ISSN 0317-1671

THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

VOL. 3 NO. 1 FEBRUARY 1976

AKINETON®

works well in any Parkinsonism syndrome, regardless of etiology. Organic or drug-induced.

- effective at low daily doses
- reduces rigidity and tremors
- infrequent adverse reactions
- versatile – available in 2 mg. tablets and injectable
- can be used concomitantly with other anti-parkinson drugs

AKINETON® (biperiden hydrochloride) Tablets

Contraindications: The only known contraindication is sensitivity to Akineton hydrochloride.

Warnings: Isolated instances of mental confusion, euphoria, agitation and disturbed behavior have been reported in susceptible patients.

Precautions: Caution should be observed in patients with manifest glaucoma, though no prohibitive rise in intraocular pressure has been noted following either oral or parenteral administration. Patients with prostatism or cardiac arrhythmia should be given this drug with caution. Occasionally, drowsiness may occur.

Adverse reactions: Adverse reactions encountered are primarily dry mouth and blurred vision. These side effects are usually slight and can be overcome by judicious reduction of dosage. If gastric irritation occurs, it can be avoided by administering during or after meals.

Dosage and Administration: Doses required to achieve the therapeutic goal are variable and must be individually and gradually adjusted.

Parkinson's disease: 1 tablet, 2 mg. three or four times daily.

Drug-induced extrapyramidal disorders: 1 tablet, 2 mg. one to three times daily.

How Supplied:

Akineton hydrochloride tablets, 2 mg. each, bisected – bottles of 100 and 1000.

https://doi.org/10.1017/S0317167100025919 Published online by Cambridge University Press

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Papers will be accepted in French or English. All papers should be accompanied by a short résumé in the other language. 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 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 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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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.

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.

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.

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*Trademark (MC-973a)

https://doi.org/10.1017/S0317167100025919 Published online by Cambridge University Press

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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.

*Trademark

(MC-973)

