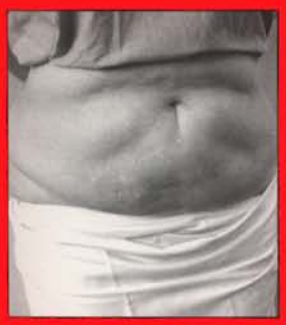
Volume 31 Number 1 February 2004

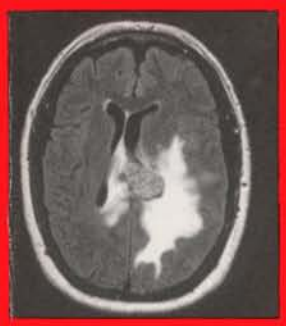
30th ANNIVERSARY
1974 • 2004

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques



Lipoatrophy

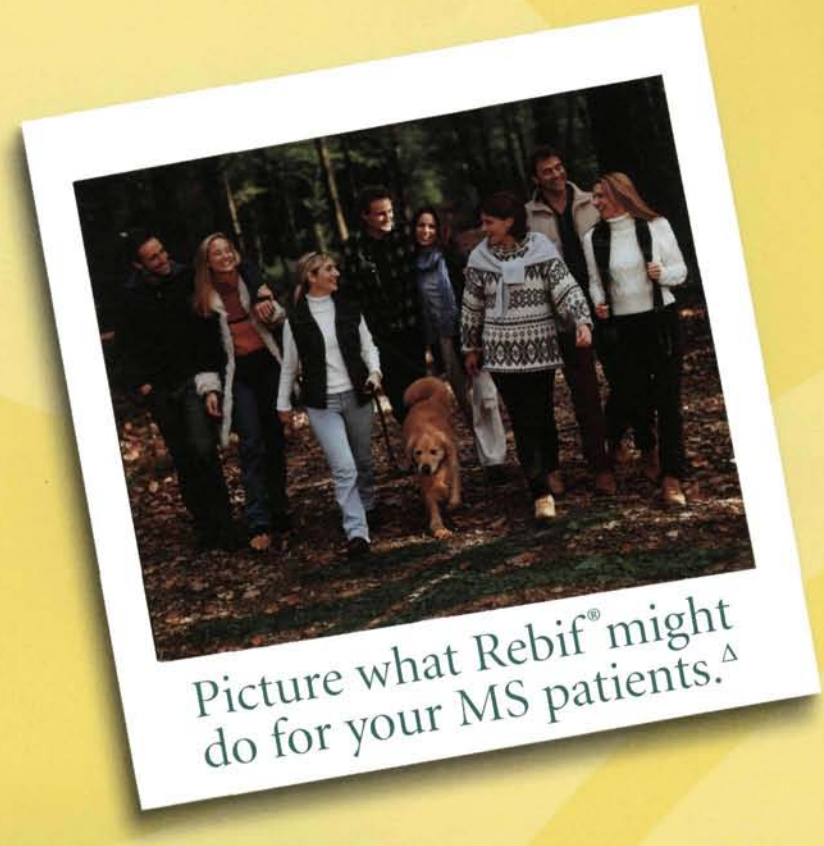


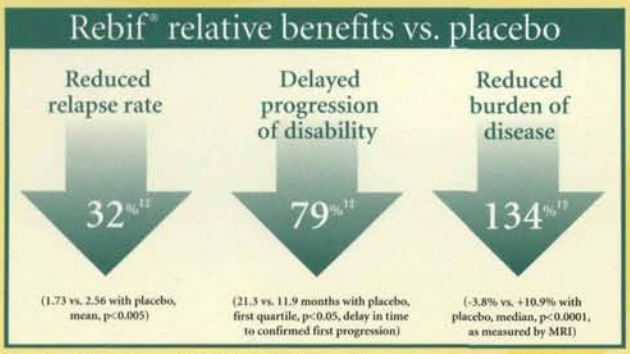
Renal Cell Carcinoma

39th CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES
June 8–12, 2004
Calgary, Alberta

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





Results of the 44 mcg TIW dose at 2 years.[1]

In two pivotal studies, including a total of 628 patients, Rebif showed significant efficacy in three major outcomes (relapses, disability progression and MRI).[1,2]

Its ability to affect the course of the disease[2] has made Rebif not only a good first-line choice for relapsing-remitting MS, but the leading drug in its class.[3]

Rebif is generally well-tolerated. The most common adverse events are often manageable and decrease in frequency and severity over time.[2†]

Rebif alters the natural course of relapsing-remitting MS.[2]

Rebif® is indicated for the treatment of relapsing-remitting multiple sclerosis in patients with an EDSS between 0 and 5.0, 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. The efficacy of Rebif has been confirmed by T_1–Gd enhanced and T_2 (burden of disease) MRI evaluations.[2]

† The most common adverse events reported are injection-site disorders (all) (92.4% vs. 38.5% placebo), upper respiratory tract infections (74.5% vs. 85.6% placebo), headache (70.1% vs. 62.6% placebo), flu-like symptoms (58.7% vs. 51.3% placebo), fatigue (41.3% vs. 35.8% placebo) and fever (27.7% vs. 15.5% placebo). Evidence of safety and efficacy derived from 2-year data only. Please see product monograph for full prescribing information.[2]

‡ Randomized, double-blind, placebo-controlled trial. Rebif 44 mcg TIW group (n=184), Rebif 22 mcg TIW group (n=189), placebo group (n=187).[1]

Δ Fictitious case may not be representative of results for the general population.

