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— Continued on page viii

NEUROSCIENCE SYMPOSIUM

KINDLING

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Pr Symmetrel® 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. benztropine 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 phlebothrombosis.

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.

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THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES
LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

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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 Reimenshender (1951) demonstrated, etc."* References should be typed in alphabetical order on a separate sheet and include author's name, initials, year, title in full, publication in full, volume, first and last page, i.e. Isacson, P. (1967). Myxoviruses and autoimmunity. Progress in Allergy, 10, 256-292.

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

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OURS IS HEADACHE THERAPY.

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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

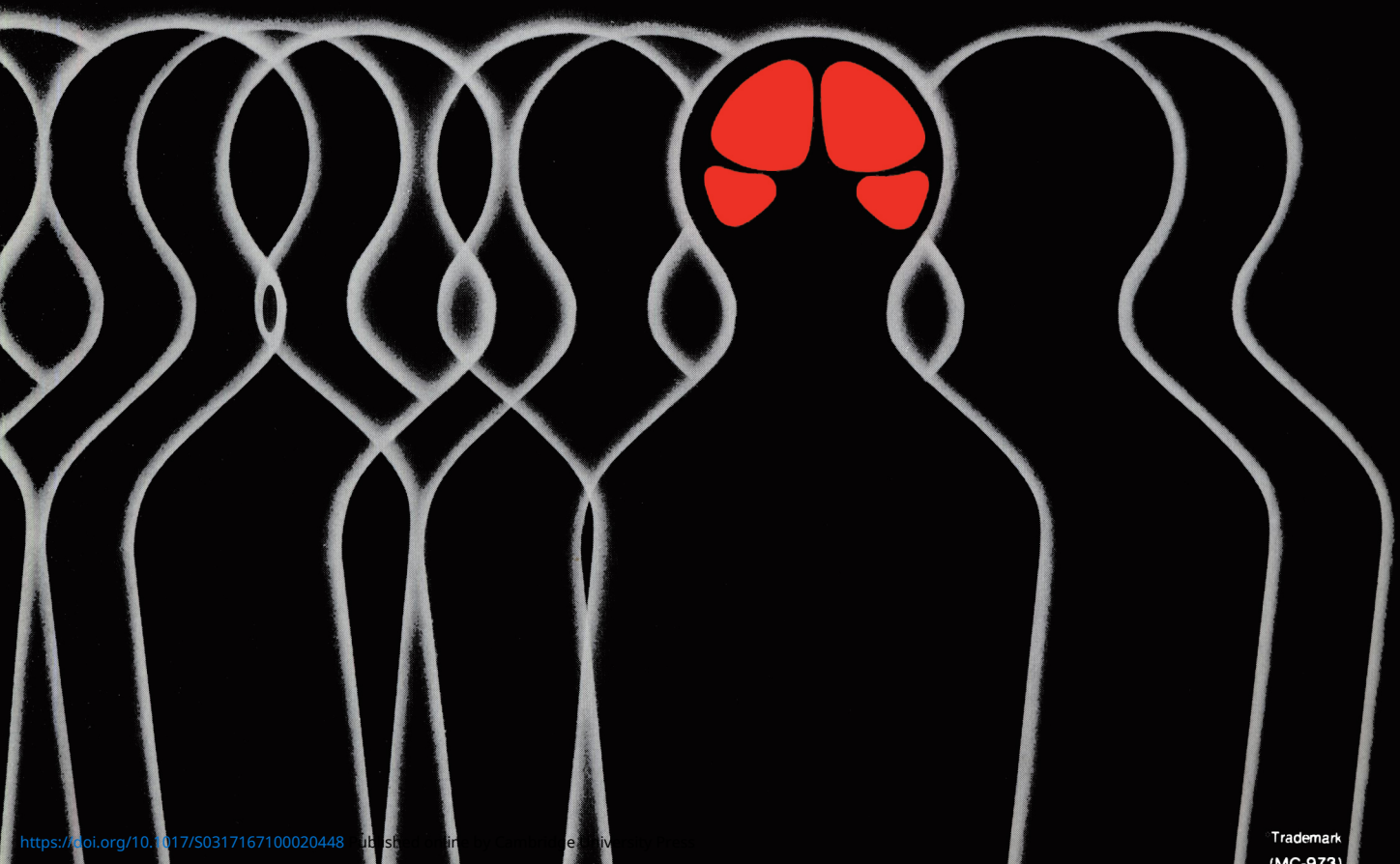
SINEMET* reduces or eliminates peripheral adverse reactions, such as nausea, vomiting and possibly cardiac arrhythmias, frequently seen with plain levodopa. Combined therapy does not decrease adverse reactions due to central effects of levodopa.

