

THE CANADIAN JOURNAL OF

Neurological Sciences

LE JOURNAL CANADIEN DES

Sciences Neurologiques



Metastatic hemangiopericytoma



Galvanism being applied on the head

40th CANADIAN

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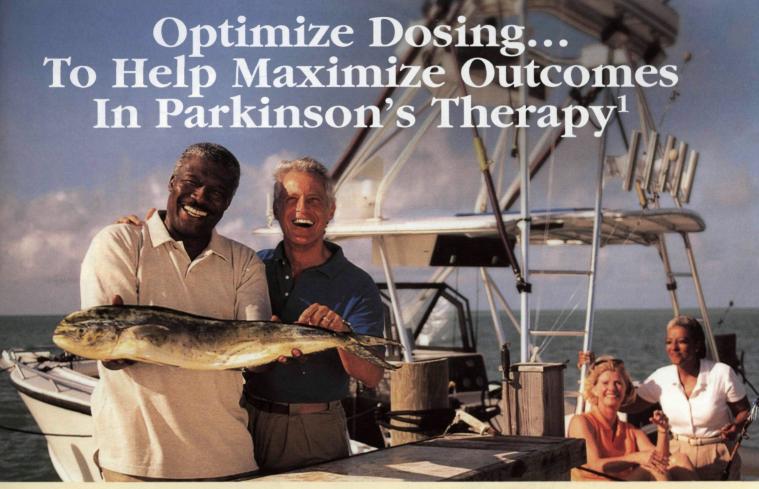
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- x Data from 3 large phase III double-blind trials of ropinirole monotherapy in early Parkinson's disease were examined: a 5-year L-dopa-controlled trial (n=179), a 3-year bromocriptine-controlled trial (n=168), both with planned interim analysis and a 6-month placebo-controlled
- † Please consult the Warnings section of the Product Monograph.³
- ® REQUIP is a registered trademark, used under license by GlaxoSmthKline Inc.

References: 1. Korczyn AD *et al.* Dosing with ropinirole in a clinical setting. *Acta Neurologica Scandinavica* 2002;106:200-204. 2. Rascol O *et al.* A five-year study of the incidence of dyskinesia in patients with early Parkinson's disease who were treated with ropinirole or levodopa. *N Eng J Med* 2000;342(20):1484-1491. 3. Product Monograph of REQUIP® (ropinirole hydrochloride), GlaxoSmithKline, March 2004.

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References

- 1. REMINYL* (galantamine hydrobromide) Product Monograph, JANSSEN-ORTHO Inc., October 29,2003.
- 2. Maelicke A, Albuquerque EX. Eur J Pharmacol 2000:393:165-170.
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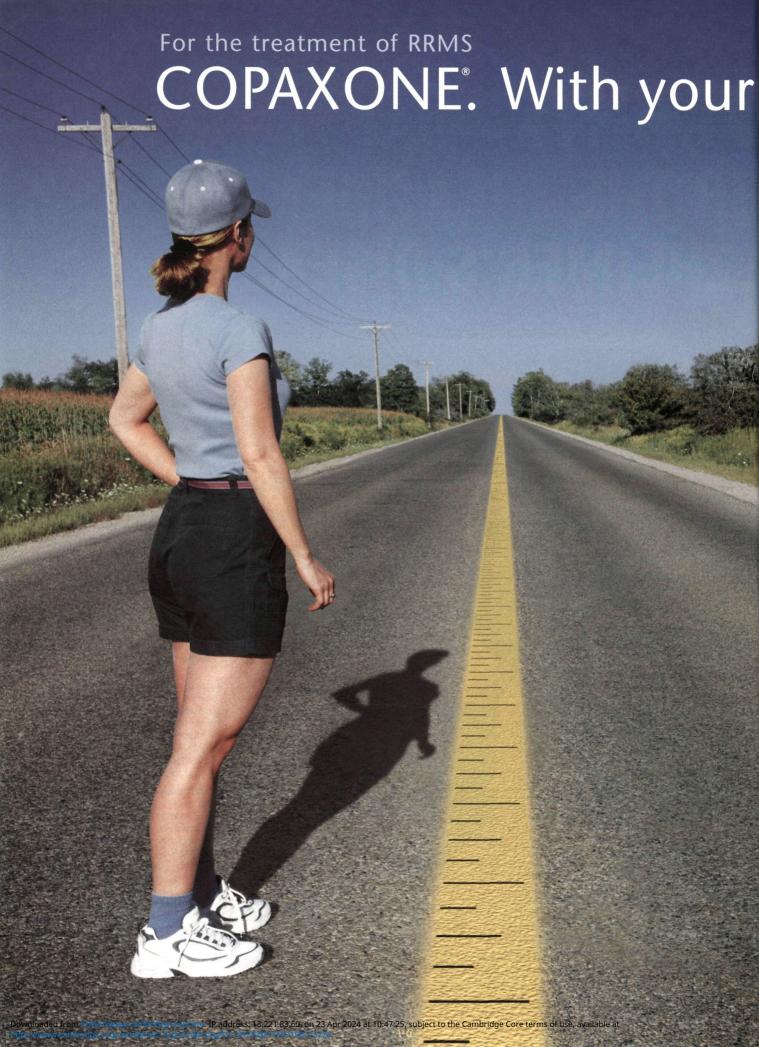
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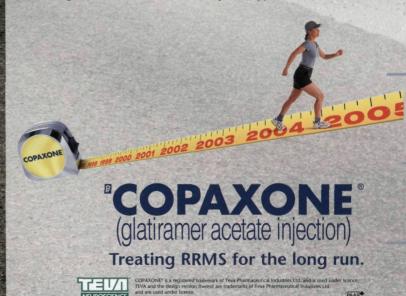
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1 Prescribed anti-epileptic among Canadian neurologists¹





19 Green Belt Drive, Toronto, Ontario M3C 1L9 www.janssen-ortho.com

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† Clinical significance is unknown.

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^{‡ 12-}week, randomized, placebo-controlled, double-blind, multicentre trial; patients received either TOPAMAX 25 mg/day titrated weekly in 25 mg/day increments (n=85), TOPAMAX 50 mg/day titrated weekly in 22 mjg/day increments (n=85), TOPAMAX 50 mg/day titrated weekly in 50 mg/day increments (n=86), or placebo (n=92) as adjunctive therapy. Maximum daily dosage was 200 mg/day at study end for both TOPAMAX groups. Median reduction in seizures was 44% vs. 20% for placebo at week 12 (p<0.001); 22/91 placebo patients had a >50% episode reduction by week 12.