PAAB

Pr Rebif® interferon beta-1a

FOR MULTIPLE REASONS.

serono

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

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LE JOURNAL CANADIEN DES Sciences Neurologiques

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La Société Canadienne de Neurologie

The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

The Canadian Society of Clinical Neurophysiologists
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FAST MIGRAINE RELIEF

THAT LASTS

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.

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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AXJA041005A

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For brief prescribing information see pages A-48, A-49, A-51

atients for the long run.

Demonstrated impact on disability

- COPAXONE®-treated patients experienced a significant improvement in mean EDSS change: 123% treatment effect vs. placebo over 2 years
  (-0.05 {n=125} vs. +0.21 {n=126}, 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

PM481

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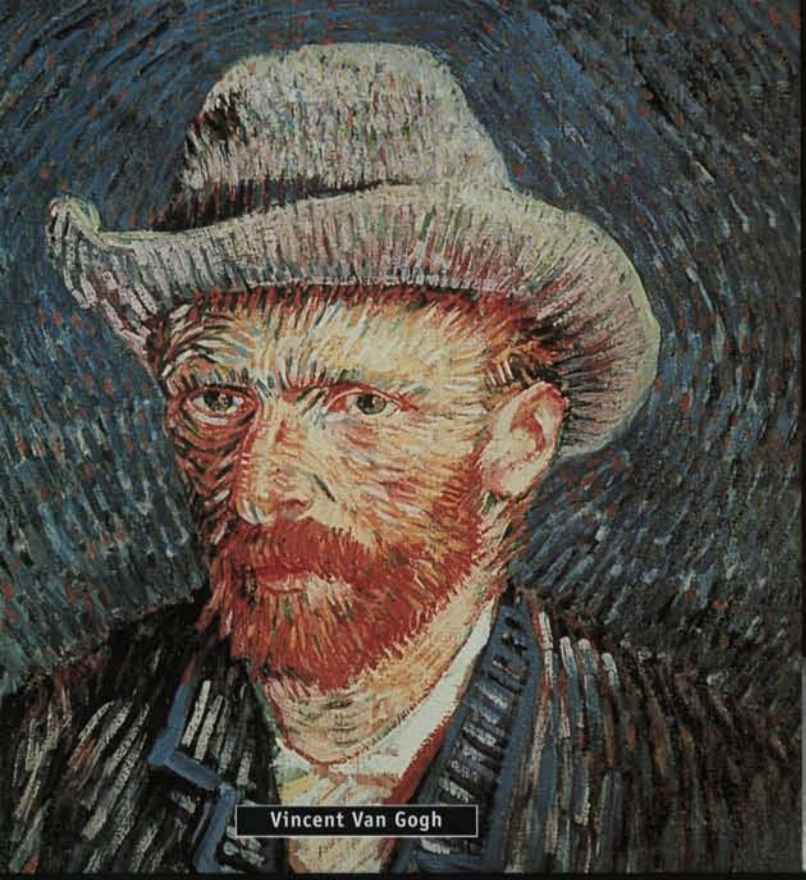
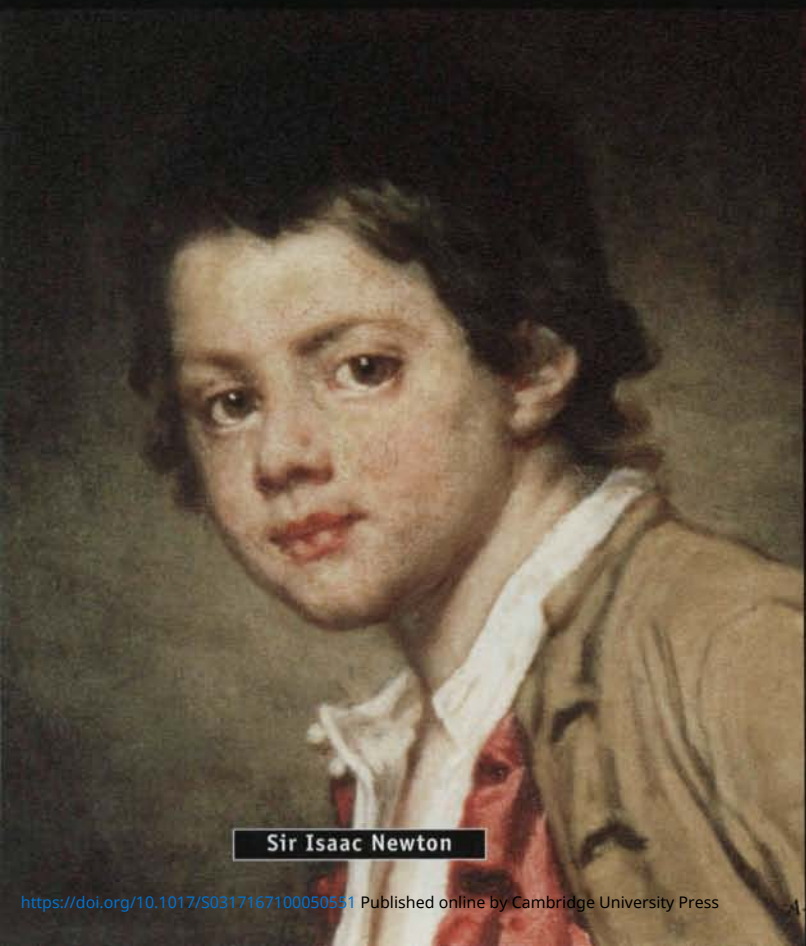
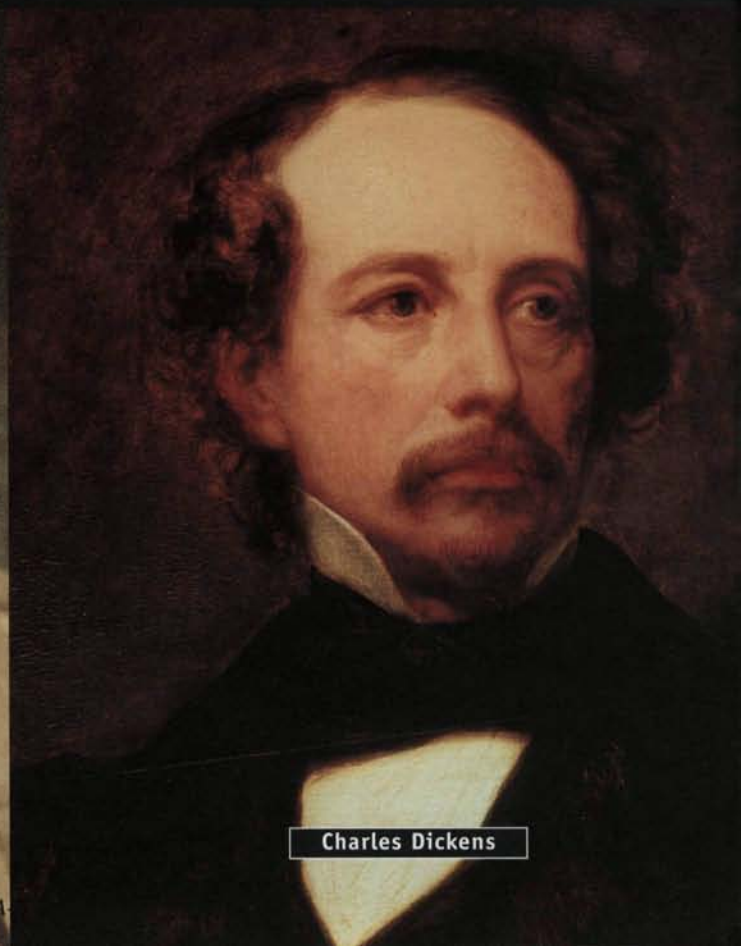
For brief prescribing information see pages A-34, A-35



YESTERDAY, PEOPLE WITH EPILEPSY HAD TO BE EXTRAORDINARY TO SUCCEED.





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EFFICACY ACROSS A BROAD RANGE OF SEIZURES.

- TOPAMAX demonstrates efficacy in Partial Onset, Primary Generalized Tonic-Clonic, and Lennox-Gastaut Seizures[1]
- Desirable seizure-free results were shown in both Adults (19%)† and Children (22%)‡ with Partial Onset Seizures[2,3]

NO EVIDENCE OF LIFE-THREATENING SIDE EFFECTS.

- Like most antiepileptics, the most common side effects are CNS related, usually mild to moderate and transient§[1]

ADULT PATIENTS MAY EXPERIENCE WEIGHT LOSS.

- 73% of patients (n = 52) showed a mean weight decrease of 5.97 lb (Interim analysis. Average duration 60 days)[4]
- 96% of children in clinical trials (≥ one year) who lost weight showed resumption of weight gain in test period**[1]

TODAY, THERE'S TOPAMAX.

B.I.D. DOSING WITH THE PATIENT IN MIND.

