Volume 31 Number 4 November 2004

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Neurological Sciences
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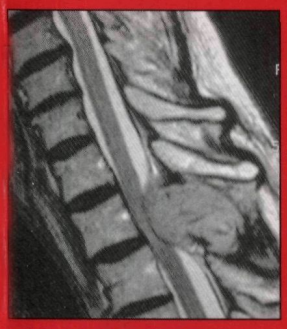
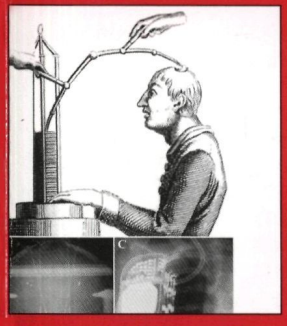


Metastatic hemangiopericytoma



Galvanism being applied on the head

She Has Dreams. Controlling MS Could Help Her Live Them.

Jennifer M. is a MS patient who has been taking Rebif® since 1999. She lives in Vancouver.

In PRISMS 4 – Patients treated early attained more benefit at 4 years than those delaying treatment.[1,2]*

- Rebif® 44mcg x3 reduced the number and severity of MS relapses.[1,2]*
- Time to sustained disability progression was prolonged by 18 months in the Rx44 group. (42.1 months vs. 24.2 months, p=0.047)[2]

Rebif® is indicated for the treatment of relapsing forms of multiple sclerosis, to reduce the number and severity of clinical exacerbations, slow the progression of physical disability, reduce the requirement for steroids, and reduce the number of hospitalizations for treatment of multiple sclerosis and reduction in T_1-Gd enhanced and T_2 (burden of disease) as seen on MRI.[1] The most common adverse events reported in controlled clinical trials with high-dose Rebif® (44mcg x3) are: injection site inflammation 66.5%, injection site reaction 31.7%, injection site pain 13.8%, upper respiratory tract infections 20.4%, headache 46.7%, flu-like symptoms 42.5%, fatigue 27.5%, and fever 12.0%. Evidence of safety and efficacy derived from 3- and 4-year data.[1]

* Randomized, 4-year, placebo-controlled study. Patients receiving placebo in first 2 years were randomized to blinded interferon ß-1a, 22 or 44mcg x3 (n=172; crossover group) while others remained on assigned dose 22mcg (Rx22 group) or 44mcg (Rx44 group) *tiw* (n=167 per group). Patients had 3- to 6-month clinical and annual MRI assessments.

Pr Rebif® 44mcg x3.
Interferon beta-1a

Because life is more than MS

For brief prescribing information see pages A-32, A-33

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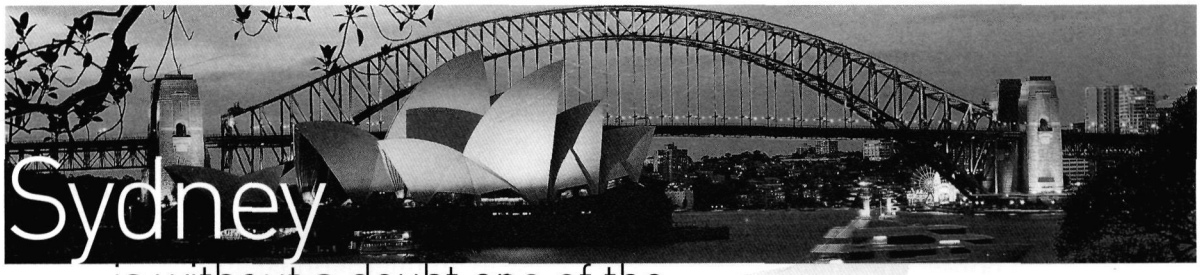
5-11 November 2005 Sydney Australia



is without a doubt one of the
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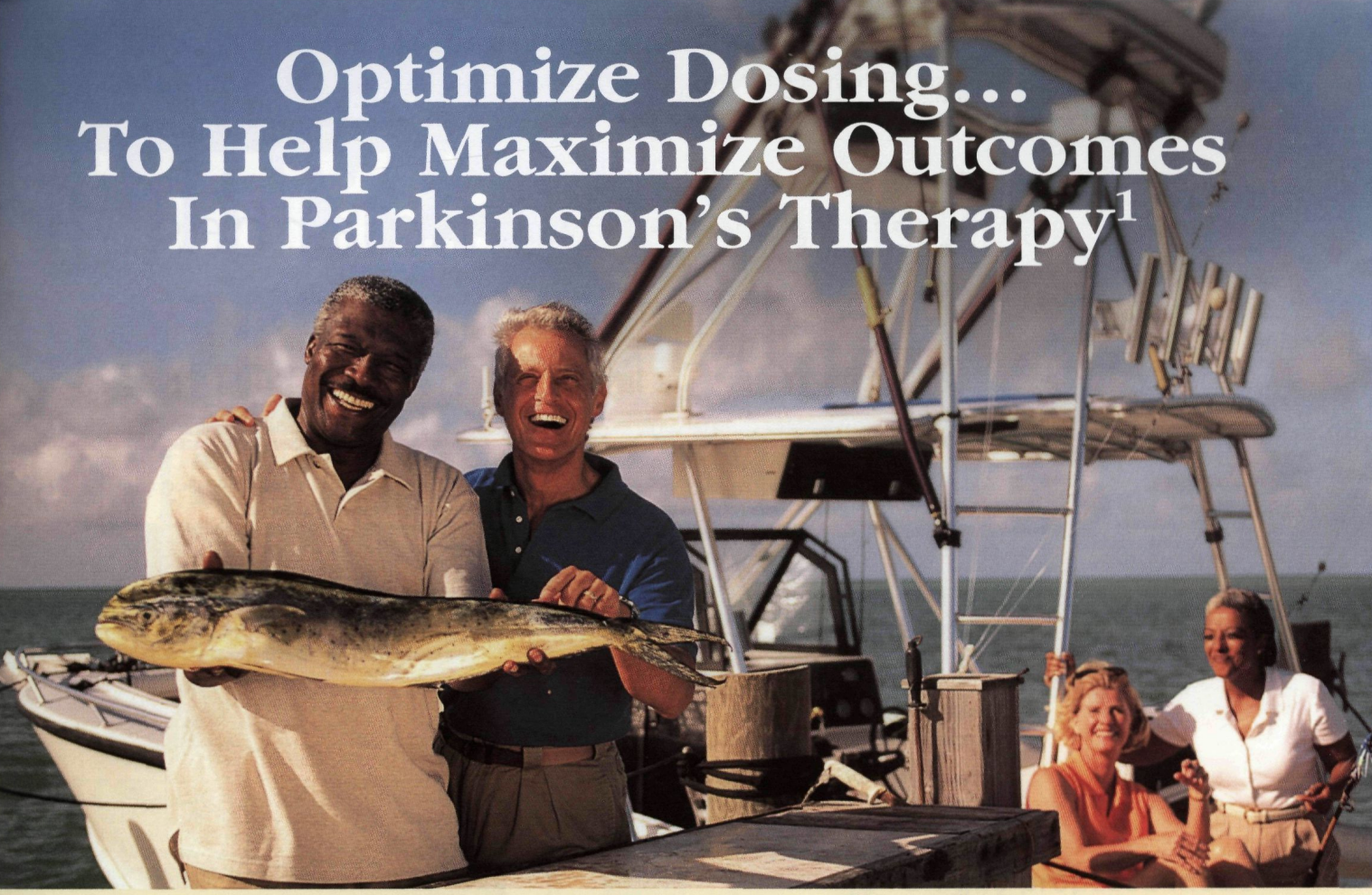
THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