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The Canadian Journal of Neurological Sciences publishes original articles in neurology, neurosurgery and basic neurosciences. Manuscripts are considered for publication with the understanding that they, or the essence of their content, have not been published elsewhere except in abstract form and are not under simultaneous consideration by another journal. A cover letter that states the above must accompany the submission. Articles undergo peer review. Manuscripts should be submitted to: Douglas Zochodne, M.D., Editor, Canadian Journal of Neurological Sciences, 7015 Macleod Trail SW, Suite 709, Calgary, AB, Canada T2H 2K6

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- Submit five high quality copies of the manuscript and original illustrations. Papers will be accepted in English or French. Manuscripts must be double spaced throughout including references, tables and legends for illustrations. Margins of at least 25mm should be left on all sides.
- After a paper has been reviewed, the author will be requested to submit four copies of the revised manuscript, including illustrations. Supply a computer diskette (3 1/2" size) containing the article saved in an RTF format. Identify clearly first author's name, file name, word processing program and version, and system (i.e. PC or Mac). Clearly indicate the order and importance of headings.
- For detailed instructions regarding style and layout refer to "Uniform requirements for manuscripts submitted to biomedical journals". Copies of this document may be obtained on the website www.icmje.org, but the main points are summarized here. Articles should be submitted under conventional headings of introduction, methods and materials, results, discussion, but other headings will be considered if more suitable. Clinical trials must be reported in Consort format (www.cjns.org). Pages of text should be numbered consecutively.
- A title page should identify the title of the article which should be no more than 80 characters including spaces; name of institution(s) from which the work originated; and the name, address, telephone, and fax number of the corresponding author.
- Abstract Original Articles should be accompanied by an abstract of 250 words or less on a separate page, preferably in English and French, although the Journal will provide translation if required. Abstracts of original articles should consist of four paragraphs headed: Background (or objective), Methods, Results and Conclusions. Review articles should be accompanied by an abstract of 150 words or less.
- Acknowledgements including recognition of financial support should be typed on a separate page at the end of the text.
- The SI system (système international d'unités) should be used in reporting all laboratory data, even if originally reported in another system. An *Ethics approval statement* must be provided, if applicable. Temperatures are reported in degrees celsius. English language text may use either British or American spelling, but should be consistent throughout.
- References should be numbered in the order of their citation in the text. Those cited only in tables and legends for illustrations are numbered according to the 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 list the names of up to five authors; if there are more, cite the first three, then et al. Provide the full title, year of publication, volume number and inclusive pagination for journal articles. For any reference cited as "in press", five copies of the article must accompany the author's manuscript. Do not reference unpublished or "submitted" papers; these can be mentioned in the body of the text and authors must provide five copies of "submitted" manuscripts. Avoid "personal communications" and, if necessary, include them in the body of the text, not

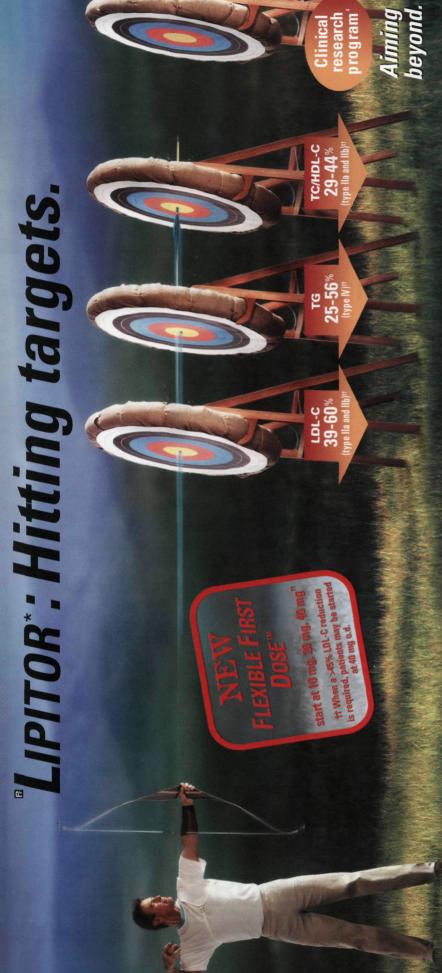
among the references. Reference citations should not include unpublished presentations or other non-accessible material. Books or chapter references should also include the place of publication and the name of the publisher. Examples of correct forms of reference follow:

Journals

Yang JF, Fung M, Edamura R, et al. H-Reflex modulation during walking in spastic paretic subjects. Can J Neurol Sci 1991; 18: 443-452. 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* Submit five original sets of illustrations. We will not return illustrations; therefore, authors should keep negatives for all photographs. Submit high quality glossy black and white photographs preferably 127 x 173 mm (5" x 7"). This includes graphs and diagrams. Do NOT send photocopies of illustrations. Original artwork and radiographs should not be submitted. The additional cost of coloured illustrations must be borne by the author; quotations are available upon request from the Journal office. Identify each figure with a label at the back indicating top, figure number and first author. 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 a scale indicated on the figure or in the legend. Legends for illustrations should be typed on a separate page from the illustrations.
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LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control4

LPTTOR is an HMG-CoA reductase inhibitor (statin). LIPITOR is indicated as an adjunct to lifestyle changes, including diet, for the reduction of elevated total cholesterol, LDL-C, TG and apolipoprotein B in hyperlipidemic and dyslipidemic conditions (including primary hypercholesterolemia, combined [mixed] hyperlipidemia, dysbetalipoproteinemia, hypertriglyceridemia and familial hypercholesterolemia) when response to diet and other non-pharmacological measures alone has been inadequate.

.IPITOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and Total-C/HDL-C ratios (Fredrickson Type

Less than 2% of patients discontinued therapy due to adverse experiences. Most common adverse effects were consti-pation, diarrhea, dyspepsia, flatulence, nausea, headache, pain, myalgia and asthenia. lla and IIb)

LIPITOR is contraindicated: During pregnancy and lactation; active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal; hypersensitivity to any component of this medication. Lipid levels should be monitored periodically and, if necessany, the dose of LIPITOR adjusted based on target lipid levels

Caution should be exercised in severely hypercholesterolemic patients who are also renally impaired, elderly, or are con-

Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should comitantly being administered digoxin or CYP 3A4 inhibitors. be repeated promptly and then performed more frequently.

