Volume 32 Number 3 August 2005

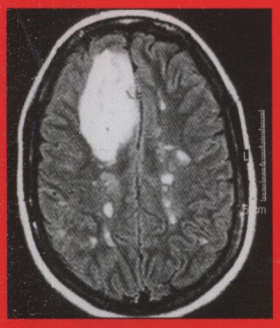
THE CANADIAN JOURNAL OF

Neurological Sciences

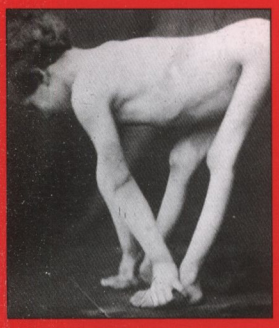
LE JOURNAL CANADIEN DES

Sciences Neurologiques

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL



Neuroimaging Highlight



Duchenne on clinical pathology

PM 40007777 R 9824

The official Journal of: The Canadian Neurological Society, The Canadian Neurosurgical Society, The Canadian Society of Clinical Neurophysiologists, The Canadian Association of Child Neurology

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.

Rebif® is a registered trademark of Serono Canada Inc.

PAAB

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

Because life is more than MS

For brief prescribing information see pages A-18, A-19

https://doi.org/10.1017/S031716710011594X Published online by Cambridge University Press

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Canada

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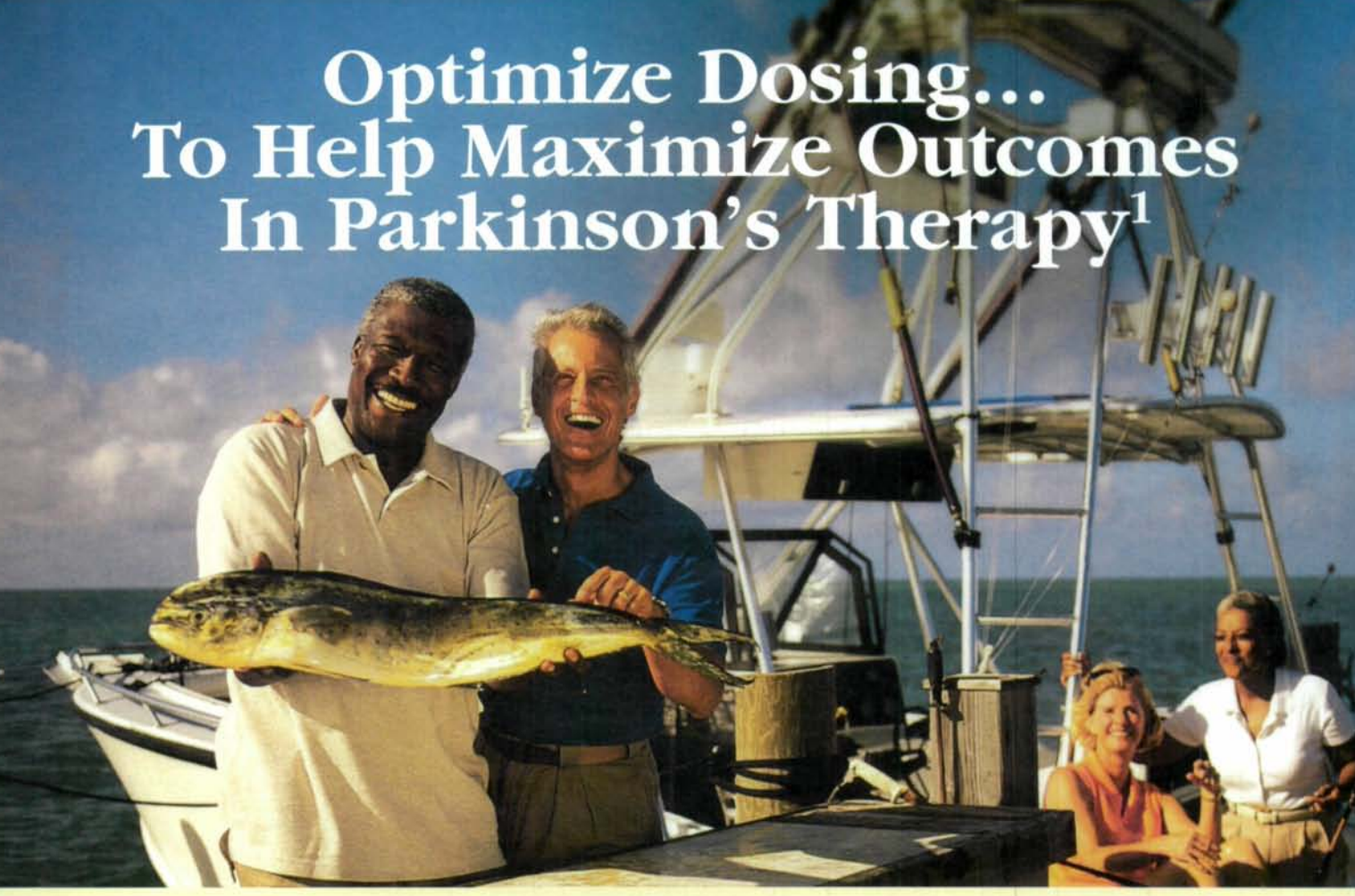
Optimize Dosing... To Help Maximize Outcomes In Parkinson's Therapy[1]



