The Canadian Journal of Neurological Sciences

Le Journal Canadien des Sciences Neurologiques

XXI Canadian Congress of Neurological Sciences
London, Ontario

June 24 - 28, 1986

The Official Journal of

The Canadian Neurological Society
The Canadian Neurosurgical Society
The Canadian Society of Clinical Neurophysiologists
The Canadian Association for Child Neurology

Volume 13, No. 1 **February 1986**

When patients show prominent dyskinesia or wearing-off reactions on long-term levodopa

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

The Canadian Journal of Neurological Sciences

Le Journal Canadien des Sciences Neurologiques

The Official Journal of:/La Revue Officielle de:

The Canadian Neurological Society
La Société Canadienne de Neurologie
President/Président — Robert F. Nelson
Secretary-Treasurer/ — Garth M. Bray,
Secrétaire-Trésorier 650 Cedar Avenue,
Montreal, Quebec
H3G 1A4

The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie
President/Président — Charles Tator
Secretary-Treasurer/ — Alain Godon,
Secrétaire-Trésorier 12361 Notre-Dame-des Anges St.,
Montreal, Quebec
H4J 2C3

The Canadian Society of Clinical Neurophysiologists
La Société Canadienne de Neurophysiologues Clinics
President/Président — Terence Picton
Secretary-Treasurer/ — R. Gordon Blair
Secrétaire-Trésorier 25 Leonard Avenue
Suite 309
Toronto, Ontario
M5T 2R2

The Canadian Association for Child Neurology
L'Association Canadienne de Neurologie Pédiatrique
President/Président — Frederick Andermann
Secretary-Treasurer/ — Daune L. McGregor,
Secrétaire-Trésorier Hospital for Sick Children
555 University Avenue
Toronto, Ontario
M5G 1X8

The Canadian Journal of Neurological Sciences is published quarterly by University of Calgary Press. The annual subscription rate is $40.00 for Canada and the U.S.A. $44.00 elsewhere. Interns, Residents Pre- and Post-Doctoral Students $20.00 per annum. Single copies $12.00 each. All communications and subscriptions should be sent to the Editor, Canadian Journal of Neurological Sciences, Room 1496, Faculty of Medicine, University of Calgary, 3330 Hospital Drive N.W., Calgary, Alberta, Canada T2N 4N1. Telephone: (403) 220-3062.

Mailed under second class registration number 3307. Postage paid at Calgary, Alberta. This journal is indexed by *Index Medicus*, *Excerpta Medica* and *Current Contents — Clinical Practice and Life Sciences*.

Le Journal Canadien des Sciences Neurologiques est publié trimestriellement par les Presses de l'Université de Calgary. L'abonnement annuel est de $40.00 pour le Canada et les Etats-Unis; $44.00 ailleurs. Internes, résidents, fellows pré et post-doctoral: $20.00 par an. Toutes les communications et les abonnements doivent être adressés à l'Editeur, Journal des Sciences Neurologiques, chambre 1496, Faculté de Médecine, Université de Calgary, 3330 Hospital Drive N.W., Calgary, Alberta, T2N 4N1. Téléphone (403) 220-3062.

Posté sous permis de second classe no 3307. Port payé à Calgary, Alberta. Le Journal est cité et indexé dans *Index Medicus*, *Excerpta Medica* et *Current Contents — Clinical Practice et Life Sciences*.

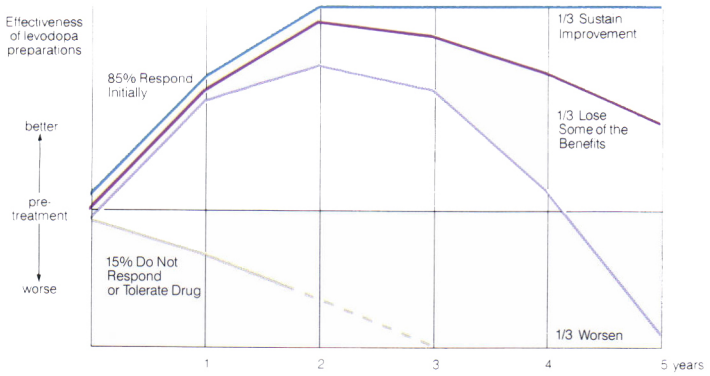
Advertising representative/Représentant de publicité Keith Health Care Communications, 289 Rutherford Road S., Suite 11, Brampton, Ontario, Canada L6W 3R9 — (416) 457-8009

Printer/Imprimeur McAra Printing Limited, 105, 2507 - 12th Street N.E., Calgary, Alberta T2E 7L5

ISSN 0317 - 1671

NEW INDICATION!
Listed on all provincial formularies!

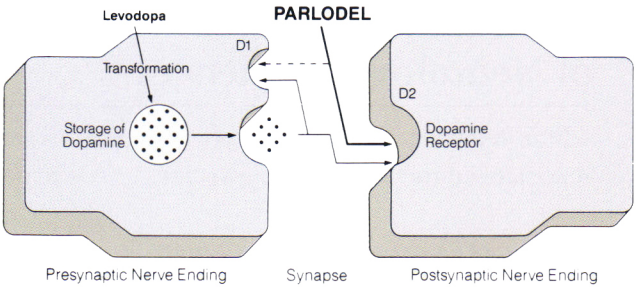
Frequent problems of long-term levodopa therapy[8]



With time, the benefits of levodopa can decline, and patients may demonstrate prominent dyskinesia or signs of wearing-off such as:

- ☐ performance fluctuations
- ☐ early morning stiffness
- ☐ foot cramps
- ☐ end-of-dose deterioration
- ☐ on-off phenomenon

Dopamine-like action[3]



Help protect the quality of life for your Parkinson patients over the long term with Parlodel.[2,4] Added to levodopa, it may allow lower doses for fewer long-term levodopa side effects[4,5,6], and prolong the total useful period of active treatment.[1]

- ☐ Primary effect is directly on postsynaptic receptors.[3]
- ☐ Does not require transformation for its dopaminomimetic effect.[3]
- ☐ Combined therapy with levodopa often leads to significantly improved control.[9]
- ☐ May permit lower levodopa doses.[4,5]
- ☐ Longer plasma half-life (Parlodel 2-8 hours vs. levodopa 1 hour).[9]
- ☐ Mainly type D2 dopamine receptor agonist activity.