Pfizer

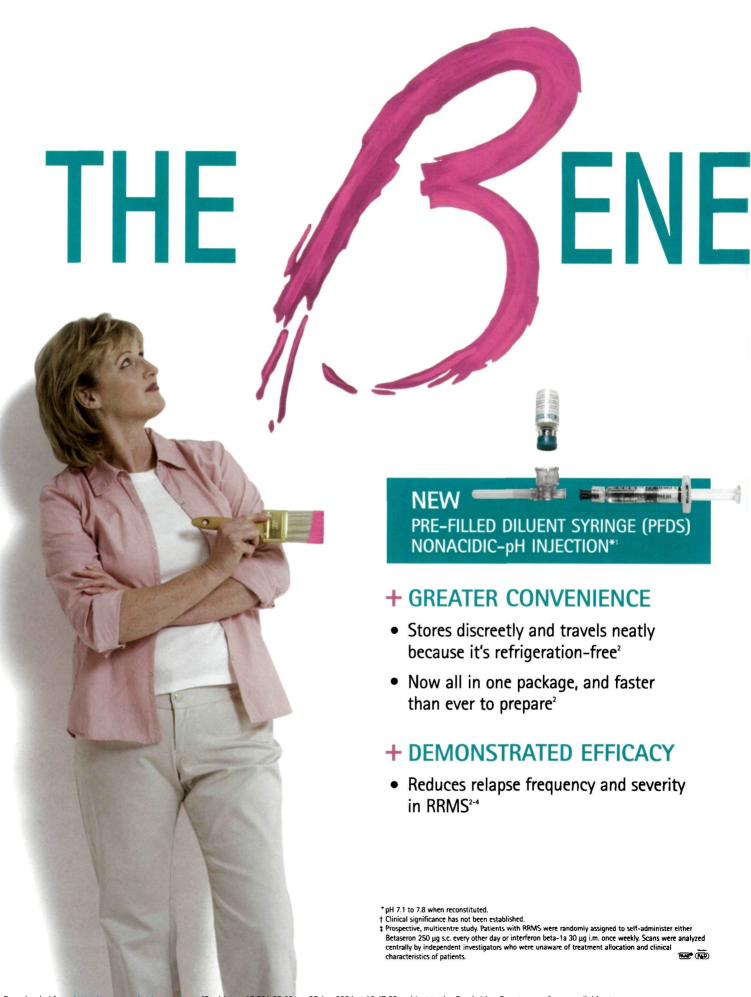
† A powerful demonstrated effect across key lipid parameters¹ More than **57** million patient-years of experience² A EXPERIENCE EVIDENCE **EFFICACY**

in patients with stable coronary artery disease and LDL-C at least 3.0 mmol/L in patients referred for percutaneous transluminal coronary angioplasty (PTCA). Patients were randomized for 18 months to LIPITOR 80 mg daily or to PTCA with usual medical care which could include lipid metabolism regulators. The results of the AVERT study should be The Atorvastatin Versus Revascularization Treatments (AVERT) study examined the effect of intensive lipid-lowering Demonstrated delayed time to first ischemic event in stable CAD patients³⁴ (n=341, p=0.03)

considered as exploratory since several limitations may affect its design and conduct. In the medical-treated group with LIPITOR there was a trend for a reduced incidence of The results also suggest that intensive treatment to target LDL-C levels with LIPITOR is additive and complementary to angioplasty and would benefit patients referred for this ischemic events and a delayed time to first ischemic event.







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+ PERSONALIZED CARE

- Your dedicated MS Pathways[™] nurse is just a phone call away
- Specialized MS Pathways[™] support to help meet your needs and those of your patients

+ SHOWED SIGNIFICANT MRI IMPACT[†]

60% relative risk reduction (29% absolute risk reduction; p<0.001) in the appearance of new T₂ lesions with Betaseron® (n=76) vs. interferon beta-1a i.m. (n=73) after two years (comparative clinical significance has not been established)*5

BETASERON* (interferon beta-1b) is indicated for the reduction of the frequency of clinical exacerbations in ambulatory patients with relapsing-remitting multiple sclerosis and for the slowing of progression in disability and the reduction of the frequency of clinical exacerbations in patients with secondary-progressive multiple sclerosis.

The safety and efficacy of BETASERON® in primary-progressive MS have not been evaluated. Efficacy of treatment for longer than two years has not been substantially demonstrated in relapsing-remitting multiple sclerosis (RRMS).

The most common side effects related to BETASERON® in patients with RRMS are: flu-like symptom complex (76%); fever (59%); chills (46%); injection site reactions (85%); myalgia (44%); asthenia (49%) and malaise (15%).

FOR COMPLETE WARNINGS AND PRECAUTIONS, PLEASE REFER TO THE PRODUCT MONOGRAPH, AVAILABLE TO HEALTH CARE PROFESSIONALS UPON REQUEST.



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25 Years Ago in the Canadian Journal of Neurological Sciences

PROBLEMS IN THE DIAGNOSIS OF PROGRESSIVE SUPRANUCLEAR PALSY (STEELE–RICHARDSON–OLSZEWSKI SYNDROME)

George David Perkin, Andrew John Lees, Gerald Malcolm Stern and Roman Stefan Kocen

SUMMARY: Five patients with progressive supranuclear palsy are described, in whom the ophthalmoplegia developed late in the course of the disease. In two, an internuclear component was identified in the ophthalmoplegia, and one patient had an alternating nystagmus of a type not previously described in this condition.

The late appearance of the ophthalmoplegia, with a corresponding delay in establishing the diagnosis, is compared to the similar experience of Pfaffenbach et al (1972) in six patients.

Other clinical features, previously seldom described, have been encountered. Dysphasia was seen in two cases, both of whom had evidence of cortical atrophy on neuroradiological investigation. The evidence that cortical changes, in particular the presence of neurofibrillary tangles, may be a specific morphological characteristic of the disease rather than a chance association is discussed. Disorders of respiratory rhythm in four patients were similar to those described by Mastaglia et al (1973), and indistinguishable from those occurring after encephalitis lethargica.

A review of cases resembling progressive supranuclear palsy in the early part of the century fails to show any with postencephalitic features, nor does a search of reviews of eye movement disorders in encephalitis lethargica and postencephalitic Parkinsonism provide comparable cases. None of the forty patients with postencephalitic Parkinsonism examined at the Highlands Hospital had a clinical picture resembling progressive supranuclear palsy.

It is suggested that neither on clinical nor pathological grounds is it justifiable to equate this disorder with known postencephalitic syndromes.

Can. J. Neurol. Sci. 1978;5: 167

MULTIPLE SCLEROSIS TREATED WITH ANTITHYMOCYTE GLOBULIN – A FIVE YEAR FOLLOW-UP

L. F. Kastrukoff, D. R. McLean, and T. A. McPherson

SUMMARY: Multiple sclerosis patients treated with antithymocyte globulin (ATG) were re-evaluated after five years. No long term benefit was found. Notably, the group of patients with an elevated gamma globulin to total protein ration in their CSF and who did particularly well after treatment with ATG also failed to show any long term benefit. Few long term detrimental effects of ATG immunosuppression were identified. The implications of the results are discussed as they relate to the use of immunosuppression in multiple sclerosis.

Can. J. Neurol. Sci. 1978;5: 175

TIMING OF THE ELECTRORETINGGRAM RESPONSE AND DARK ADAPTATION

Jean Real Brunette and Gilles Lafond

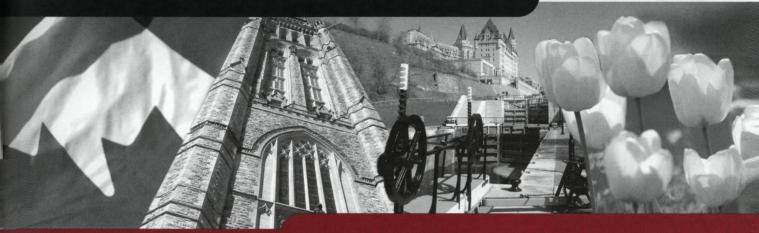
SUMMARY: The time response of the Electroretinogram (ERG) is an essential part of the examination. Peak time of response increases with dark adaptation and decreases with the intensity of stimulation. When working with constant amplitude during dark adaptation sensitivity increases but the intensity of stimulation decreases. It is essential to clarify the relationship of these two factors for valid interpretation of results. The present work suggests that the state of adaptation or retinal sensitivity affects amplitude, while peak time of the response is modified by the absolute value of the stimulating source whatever the state of adaptation. This observation has been done on rod responses and is valid as long as pigments remain unbleached and able to respond.

