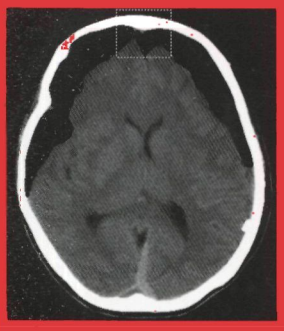
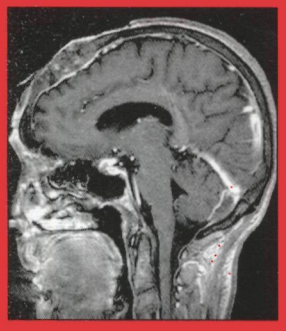
Volume 32 Number 4 November 2005

THE CANADIAN JOURNAL OF
Neurological Sciences
LE JOURNAL CANADIEN DES
Sciences Neurologiques

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL



Tension pneumocephalus



Basal cell carcinoma

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.

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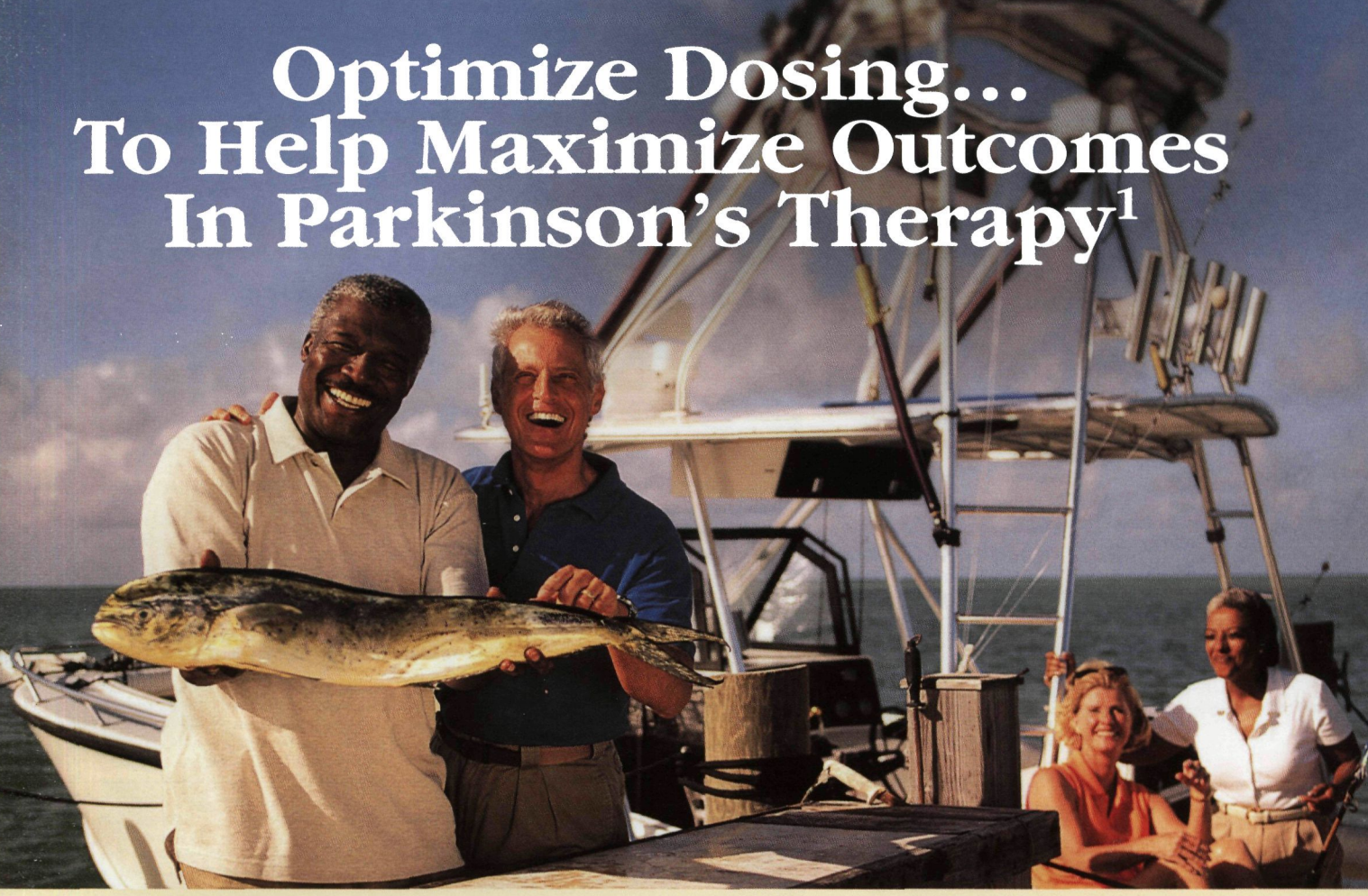
Optimize Dosing... To Help Maximize Outcomes In Parkinson's Therapy[1]