PARLODEL®
(bromocriptine mesylate)

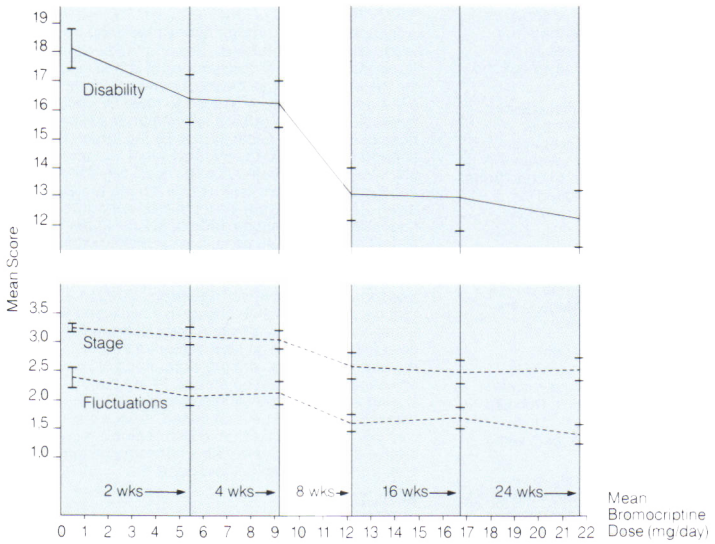
Can help prolong effective control[1]

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

Add Parlodel for improved quality of life[4,7]

In combination with levodopa, Parlodel may provide effective long-term control of Parkinson symptoms[9], with decreased functional disability and increased mobility.[2]

Mean improvement chart



n = 33
Mean improvements during adjunctive therapy with Parlodel [4]

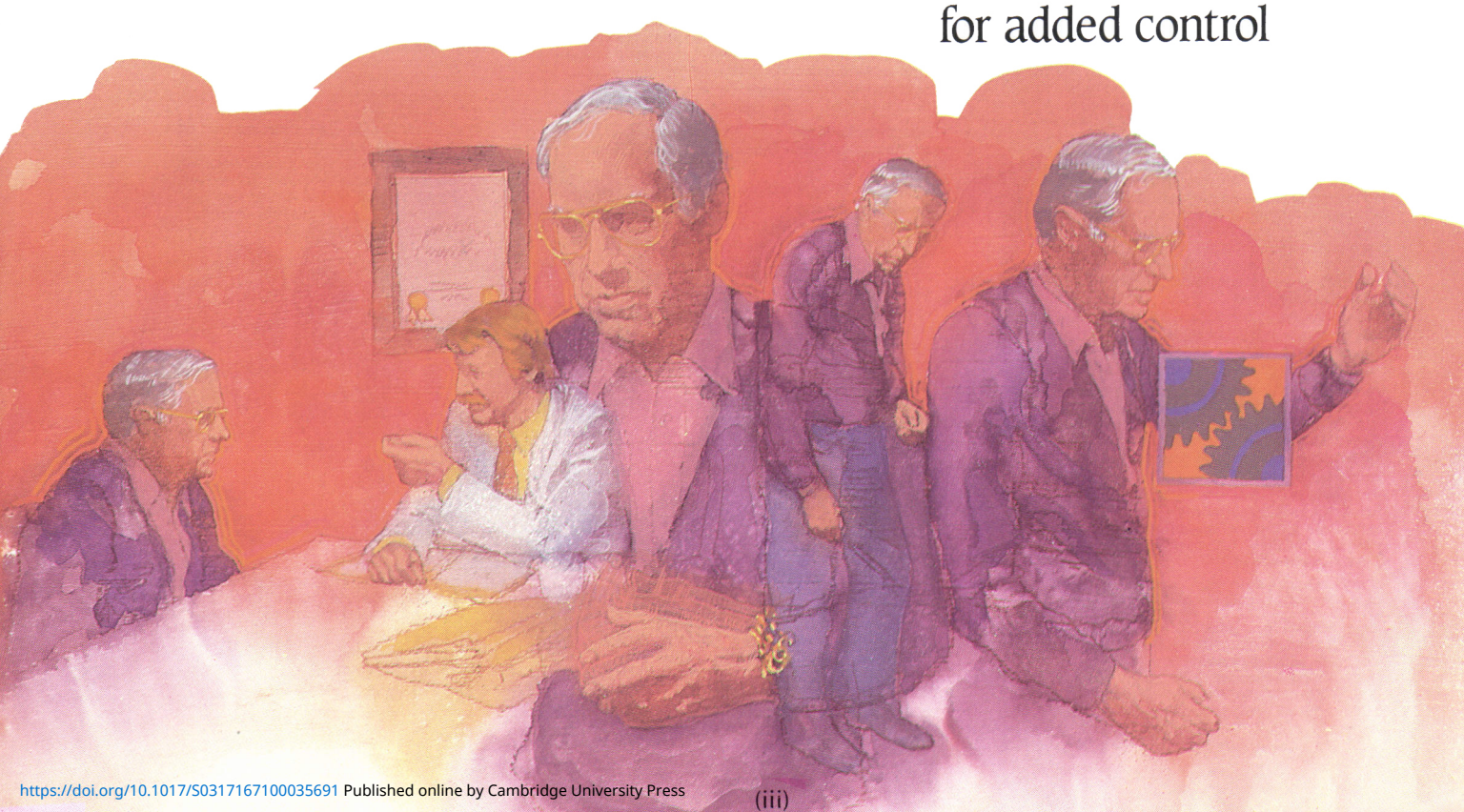
In a recently reported Canadian multicentre trial of Parlodel as adjunctive therapy[4]