Optimize Dosing... To Help Maximize Outcomes In Parkinson's Therapy[1]



Titrate to help maximize patient benefit. In at least 75% of the patients who responded to REQUIP®, doses of up to 9 mg/day were necessary to ensure a first therapeutic response.[1x]

Three Reasons to Prescribe REQUIP®

REQUIP® delayed the use of L-dopa

34% (n=29 of 85) of REQUIP® monotherapy patients completed the entire 5-year study without requiring L-dopa supplementation[2∂]

Low risk of dyskinesia

Only 5% of REQUIP® monotherapy patients developed dyskinesia compared with 36% of L-dopa patients[2]*

Low supplementary dose of L-dopa needed

When used with adjunct L-dopa, REQUIP® patients required an average of 43% less L-dopa (427 ± 221 mg) than patients on L-dopa alone (753 ± 398 mg)[2]

∂ In early treatment of Parkinson's disease over the course of a 5-year multicentre, prospective, double-blind, flexible-dose study, with 268 patients randomized to either REQUIP® (*n*=179) or L-dopa and benserazide (a decarboxylase inhibitor) (*n*=89). Open label L-dopa was available as supplementary medication.[2,3] $p<0.001$

* Prior to supplementation with L-dopa

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 trial (n=116).[1]

† 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.

REQUIP® (ropinirole hydrochloride) is indicated in the treatment of the signs and symptoms of idiopathic Parkinson's disease. REQUIP® can be used both as early therapy, without concomitant levodopa and as an adjunct to levodopa. Patients receiving treatment with REQUIP® and other dopaminergic agents have reported the sudden onset of sleep while engaged in daily activities. Patients should be warned not to drive or engage in other activities where impaired alertness could put themselves or others at risk.[3†]

Adverse events occurring with an incidence of greater than, or equal to, 10% were as follows: *Early therapy:* nausea, dizziness, somnolence, headache, peripheral edema, vomiting, syncope, fatigue and viral infection. *Adjunct therapy:* dyskinesia, nausea, dizziness, somnolence and headache. REQUIP® is contraindicated in patients with a known hypersensitivity to ropinirole hydrochloride or the excipients of the drug product.[3]

Pr REQUIP® ropinirole

Rethinking Parkinson's.

Member R&D PAAB

gsk GlaxoSmithKline

For brief prescribing information see pages A-61, A-62

Volume 31 Number 4 November 2004

THE CANADIAN JOURNAL OF Neurological Sciences

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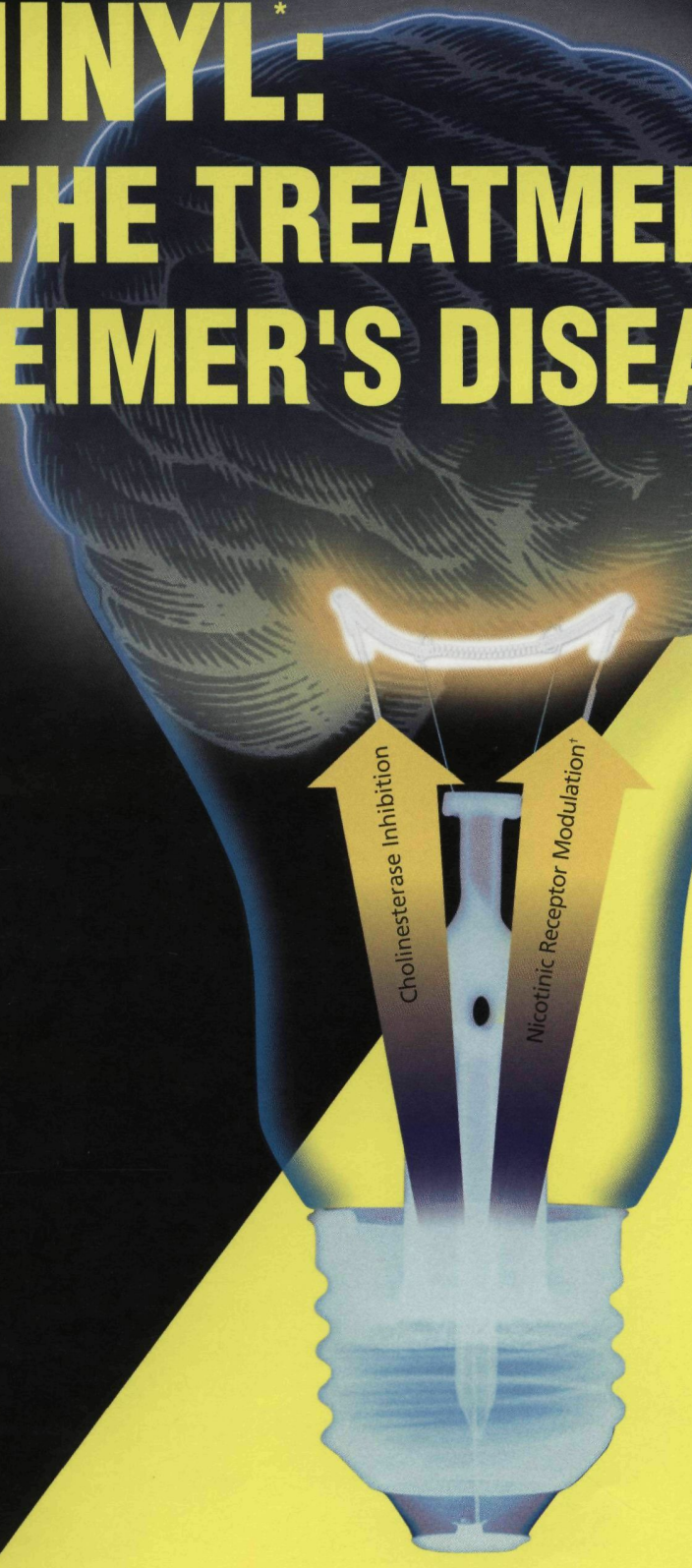
††Now on provincial formularies for Ontario, Quebec, Alberta, Saskatchewan, Manitoba, New Brunswick, Nova Scotia and Newfoundland