- TOPAMAX is initiated and titrated to clinical response regardless of existing anticonvulsant therapy
- Tablets available on formulary††

NOW AVAILABLE IN SPRINKLE CAPSULES

TOPAMAX* topiramate

NOW INDICATED FOR CHILDREN

HELPING PATIENTS MAKE MORE OF THEIR LIVES.

TOPAMAX topiramate Tablets and Sprinkle Capsules: 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 topiramate in monotherapy at this time.*

† Open label, 20 week trial (n = 450 Adults). Optimal dosing was 300-350 mg/day(Average 288 mg/day).
‡ Open label trial for children (n = 72) treated for ≥ 3 months. Average dose of 10 mg/kg/day.
§ CNS adverse events: 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 concentration/attention (8.0%), confusion (9.7%), depression (8.0%), anorexia (5.3%), language problems (6.2%) and mood problems (3.5%). In an audit of 1446 adults and 303 children, there appeared to be a similar pattern of adverse events.
** The long-term effects of weight loss in pediatric patients are not known.
†† Limited use benefit: Ontario, Nova Scotia, New Brunswick, PEI. Full benefit: Quebec, Saskatchewan, British Columbia, Alberta, Manitoba.
Please refer to the TOPAMAX Prescribing Information for complete prescribing details.

REFERENCES: 1. TOPAMAX* topiramate Tablets and Sprinkle Capsules Product Monograph, May 11, 1999. 2. Kamin M, Kraut L, Olson W. Dose optimization of topiramate as add-on therapy in adults with treatment-resistant partial-onset seizures *Neurology* 1999;52 (Suppl 2):A525-526. 3. Glauser TA, Elterman R, Wyllie E et al. Open label topiramate in paediatric partial epilepsy *Epilepsia* 1997:38 (Suppl 3):94. 4. Rosenfeld WE et al.Topiramate and concomitant weight loss. *Epilepsia* 1997:38 (Suppl 8):98.

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• Submit five high quality copies of the manuscript and original illustrations. Papers will be accepted in English or French. Manuscripts must be double spaced throughout including references, tables and legends for illustrations. Margins of at least 25mm should be left on all sides.

• After a paper has been reviewed, the author will be requested to submit four copies of the revised manuscript, including illustrations. Supply a computer diskette (3 1/2" size) containing the article *saved in an RTF format*. Identify clearly first author's name, file name, word processing program and version, and system (i.e. PC or Mac). Clearly indicate the order and importance of headings.

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• ***Abstract*** Original Articles should be accompanied by an abstract of 250 words or less on a separate page, preferably in English and French, although the Journal will provide translation if required. Abstracts of original articles should consist of four paragraphs headed: *Background (or objective), Methods, Results and Conclusions*. Review articles should be accompanied by an abstract of 150 words or less.

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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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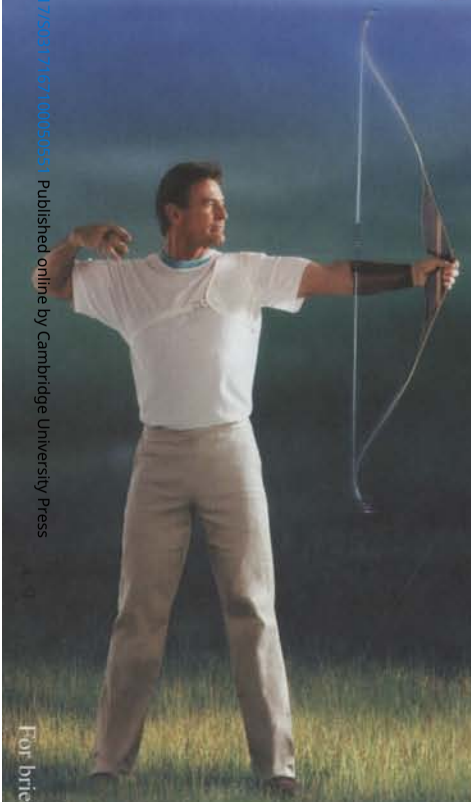
LIPITOR*: Hitting targets.



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.

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).

See Prescribing Information for complete warnings, precautions, dosing and administration.

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.

‡ A patient-year represents the total time of exposure to LIPITOR as defined by the sum of each patient's time on LIPITOR.[3]

¥ 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.[4]

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)