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[2ə]

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]

ə 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 GlaxoSmithKline 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

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For brief prescribing information see pages A-39, A-40

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LE JOURNAL CANADIEN DES Sciences Neurologiques

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The Canadian Neurosurgical Society
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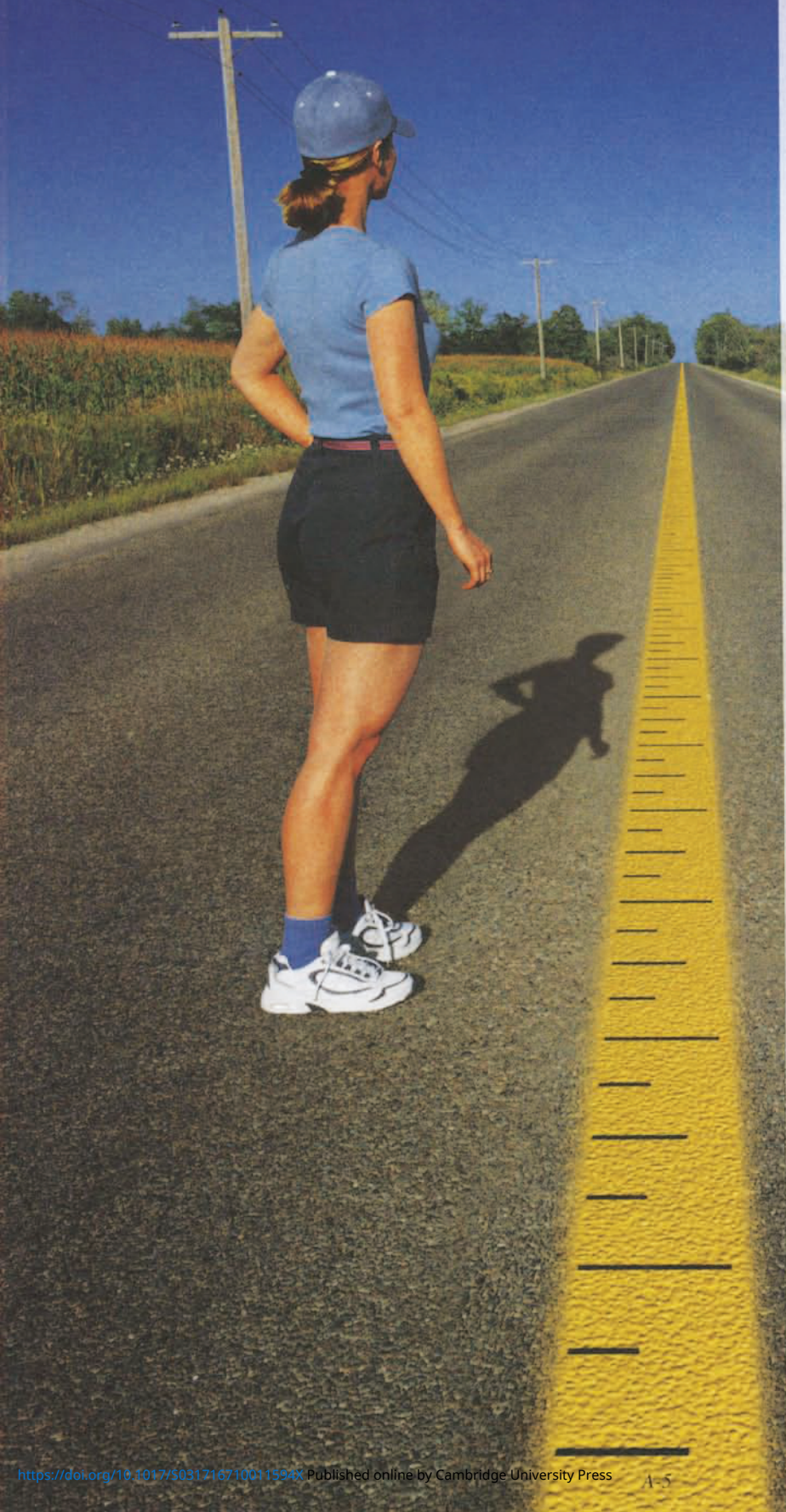
For the treatment of RRMS