- ☐ 43% improvement in end-of-dose deterioration in a majority of patients
- ☐ 33% reduction in total disability scores
- ☐ low mean daily doses of Parlodel
  12 mg (8 weeks)
  22 mg (24 weeks)
- ☐ 15% average decrease of levodopa

Add Parlodel

When levodopa no longer provides sufficient control, adding Parlodel is an alternative to increasing the dose of levodopa. Likewise, Parlodel can be an important adjunct when prominent dyskinesia appear. Parlodel — a new era in the treatment of Parkinson's disease.

PARLODEL®
(bromocriptine mesylate)
for added control



https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

Information for Authors

The Canadian Journal of Neurological Sciences publishes original articles in the clinical and basic neurosciences. Manuscripts are considered for publication with the understanding that, except for identified review articles, they have not been published elsewhere except in abstract form and are not under simultaneous consideration by another publication. Manuscripts should be submitted to:

The Editor
Canadian Journal of Neurological Sciences
Faculty of Medicine,
University of Calgary
3330 Hospital Drive N.W.
Calgary, Alberta T2N 4N1

Manuscripts and all illustrations should be submitted in triplicate. Papers will be accepted in English or French. All papers should be accompanied by an abstract or a résumé of approximately 150 words on a separate page, preferably in both languages, although the Journal will provide the translation if requested. All manuscripts should be double spaced throughout, including references and legends for illustrations. Margins of at least 25 mm should be left on all sides.

For detailed instructions regarding style and layout, authors should refer to "Uniform requirements for manuscripts submitted to biomedical journals". Copies of this document may be obtained by writing to the Journal office, but the main points will be summarized here. Articles should be subdivided under conventional headings of "introduction", "methods and materials", "results" and "discussion" but other headings and subheadings will be considered if more suitable for a particular manuscript. A title page should identify the title of the article, authors, name of institution(s) from which the work originated, and the address and telephone number of the author to whom communications should be addressed. Pages of text should be numbered consecutively. Acknowledgements, including recognition of financial support, should be typed on a separate page at the end of the text.

References are to be numbered in the order of citation in the text. Those cited only in tables or in legends for illustrations are numbered in accordance with a sequence established by the first identification in the text of a particular table or illustration. Titles of journals should be abbreviated according to the style used in Index Medicus. References should be complete including the names of the first three authors followed by "et al" if there are more than three authors, full title, year of publication, volume number, and inclusive pagination for journal articles. Book or chapter references should also include the place of publication and name of the publisher. Examples of correct forms of references follow:

Journals

Poirier LJ, Filion M, Larochelle L, et al. Physiopathology of experimental parkinsonism in the monkey. Can J Neurol Sci 1975; 2: 255-263

Chapter in a book

McGeer PL, McGeer EG. Amino acid neurotransmitters. In: Siegel GJ, Albers RW, Agranoff BW, Katzman R, eds. Basic Neurochemistry. Boston: Little, Brown & Co, 1981: 233-254

Illustrations should be high quality glossy black-and-white photographic prints, preferably 127 x 173 mm (5 x 7"). Original artwork and radiographs should not be submitted. The additional cost of colour illustration must be borne by the author; quotations are available upon request from the Journal office. All figures should be identified on the back with the author's name and figure number. Letters and arrows applied to the figures to identify particular findings should be professional appliques suitable for publication. Photomicrographs should include a calibration bar with the scale indicated on the figure or in the legend. Legends for illustrations should be typed on a separate page from the illustrations themselves.

Tables should each be on a separate page and be identified with the title or heading. Particular care should be taken in the preparation of tables to ensure that the data are presented in the most clear and precise format. Each column should have a short or abbreviated heading. Place explanatory matter in footnotes, not in the heading. Do not submit tables as photographs.

The SI system (système international d'unités) should be used in reporting all laboratory data, even if originally reported in another system. Temperatures are reported in degrees Celsius. Other measurements should be reported in the metric system. English language text may use either British or American spelling, but should be consistent throughout.

Review articles on selected topics also are published by the Journal. These are usually invited, but unsolicited reviews will be considered. It is suggested that authors intending to submit reviews contact the Editor in advance.

Letters to the Editor are welcome. These should be limited to two double-spaced pages and may include one illustration and a maximum of four references.