REMINYL*: FOR THE TREATMENT OF ALZHEIMER'S DISEASE



Unique proposed mode of action:

Cholinesterase inhibition and nicotinic modulation[1,2†]

New REMINYL: The difference may be nicotinic modulation†

More than just cholinesterase inhibition, REMINYL enhances the action of acetylcholine through binding to an allosteric site on the nicotinic receptors[1,2†]

† Based on *in vitro* data. The clinical relevance to humans is unknown. The majority of common side effects occurred during the dose-escalation period and were primarily gastrointestinal. During maintenance therapy, the most common side effects were: REMINYL 16 mg/day-nausea (4%) and diarrhea (5%); REMINYL 24 mg/day-nausea (6%), vomiting (6%) and anorexia (5%).

REMINYL (galantamine hydrobromide) is indicated for the symptomatic treatment of patients with mild to moderate dementia of the Alzheimer's type. REMINYL has not been studied in controlled clinical trials for longer than 6 months. There is no evidence that galantamine alters the course of the underlying dementing process.

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.

†† Exception drug status

RMJA041001A

JANSSEN-ORTHO Inc.
19 Green Belt Drive,
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www.janssen-ortho.com

Pr Reminyl* Galantamine hydrobromide tablets

Think Cognition


For the treatment of RRMS
COPAXONE®. With your

patients for the long run.

Demonstrated impact on disability

- COPAXONE®-treated patients had a mean reduction in EDSS scores of -0.05 compared with an increase in EDSS scores of +0.21 in the placebo group over 2 years
  ({n=125} vs. {n=126} placebo, p=0.023)[1]

Reduced relapse rates*

- 35% reduction at 9 months
  (0.50 {n=113} vs. 0.77 {n=115} placebo, mean, p=0.0077)[1]
- 75% reduction at 2 years
  (0.60 {n=25} vs. 2.40 {n=25} placebo, mean, p=0.005)[1]
  *Two independent studies

Established safety profile

- Demonstrated for over 7 years in clinical trials[1]
- No recommended monitoring of liver and thyroid function or complete blood count[1]

COPAXONE® is indicated for use in ambulatory patients with Relapsing-Remitting Multiple Sclerosis (RRMS) to reduce the frequency of relapses.

The safety and efficacy of COPAXONE® in chronic progressive MS have not been established.

The most commonly observed adverse events associated with the use of COPAXONE® in controlled trials which occurred at higher frequency than placebo were: injection site reactions (2.4-66.4% vs. 0-36.5%), vasodilation (27.2% vs. 11.1%), chest pain (26.4% vs. 10.3%), asthenia (64.8% vs. 61.9%), infection, pain, nausea (23.2% vs. 17.5%), arthralgia (24.8% vs. 17.5%), anxiety and hypertonia (35.2% vs. 29.4%).

℗ COPAXONE®
(glatiramer acetate injection)

Treating RRMS for the long run.

TEVA NEUROSCIENCE

PAAB

For brief prescribing information see pages A-51, A-52

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

TOPAMAX works at multiple sites in the brain, including GABA receptors, sodium channels, and glutamate receptors.†

† Clinical significance is unknown.

The Strength of Growing Experience

Rapid and Effective Control

- Significant therapeutic effect was observed at the first treatment visit (week 2) in the 50/50 titration group ($p<0.001$ vs. placebo)[2‡]
- More than half of these patients had a ≥ 50% episode reduction at 12 weeks (n=42/83; $p=0.001$ vs. placebo)[3‡]

Favourable Tolerability and Safety Profiles

- No reported contraindications other than hypersensitivity to the drug or any ingredients in the formulation[2]
- Patients may experience some weight loss[§]

Convenient to Use

- Flexible dosing and titration
- No monitoring of topiramate plasma levels required[2]

TOPAMAX (topiramate) is indicated as adjunctive therapy for the management of patients (adults and children two years and older) with epilepsy who are not satisfactorily controlled with conventional therapy. There is limited information on the use of TOPAMAX in monotherapy at this time.

In combinations with other AEDs, CNS adverse events include: somnolence (30.1%), dizziness (28.3%), ataxia (21.2%), speech disorders (16.8%), psychomotor slowing (16.8%), nystagmus (15.0%), paresthesia (15.0%), nervousness (15.9%), difficulty with memory (12.4%), difficulty with concentration/attention (8.0%), confusion (9.7%), depression (8%), anorexia (5.3%), language problems (6.2%), agitation (4.4%) and mood problems (3.5%). In an audit of 1446 adults and 303 children, there appeared to be a similar pattern of adverse events.[2]

Low discontinuation rates in adults (10.6% vs 5.8% for placebo) at the recommended maintenance dose of 200-400 mg/day.[3‡]

Physicians are urged to consult the Product Monograph/Prescribing Information for complete information on warnings, precautions (including metabolic acidosis), and patient selection.