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

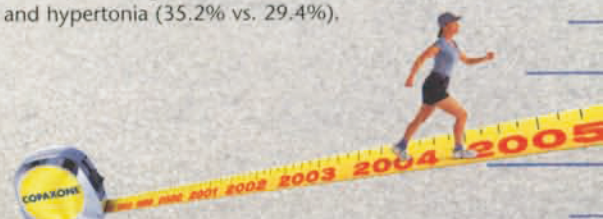
Established safety profile

- 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

For brief prescribing information see pages A-28, A-29

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† 28-week, randomized, multicentre, double-blind, parallel-group, placebo-controlled U.S. study in patients (≥50 years) with moderate to severe Alzheimer's disease. Patients were randomized to treatment with EBIXA® 20 mg daily (n=126) or placebo (n=126).

* Function was measured on the Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADL$_{19}$) scale with LOCF data - Change from baseline at study endpoint for EBIXA® vs. placebo: 2.1 units, p=0.02.

** Cognition was measured on the Severe Impairment Battery (SIB) with LOCF data - Change from baseline at study endpoint for EBIXA® vs. placebo: 5.9 units, p<0.001.

Ω Less caregiver time was needed per month (45.8 hrs) for patients treated with EBIXA® vs. placebo, p=0.01.

1. Cummings JL. Alzheimer's disease (review). *N Engl J Med* 2004;351:56-67. 2. EBIXA® Product Monograph. Lundbeck Canada Inc., 2004. 3. Reisberg B, Doody R, Stöffler A, Schmitt F, Ferris S, Möbius HJ for the Memantine Study Group. Memantine in Moderate-to-Severe Alzheimer's Disease. *N Engl J Med* 2003;348(14):1333-1341.

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I've been living with Alzheimer's disease for three years.

My mother has the disease. But I feel just as helpless. Only someone who takes care of the patient truly knows how debilitating Alzheimer's disease is.[1] Introducing EBIXA®.

- **A new class of therapy**[2]
- **Effective in moderate to severe stages**[2]
- **Extended daily functioning (ADCS-ADL$_{sev}$)**[2,3†*] **and cognition (SIB)**[2,3†**] **vs. placebo**
- **Excellent safety and tolerability profile**[2]
- **45.8 hrs less caregiver time demonstrated per month vs. placebo**[3Ω]

A new hope for patients with moderate to severe Alzheimer's disease.

EBIXA®, indicated for the symptomatic treatment of patients with moderate to severe dementia of the Alzheimer's type, has been issued marketing authorization with conditions, to reflect the promising nature of the clinical evidence and the need for a confirmatory study to verify the clinical benefit. Patients should be advised of the nature of the authorization assessment.

NEW Pr **Ebixa®**
memantine
A Name To Remember

Most common adverse events vs. placebo: dizziness (6.9% vs. 4.6%), constipation (6.1% vs. 3.5%), confusion (5.7% vs. 5.5%), and headache (5.6% vs. 3.6%).

EBIXA® (memantine hydrochloride) may be useful as monotherapy or as adjunctive therapy with cholinesterase inhibitors[∂] for the symptomatic treatment of patients with moderate to severe dementia of the Alzheimer's type. EBIXA® has not been studied in controlled clinical trials for the symptomatic treatment of moderate to severe Alzheimer's disease for more than 6 months. There is no clinical evidence that EBIXA® alters the course of the underlying disease. Periodic monitoring of the patient's ophthalmic condition is recommended.

Caution should be observed when EBIXA® is initiated in patients with cardiovascular conditions or in patients with a history of seizure disorder as these patient groups were not included in the clinical trials.

The renal elimination rate of EBIXA® under alkaline urine conditions may be reduced by a factor of 7 to 9, resulting in increased plasma levels of EBIXA®.

Lundbeck

∂ Cholinesterase inhibitors refers to only those which are approved in Canada for the symptomatic treatment of Alzheimer's disease.