Can. J. Neurol. Sci. 1978;5: 179



40TH MEETING OF THE

CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES



PRELIMINARY PROGRAM

Tuesday, June 14th, 2005

- Neurobiology Review Course
- ALS Strategies for Quality Life/Quality Care
- Movement Disorders Video Session
- Epilepsy Video Session

Wednesday, June 15th, 2005

- Spinal Course
- Epilepsy Consensus and Controversies in Epilepsy
- EMG
- Neuroanatomy
- EEG
- Brain Tumours Current Standard and Advances in Neuro-Imaging for Treatment of Brain Tumours
- MRI in MS and Stroke and Functional MRI
- Sleep Review and Update in Neurology-Related Pediatric and Adult Sleep Disorders
- Welcome Reception

Thursday, June 16th, 2005

- Plenary Session I Topics on Peripheral Nerve Function, Disease and Repair
- Platform and Poster Sessions
- Grand Rounds
- Dementia

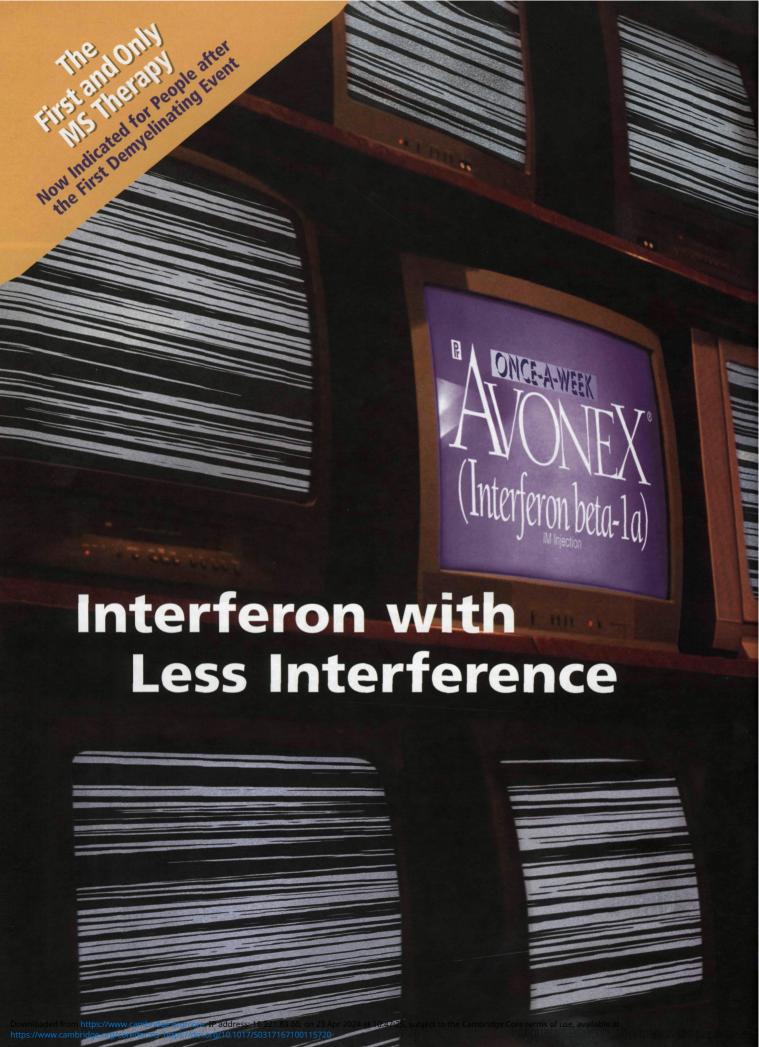
Friday, June 17, 2005

- Plenary Session II Leaders in Canadian Neurosciences
- Platform and Poster Sessions
- Plenary Session III Joint Session with Canadian Association of Physical Medicine and Rehabilitation: Perspectives on neuromuscular disease
- Friday Night Social

Saturday, June 18th, 2005

- Mini-symposia:
 - A Pain in the Head
 - Maximizing CME/Maintenance of Certification Opportunities
 - Neurocritical Care
- Child Neurology Day Advances in the Diagnosis and Treatment of Pediatric Neuromuscular Diseases
- Stroke
- Multiple Sclerosis







Neutralizing antibodies (NAbs) may significantly impact IFNB's ability to bind to receptors and initiate an immunomodulatory process.

AVONEX® has demonstrated the lowest incidence of NAbs. £,1,2,3,4

- AVONEX® (interferon beta-1a) treated patients had the lowest risk of becoming persistent NAb-positive; 2% of patients versus 15% and 31% for Rebif® (IFNβ-1a 22 μg) and Betaseron® (IFNβ-1b) respectively.² (Betaseron® vs AVONEX® p=0.001, Betaseron® vs Rebif® p=0.19, Rebif® vs AVONEX® p=0.04, n=125)
- ► The majority of NAbs usually appear during the first 12 months after initiation of IFNß therapy (ranging from 3 to 18 months).^{2,5}

Once-a-week AVONEX® – Efficacy that Lasts:

- ➤ 37% reduction in the probability of disability progression at 2 years (21.9% vs. 34.9%; p=0.02).^{1,5}
- ➤ 32% reduction in annual exacerbation rate over 2 years (0.61 vs. 0.90; p=0.002).*5
- ► Significant reduction in the number (0.8 vs. 1.6; p≤0.05) and volume (p=0.03) of Gd-enhanced lesions at 2 years Ω,#,5, and in the number of new and enlarging T2 lesions over 2 years (2.0 vs. 3.0; p=0.002).#,**,5
- ► Delayed worsening in brain atrophy during the second year (p=0.03).+,∆,5
- ► Delayed worsening in cognitive function demonstrated on 2 neuropsychological parameters (Information Processing/Memory[†], p=0.011 and PASAT^{*} p=0.023).^{Δ,0,5}

AVONEX® (Interferon beta-1a) is indicated for the treatment of relapsing forms of MS and for the treatment of people who have experienced a single demyelinating event, accompanied by abnormal Magnetic Resonance Imaging (MRI) scans with lesions typical of MS, to delay the onset of clinically definite multiple sclerosis (as determined by a second demyelinating event), and to decrease the number and volume of active brain lesions and overall disease burden (as identified by MRI scans). Before initiating treatment with AVONEX®, alternate diagnoses should first be excluded.