‡ 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 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.

§ The long-term effects of reduced weight gain in pediatric patients are unknown.

Pr TOPAMAX* topiramate

The Strength of Experience

TXJA041030A

Member R&D PAAB

For brief prescribing information see pages A-36, A-37

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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.

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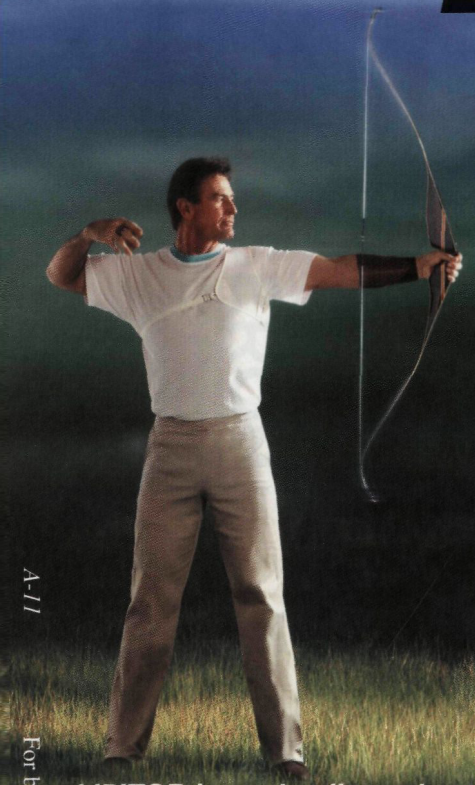
PrLIPITOR*: Hitting targets.



NEW
FLEXIBLE FIRST DOSE™
start at 10 mg, 20 mg, 40 mg††
†† When a >45% LDL-C reduction is required, patients may be started at 40 mg o.d.

Clinical research program[4]

Aiming beyond.

LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control[4]

LIPITOR 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.

LIPITOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and Total-C/HDL-C ratios (Fredrickson Type IIa and IIb).

Less than 2% of patients discontinued therapy due to adverse experiences. Most common adverse effects were constipation, diarrhea, dyspepsia, flatulence, nausea, headache, pain, myalgia and asthenia.

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 necessary, the dose of LIPITOR adjusted based on target lipid levels recommended by guidelines.

Caution should be exercised in severely hypercholesterolemic patients who are also renally impaired, elderly, or are concomitantly being administered digoxin or CYP 3A4 inhibitors.

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 be repeated promptly and then performed more frequently.

EFFICACY ➢ † A powerful demonstrated effect across key lipid parameters[1]

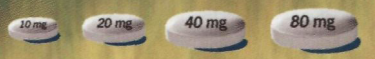
EXPERIENCE ➢ More than **57** million patient-years of experience[2]

EVIDENCE ➢ Demonstrated delayed time to first ischemic event in stable CAD patients[3¥] (n=341, *p*=0.03)

¥ *The Atorvastatin Versus Revascularization Treatments* (AVERT) study examined the effect of intensive lipid-lowering 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 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 ischemic events and a delayed time to first ischemic event. 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 procedure.[1]

PrLIPITOR
atorvastatin calcium
tablets

power you can trust™



Pfizer
Life is our life's work

PAAB Member R&D

A-11

For brief prescribing information see pages A-40, A-41

THE BENE

NEW
PRE-FILLED DILUENT SYRINGE (PFDS)
NONACIDIC-pH INJECTION*[1]

+ GREATER CONVENIENCE

- Stores discreetly and travels neatly because it's refrigeration-free[2]
- Now all in one package, and faster than ever to prepare[2]

+ DEMONSTRATED EFFICACY

- Reduces relapse frequency and severity in RRMS[2-4]

*pH 7.1 to 7.8 when reconstituted.
† Clinical significance has not been established.
‡ Prospective, multicentre study. Patients with RRMS were randomly assigned to self-administer either Betaseron 250 µg s.c. every other day or interferon beta-1a 30 µg i.m. once weekly. Scans were analyzed centrally by independent investigators who were unaware of treatment allocation and clinical characteristics of patients.

FITS ADD UP

HELPING YOU BETTER CARE FOR YOUR MS PATIENTS

+ 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 T_2 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.

BETASERON® INTERFERON BETA-1b

® BETASERON is a registered trademark of Berlex Canada Inc.
™ MS Pathways is a trademark used under license by Berlex Canada Inc.

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BERLEX
www.betaseron.ca
www.mspathways.ca

For brief prescribing information see pages A-38, A-39

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 Electroretinogram Response and Dark Adaptation