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For brief prescribing information see pages A-34, A-35, A-36

Trust AVONEX®

The **First and Only MS Therapy**

indicated for use after a single

demyelinating event.

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✓ Low Immunogenicity

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

INTERFERON WITH LESS INTERFERENCE

- AVONEX® (Interferon beta-1a) has demonstrated the lowest incidence of neutralizing antibodies (2-6%)*[1,2,3,4]

✓ Lasting Efficacy in MS Disease Activity**

- **44% reduction** in the risk of developing clinically definite MS in patients with a single demyelinating event over 3 years compared to placebo (confidence interval = 0.38 to 0.81; p=0.002)[Δ,5]
- **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]

✓ Patient Convenience

- The only once-a-week MS therapy.

AVONEX® (Interferon beta-1a) is indicated for the treatment of relapsing forms of multiple sclerosis to slow the progression of disability, decrease the frequency of clinical exacerbations, and reduce the number and volume of active brain lesions identified on Magnetic Resonance Imaging (MRI) scans. AVONEX® is also indicated 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®.

* Comparative clinical significance has not been established.
** As demonstrated in 3 years of clinical trials.
Δ Rate ratio = 0.56.
+ Kaplan-Meier methodology. AVONEX® n=158, placebo n=143.
◊ AVONEX® n=85, placebo n=87.

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

EFFICACY THAT LASTS
As demonstrated in 3 years of clinical trials

biogen idec™

PAAB

2004-AVX-038

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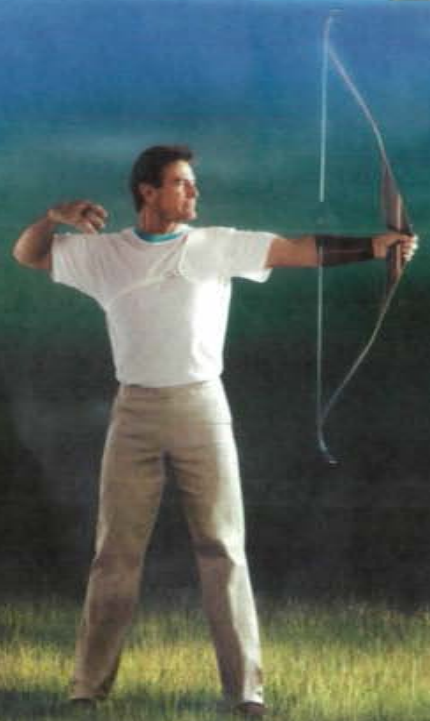
For brief prescribing information see pages A-37, A-42

LIPITOR*: Hitting targets.



Powerful NEW Indication

Aiming beyond.

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).

NEW § LIPITOR is indicated to reduce the risk of myocardial infarction in adult hypertensive patients without clinically evident coronary heart disease, but with at least three additional risk factors for coronary heart disease such as age ≥55 years, male sex, smoking, type 2 diabetes, left ventricular hypertrophy, other specified abnormalities on ECG, microalbuminuria or proteinuria, ratio of plasma total cholesterol to HDL-cholesterol ≥6, or premature family history of coronary heart disease.

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.

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

EFFICACY ➢ **Power to start with a *FLEXIBLE FIRST DOSE*™ at 10 mg, 20 mg, 40 mg[11]**

† When a >45% LDL-C reduction is required, patients may be started at 40 mg o.d.[1]

EXPERIENCE ➢ **More than 76 million patient-years of experience[2¥‡]**

EVIDENCE NEW ➢ **ASCOT£ demonstrated LIPITOR's efficacy in reducing the risk of myocardial infarction in adult hypertensive patients without clinically evident CHD, but with at least three additional risk factors for CHD[1§]**

LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control[3]

¥ Based on Pfizer's analysis of IMS Health data.[2]

‡ A patient-year represents the total time of exposure to LIPITOR as defined by the sum of each patient's time on LIPITOR.[4]

£ ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial.