Information aux Auteurs

Le Journal Canadien des Sciences Neurologiques publie des articles originaux dans les sciences neurologiques, cliniques et fondamentales. Les manuscrits ne sont considérés pour publication qu'à la condition expresse, à l'exception des articles de revue clairement identifiés comme tel, qu'ils n'aient pas été publiés ailleurs, sauf sous forme de résumé et qu'ils ne soient pas sous considération simultanée par un autre journal. Les manuscrits doivent être soumis à:

L'Editeur
Journal Canadien des Sciences Neurologiques,
Faculté de Médecine,
Université de Calgary,
3330 Hospital Drive, N.W.,
Calgary, Alberta T2N 4N1

Les manuscrits et toutes les illustrations doivent être soumis en triplicata. Les articles seront acceptés en français ou en anglais. Tous les articles doivent être accompagnés d'un résumé d'environ 150 mots, sur page séparée, préférablement dans les deux langues, quoique le Journal puisse fournir cette traduction sur requête. Les manuscrits doivent être dactylographiés complètement à double interligne y compris les références et les légendes pour illustrations. Des marges d'au moins 25 mm doivent être laissées de tous les côtés.

Pour les conseils plus détaillés sur le style et la présentation du texte, les auteurs doivent se référer au texte intitulé "Règlements uniformes pour les manuscrits soumis aux journaux biomédicaux". On peut obtenir une copie de ce document en écrivant au bureau du Journal, mais en voici les principaux points: Les articles doivent être présentés selon le plan habituel: "Introduction", "Matériel et méthodes", "Résultats" et "Discussion", mais il est possible d'employer d'autres titres ou sous-titres si nécessaire pour un manuscrit en particulier. Sur une page titre séparée on doit identifier le titre de l'article, les auteurs, les institutions d'où origine le travail, ainsi que l'adresse et le numéro de téléphone de l'auteur à qui devront être adressées les communications. Les remerciements, incluant ceux pour l'appui financier, doivent être dactylographiés sur page séparée à la fin du texte. Les références doivent être numérotées dans l'ordre où elles sont citées dans le texte. Celles qui sont citées seulement dans les tableaux ou légendes d'illustrations sont numérotées selon la séquence établie par la première identification dans le texte de ces tableaux ou illustrations particulières. Les titres des Journaux doivent être abrégés selon le style utilisé dans Index Medicus. Les références doivent être complètes, incluant le nom des trois premiers auteurs suivis de "et al", s'il y a plus de trois auteurs, le titre complet, l'année de publication, le numéro du volume et les premières et dernières pages de l'article. Les références aux livres et chapitres de livres doivent aussi inclure le lieu de la publication et le nom de la maison d'édition. Les exemples corrects suivants peuvent être utilisés:

Journaux

Poirier LJ, Filion M, Larochelle L, et al. Physiopathology of experimental parkinsonism in the monkey. Can J Neurol Sci 1975; 2: 255-263

Chapitre de livre

McGeer PL, McGeer EG, Amino acid neurotransmitters. In: Siegel GJ, Albers RW, Agranoff BW, Katzman R, eds. Basic Neurochemistry. Boston: Little, Brown & Co, 1981: 233-254

Les **illustrations** doivent être sur papier brillant de haute qualité et imprimés en blanc et noir, préférablement 127 x 173 mm (5 x 7"). Les illustrations et photographies originales ne doivent pas être soumises. Le coût supplémentaire des illustrations en couleur revient entièrement à l'auteur; les coûts détaillés peuvent être obtenus directement au bureau du Journal. Il faut identifier toutes illustrations en inscrivant au dos le nom de l'auteur et le numéro. Toutes lettres ou flèches appliquées aux illustrations pour identifier un aspect particulier doivent être de qualité professionnelle. Les photomicrographies doivent inclure une barre de calibration dont l'échelle est mentionée dans la légende. Les légendes des illustrations doivent être dactylographiées sur une page séparée de celles-ci.