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.



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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 childbearing 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 Antihypertensive Therapy:* As symptomatic 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 paradoxica (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 paradoxica", 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, nonspecific 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
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.

MSD | MERCK SHARP & DOHME CANADA LIMITED

*Trademark (MC-973a)

In epilepsy
Tegretol®
provides control of seizures and alleviation of personality disorders

References
1 Livingston, S. F.: Comprehensive Management of Epilepsy in Infancy, Childhood and Adolescence, Charles C. Thomas, 1972.
2 Rodin, E. A., Rim, G. S., and Rennick, P.: Abstract from Program of the American Epilepsy Society Annual Meeting (Dec. 6) 1973, N.Y.
3 Livingston, S. F., et al: Carbamazepine (Tegretol) in Epilepsy Nine Year Follow-up Study with Special Emphasis on Untoward Reactions, Dis. Nerv. System 35:103-107 (March) 1974.

Brief Prescribing Information
Tegretol® 200 mg
Anticonvulsant
Properties
Tegretol has a proven anticonvulsant effect. In addition, Tegretol also has a distinct psychotropic effect, improving the mood and relieving irritability of the epileptic patient with associated behavioral or personality disturbances. Tegretol relieves or diminishes the pain associated with trigeminal neuralgia, usually within 24 - 48 hours.
Indications
1 Epilepsy
Temporal lobe (psychomotor) epilepsy, and as an adjunct in secondary epilepsy or partial epilepsy with complex symptoms or secondarily generalized seizures.
2 Neuralgia
Trigeminal neuralgia (tic douloureux), glossopharyngeal neuralgia.
Dosage
A gradual increasing schedule is recommended with adjustment to suit the needs of the individual. When Tegretol is added to, or substituted for, existing anticonvulsant therapy, the dosage of the other drugs(s) should be gradually reduced.
Epilepsy
Initially ½ - 1 tablet (100 mg - 200 mg) twice daily increasing over a period of 4 - 6 days until optimal control is achieved (usually with 3 tablets daily).
Trigeminal Neuralgia
Initially — 200 mg daily in divided doses of 100 mg (½ tablet), increasing by 200 mg (1 tablet) daily until pain relief is obtained. Dosage in excess of 1200 mg (6 tablets) daily is not recommended.
All patients should be maintained on the minimum effective dose.
Adverse Reactions
Most frequently reported are: drowsiness, disturbances of accommodation, vertigo, dizziness and gastrointestinal disturbances. They usually occur only during initial phase of therapy and can be minimized, if not prevented, by starting treatment at a low dosage. Although rare, effects on the blood forming elements, skin, genitourinary and circulatory system have been reported. The most serious adverse reactions which may require discontinuation of therapy are the haematological including blood dyscrasias, the hepatic including jaundice, the dermatological, the neurological, the cardiovascular, the genito-urinary, the digestive, and the ocular. Miscellaneous including fever and chills, lymphadenopathy aching joints and muscles, leg cramps and conjunctivitis.
Precautions
Careful clinical and laboratory supervision should be instituted prior to and maintained throughout treatment. Caution should be observed while treating patients with increased ocular pressure or urinary retention and also in patients with a history of coronary artery disease, organic heart disease or congestive failure. There is a possibility of agitation and confusion in the elderly or activating a latent psychosis.
Contraindications
Concomitant use of monoamine oxidase inhibitors (two weeks should elapse before Tegretol is prescribed for patients who have received MAOI drugs), first trimester of pregnancy, nursing mothers, patients with a history of hepatic disease or serious blood disorder, or known sensitivity to any tricyclic compound. Tegretol should not be given to women of child-bearing potential unless, in the opinion of the physician, the expected benefits to the patient outweigh the possible risk to the foetus.
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.
Treatment of Overdosage
No specific antidote.
Availability
Tegretol 200 mg:
Each round, white, single scored tablet with Geigy seal contains: carbamazepine 200 mg, available in bottles of 50 and 500.
Full information is available on request.

Geigy
Dorval, P.Q. H9S 1B1 G-5052

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