Volume 32 Number 2 May 2005

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

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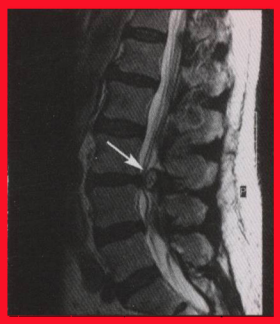
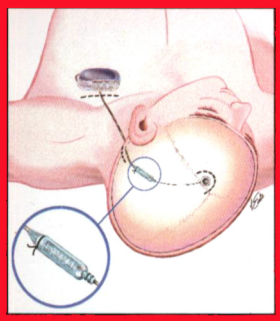


Ligamentum flavum cysts



Deep brain stimulation

40th CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES
June 14-18, 2005
Ottawa, Ontario

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

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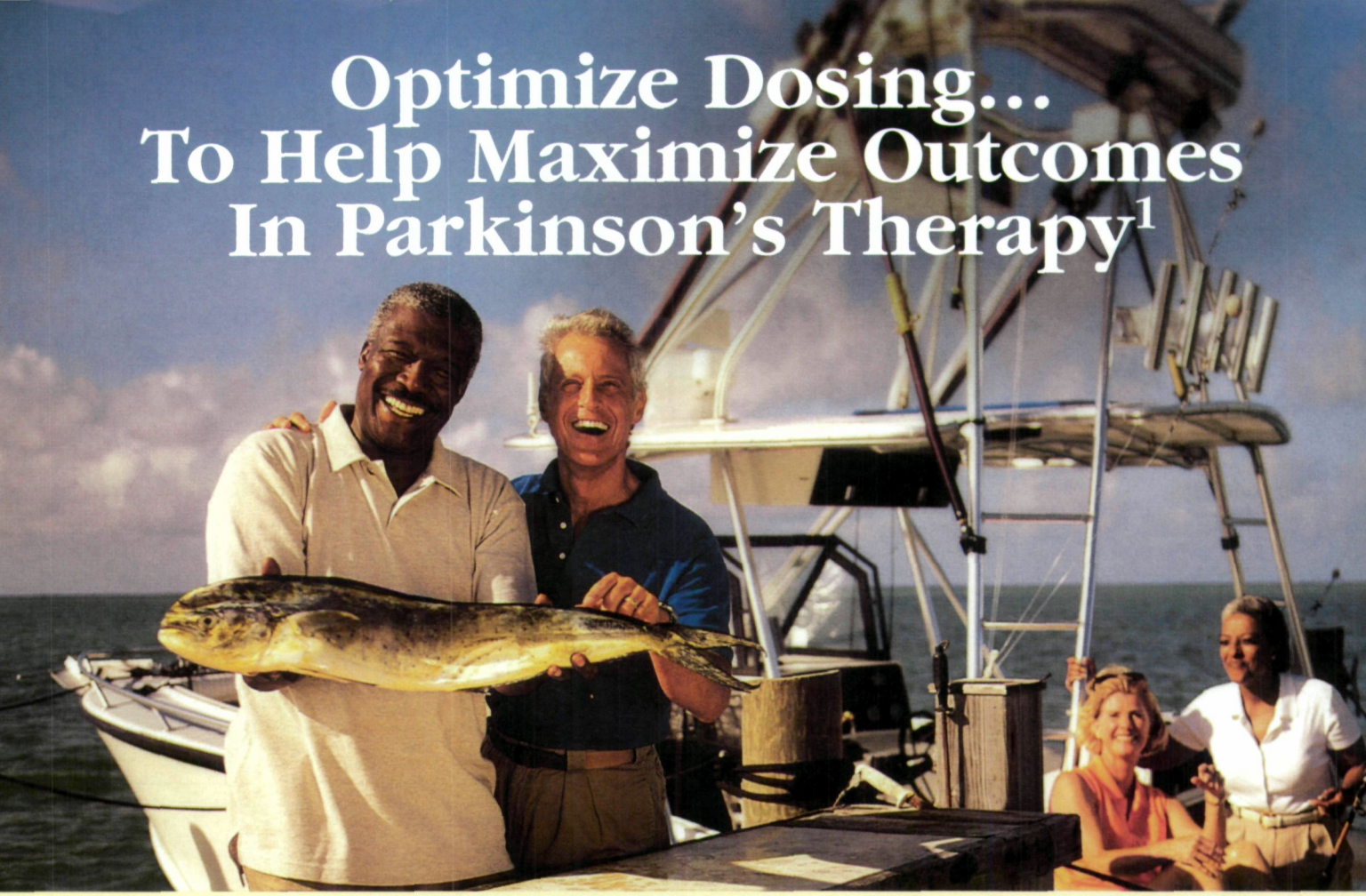
Optimize Dosing... To Help Maximize Outcomes In Parkinson's Therapy[1]