AVONEX® is generally well tolerated. The most common side effects associated with treatment are flu-like symptoms, muscle ache, fever, chills, and asthenia. AVONEX® should be used with caution in patients with depression and in patients with seizure disorders. Patients with cardiac disease should be closely monitored. Routine periodic blood chemistry and hematologic tests are recommended during treatment with AVONEX®.5

£ Comparative clinical significance has not been established. ¶ Kaplan-Meier methodology, AVONEX® n=158, placebo n=143. * AVONEX® n=85, placebo n=87. Ω Using the Mann-Whitney rank-sum test. AVONEX® n=83, placebo n=82. # The exact relationship between MRI findings and clinical status is unknown. ** Analyzed by Wilcoxon rank-sum test. AVONEX® n=78, placebo n=80. + As measured by brain parenchymal fraction in a retrospective analysis, n=140, AVONEX®: 68, placebo: 72. Δ The clinical correlation and significance of these findings require further assessment. † AVONEX® 67, placebo 70, n=137. ¥ AVONEX® 77, placebo 71, n=148. \Diamond As demonstrated in the second year of the Phase III pivotal trial.

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25 Years Ago in the Canadian Journal of Neurological Sciences

LIPOTROPIN, MELANOTROPIN AND ENDORPHIN: IN VIVO CATABOLISM AND ENTRY INTO CEREBROSPINAL FLUID

P.D. Pezalla, M. Lis, N.G. Seidah and M. Chrétien

SUMMARY: Anesthetized rabbits were given intravenous injections of either beta-lipotropin (beta-LPH), beta-melanotropin (beta-MSH) or beta-endorphin. The postinjection concentrations of these peptides in plasma and cerebrospinal fluid (CSF) were measured by radioimmunoassay (RIA). The plasma disappearance half-times were 13.7 min for beta-LPH, 5.1 min for beta-MSH, and 4.8 min for beta-endorphin. Circulating beta-LPH is cleaved to peptides tentatively identified as gamma-LPH and beta-endorphin. Each of these peptides appeared in the CSF within 2 min postinjection. The maximum CSF to plasma ratios were 0.08 for beta-LPH, 1.48 for beta-MSH, and 0.23 for beta-endorphin.

Can. J. Neurol. Sci. 1978;5: 183

THE NEURAL HYPOTHESIS OF MUSCULAR DYSTROPHY: A REVIEW OF RECENT EXPERIMENTAL EVIDENCE WITH PARTICULAR REFERENCE TO THE DUCHENNE FORM

R.E.P. Sica and A.J. McComas

SUMMARY: Recent observations are considered to provide further evidence for an abnormality involving motorneurones in DMD. The dystrophic process appears to take place in two stages of which the first occurs during early embryonic life. This stage is thought to involve faulty inductive actions of the neural tube upon mesoderm and upon itself. The neural consequences vary among individuals and are manifested as mental retardation, EEG abnormalities and losses of functioning motor units. While the first two abnormalities are nonprogressive, a further loss of motor units, associated with striking reductions in the numbers of excitable muscle fibers, takes place in trunk and large limb muscles at 9-12 years. The latter process, the cause of which is uncertain, constitutes the second stage of DMD.

Can. J. Neurol. Sci. 1978;5: 189

THE UPTAKE OF 3H(G)L LEUCINE INTO SINGLE MUSCLE FIBERS IN CHARCOT-MARIE-TOOTH DISEASE

George Monckton and Halyna Marusyk

SUMMARY: In previous studies, the incorporation of 3H(G)L-leucine into muscles of patients with Charcot-Marie-Tooth (CMT) disease was shown to be increased in comparison with that observed in motor neuron disease. To determine the cause of the increased uptake in CMT, studies of single fiber leucine incorporation have been undertaken. The results of this study indicate that the increased incorporation is into those muscle fibers which are undergoing regeneration following reinnervation. These results do not support the thesis that there is an associated myopathic process in CMT.

Can. J. Neurol. Sci. 1978;5: 199

Help Provide Relief From Spasticity And Painful Muscle Spasms

ZANAFLEX® targets both the brain and the spinal cord to help provide relief from symptoms of spasticity with no demonstrated effect on muscle weakness.^{1,2}

ZANAFLEX® significantly reduced the frequency of painful daytime spasms by up to 50%

(response ratios at week 8: ZANAFLEX® -0.25, placebo -0.12)****3,4

Statistically significant reductions in spasms were reported at:3,4

- All patient evaluation visits (weeks 1, 2, 3, 5; p=0.0097 p=0.0005)
- Endpoint (week 8; p-value not available)
- * Response ratio = $\frac{\text{count at visit + count at baseline}}{\text{count at visit count at baseline}}$
- **A randomized, parallel-group, double-blind, multicenter, placebo-controlled trial of patients with spasticity secondary to spinal cord injury: ZANAFLEX® n=59 vs. placebo n=59. 4

ZANAFLEX®:

- Significantly reduced muscle tone^{†3,4,5}
- Significantly reduced painful muscle spasms**3,4
- Preserves healthy muscle strength^{3,4,6}
- Has demonstrated a proven safety profile³
- Offers flexible dosing to help maximize efficacy³

ZANAFLEX® is a short-acting drug for the treatment of spasticity.3

In multiple-dose, placebo-controlled studies, the most frequently reported adverse events included dry mouth (49%), sedation/somnolence (48%), asthenia (weakness, fatigue and/or tiredness) (41%) and dizziness (16%). Patients report that side effects are dose related and tend to diminish as they continue to take ZANAFLEX®. The most common adverse events leading to discontinuation of therapy were asthenia (3%), somnolence (3%) and dry mouth (3%). Sedation may be additive when ZANAFLEX® is taken in conjunction with drugs or substances that act as CNS depressants.

Caution is advised when treatment is used in patients who have a history of orthostatic hypotension or are currently receiving concurrent antihypertensive therapy. Monitoring of aminotransferase levels is recommended during the first six months of treatment, and periodically thereafter, based on clinical status. Please refer to Product Monograph for full prescribing information.

'A randomized, double-blind, placebo-controlled, dose-response study of patients with MS. Muscle tone was assessed using the Ashworth scale and the pendulum test: 8-mg ZANAFLEX® group, n=45; 16-mg ZANAFLEX® group, n=49; placebo group, n=48, p<0.001 vs placebo at 1, 2 and 3 hours post dose.

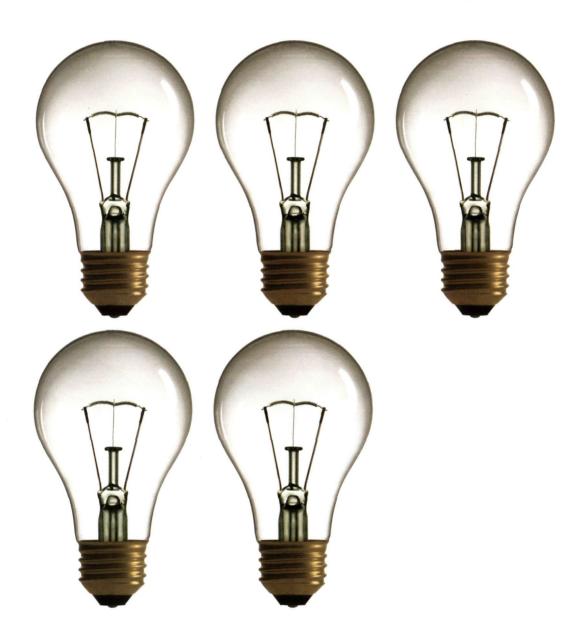




Relieves Spasticity. Restores Possibilities.