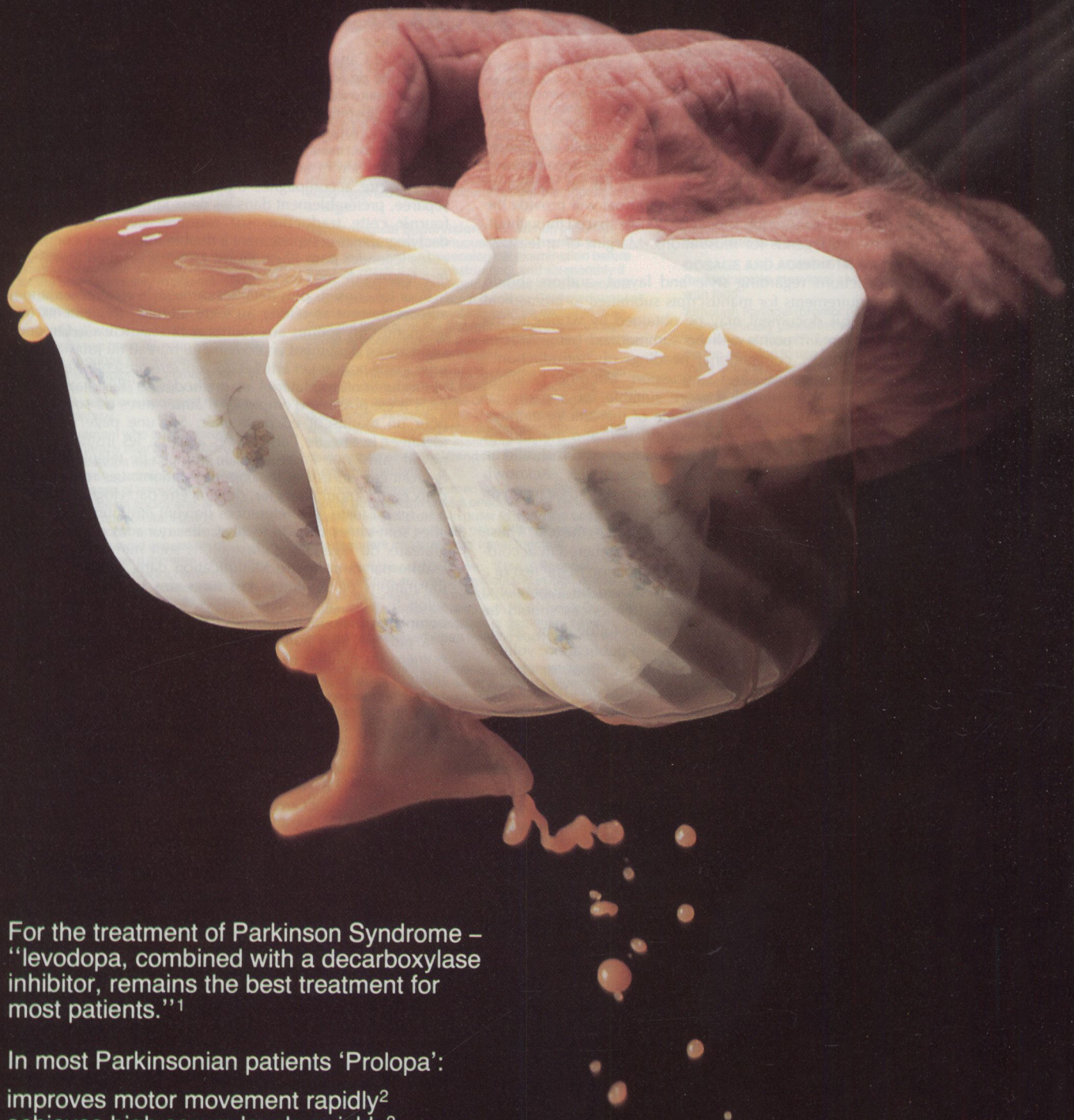
Les **tableaux** doivent être sur des pages séparées et être identifiés avec titre. On doit prendre un soin particulier dans la préparation de ces tableaux afin d'assurer que les données soient présentées avec le format le plus clair et le plus précis possible. Chaque colonne doit avoir un court titre. Les explications doivent être placées en dessous du tableau et non en sous-titre. Un tableau ne doit pas être soumis sous forme de photographie.

On doit employer le système international d'unités (SI) pour toutes données de laboratoire, même si celles-ci sont originellement présentées dans un autre système. Les températures doivent être citées en degrés Celcius. Les autres données doivent utiliser le système métrique. Les textes en anglais peuvent utiliser l'orthographe anglais ou américain, mais cet usage doit être constant.

Le Journal publie également des **articles de revue** sur des sujets sélectionnées. Ces articles sont généralement sur invitation, mais, à l'occasion, une revue non sollicitée peut être acceptée. Il serait préférable que les auteurs ayant l'intention de soumettre une telle revue contactent d'abord l'Editeur.

Nous accueillons les **lettres à l'Editeur**. Celles-ci doivent se limiter à deux pages, double interligne et peuvent contenir une seule illustration et ne citer qu'un maximum de quatre références.

HOLD IT!



For the treatment of Parkinson Syndrome – "levodopa, combined with a decarboxylase inhibitor, remains the best treatment for most patients."[1]

In most Parkinsonian patients 'Prolopa':

- ☐ improves motor movement rapidly[2]
- ☐ achieves high serum levels quickly[2]
- ☐ minimizes common side effects like nausea and vomiting
- ☐ all three 'Prolopa' dose forms contain the established 4:1 ratio

The use of the 4:1 levodopa/decarboxylase inhibitor combination has been shown to reduce significantly the incidence of side effects attributed to the 10:1 ratio[3,4,5]

Prolopa®
(levodopa/benserazide) 4:1

Helps return the simple pleasures of living.

ROCHE®

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

PAAB
CCPP

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

Intermediate Prescribing Information

Ⓟ Tegretol® 200 mg tablets
(carbamazepine)

Ⓟ Tegretol® Chewtabs™ 100 mg and 200 mg
(carbamazepine chewable tablets)

For Symptomatic Relief of Trigeminal Neuralgia Anticonvulsant

Action:
TEGRETOL (carbamazepine) has anticonvulsant properties which have been found useful in the treatment of psychomotor and other partial epilepsies, when administered in conjunction with other anticonvulsant drugs to prevent the possible generalization of the epileptic discharge. A mild psychotropic effect has been observed in some patients, which seems related to the effect of the carbamazepine in psychomotor or temporal lobe epilepsy. TEGRETOL relieves or diminishes the pain associated with trigeminal neuralgia often within 24 to 48 hours.

Indications and Clinical Use

A. Trigeminal Neuralgia:
For the symptomatic relief of pain of trigeminal neuralgia only during periods of exacerbation of true or primary trigeminal neuralgia (tic douloureux). Do not use 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:
1) in 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.
3) as an alternative medication in patients with generalized tonic-clonic seizures who are experiencing marked side effects or fail to respond to other anticonvulsant drugs.

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

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. Long-term toxicity studies in rats indicated a potential carcinogenic risk. Therefore, the possible risk of drug use must be weighed against the potential benefits before prescribing carbamazepine to individual patients.

Contraindications
Hepatic disease, serious blood disorder, less than 14 days either before or after monoamine oxidase inhibitor (then the dosage of TEGRETOL should be low initially, and increased very gradually), atrioventricular heart block, hypersensitivity to tricyclic compounds, lactation, first trimester of pregnancy.