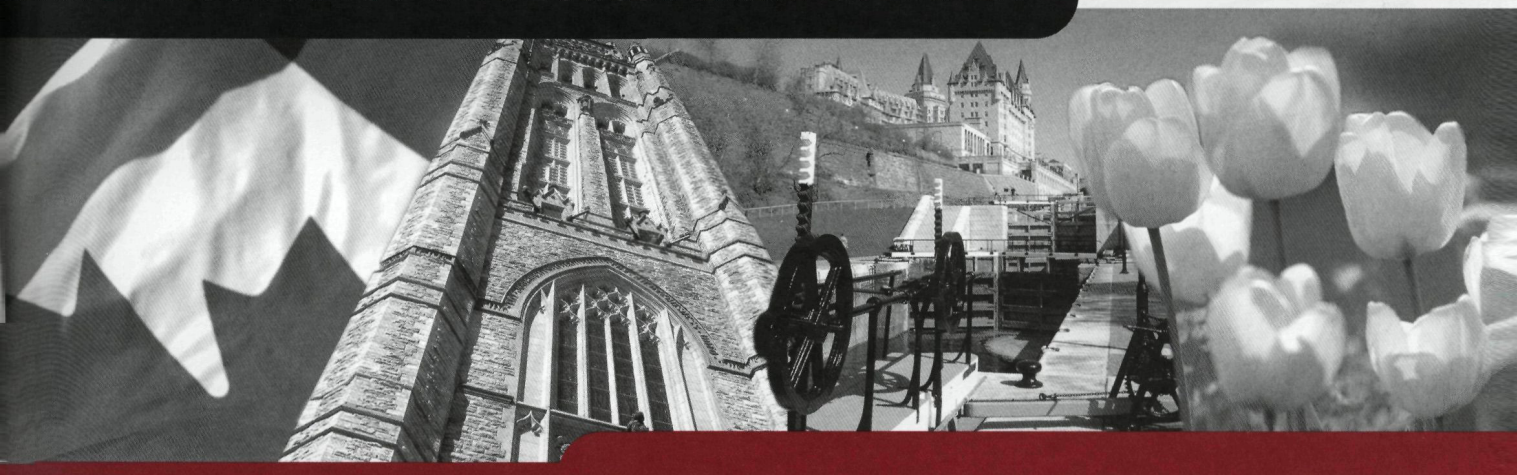
Jean Real Brunette and Gilles Lafond

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

2005
OTTAWA
CCNS/CCSN
June 14-18 Juin 2005

40TH MEETING OF THE
CANADIANCONGRESS 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

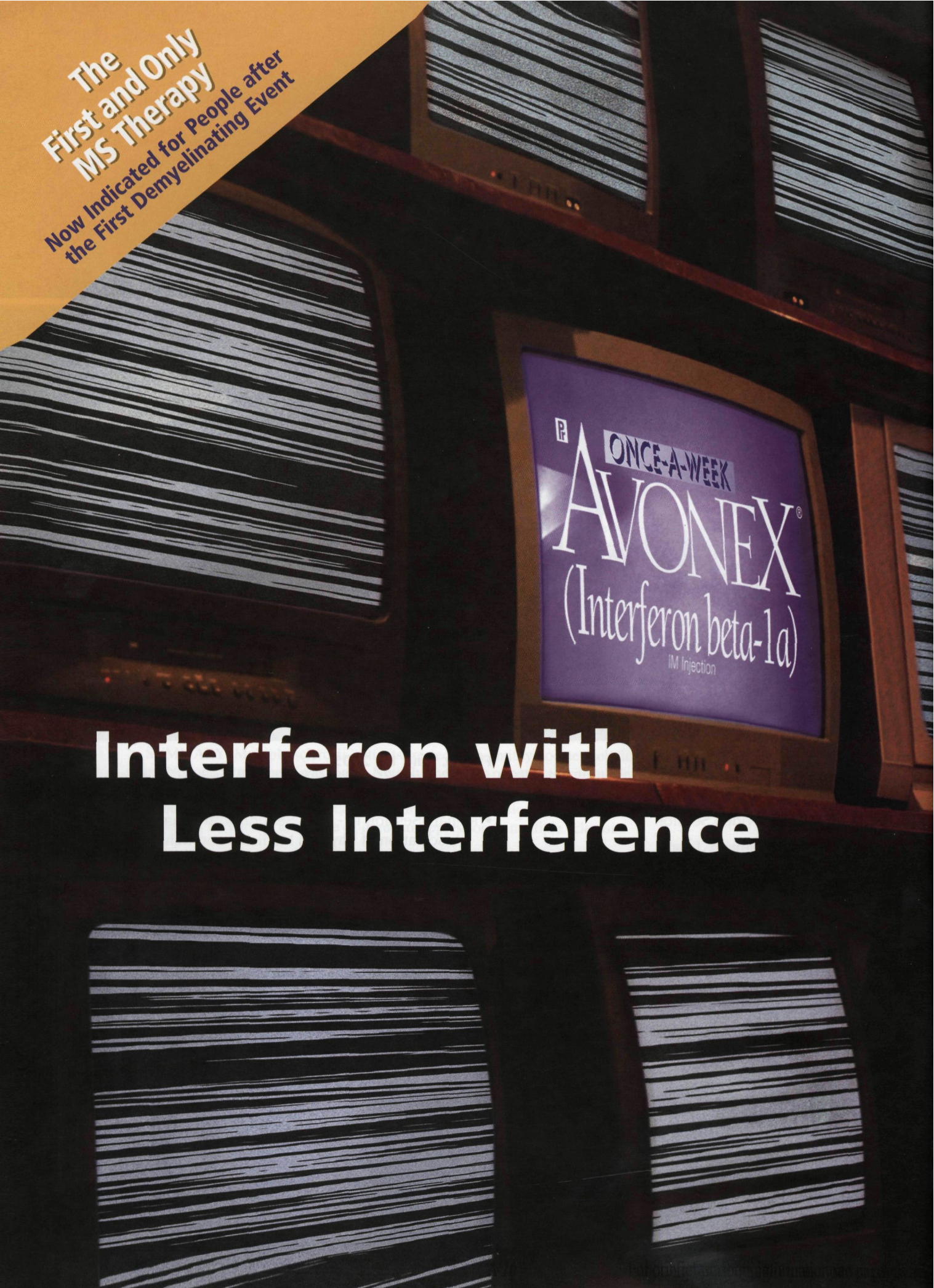
Wednesday, June 15th, 2005
- Spinal Course
- Epilepsy – Consensus and Controversies in Epilepsy
- EMG
- Neuroanatomy
- EEG
- Brain Tumours - Current Standard and Advances in Neuro-Imaging for Treatment of Brain Tumours
- MRI in MS and Stroke and Functional MRI
- Sleep – Review and Update in Neurology-Related 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

2005
OTTAWA
CCNS/CCSN
June 14-18 Juin 2005


The
First and Only
MS Therapy
Now Indicated for People after
the First Demyelinating Event
ONCE-A-WEEK
AVONEX®
(Interferon beta-1a)
IM Injection
Interferon with
Less Interference

Neutralizing antibodies (NAbs) may significantly impact IFNß'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® (IFNß-1a 22 µg) and Betaseron® (IFNß-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).[¶,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).[+,Δ,5]
- Delayed worsening in cognitive function demonstrated on 2 neuropsychological parameters (Information Processing/Memory[†], p=0.011 and PASAT[¥] p=0.023).[Δ,◊,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. ◊ As demonstrated in the second year of the Phase III pivotal trial.*