If you think all IGIVs are the same,



Gamunex™ (Immune Globulin Intravenous [Human], 10%, Caprylate/Chromatography Purified) is indicated: as replacement therapy of primary immune deficiency states in which severe impairment of antibody forming capacity has been shown; in idiopathic thrombocytopenic purpura (ITP) to rapidly raise platelet counts to prevent bleeding or to allow an ITP patient to undergo surgery; for the reduction of septicemia and other infections, interstitial pneumonia and acute graft vs host disease in first 100 days post-transplant in allogeneic bone marrow transplantation patients ≥ 20 years of age; for the reduction of recurrent serious bacterial infections in those children with HIV who do not respond to or cannot tolerate antiretroviral combination therapy.

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Gamunex $^{\text{TM}}$ is contraindicated in individuals with known anaphylactic or severe systemic response to immune globulin (human). Individuals with severe, selective IgA deficiencies (serum IgA <0.05 g/L) who have known antibody against IgA (anti-IgA antibody) should only receive Gamunex $^{\text{TM}}$ with utmost cautionary measures.

Immune globulin intravenous (human) products have been associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients predisposed to acute renal failure should be administered the minimum concentration of human immune globulin products at the minimum rate of infusion.

Please see complete Prescribing Information on adjacent pages.

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new Gamunex could change your mind.

The Gamunex™ Difference.

Innovative manufacturing process.

- Novel process designed to protect fragile IgG molecules.
- Utilizes new caprylate/chromatography process as an effective alternative to solvent-detergent for inactivating and removing enveloped viruses.

Excellent tolerability profile.

• In a study of 97 ITP patients, 90% of adverse events were mild-to-moderate and transient. **

Designed with convenience in mind.

- Liquid 10% formulation reduces volume load vs 5% formulations.1#
- High maximum infusion rate reduces infusion time.11
- 5 months room temperature storage. 14
- · Osmolality similar to physiologic osmolality.
- No added sugar stabilizers (such as sucrose or glucose).
- *Most common adverse events reported in a study of 97 ITP patients: headache (50%), vomiting (13%), fever (10%), nausea (10%), rash (6%), back pain (6%).
- † Initial infusion rate is 0.01 to 0.02 mL/kg body weight/min for 30 minutes; if well tolerated, the rate may be gradually increased to a maximum of 0.14 mL/kg body
- ‡ May be stored at room temperature (≤ 25°C) for 5 months during first 18 months of manufacture after which product must be used or discarded.
- § Based on sizes of studies listed in Product Monographs of IGIV products currently marketed in Canada.
- ¶Double-blind trial of 172 PID patients randomized to Gamunex™ or Gamimune® N, 10%. **Double-blind trial of 97 ITP patients randomized to Gamunex™ or Gamimune® N, 10% response rate by day 7.
- †† ITP study above; maintenance rate (≥50 x 10° for 7 days); p = 0.066.
- ## Comparative clinical significance unknown.

Most common adverse events reported in PID were: cough increased

New Gamunex™ trials design.

- · Largest pivotal trials in IGIV in patients with primary humoral immunodeficiency (PID) and idiopathic thrombocytopenic purpura (ITP).15
- Head-to-head comparison in more than 350 patients vs Gamimune® N, 10%.

Proven efficacy in immune replacement therapy.

· Reduced the annual rate of validated sinopulmonary infection in PID (Gamunex™: 0.18 vs Gamimune® N. 10%: 0.43, p = 0.023).

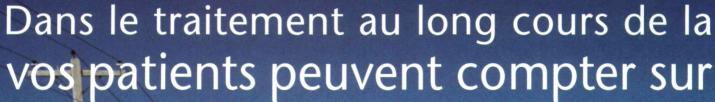
Proven efficacy in immunomodulatory therapy.

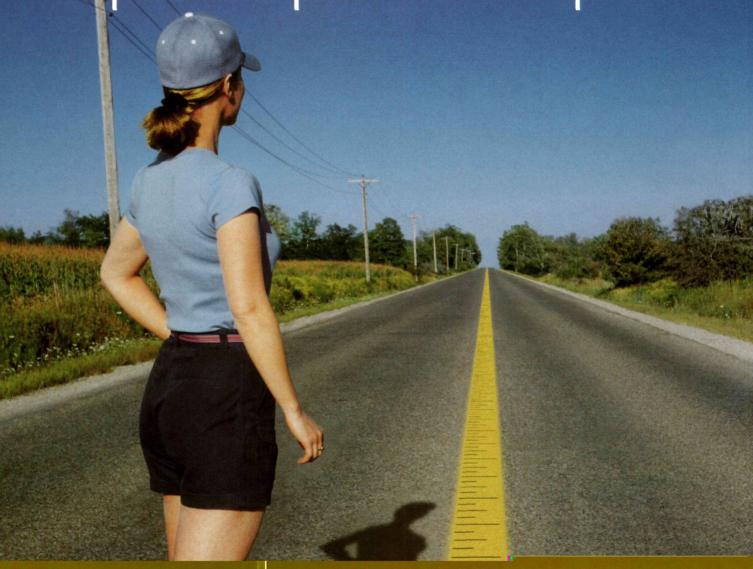
- Gamunex[™] demonstrated excellent response rates in chronic ITP (100%) and acute ITP (90%).2**
- Excellent duration of platelet response (Gamunex[™]: 74% vs Gamimune[®] N, 10%: 60%).²



immune globulin intravenous (human), 10% caprylate/chromatography purified

For brief prescribing information see pages A-44,





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SP rémittente, COPAXONE.

Effet démontré sur l'incapacité

■ Les patients traités par COPAXONE® ont présenté une réduction moyenne de leur cote EDSS de -0,05 comparativement à une augmentation de la cote EDSS de +0,21 dans le groupe placebo sur une période de deux ans

 $({n=125} c. {n=126} placebo, p = 0.023)^{1}$.

Réduction de la fréquence des poussées*

- Réduction de 35 % après neuf mois (0,50 {n = 113} c. 0,77 {n = 115} placebo, moyenne, p = 0,0077)¹.
- Réduction de 75 % après deux ans (0,60 {n = 25} c. 2,40 {n = 25} placebo, moyenne, p = 0,005)¹.

*Deux études indépendantes

Profil d'innocuité établi

- Innocuité démontrée depuis plus de sept ans dans les essais cliniques¹.
- Aucune surveillance en laboratoire des anomalies hépatiques ou sanguines n'est recommandée¹.

L'emploi de COPAXONE® est indiqué chez les patients ambulatoires atteints de sclérose en plaques (SP) rémittente en vue de réduire la fréquence des poussées. L'innocuité et l'efficacité de COPAXONE® dans la sclérose en plaques chronique progressive n'ont pas été établies.