Usage in Pregnancy
As safety has not been established, 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.

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 and frequent clinical and laboratory supervision should be maintained throughout treatment. If any signs or symptoms or abnormal laboratory findings suggestive of blood dyscrasia or liver disorder occur, TEGRETOL should be immediately discontinued.
Urinary Retention and Increased Intraocular Pressure:
Caution is advised in patients with increased intraocular pressure or urinary retention due to the drug's anticholinergic action.
Occurrence of Behavioural Disorders:
TEGRETOL may activate a latent psychosis, or, in elderly patients, produce agitation or confusion. Caution is advised in alcoholics.
Use in Patients with Cardiovascular Disorders:
Caution is advised in patients with a history of coronary artery disease, organic heart disease, or congestive failure. An E.K.G. should be performed if a defective conductive system is suspected before administering TEGRETOL, in order to exclude patients with atrioventricular block.
Use in Patients taking Oral Contraceptives:
Women under treatment with TEGRETOL and oral contraceptives, should be advised to use some alternative, non-hormonal method of contraception as the reliability of oral contraceptives may be adversely affected.
Driving and Operating Hazardous Machinery:
Warn patients about the possible hazards of operating machinery or driving automobiles as dizziness and drowsiness are possible side effects of TEGRETOL.

Adverse Reactions
Haematological reactions: Transitory leucopenia, eosinophilia, leucocytosis, thrombocytopenic purpura, agranulocytosis, macrocytic anemia and aplastic anemia. In a few instances, deaths have occurred.
Hepatic Disturbances: Abnormalities in liver function tests, cholestatic or hepatocellular jaundice.
Dermatological Reactions: 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: Vertigo, dizziness, somnolence, disturbances of coordination, confusion, headache, fatigue, blurred vision, transient diplopia and oculomotor disturbances, speech disturbances, abnormal involuntary movements, increase in motor seizures, peripheral neuritis, paresthesia, depression with agitation, talkativeness, nystagmus, tinnitus, paralysis and other symptoms of cerebral arterial insufficiency.
Cardiovascular Systems: Recurrence of thrombophlebitis, congestive heart failure, aggravation of hypertension, Stokes-Adams in patients with AV block, hypotension, syncope and collapse, edema, aggravation of coronary artery disease. Some of these complications (including myocardial infarction and arrhythmia) have been associated with other tricyclic compounds.
Genitourinary Reactions: Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, impotence, elevation of BUN, albuminuria, and glycosuria.
Digestive Tract: Nausea, vomiting, gastric or abdominal discomfort, diarrhoea, anorexia, 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 slitlamp fundoscopy and tonometry, are recommended.
Other Reactions: Fever and chills, lymphadenopathy, aching joints and muscles, leg cramps and conjunctivitis.

Symptoms and Treatment of Overdosage
Symptoms: Dizziness, ataxia, drowsiness, stupor, nausea, vomiting, restlessness, agitation, disorientation; tremor, involuntary movements, opisthotonos, abnormal reflexes (slowed or hyperactive); mydriasis, nystagmus; flushing, cyanosis, urinary retention, hypotension, hypertension, coma. The EEG may show dysrhythmias. The laboratory findings have included leukocytosis, reduced leukocyte count, glycosuria and acetonuria.
Treatment: No known specific antidote. Induce emesis. Perform gastric lavage. Watch vital signs and administer symptomatic treatment as required. Hyperirritability may be controlled by the administration of parenteral barbiturates. Barbiturates should not be used if monoamine oxidase inhibitors have also been taken by the patient, either in overdosage or in recent therapy (within two weeks). Barbiturates may induce respiratory depression, particularly in children, therefore, have equipment available for artificial ventilation and resuscitation. Paraldehyde may be used to counteract muscular hypertonus without producing respiratory depression. Treat shock (circulatory collapse) with supportive measures, including intravenous fluids, oxygen, and corticosteroids. Electrocardiogram should be monitored, particularly in children, to detect any cardiac arrhythmias or conduction defects.

Dosage and Administration
Use in Epilepsy (see Indications): A low initial daily dosage with a gradual increase in dosage is advised. Dosage should be adjusted to the needs of the individual patient.
Adults and Children over 12 years of age: Initially: 100 to 200 mg once or twice a day. The initial dosage is progressively increased, until the best response is obtained, up to 600 mg daily. Usual Daily Dosage: 600 mg, however 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.
Children 6-12 Years of Age: Initially, 100 mg in divided doses on the first day. Increase gradually by adding 100 mg per day until the best response is obtained. Dosage should generally not exceed 1000 mg daily. 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: Initial daily dosage: 100 mg twice daily may be increased by 200 mg per day until relief of pain is obtained. Usual dosage: 200 to 800 mg daily. Up to 1200 mg daily 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 in trigeminal neuralgia is not recommended.
Administer in two or three divided doses daily, with meals whenever possible.

Dosage Forms
TEGRETOL® *tablets 200 mg:* Each white, round, flat, bevelled-edge double-scored tablet engraved GEIGY on one side contains 200 mg carbamazepine.
TEGRETOL® *Chewtabs™ 100 mg:* Pale pink, round, flat, bevel-edged tablets with distinct red spots. GEIGY engraved on one side and MR on the other. Fully bisected between the M and R. Each chewable tablet contains 100 mg carbamazepine.
TEGRETOL® *Chewtabs™ 200 mg:* Pale pink, oval biconvex tablets with distinct red spots. GEIGY engraved on one side and PU on the other. Fully bisected between the P and U. Each chewable tablet contains 200 mg carbamazepine.