LIPITOR atorvastatin calcium tablets

power you can trust™

10 mg 20 mg 40 mg 80 mg

Pfizer
Life is our life's work

PMAB Member R&D

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CONSIDER KEPPRA

NOW AVAILABLE ON PROVINCIAL FORMULARIES:*

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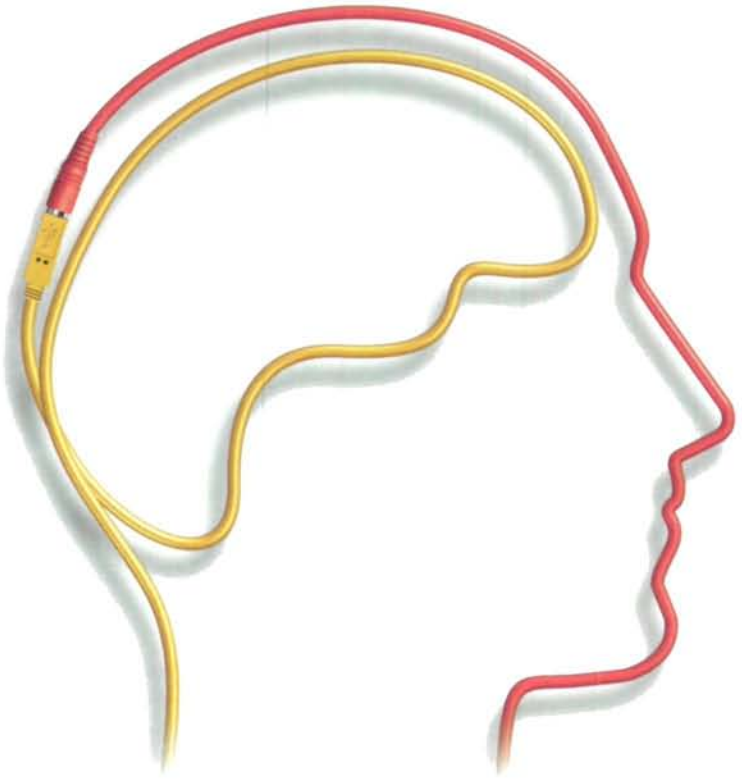
to control



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)§

¶ 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

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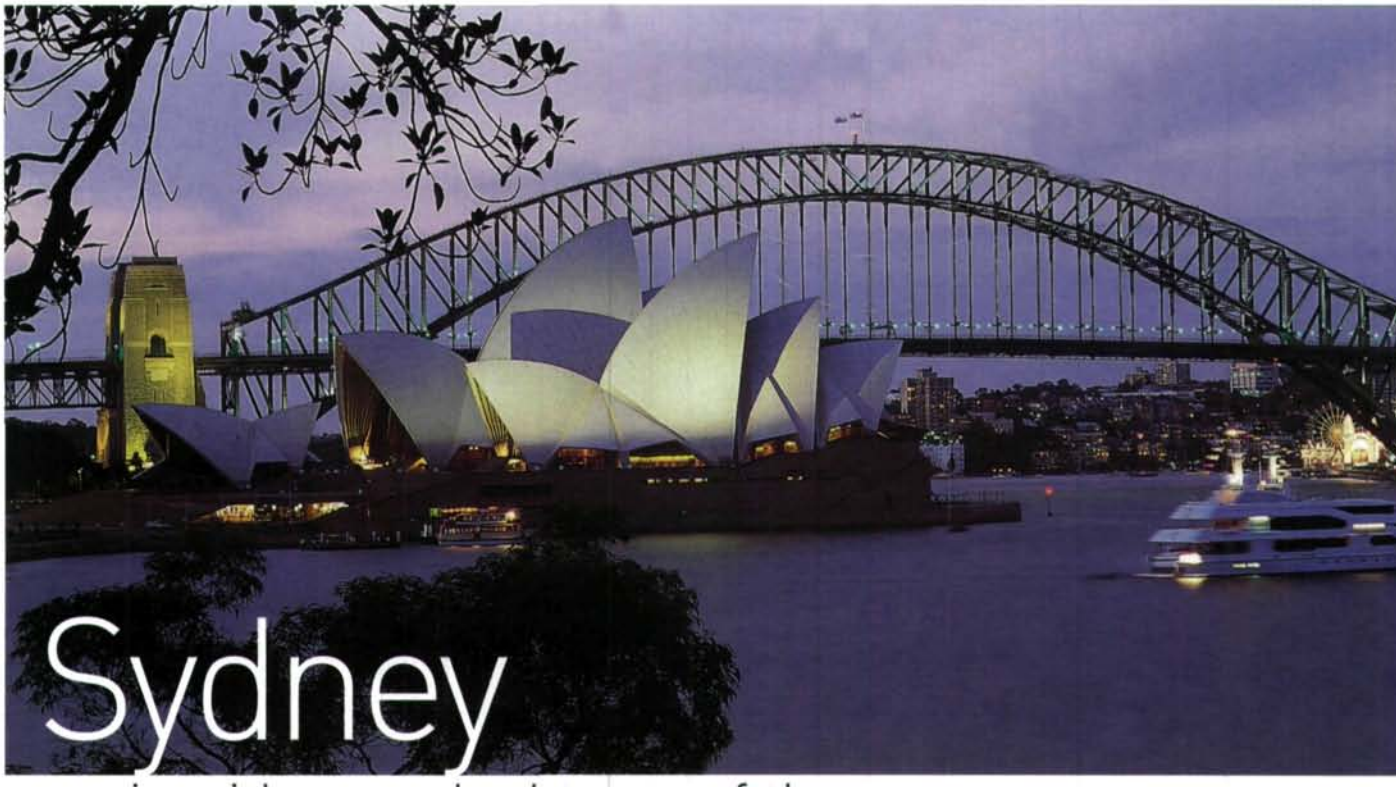
For brief prescribing information see pages A-26, A-27