ONCE-A-WEEK
AVONEX®
(Interferon beta-1a)
IM Injection

EFFICACY THAT LASTS
As demonstrated in 3 years of clinical trials

biogen idec

PAAB

For brief prescribing information see pages A-56, A-57

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

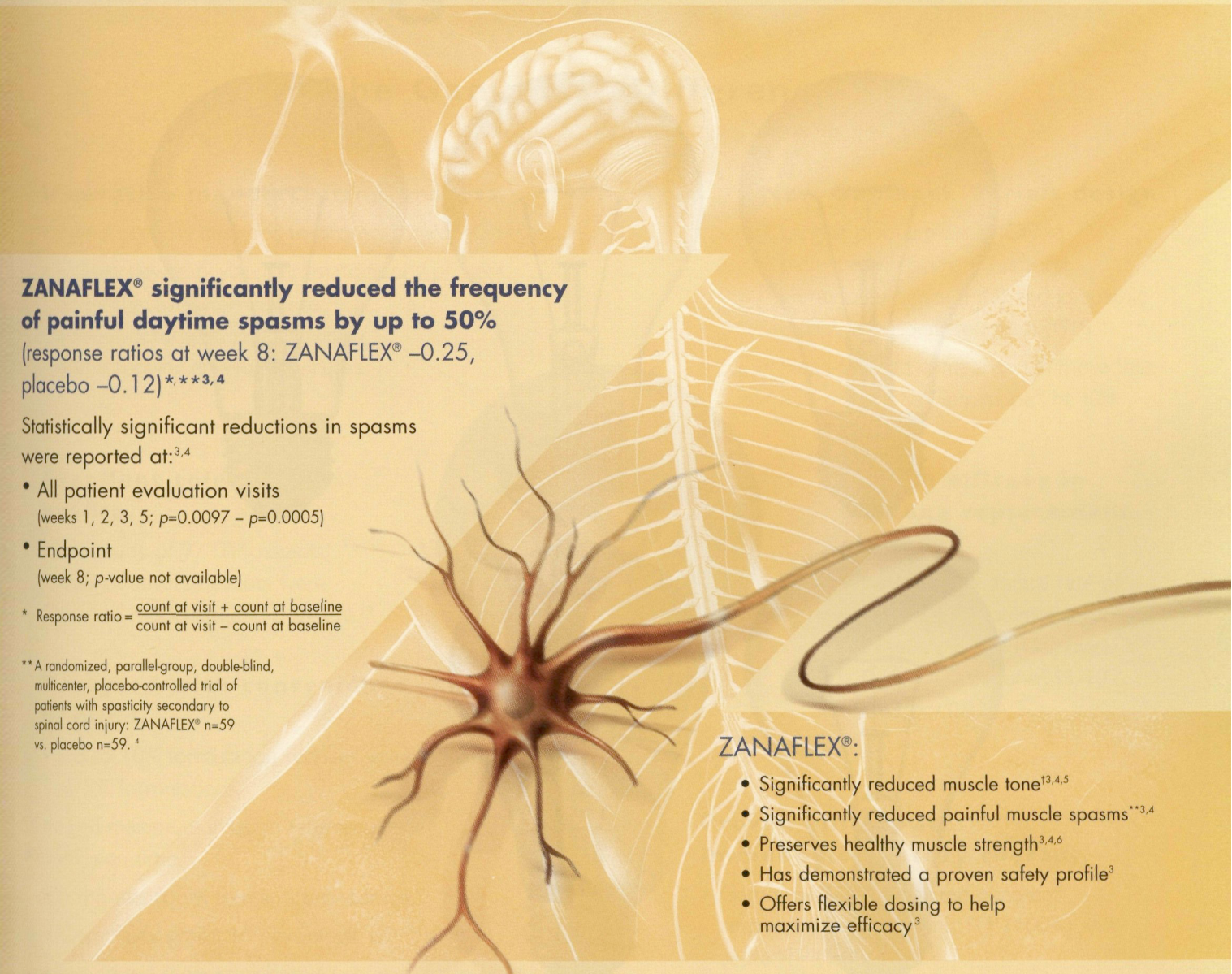
George Monckton and Halyna Marusyk

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 profile[3]
- Offers flexible dosing to help maximize efficacy[3]

ZANAFLEX®[3] 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%).[3] Patients report that side effects are dose related and tend to diminish as they continue to take ZANAFLEX®.[7] The most common adverse events leading to discontinuation of therapy were asthenia (3%), somnolence (3%) and dry mouth (3%).[3] Sedation may be additive when ZANAFLEX® is taken in conjunction with drugs or substances that act as CNS depressants.[3]

Caution is advised when treatment is used in patients who have a history of orthostatic hypotension or are currently receiving concurrent antihypertensive therapy.[3] Monitoring of aminotransferase levels is recommended during the first six months of treatment, and periodically thereafter, based on clinical status.[3] 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.

Pr Zanaflex® (tizanidine hydrochloride)