Au cours des essais comparatifs, les effets indésirables le plus fréquemment associés à l'utilisation de COPAXONE® et dont l'incidence était supérieure à celle qui a été observée chez les sujets qui recevaient le placebo étaient les suivants : réactions au point d'injection (2,4-66,4 % c. 0-36,5 %), vasodilatation (27,2 % c. 11,1 %), douleur thoracique (26,4 % c. 10,3 %), asthénie (64,8 % c. 61,9 %), infection, douleur, nausées (23,2 % c. 17,5 %), arthralgie (24,8 % c. 17,5 %), anxiété et hypertonie (35,2 % c. 29,4 %).



"COPAXONE" (acétate de glatiramère injectable)

Traitement au long cours de la SP rémittente



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25 Years Ago in the Canadian Journal of Neurological Sciences

THE SYNDROME OF CARNITINE DEFICIENCY: MORPHOLOGICAL AND METABOLIC CORRELATIONS IN TWO CASES

G. Scarlato, G. Pellegrini, C. Cerri, G. Meola and A. Veicsteinas

SUMMARY: Two cases of systemic carnitine deficiency are described. In both patients, carnitine concentration was lower than normal in serum and muscle tissue. In the first case, the illness began at age 35; the clinical manifestations were only muscular. In the second case, the illness began in childhood; there were intermittent episodes of hepatic enlargement and coma. An excessive lipid content was present in muscle tissue, especially in type I fibers, of both cases, and in the liver of the second patient. Ultrastructural studies of muscle tissue revealed important changes of mitochondria.

During muscular exercise, aerobic and anaerobic metabolism were investigated. For a given relative work intensity, these patients showed abnormally high blood lactic acid concentration and lactic acid/pyruvic acid ratios. These data, together with the morphological alterations observed in mitochondria, suggest an impaired function of the respiratory chain, leading to a shift of the red/ox potential of the tissue towards a non reduced state.

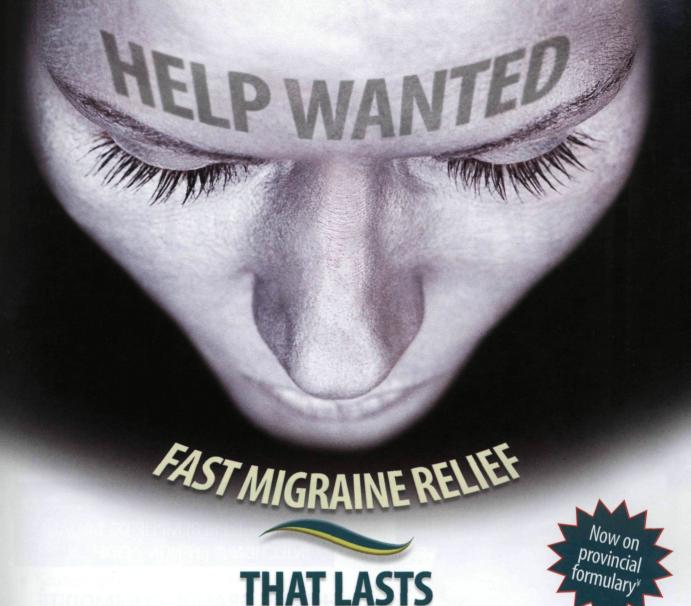
Can. J. Neurol. Sci. 1978;5: 205

THE PROLONGED ANTICONVULSANT ACTION OF TAURINE ON GENETICALLY DETERMINED SEIZURE-SUSCEPTIBILITY

R. Huxtable and H. Laird

SUMMARY: A prolonged anticonvulsant action of taurine has been shown in a strain of seizure susceptible rats. The audiogenic rat (AS) has lower intracerebral electroshock thresholds in three auditory nuclei; the ventral cochlear, the inferior colliculi and the medial geniculate, and in one nonauditory structure; the reticular formation, than a strain of nonaudiogenic rats (NAS). Furthermore, the AS animals routinely display maximal (tonic-clonic) convulsion, regardless of brain structure stimulated, whereas NAS subjects respond with minimal (clonic) convulsions. Within three minutes of intraventricular injection of 8µ moles, taurine reduces the susceptibility of AS rats to intracerebral electroshock seizures along with attenuation of the severity of the convulsion. The initial elevation in intracerebral electroshock threshold returns to pretreatment value at 24 hours, only to rise again at 48 hours and to remain elevated through day six after injection. In contrast, the severity of convulsions remains attenuated through 24 hours, after which it returns to pre-injection level. By comparison, NAS animals injected intracerebroventricularly in an identical fashion to the AS rats showed no changes in either seizure threshold or severity of convulsion. The direct injection of 200n-moles of taurine in the inferior colliculi of AS rats produced a slow developing, but prolonged, elevation of intracerebral electroshock threshold of this auditory nuclei. However, at no time after the intracerebral injection of taurine was convulsive severity changed. Injection of taurine into the inferior colliculi of NAS subjects did not change either susceptibility or severity of intracerebral electroshock seizures. The data indicate that taurine produces an anticonvulsant effect which is slow in onset, potent, selective and prolonged.

Can. J. Neurol. Sci. 1978;5: 215



THAT LASTS

Fast onset.

Significant migraine pain relief attained as early as 30 minutes after treatment 11

Lasting relief.Demonstrated low incidence of migraine recurrence within 24 hours^{2‡}

No recurrence seen in 4 out of 5 patients.

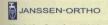
After a single 12.5 mg dose, 82% of responders had no recurrence of their migraine attack within 24 hours, in a clinical trial²⁺

AXERT* (almotriptan malate) tablets are indicated for the acute treatment of migraine with or without aura in adults. AXERT* is not indicated for the prophylactic therapy of migraine or for use in the management of hemiplegic, ophthalmoplegic or basilar migraine. Safety and effectiveness of AXERT* have not been established for cluster headache, which presents in older, predominately male population.

Overall, in controlled clinical trials, only three side effects occurred in more than 1% of AXERT* patients and more frequently than in patients taking placebo: nausea (2%), dry mouth (1%) and paresthesia (1%).

As with other triptans, AXERT* is contraindicated in patients with history, symptoms or signs of ischemic cardiac, cerebrovascular or peripheral vascular syndromes, valvular heart disease, cardiac arrhythmias, uncontrolled hypertension, or in patients with other significant underlying cardiovascular disease. AXERT* should not be administered within 24 hours of treatment with another 5-HT₁ agonist or an ergotamine-containing or ergot-type medication.

uct Monograph, Janssen-Ortho Inc., October 2003



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Fastlasting™ Relief

almotriptan malate tablets

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OFFRIR DE MEILLEURS SOINS À VOS PATIENTS ATTEINTS DE SEP

+ SOINS PERSONNALISÉS

- Un appel suffit pour parler à votre infirmière de SEP LeParcours^{MC}
- Soutien spécialisé de SEP LeParcours[™] pour répondre à vos besoins et à ceux de vos patients atteints de SEP

+ RÉSULTATS SIGNIFICATIFS OBSERVÉS À L'IRM[†]

 Diminution de 60 % du risque relatif (diminution de 29 % du risque absolu; p < 0,001) d'apparition de nouvelles lésions T₂ avec Betaseron® (n = 76) comparativement à l'interféron bêta-1a i.m. (n = 73) après deux ans (la signification clinique comparative n'a pas été établie)^{‡5} BETASERON® (interféron bêta-1b) est indiqué pour réduire la fréquence des poussées cliniques chez les patients ambulatoires atteints de sclérose en plaques rémittente. Il est également indiqué pour ralentir la progression de l'incapacité et réduire la fréquence des poussées cliniques chez les patients atteints de sclérose en plaques progressive-secondaire.