XVIIIth World Congress of Neurology

5-11 November 2005 Sydney Australia



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The Australian Association of Neurologists (AAN)

Sydney, the host city for the World Congress of Neurology 2005, is without doubt one of the most beautiful cities in the world with a reputation for friendly people, a cosmopolitan lifestyle, wonderful shopping and world-class entertainment. The magnificent harbour, renowned Opera House and sunny beaches combine to make Sydney a unique destination.

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  - Stroke
  - Multiple Sclerosis
  - Headache/ Pain
  - Dementia/ Movement Disorders, Neurological Infections
- Frontiers of Neuroscience Lectures presented by: Professor Salvatore DiMauro • Professor Peter Doherty • Professor Colin Masters • Professor Yoshikuni Mizuno • Professor Bert Sakmann
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Key dates	
Abstract submission deadline	31 May 2005
Notification of acceptance of abstracts	July 2005
End of early rate registration fee	5 August 2005
Accommodation booking deadline	23 September 2005
World Congress of Neurology 2005	5-11 November 2005

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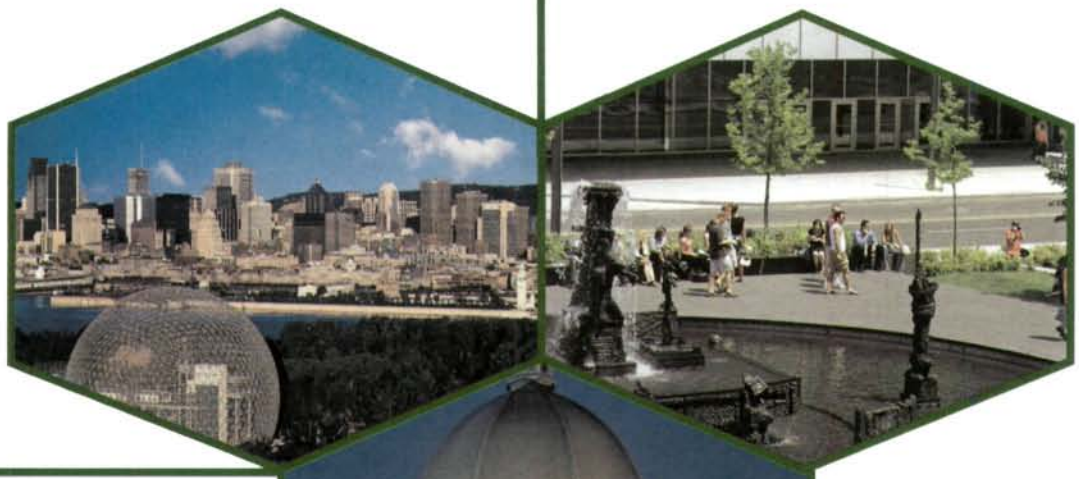

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Les symptômes de douleur neuropathique[1]...

...prennent naissance en profondeur

Nouveau

PrLYRICA* PRÉGABALINE

BIENTÔT

LYRICA est indiqué pour le traitement de la douleur neuropathique associée à :

- la neuropathie diabétique périphérique
- la névralgie postzostérienne

Veuillez consulter les renseignements thérapeutiques pour obtenir de l'information importante sur les mises en garde, les précautions, les effets indésirables et les critères de sélection des patients.

1. Dworkin RH. An Overview of Neuropathic Pain: Syndromes, Symptoms, Signs, and Several Mechanisms. *The Clinical Journal of Pain* 2002;18:343-349.

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