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-38, A-39

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LE JOURNAL CANADIEN DES Sciences Neurologiques

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La Société Canadienne de Neurologie

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For brief prescribing information see pages A-24, A-25

† 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$_{severe}$) 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-30, A-31, A-32

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

sting 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]

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The only once-a-week MS therapy.

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• For detailed instructions regarding style and layout refer to *"Uniform requirements for manuscripts submitted to biomedical journals"*. Copies of this document may be obtained on the website www.icmje.org, but the main points are summarized here. Articles should be submitted under conventional headings of *introduction, methods and materials, results, discussion,* but other headings will be considered if more suitable. Clinical trials must be reported in Consort format (www.cjns.org). Pages of text should be numbered consecutively.

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Journals

Yang JF, Fung M, Edamura R, et al. H-Reflex modulation during walking in spastic paretic subjects. Can J Neurol Sci 1991; 18: 443-452.

Chapter in a book

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

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tting targets.

EFFICACY ➢ Power to start with a *FLEXIBLE FIRST DOSE*™ at 10 mg, 20 mg, 40 mg[1†]

† 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[ε] 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[3]

s that may extend beyond lipid control[3]

P LIPITOR*: Hi

A-11

For brief prescribing information se

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

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

Less than 2% of patients discontinued therapy due to adverse experiences. Most common adverse effect

LIPITOR

new area

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CONSIDER KEPPRA

NOW AVAILABLE ON PROVINCIAL FORMULARIES:*

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MANITOBA
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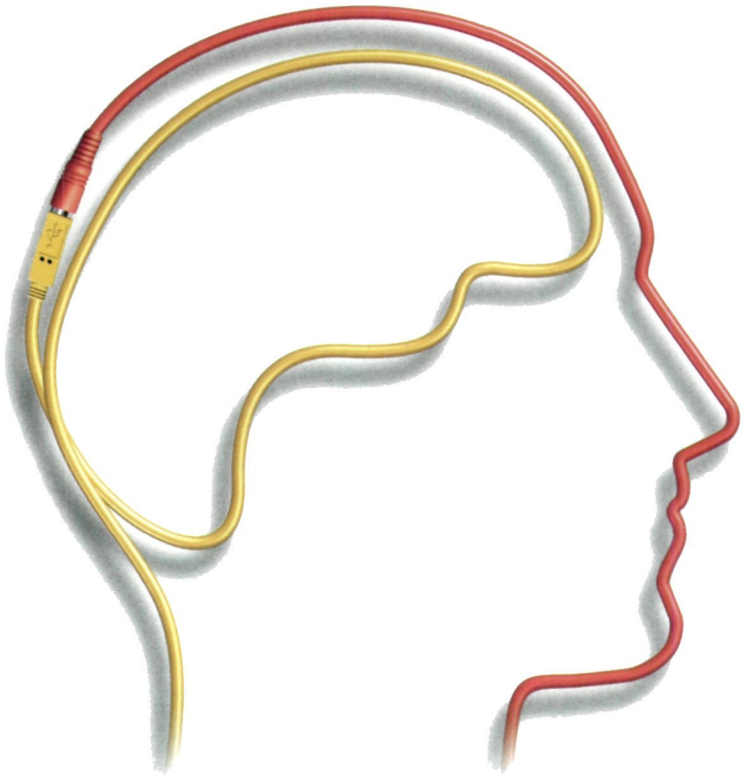
NOVA SCOTIA
ONTARIO

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‡

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-22, A-23

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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 among cardiologists.*

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

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