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

Pfizer
Life is our life's work

*TM Pfizer Ireland Pharmaceuticals
Pfizer Canada Inc., licensee

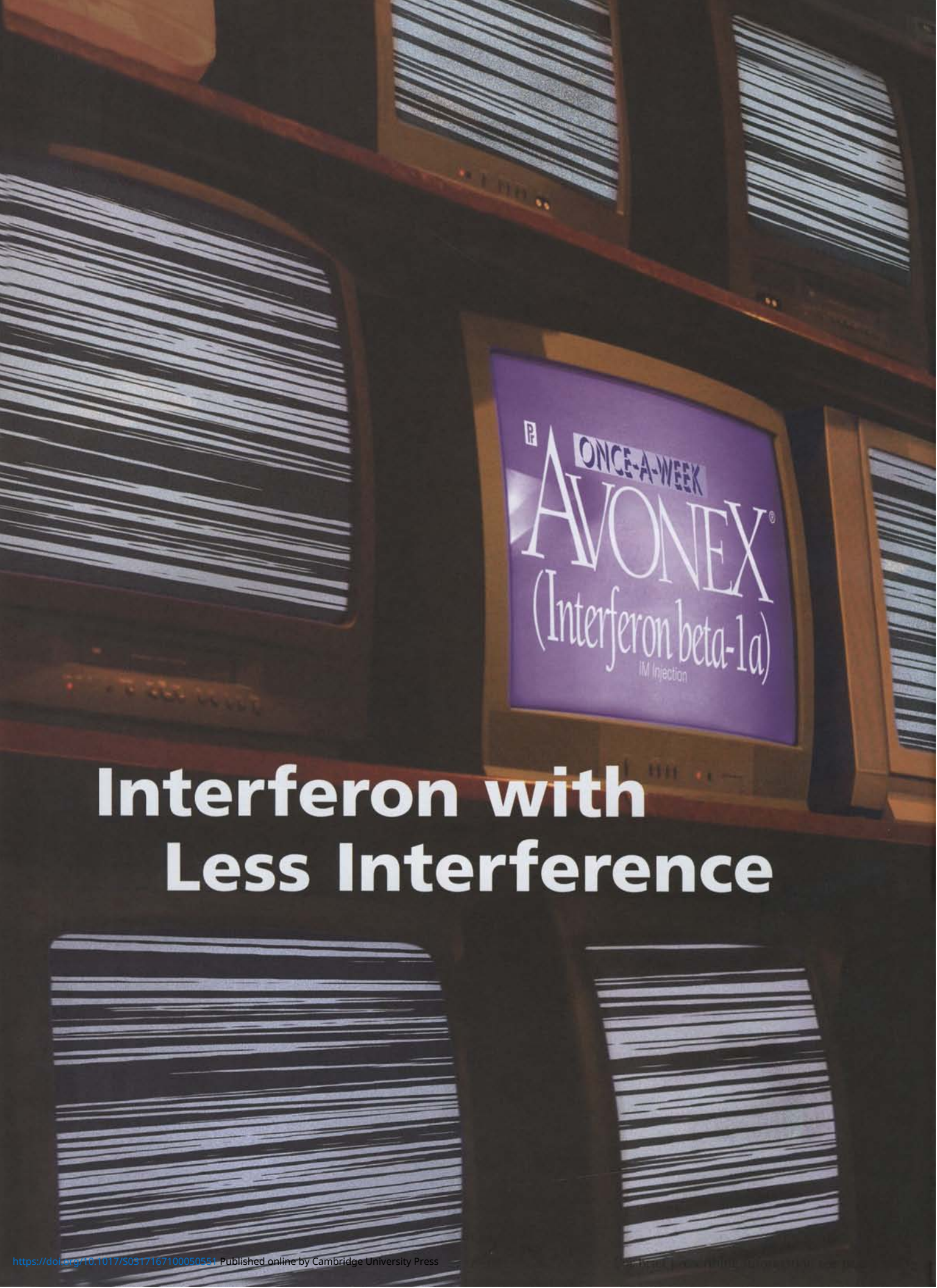
PAAB Member R&D

LIPITOR
atorvastatin calcium
tablets

power you can **trust**™

10 mg 20 mg 40 mg 80 mg

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



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 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 (Betaseron® vs AVONEX p=0.001, Betaseron® vs Rebif® p=0.19, Rebif® vs AVONEX p=0.04, n=125).[2]
- 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 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

55% reduction in whole brain atrophy progression in year 2 (-0.233 vs. -0.521; p=0.03).Ø,6

89% reduction in Gd-enhanced lesions in patients with enhancement at baseline (0.11 vs 0.50; p=0.041).†,7

AVONEX is indicated for the treatment of relapsing forms of MS.[5] AVONEX is generally well tolerated.[5] The most common side effects associated with treatment are flu-like symptoms (muscle ache [myalgia], 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.

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

EFFICACY THAT LASTS
As demonstrated in 2 years of clinical trials

£ Comparative clinical significance has not been established.
¶ Kaplan-Meier methodology, AVONEX n=158, placebo n=143. * AVONEX n=85, placebo n=87.
Ø As measured by brain parenchymal fraction, AVONEX n=68, placebo n=72.
† AVONEX n=44, placebo n=44. The exact relationship between MRI findings and clinical status is unknown.
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PAAB