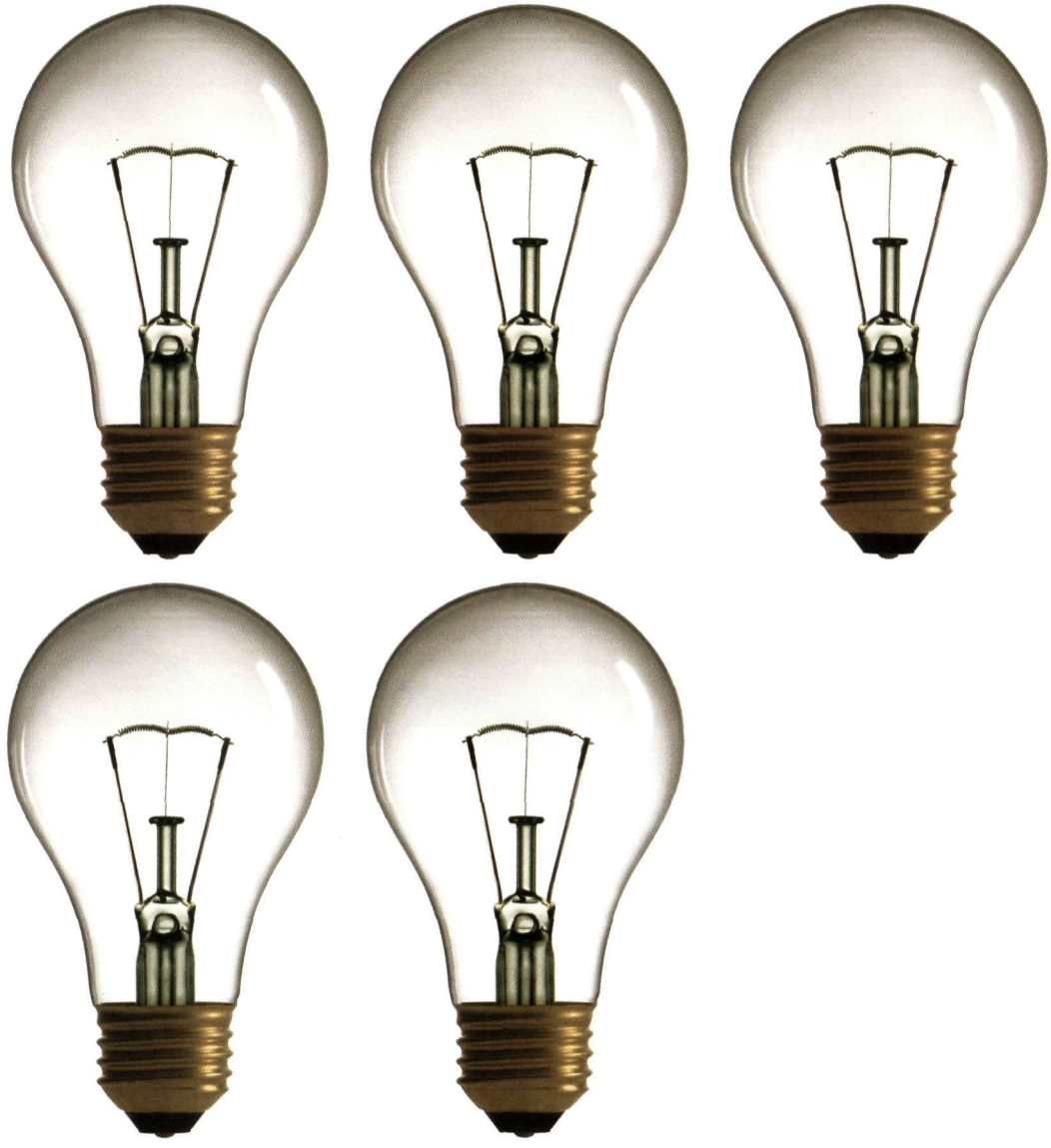
Shire
Shire BioChem Inc.
Laval, Quebec

Relieves Spasticity. Restores Possibilities.

Member PAAB R&D

For brief prescribing information see pages A-46, A-47

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.

Gamunex™ 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™ 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.

Bayer HealthCare
Biological Products Division

Member PAAB R&D

BP279-0104E

new Gamunex™ could change your mind.

The Gamunex™ Difference.

Innovative manufacturing process.

- Novel process designed to protect fragile IgG molecules.[1]
- Utilizes new caprylate/chromatography process as an effective alternative to solvent-detergent for inactivating and removing enveloped viruses.[1]

New Gamunex™ trials design.

- Largest pivotal trials in IGIV in patients with primary humoral immunodeficiency (PID) and idiopathic thrombocytopenic purpura (ITP).[1§]
- Head-to-head comparison in more than 350 patients vs Gamimune® N, 10%.[1]

Excellent tolerability profile.

- In a study of 97 ITP patients, 90% of adverse events were mild-to-moderate and transient.[1*]

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, $p = 0.023$).[1¶]

Designed with convenience in mind.

- Liquid 10% formulation reduces volume load vs 5% formulations.[1‡‡]
- High maximum infusion rate reduces infusion time.[1†]
- 5 months room temperature storage.[1‡]
- Osmolality similar to physiologic osmolality.[1]
- No added sugar stabilizers (such as sucrose or glucose).[1]

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††]

*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 weight/min.

‡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 10^9 for 7 days); $p = 0.066$.

‡‡Comparative clinical significance unknown.

Most common adverse events reported in PID were: cough increased (1.7%), headache (0.8%), fever (0.1%) and pharyngitis (0.8%).

new gamunex™

A different IGIV.

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

For brief prescribing information see pages A-44, A45

Dans le traitement au long cours de la
vos patients peuvent compter sur

g cours de la
ompter sur

Dans le traitement au lo
vos patients peuvent

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 cliniques[1].
- Aucune surveillance en laboratoire des anomalies hépatiques ou sanguines n'est recommandée[1].

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 %).

PrCOPAXONE®

(acétate de glatiramère injectable)

Traitement au long cours de la SP rémittente

Pour documentation voir pages A-53, A-54, A-55

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

FAST MIGRAINE RELIEF

THAT LASTS

Now on provincial formulary¥

Fast onset.

Significant migraine pain relief attained as early as 30 minutes after treatment[1†]

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 trial[2‡]

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%).[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-HT_1 agonist or an ergotamine-containing or ergot-type medication.

† AXERT 12.5 mg (n=164) compared to placebo (n=80) at 30 minutes, p=0.0485.

‡ Randomized, single-dose, double-blind, parallel-group multicentre study of 668 patients with acute migraine; response (n=104/183) was defined as a reduction to mild or no pain at 2 hours post-medication.

¥ Ontario, Quebec, Albert, Nova Scotia, Saskatchewan

References

1. AXERT® Product Monograph, Janssen-Ortho Inc., October 2003.
2. Dowson AJ, Massiou H, Lainez JM, *et al.* Almotriptan is an effective and well-tolerated treatment for migraine pain: results of a randomized, double-blind, placebo-controlled clinical trial. *Cephalalgia* 2002; 22(6): 453–61.