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[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 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-35, A-36

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LE JOURNAL CANADIEN DES Sciences Neurologiques

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The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

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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 ($ADCS\text{-}ADL_{sev}$) 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.

§ Restrictions exist. Please refer to your formulary for details.

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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NOW AVAILABLE ON THE
QUEBEC FORMULARY[§]

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-30, A-31, A-32

Neuropathic Pain

Scalded From Within

LYRICA is contraindicated in patients who are hypersensitive to pregabalin or to any ingredient in the formulation or component of the container.

The most commonly observed adverse events (twice the rate as that seen with placebo) were dose related for PHN and DPN patients in the recommended dose range of 150 mg/day to 600 mg/day: dizziness (9-37%), somnolence (6.1-24.7%), peripheral edema (6.1-16.2%) and dry mouth (1.9-14.9%).

Dosage reduction is required in patients with renal impairment as pregabalin is primarily eliminated by renal excretion.

¥ Pharmacodynamic interactions were reported with oxycodone, lorazepam, ethanol and thiazolidinedione antidiabetic agents. Please consult Prescribing Information for complete interaction information.

Please see Prescribing Information for complete Warnings and Precautions, Dosage and Administration, and patient selection criteria.

† A 13-week, multicentre, double-blind, placebo-controlled trial in 368 patients with PHN. A significant difference was shown over placebo for all doses: 150 mg/day, 300 mg/day, and 600 mg/day at week 1, $p<0.001$ for pain and $p<0.01$ for sleep.

‡ A 12-week, multicentre, randomised, double-blind, placebo-controlled study in 338 patients with neuropathic pain (DPN [n=249] or PHN [n=89]), resulting in a significant difference from placebo in the flexible dose range 150-600 mg/day ($p\leq0.05$, week 2 and $p\leq0.01$, weeks 3-12), and the fixed dose of 600 mg/day ($p\leq0.05$, week 1 and $p\leq0.01$, weeks 2-12).

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For brief prescribing information see pages A-26, A-27, A-28, A-29

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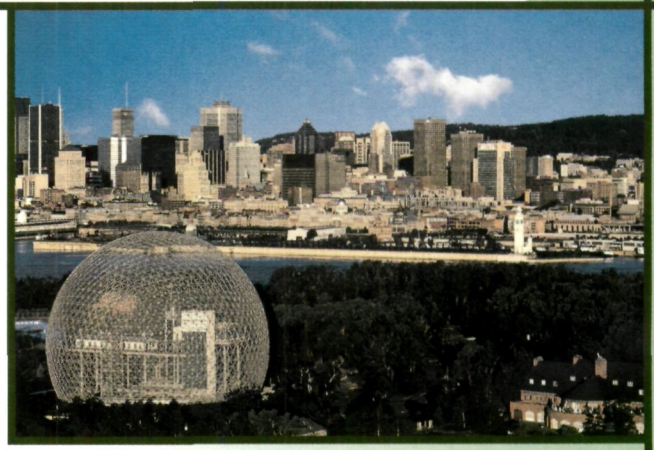
June 13 - 17 juin 2006



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JOIN US IN MONTREAL FOR THE 41ST MEETING OF THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

JUNE 13 – 17, 2006

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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 in Canada and the ACEI most prescribed by cardiologists.*

*IMS Health Canada: Canadian CompuScript Audit, Moving Annual Total ending March 2005, Total Dispensed Prescriptions.