BIOGEN CANADA

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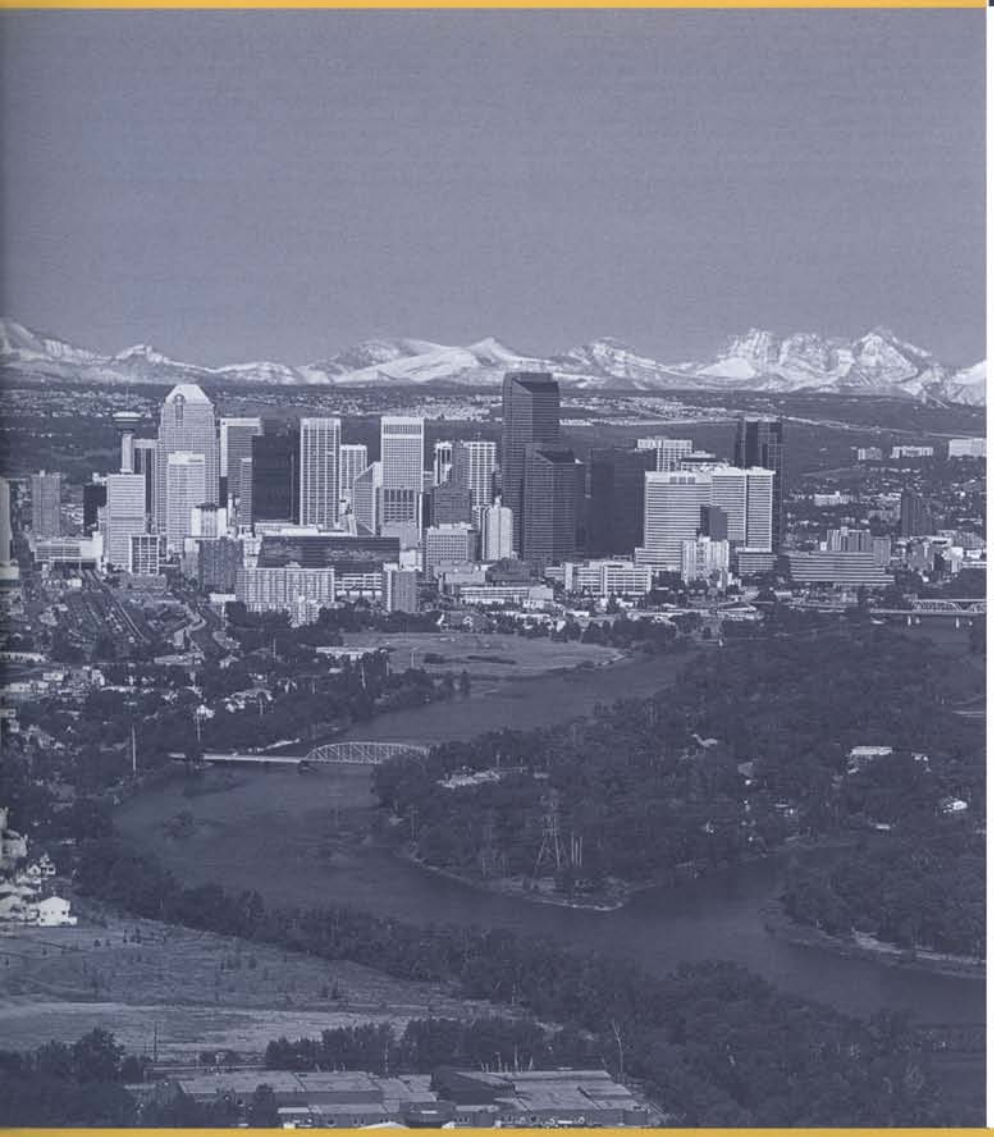
PROVISIONAL PROGRAM



39th

meeting of the

Canadian Congress of Neurological Sciences

Calgary

CCNS • CCSN

June 8-12 juin 2004

Tuesday June 8, 2004

Pre-Congress Courses

08:00-17:30	Neurobiology Review Course
09:00-16:00	ALS-Strategies for Quality Life/Quality Care
18:00-21:00	Movement Disorders Video Session
18:00-21:00	Headache Case Studies

Wednesday, June 9, 2004

08:00-17:30	Complex Spinal Neurosurgery Course
08:00-12:00	Brain Tumour Course – Advances in Neuro-Oncology
08:00-12:00	Epilepsy Course
08:00-12:00	Update on Electromyography and its Clinical Applications
13:30-17:30	Alzheimer's Disease Course
13:30-17:30	Radiosurgery Course – Current Role in Neurosurgical Practice
13:30-17:30	Movement Disorders Course – Cognitive and Behavioral Aspects of Parkinson's Disease
13:30-17:30	EEG Course
18:00-20:00	Welcome Reception

Thursday, June 10, 2004

08:30-10:30	Plenary Session I: Neurology and Neurosurgery in the Developing World
11:00-13:00	Platform Session
13:00-14:30	Poster Session
14:30-16:00	Platform Session
16:00-17:30	Grand Rounds
17:30-19:00	Poster Tours