L'efficacité et l'innocuité de BETASERON® dans la SEP progressiveprimaire n'ont pas été évaluées. On ne dispose pas de données probantes sur l'efficacité du traitement de la SEP rémittente au-delà de deux ans.

Chez les patients atteints de SEP rémittente, les effets indésirables les plus courants liés à l'utilisation de BETASERON® sont : syndrome grippal (76 %) ; fièvre (59 %) ; frissons (46 %) ; réactions au point d'injection (85 %) ; myalgie (44 %) ; asthénie (49 %) et malaise (15 %).

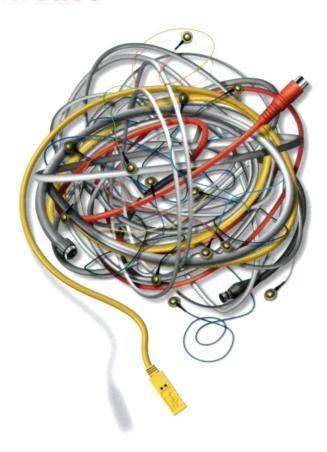
POUR PLUS DE DÉTAILS SUR LES MISES EN GARDE ET LES PRÉCAUTIONS, VEUILLEZ CONSULTER LA MONOGRAPHIE DE PRODUIT FOURNIE SUR DEMANDE AUX PROFESSIONNELS DE LA SANTÉ.







From uncontrolled



Keppra — connecting excellent profiles in efficacy and tolerability

Effective control of seizures

- Shown to provide up to 4 out of 10 refractory patients with \geq 50% reduction in partial onset seizures (p < 0.001)
- Rapid clinical improvement demonstrated by week 2 during a 14-week evaluation period $(p < 0.001)^{11}$



For more information, please refer to the complete Keppra Product Monograph.

• Keppra is a registered trademark of UCB SA. Distributed by Lundbeck Canada Inc.

Keppra is indicated as adjunctive therapy in the management of patients with epilepsy who are not satisfactorily controlled by conventional therapy.

The most significant CNS adverse events were somnolence (Keppra 15% vs placebo 10%) and asthenia (Keppra 14% vs placebo 10%), behavioural/psychiatric symptoms (nonpsychotic: Keppra 14% vs placebo 6%; psychotic: Keppra 1% vs placebo 0%) and coordination difficulties (Keppra 3% vs placebo 2%). These adverse events were observed in controlled clinical trials with concomitant AEDs.

NOW **AVAILABLE ON PROVINCIAL FORMULARIES:***

ALBERTA MANITOBA NEWFOUNDLAND NOVA SCOTIA ONTARIO

QUEBEC SASKATCHEWAN

to control



Generally well tolerated

- Favourable adverse event profile
- Adverse events not dose dependent
- Low discontinuation or dosage reduction (Keppra 14.3% vs placebo 11.7%) due to adverse events

Efficacy and manageability right from the start

- Starting dose of 1000 mg/day (500 mg bid) shown to be effective and may be adjusted to a maximum of 3000 mg/day if required
- No blood level monitoring required
- No drug/drug interactions[§] with other AEDs, warfarin, digoxin or between Keppra 500 mg bid and a combination oral contraceptive (0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel)⁵
- ¶ Note: Pharmacokinetic interaction studies with contraceptives have not been conducted 1) Note: Priarmacoinetic interaction studies with contractipities have not been consolidated covering the full recommended dosage range of Keppra. Physicians should advise their female patients to be alert to any irregular vaginal bleeding or spotting and report any occurrences. Restrictions may exist by province. Please refer to your formulary for details.
 † Data from a 38-week multicentre, randomised, add-on, double-blind, placebo-controlled, parallel-
- † Data from a 38-week multicentre, randomised, add-on, double-blind, placebo-controlled, parallel-group trial. Study consisted of a 4-week titration period followed by a 14-week evaluation period. Patients received either levetiracetam 1000 mg/day (n = 98), 3000 mg/day (n = 101) or placebo (n = 95). Patient weekly seizure frequency was reduced over placebo, at week 2 of the evaluation period, by 24.9% (1.120/1.406) for Keppra 1000 mg/day and 38.6% (0.918/1.406) for Keppra 3000 mg/day. The percentage of patients achieving ≥ 50% seizure reduction from baseline after the 18-week titration and evaluation period was 7.4% for placebo, 37.1% for Keppra 1000 mg/day and 39.6% for Keppra 3000 mg/day.
 ‡ Based on observations in clinical studies.
 § C_{max} of levetiracetam's metabolite (ucb L057) was approximately doubled in presence of probenecid. Renal clearance of ucb L057 decreased by 60% in presence of probenecid.





PORTRAIT OF A FAMILY HISTORY

HISTORY DOESN'T HAVE TO REPEAT ITSELF



Roger, History of angina.

> Died age 57 of MI.

Help Reduce the Risk of CV Death

(p<0.001; 6.1% vs. 8.1%)

of stroke.



GUARDING AGAINST CV DEATH

ALTACE is indicated in the treatment of essential hypertension, normally when beta-blockers and diuretics are inappropriate. It may be used alone or in association with thiazide diuretics. ALTACE is indicated following acute myocardial infarction in clinically stable patients with signs of left ventricular dysfunction to improve survival and reduce hospitalizations for heart failure.

Results from the HOPE study showed that ALTACE improved survival in patients by reducing the risk of CV death by 26% (p<0.001; 6.1% vs. 8.1%). ALTACE may be used to reduce the risk of MI, stroke, or CV death in patients over age 55 who are at high risk of CV events because of a history of CAD, stroke, peripheral artery disease, or diabetes accompanied by at least 1 other CV risk factor such as hypertension, elevated total cholesterol levels, low HDL levels, cigarette smoking, or documented microalbuminuria.

Like other ACE inhibitors, ALTACE is not recommended for pregnant or lactating women and should be used with caution in patients with renal insufficiency. The most frequent adverse events occurring in clinical trials with ALTACE monotherapy in hypertensive patients who were treated for at least 1 year (n=651) were: headache (15.1%); dizziness (3.7%); asthenia (3.7%); chest pain (2.0%). Discontinuation of therapy due to clinical adverse events was required in 5 patients (0.8%).

The reasons for stopping treatment were cough (ramipril 7.3% vs. placebo 1.8%); hypotension/dizziness (1.9% vs. 1.5%) and edema (0.4% vs. 0.2%).

ALTACE is the most prescribed ACEI among cardiologists.

*IMS Health Canada: Canadian CompuScript Audit, Moving Annual Total ending June 2004, Total Prescriptions.

(R&D) PAAB

Product Monograph available to physicians and pharmacists upon request.

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