Availability
TEGRETOL® *tablets 200 mg:* Bottles of 100 and 500 tablets. Protect from heat and humidity. TEGRETOL® *Chewtabs™ 100 mg:* Bottles of 100. Protect from heat and humidity.
* TEGRETOL® *Chewtabs™ 200 mg:* Bottles of 100. Protect from heat and humidity. (Available September 1985.)

Full information available on request.

Geigy
Mississauga, Ontario
L5N 2W5

G-5088

See OBC

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

Prolopa®

Rx Summary

Indications

Treatment of Parkinson's syndrome when not drug-induced.

Contraindications

Known hypersensitivity to levodopa or benserazide; in patients in whom sympathomimetic amines are contraindicated; concomitantly with, or within 2 weeks of, MAOI administration; uncompensated cardiovascular, endocrine, renal, hepatic, hematologic or pulmonary disease; narrow-angle glaucoma.

Warnings

Discontinue levodopa at least 12 hours before initiating 'Prolopa'. See Dosage section for substitution recommendations.

Not indicated in intention tremor, Huntington's chorea or drug-induced Parkinsonism.

Increase dosage gradually to avoid CNS side effects (involuntary movements). Observe patients for signs of depression with suicidal tendencies or other serious behavioural changes. Caution in patients with history of psychotic disorders or receiving psychotherapeutic agents.

In patients with atrial, nodal or ventricular arrhythmias or history of myocardial infarction initiate treatment cautiously in hospital. Caution in patients with history of melanoma or suspicious undiagnosed skin lesions.

Safety in patients under 18 years has not been established. In women who are or may become pregnant, weigh benefits against possible hazards to mother and fetus. Not recommended for nursing mothers.

Precautions

Monitor cardiovascular, hepatic, hematopoietic and renal function during extended therapy. Caution in patients with history of convulsive disorders. Upper gastrointestinal hemorrhage possible in patients with a history of peptic ulcer.

Normal activity should be resumed gradually to avoid risk of injury.

Monitor intraocular pressure in patients with chronic wide-angle glaucoma. Pupillary dilation and activation of Horner's syndrome have been reported rarely. Exercise caution and monitor blood pressure in patients on antihypertensive medication. 'Prolopa' can be discontinued 12 hours prior to anesthesia. Observe patients on concomitant psychoactive drugs for unusual reactions.

Adverse Reactions

Most common are abnormal involuntary movements, usually dose dependent, which necessitate dosage reduction. Other serious reactions are periodic oscillations in performance (end of dose akinesia, on-off phenomenon and akinesia paradoxica) after prolonged therapy, psychiatric disturbances (including paranoia, psychosis, depression, dementia, increased libido, euphoria, sedation and stimulation), and cardiovascular effects (including arrhythmias, orthostatic hypotension, hypertension, ECG changes and angina pectoris).

Neurologic, intellectual, gastrointestinal, dermatologic hematologic, musculoskeletal, respiratory, genitourinary and ophthalmologic reactions have also been reported. Consult Product Monograph for complete list.

Dosage

Individualize therapy and titrate in small steps to maximize benefit without dyskinesias. Do not exceed the recommended dosage range.

Initially, one capsule 'Prolopa' 100-25 once or twice daily, increased carefully by one capsule every third or fourth day (slower in post-encephalitic Parkinsonism) until optimum therapeutic effect obtained without dyskinesias. At upper limits of dosage, increment slowly at 2-4 week intervals. Administer with food.

Optimal dosage is usually 4-8 'Prolopa' 100-25 capsules daily, in 4-6 divided doses.

'Prolopa' 200-50 capsules are intended for maintenance therapy once optimal dosage has been determined using 'Prolopa' 100-25 capsules. No patient should receive more than 1000 - 1200 mg levodopa daily during the first year of treatment. 'Prolopa' 50-12.5 capsules should be used when frequent dosing is required to minimize adverse effects.

For patients previously treated with levodopa, **allow at least 12 hours to elapse** and initiate 'Prolopa' at 15% of previous levodopa dosage.

During maintenance, reduce dosage slowly, if possible, to a maximum of 600 mg levodopa daily.

Supply

'Prolopa' 50-12.5 capsules containing 50 mg levodopa and 12.5 mg benserazide.

'Prolopa' 100-25 capsules containing 100 mg levodopa and 25 mg benserazide.

'Prolopa' 200-50 capsules containing 200 mg levodopa and 50 mg benserazide.

Bottles of 100.

Product Monograph available on request.

References:

1. Editorial Parkinson's disease, 1984. Lancet 1984;1: 829-30.
2. Lieberman AN, Goldstein M, Gopmathan G, et al. Combined use of benserazide and carbidopa in Parkinson's disease. Neurology 1984;34:227-9.
3. Rinne UK, Mölsä P. Levodopa with benserazide or carbidopa in Parkinson's disease. Neurology 1979; 29:1584-9.
4. Weiner WJ, Nausieda PA. Carbidopa - levodopa ratio in Parkinson's disease. Arch Neurol 1981; 38:534.
5. Hoehn MM. Increased dosage of carbidopa in patients with Parkinson's disease receiving low doses of levodopa. A pilot study. Arch Neurol 1980; 37:146-9.

Hoffmann-La Roche Limited
Etobicoke, Ontario M9C 5J4

5034

PAAB CCPP

ROCHE®

See page vi

Original Research in Medicine and Chemistry

BRIEF PRESCRIBING INFORMATION

DILANTIN®

Extended Phenytoin Sodium Capsules, U.S.P.
100 mg
ANTICONVULSANT

INDICATIONS

Dilantin is indicated for the control of generalized tonic-clonic (grand mal) seizures and complex partial (psychomotor) seizures.