Friday, June 11, 2004

08:30-10:30	Plenary Session II: New Directions in the Neurosciences
11:00-13:00	Platform Session
13:00-14:30	Poster Session
14:30-16:30	Plenary Session III: Risk Reduction in the Clinical Neurosciences
18:00	Social Night

Saturday, June 12, 2004

08:00-10:00	Neurocritical Care Mini-Symposium – Traumatic Brain Injury
08:00-10:00	What's New in Neurology? Mini-symposium
08:00-10:00	How I do it … Neurosurgery. Mini-symposium
08:00-17:30	Child Neurology Day: Pediatric Brain Injury
10:30-17:00	Stroke Symposium
10:30-17:30	Multiple Sclerosis

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ALTACE® ramipril

PHARMACOLOGIC CLASSIFICATION:
Angiotensin Converting Enzyme Inhibitor

ACTION AND CLINICAL PHARMACOLOGY
ALTACE (ramipril) is an angiotensin converting enzyme (ACE) inhibitor.

Following oral administration, ALTACE is rapidly hydrolyzed to ramiprilat, its principal active metabolite.

INDICATIONS AND CLINICAL USE: *Essential Hypertension.* ALTACE (ramipril) is indicated in the treatment of essential hypertension. It may be used alone or in association with thiazide diuretics. ALTACE should normally be used in patients in whom treatment with a diuretic or a beta-blocker was found ineffective or has been associated with unacceptable adverse effects. ALTACE can also be tried as an initial agent in those patients in whom use of diuretics and/or beta-blockers are contraindicated or in patients with medical conditions in which these drugs frequently cause serious adverse effects. The safety and efficacy of ALTACE in renovascular hypertension have not been established and therefore, its use in this condition is not recommended. The safety and efficacy of concurrent use of ALTACE with antihypertensive agents other than thiazide diuretics have not been established.

Treatment Following Acute Myocardial Infarction
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. Sufficient experience in the treatment of patients with severe (NYHA class IV) heart failure immediately after myocardial infarction is not yet available. (See WARNINGS – Hypotension.)

MANAGEMENT OF PATIENTS AT INCREASED RISK OF CARDIOVASCULAR EVENTS: ALTACE may be used to reduce the risk of myocardial infarction, stroke or cardiovascular death in patients over 55 years of age who are at high risk of cardiovascular events because of a history of coronary artery disease, stroke, peripheral artery disease, or diabetes that is accompanied by at least one other cardiovascular risk factor such as hypertension, elevated total cholesterol levels, low high density lipoprotein levels, cigarette smoking, or documented microalbuminuria. The incidence of the primary outcome (composite of myocardial infarction, stroke and death from cardiovascular causes) was reduced from 17.8% in the placebo-treated group to 14.0% in the ramipril-treated group.

GENERAL: In using ALTACE consideration should be given to the risk of angioedema (see WARNINGS). **When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury or even death of the developing fetus. When pregnancy is detected ALTACE should be discontinued as soon as possible (see WARNINGS – Use in Pregnancy, and INFORMATION FOR THE PATIENT).**

CONTRAINDICATIONS: ALTACE (ramipril) is contraindicated in patients who are hypersensitive to this drug, or to any ingredient in the formulation, or in those patients who have a history of angioedema.

WARNINGS: *Angioedema:* Angioedema has been reported in patients with ACE inhibitors, including ALTACE (ramipril). Angioedema associated with laryngeal involvement may be fatal. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, ALTACE should be discontinued immediately, the patient treated appropriately in accordance with accepted medical care, and carefully observed until the swelling disappears. In instances where swelling is confined to the face and lips, the condition generally resolves without treatment, although antihistamines may be useful in relieving symptoms. Where there is involvement of tongue, glottis, or larynx, likely to cause airway obstruction, appropriate therapy (including, but not limited to 0.3 to 0.5 mL of subcutaneous epinephrine solution 1:1000) should be administered promptly (see ADVERSE REACTIONS).

The incidence of angioedema during ACE inhibitor therapy has been reported to be higher in black than in non-black patients. Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see CONTRAINDICATIONS).

Hypotension: Symptomatic hypotension has occurred after administration of ALTACE, usually after the first or second dose or when the dose was increased. It is more likely to occur in patients who are volume depleted by diuretic therapy, dietary salt restriction, dialysis, diarrhea, or vomiting. In patients with ischemic heart disease or cerebrovascular disease, an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident (see ADVERSE REACTIONS). Because of the potential fall in blood pressure in these patients, therapy with ALTACE should be started under close medical supervision. Such patients should be followed closely for the first weeks of treatment and whenever the dose of ALTACE is increased. In patients with severe congestive heart failure, with or without associated renal insufficiency, ACE inhibitor therapy may cause excessive hypotension and has been associated with oliguria, and/or progressive azotemia, and rarely, with acute renal failure and/or death.