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

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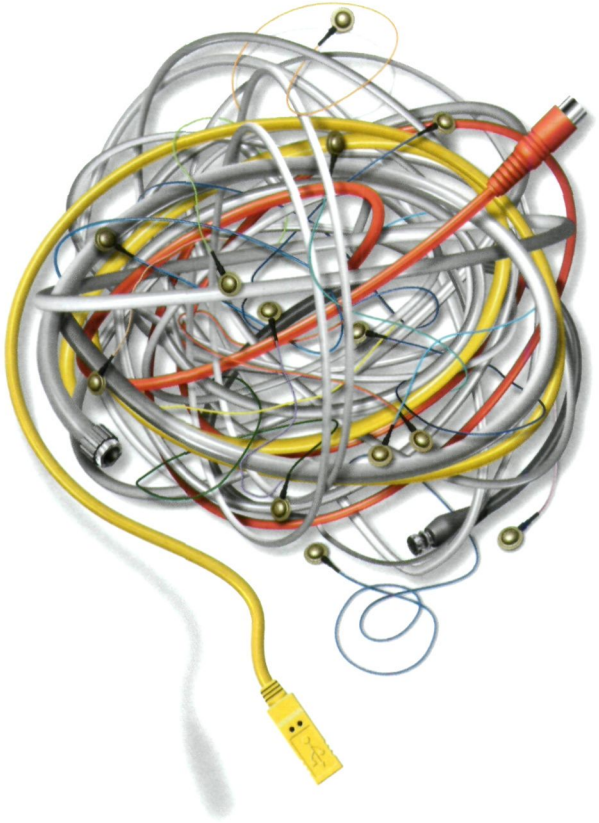
CPN 0000-05-05-04

For brief prescribing information see page A-33

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.

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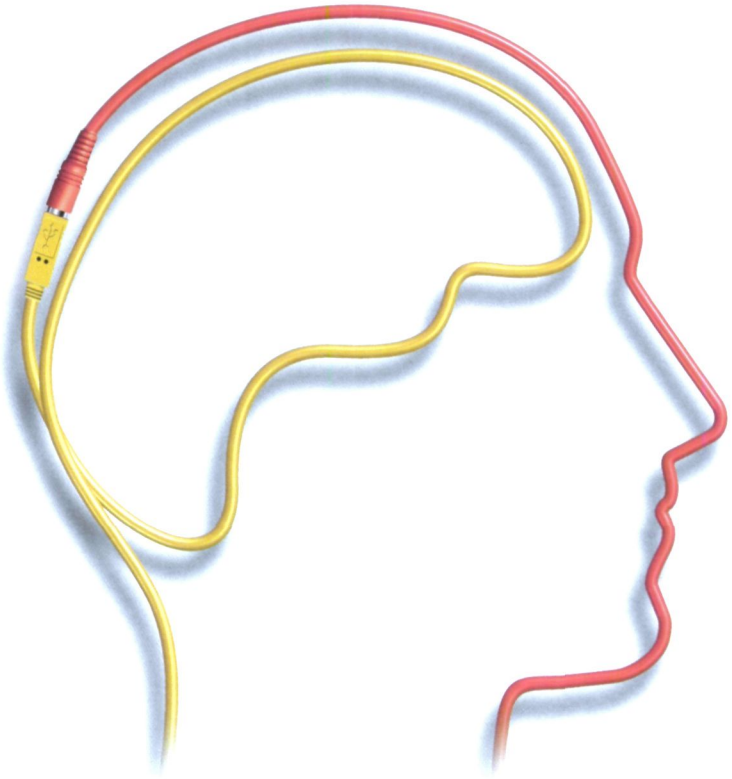
CONSIDER KEPPRA

NOW AVAILABLE ON PROVINCIAL FORMULARIES:*

NEW! BRITISH COLUMBIA
ALBERTA
SASKATCHEWAN
MANITOBA
ONTARIO
QUEBEC
NOVA SCOTIA
NEWFOUNDLAND

to control



Generally well tolerated

- Favourable side effect profile
- Adverse events not dose dependent[2]
- 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 probe-necid. 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-22, A-23

La douleur neuropathique
Ébouillanté de l'intérieur

LYRICA est contre-indiqué chez les patients qui présentent une hypersensibilité à la prégabaline ou à l'un des composants du produit ou du contenant.