CONTRAINDICATIONS

Dilantin is contraindicated in those patients with a history of hypersensitivity to hydantoin products.

WARNINGS

Abrupt withdrawal of phenytoin in epileptic patients may precipitate status epilepticus.

Phenytoin is not indicated in seizures due to hypoglycemia or other causes which may be immediately identified and corrected.

Phenytoin metabolism may be significantly altered by the concomitant use of other drugs such as:

A. Barbiturates may enhance the rate of metabolism of phenytoin. This effect, however, is variable and unpredictable. It has been reported that in some patients the concomitant administration of carbamazepine resulted in an increased rate of phenytoin metabolism.

B. Coumarin anticoagulants, disulfiram, phenylbutazone, and sulfaphenazole may inhibit the metabolism of phenytoin, resulting in increased serum levels of the drug. This may lead to an increased incidence of nystagmus, ataxia, or other toxic signs.

C. Isoniazid inhibits the metabolism of phenytoin so that with combined therapy, patients who are slow acetylators may suffer from phenytoin intoxication.

D. Tricyclic antidepressants in high doses may precipitate seizures, and the dosage of phenytoin may have to be adjusted accordingly.

Usage in Pregnancy: The effects of Dilantin in human pregnancy and nursing infants are unknown.

The prescribing physician will have to determine the risk/benefit in treating or counselling epileptic women of childbearing potential.

PRECAUTIONS

The liver is the chief site of biotransformation of phenytoin, patients with impaired liver function may show early signs of toxicity. Elderly patients or those who are gravely ill may show early signs of toxicity.

A small percentage of individuals who have been treated with phenytoin have been shown to metabolize the drug slowly. Slow metabolism may be due to limited enzyme availability and lack of induction; it appears to be genetically determined.

Phenytoin has been associated with reversible lymph node hyperplasia. If lymph node enlargement occurs in patients on phenytoin, every effort should be made to substitute another anticonvulsant drug or drug combination.

Drugs that control generalized tonic-clonic (grand mal) seizures are not effective for absence (petit mal) seizures. Therefore, if both conditions are present, combined drug therapy is needed.

Hyperglycemia, resulting from the drug's inhibitory effect on insulin release, has been reported. Phenytoin may also raise the blood sugar level in persons already suffering from hyperglycemia.

ADVERSE REACTIONS

Central Nervous System: The most common manifestations encountered with phenytoin therapy include nystagmus, ataxia, slurred speech, and mental confusion. Dizziness, insomnia, transient nervousness, motor twitchings, and headache have also been observed. These side effects may disappear with continuing therapy at a reduced dosage level.

Gastrointestinal System: Phenytoin may cause nausea, vomiting, and constipation. Administration of the drug with or immediately after meals may help prevent gastrointestinal discomfort.

Integumentary System: Dermatological manifestations sometimes accompanied by fever have included scarlatiniform or morbilliform rashes.

Hemopoietic System: Hemopoietic complications, some fatal, have occasionally been reported in association with administration of phenytoin. These have included thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, and pancytopenia.

Other: Gingival hyperplasia occurs frequently; this incidence may be reduced by good oral hygiene including gum massage, frequent brushing and appropriate dental care. Polyarthropathy and hirsutism occur occasionally. Hyperglycemia has been reported. Toxic hepatitis, liver damage, and periarteritis nodosa may occur and can be fatal.

MANAGEMENT OF OVERDOSAGE

The mean lethal dose in adults is estimated to be 2 to 5 grams. The cardinal initial symptoms are nystagmus, ataxia and dysarthria. The patient then becomes comatose, the pupils are unresponsive and hypotension occurs. Death is due to respiratory depression and apnea. Treatment is nonspecific since there is no known antidote. First, the stomach should be emptied. If the gag reflex is absent, the airway should be supported. Oxygen, vasopressors and assisted ventilation may be necessary for central nervous system, respiratory and cardiovascular depression. Finally, hemodialysis can be considered since phenytoin is not completely bound to plasma proteins.

DOSAGE AND ADMINISTRATION

Dosage should be individualized to provide maximum benefit. In some cases, serum blood level determinations may be necessary for optimal dosage adjustments — the clinically effective serum level is usually 10-20 mcg/mL.

Adult Dose: Patients who have received no previous treatment may be started on one 100 mg Dilantin Capsule three times daily and the dose then adjusted to suit individual requirements.

Pediatric Dose: Initially, 5 mg/kg/day in two or three equally divided doses, with subsequent dosage individualized to a maximum of 300 mg daily. A recommended daily maintenance dosage is usually 4 to 8 mg/kg. Children over 6 years old may require the minimum adult dose (300 mg/day). Pediatric dosage forms available include a 30 mg Capsule, a 50 mg palatably flavoured Infatab, or an oral suspension form containing 30 or 125 mg of Dilantin in each 5 mL.

Alternative Dose: Once-a-day dosage for adults with 300 mg of Dilantin may be considered if seizure control is established with divided doses of three 100 mg Capsules daily.

HOW SUPPLIED

Dilantin 100 mg Capsules; in bottles of 100 & 1000.

Complete prescribing information available upon request.

PARKE-DAVIS

Parke-Davis Canada Inc., Scarborough, Ontario

PAAB CCPP

*Reg T.M. Parke Davis & Company
Parke-Davis Canada Inc., auth. user

PMAC

See IBC

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100035691 Published online by Cambridge University Press