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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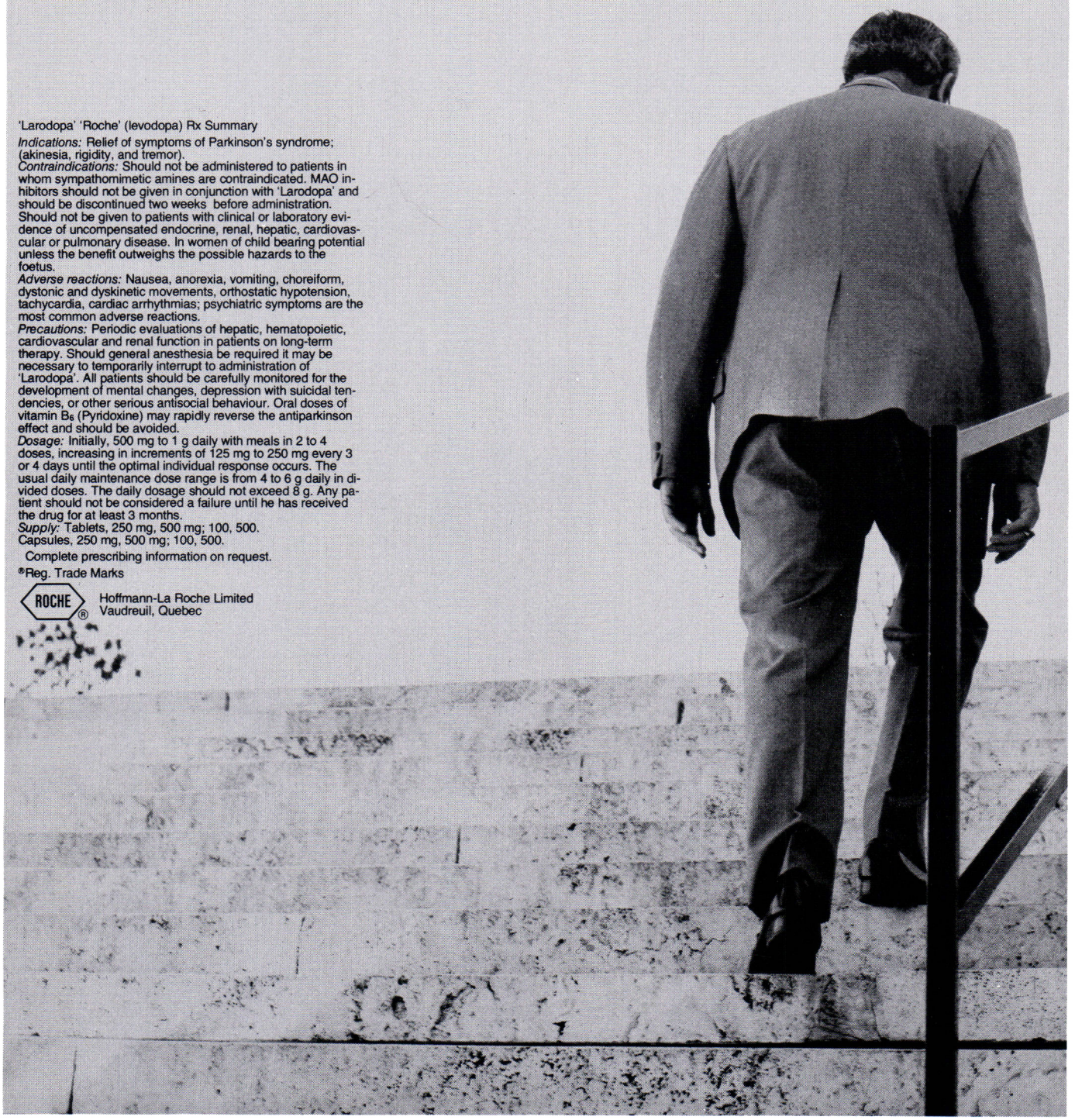
steady and more sure of himself...

and improvement is likely to continue with Larodopa® Roche®

antiparkinsonian therapy



'Larodopa' 'Roche' (levodopa) Rx Summary

Indications: Relief of symptoms of Parkinson's syndrome; (akinesia, rigidity, and tremor).
Contraindications: Should not be administered to patients in whom sympathomimetic amines are contraindicated. MAO inhibitors should not be given in conjunction with 'Larodopa' and should be discontinued two weeks before administration. Should not be given to patients with clinical or laboratory evidence of uncompensated endocrine, renal, hepatic, cardiovascular or pulmonary disease. In women of child bearing potential unless the benefit outweighs the possible hazards to the foetus.
Adverse reactions: Nausea, anorexia, vomiting, choreiform, dystonic and dyskinetic movements, orthostatic hypotension, tachycardia, cardiac arrhythmias; psychiatric symptoms are the most common adverse reactions.
Precautions: Periodic evaluations of hepatic, hematopoietic, cardiovascular and renal function in patients on long-term therapy. Should general anesthesia be required it may be necessary to temporarily interrupt to administration of 'Larodopa'. All patients should be carefully monitored for the development of mental changes, depression with suicidal tendencies, or other serious antisocial behaviour. Oral doses of vitamin B_6 (Pyridoxine) may rapidly reverse the antiparkinson effect and should be avoided.
Dosage: Initially, 500 mg to 1 g daily with meals in 2 to 4 doses, increasing in increments of 125 mg to 250 mg every 3 or 4 days until the optimal individual response occurs. The usual daily maintenance dose range is from 4 to 6 g daily in divided doses. The daily dosage should not exceed 8 g. Any patient should not be considered a failure until he has received the drug for at least 3 months.
Supply: Tablets, 250 mg, 500 mg; 100, 500.
Capsules, 250 mg, 500 mg; 100, 500.

Complete prescribing information on request.

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