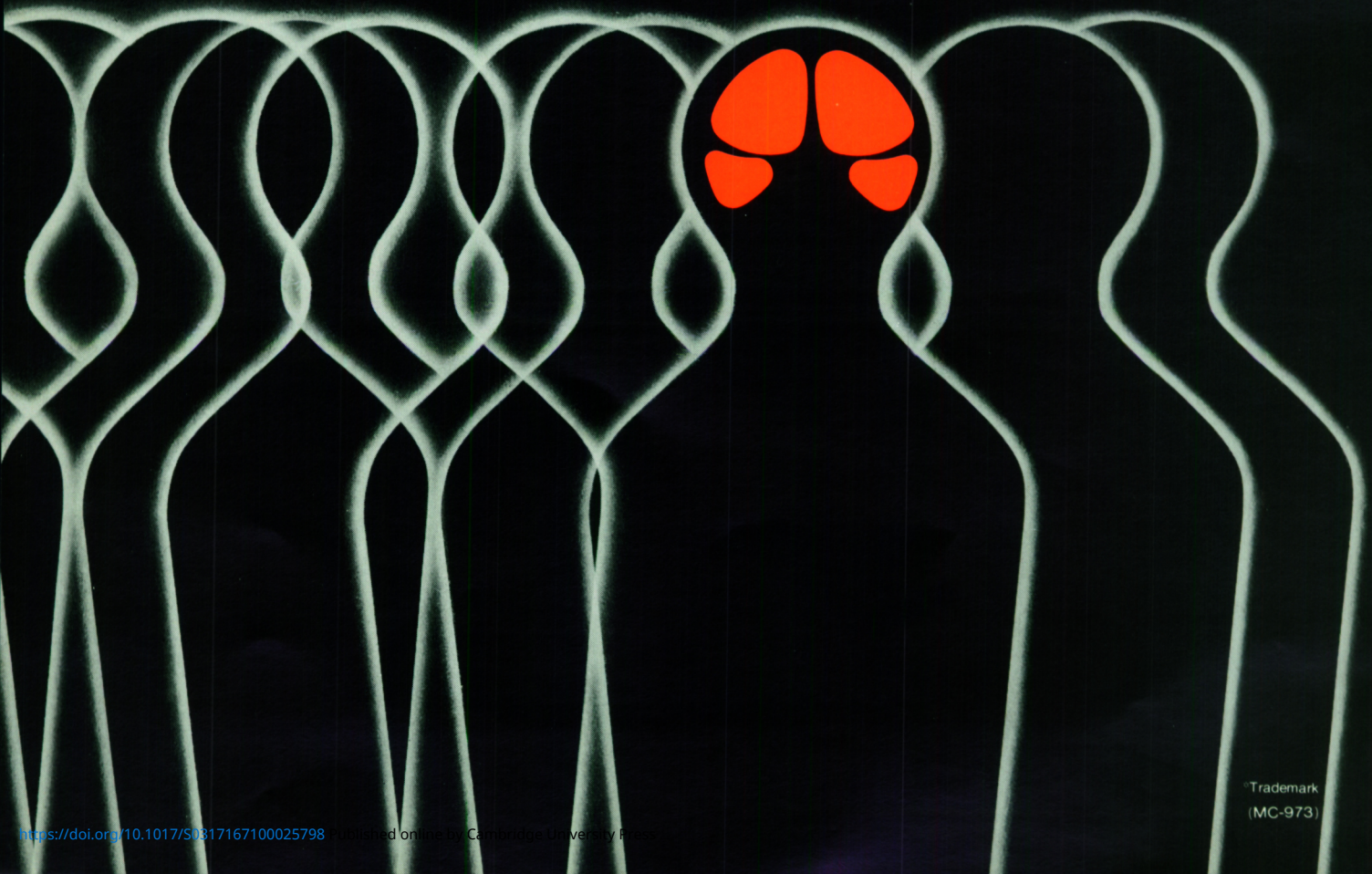
SINEMET* reduces or eliminates peripheral adverse reactions, such as nausea, vomiting and possibly cardiac arrhythmias, frequently seen with plain levodopa. Combined therapy does not decrease adverse reactions due to central effects of levodopa.

Ease of Transfer

Patients maintained on levodopa can be readily transferred to SINEMET*

(See Dosage and Administration Section of Product Monograph)

NOTE: SINEMET* is not recommended in drug-induced parkinsonism.



Trademark
(MC-973)

new 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.

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. 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 behavior, 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.

DOSE AND ADMINISTRATION

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

Ca 8804—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.



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SHARP
& DOHME**

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(MC-973a)

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"Some issues of the February number of the Canadian Journal of Neurological Sciences for 1976 were inadvertently damaged in the process of printing and or binding. Unfortunately a few of these bypassed the inspectors and were mailed to subscribers.

If you received a damaged copy please return it to the Public Press, 1760 Ellie Avenue, Winnipeg, Manitoba R3H 0B6, and we will mail you a perfect copy."

The Editor.