NEW

Pr Axert*

almotriptan malate tablets

Fastlasting™ Relief

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www.janssen-ortho.com

AXJA041022A

PAAB Member R&D

For brief prescribing information see pages A-58, A-59, A-62

LES BIENFAIT

ET VOUS AIDENT À

NOUVEAU
SERINGUE PRÉREMPLIE DE DILUANT
INJECTION À pH NON ACIDE*[1]

+ PLUS GRANDE COMMODITÉ

- Se conserve discrètement et se transporte facilement grâce à une formulation sans réfrigération[2]
- Emballage tout en un permettant une préparation plus rapide que jamais[2]

+ EFFICACITÉ ÉPROUVÉE

- Réduit la fréquence et la gravité des poussées chez les patients atteints de SEP rémittente[2-4]

* pH de 7,1 à 7,8 après la reconstitution.
† L'importance clinique n'a pas été établie.
‡ Étude prospective et multicentrique. On a assigné les patients aléatoirement soit au groupe qui devait s'administrer 250 µg de Betaseron par voie s.-c. tous les deux jours, soit à celui qui devait s'administrer 30 µg d'interféron bêta-1a par voie i.m. une fois par semaine. Les clichés ont été analysés par un service central de chercheurs indépendants qui ne connaissaient pas le traitement que recevaient les patients ni leurs caractéristiques cliniques.

S S'ADDITIONNENT

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[MC] 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 T_2 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 progressive-primaire 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.

BETASERON®
INTERFÉRON BÊTA-1b

® BETASERON est une marque déposée de Berlex Canada inc.
MC SEP LeParcours est une marque de commerce utilisée sous licence par Berlex Canada inc.

SEP LeParcours™
1 800 977-2770

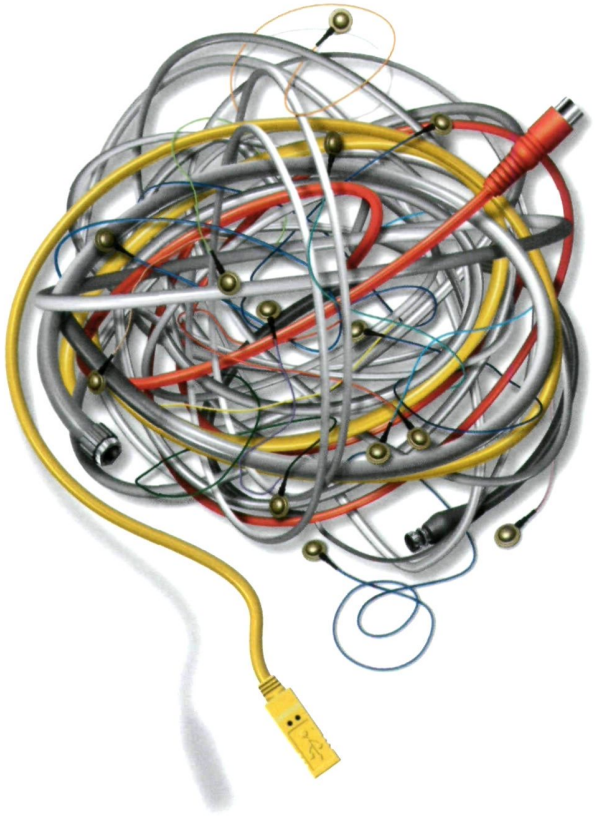
BERLEX

www.betaseron.ca
www.sepleparcours.ca

Pour documentation voir pages A-38, A-39

WHEN CONVENTIONAL THERAPY FALLS SHORT

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 ≥ 50% reduction in partial onset seizures ($p < 0.001$)
- Rapid clinical improvement demonstrated by week 2 during a 14-week evaluation period ($p < 0.001$)[1†]

Lundbeck

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.

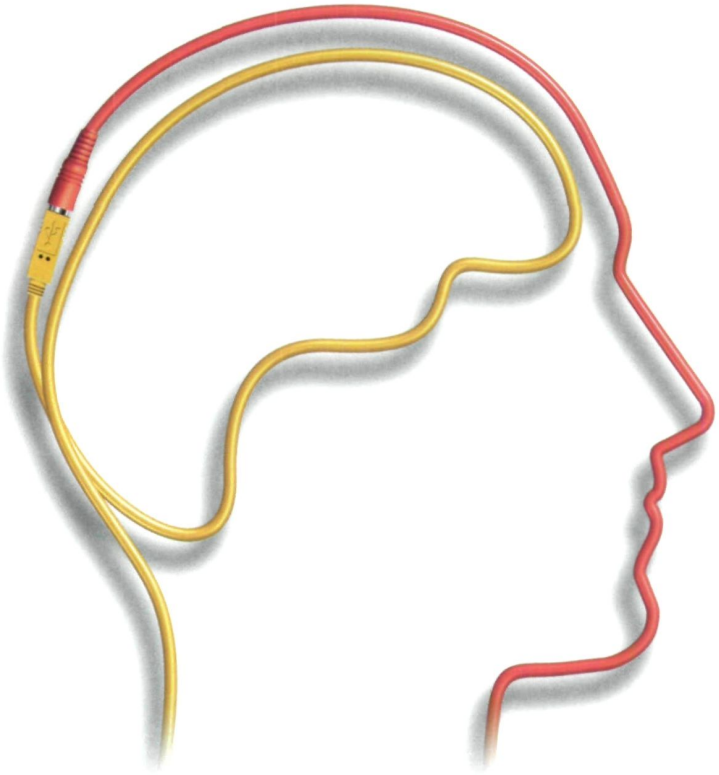
CONSIDER KEPPRA

NEW!

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[2]
- Low discontinuation or dosage reduction (Keppra 14.3% vs placebo 11.7%) due to adverse events[1]

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)[¶]

¶ Note: Pharmacokinetic interaction studies with contraceptives have not been conducted 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-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.

Pr Keppra® levetiracetam

CONNECTING EXCELLENT PROFILES IN EFFICACY AND TOLERABILITY

For brief prescribing information see pages A-42, A-43

Aventis

PORTRAIT OF A FAMILY HISTORY

HISTORY DOESN'T HAVE TO REPEAT ITSELF

Roger,
History of angina.

Died age 57 of MI.

Alice,
History of diabetes and high total cholesterol.

Died age 62 of stroke.

Help Reduce the Risk of CV Death by 26%[1]

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

ALTACE® 10 mg
ramipril

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.

Member R&D PAAB Product Monograph available to physicians and pharmacists upon request.

For brief prescribing information see page A-60