Les effets indésirables signalés le plus souvent (fréquence 2 fois plus élevée qu'avec le placebo) chez les patients souffrant de névralgie postzostérienne ou de neuropathie diabétique périphérique étaient proportionnels à la dose dans l'intervalle posologique recommandé de 150 mg/jour à 600 mg/jour et ont été les suivants : étourdissements (9 - 37 %), somnolence (6,1 - 24,7 %), œdème périphérique (6,1 - 16,2 %) et sécheresse buccale (1,9 - 14,9 %).

Comme la prégabaline est éliminée principalement par le rein, il faut réduire la dose en présence d'une dysfonction rénale.

¥ Des interactions pharmacodynamiques ont été signalées avec l'oxycodone, le lorazépam, l'éthanol et les antidiabétiques de la classe des thiazolidinediones. Veuillez consulter les renseignements thérapeutiques pour obtenir l'information complète sur les interactions médicamenteuses.

Consulter les renseignements thérapeutiques pour obtenir l'information complète sur les mises en garde, les précautions, la posologie, le mode d'administration et les critères de sélection des patients.

† Essai multicentrique d'une durée de 13 semaines, mené à double insu avec placebo auprès de 368 patients souffrant de névralgie postzostérienne. La première semaine, on a observé une différence significative par rapport au placebo à toutes les doses (150 mg/jour, 300 mg/jour et 600 mg/jour); $p < 0{,}001$ pour la douleur et $p < 0{,}01$ pour le sommeil.

‡ Essai multicentrique d'une durée de 12 semaines, mené à double insu avec placebo après répartition aléatoire de 338 patients souffrant de douleur neuropathique (*neuropathie diabétique périphérique* [$n = 249$]; *névralgie postzostérienne* [$n = 89$]). Une différence significative a été observée par rapport au placebo dans tout l'intervalle posologique flexible de 150 à 600 mg/jour ($p \leq 0{,}05$ pour la 2e semaine et $p \leq 0{,}01$ pour les semaines 3 à 12) et à la dose quotidienne fixe de 600 mg ($p \leq 0{,}05$ pour la 1re semaine et $p \leq 0{,}01$ pour les semaines 2 à 12).

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Nouveau

Pr LYRICA* PRÉGABALINE

LYRICA est indiqué pour le traitement de la douleur neuropathique associée à[1] :

- la neuropathie diabétique périphérique
- la névralgie postzostérienne

Soulagement rapide et durable démontré de la douleur neuropathique

- Un soulagement rapide de la douleur neuropathique associée à la névralgie postzostérienne dès la première semaine[2†]
- Un soulagement durable de la douleur neuropathique démontré sur une période de 3 mois[3‡]
- Une atténuation rapide des perturbations du sommeil causées par la névralgie postzostérienne dès la première semaine[2†]
- Aucune interaction pharmacocinétique médicamenteuse d'importance clinique rapportée[1*]
- Une posologie simple[1]

Nouveau Pr LYRICA* PRÉGABALINE

Effet rapide. Soulagement soutenu.

Pfizer
Notre passion, la vie

*M.C. de C.P. Pharmaceuticals International C.V.
Pfizer Canada Inc., licencié

CCPP Membre R&D

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For brief prescribing information
see pages A-26, A-27, A-28, A-29

Only Elekta gives you the ability to treat brain disorders with sub-millimeter accuracy that is three times more precise than the closest competitor. With 50 times more patients treated than any other technology, and 400 times more peer-reviewed articles, it's no wonder Leksell Gamma Knife® remains the most proven and trusted treatment for brain disorders...with equally strong results for your bottom line.

See compelling evidence – www.elekta.com/proof.

Fighting Serious Disease

www.elekta.com

Stereotactic Neurosurgery	Gamma Knife surgery	Functional Mapping	Precision Radiation Therapy	Image Guided Radiation Therapy	Stereotactic Radiation Therapy

ELEKTA

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