If hypotension occurs, the patient should be placed in a supine position and, if necessary, receive an intravenous infusion of 0.9% sodium chloride. A transient hypotensive response may not be a contraindication to further doses which usually can be given without difficulty once the blood pressure has increased after volume expansion in hypertensive patients. However, lower doses of ALTACE and/or reduced concomitant diuretic therapy should be considered. *In patients receiving treatment following acute myocardial infarction, consideration should be given to discontinuation of ALTACE (see ADVERSE REACTIONS – Treatment Following Acute Myocardial Infarction, DOSAGE AND ADMINISTRATION – Treatment Following Acute Myocardial Infarction).*

Neutropenia/Agranulocytosis: Agranulocytosis and bone marrow depression have been caused by ACE inhibitors. Several cases of agranulocytosis, neutropenia or leukopenia have been reported in which a causal relationship to ALTACE cannot be excluded. Current experience with the drug shows the incidence to be rare. Periodic monitoring of white blood cell counts should be considered, especially in patients with collagen vascular disease and/or renal disease. Use in Pregnancy: ACE inhibitors can cause fetal and neonatal morbidity and mortality when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, ALTACE should be discontinued as soon as possible.

PRECAUTIONS: Renal Impairment: *As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function have been seen in susceptible individuals. In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, such as patients with bilateral renal artery stenosis, unilateral renal artery stenosis to a solitary kidney, or severe congestive heart failure, treatment with agents that inhibit this system has been associated with oliguria, progressive azotemia, and rarely, acute renal failure and/or death. In susceptible patients, concomitant diuretic use may further increase risk. Use of ALTACE should include appropriate assessment of renal function. ALTACE should be used with caution in patients with renal insufficiency as they may require reduced or less frequent doses (see DOSAGE AND ADMINISTRATION). Close monitoring of renal function during therapy should be performed as deemed appropriate in patients with renal insufficiency.*

Anaphylactoid Reactions during Membrane Exposure: Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g. polyacrylonitrile [PAN]) and treated concomitantly with an ACE inhibitor. Dialysis should be stopped immediately if symptoms such as nausea, abdominal cramps, burning, angioedema, shortness of breath and severe hypotension occur. Symptoms are not relieved by antihistamines. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agents.

Anaphylactoid Reactions during Desensitization: There have been isolated reports of patients experiencing sustained life threatening anaphylactoid reactions while receiving ACE inhibitors during desensitization treatment with hymenoptera (bees, wasps) venom. In the same patients, these reactions have been avoided when ACE inhibitors were temporarily withheld for at least 24 hours, but they have reappeared upon inadvertent rechallenge.

Hyperkalemia and Potassium-Sparing Diuretics: Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials treated with ALTACE. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was not a cause of discontinuation of therapy in any hypertensive patient. Risk factors for the development of hyperkalemia may include renal insufficiency, diabetes mellitus, and the concomitant use of agents to treat hypokalemia or other drugs associated with increases in serum potassium (see PRECAUTIONS – Drug Interactions).

Surgery/Anesthesia: In patients undergoing surgery or anesthesia with agents producing hypotension, ALTACE may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it may be corrected by volume repletion.

Aortic Stenosis: *There is concern, on theoretical grounds, that patients with aortic stenosis might be at particular risk of decreased coronary perfusion when treated with vasodilators because they do not develop as much afterload reduction.*

Patients with Impaired Liver Function: Hepatitis (hepatocellular and/or cholestatic), elevations of liver enzymes and/or serum bilirubin have occurred during therapy with ACE inhibitors in patients with or without pre-existing liver abnormalities. In most cases the changes were reversed on discontinuation of the drug.

Elevations of liver enzymes and/or serum bilirubin have been reported with ALTACE (see ADVERSE REACTIONS). Should the patient receiving ALTACE experience any unexplained symptoms particularly during the first weeks or months of treatment, it is recommended that a full set of liver function tests and any other necessary investigations be carried out. Discontinuation of ALTACE should be considered when appropriate. There are no adequate studies in patients with cirrhosis and/or liver dysfunction. ALTACE should be used with particular caution in patients with pre-existing liver abnormalities. In such patients baseline liver function tests should be obtained before administration of the drug and close monitoring of response and metabolic effects should apply.

Nursing Mothers: *Ingestion of a single 10 mg oral dose of ALTACE resulted in* undetectable amounts of ramipril and its metabolites in breast milk. However, because multiple doses may produce low milk concentrations that are not predictable from single doses, ALTACE should not be administered to nursing mothers.

Pediatric Use: The safety and effectiveness of ALTACE in children have not been established; therefore use in this age group is not recommended.

Use in Elderly: Although clinical experience has not identified differences in response between the elderly (>65 years) and younger patients, greater sensitivity of some older individuals cannot be ruled out.

Patient Alertness: ALTACE may lower the state of patient alertness and/or reactivity, particularly at the start of treatment (see ADVERSE REACTIONS).

Cough: A dry, persistent cough, which usually disappears only after withdrawal or lowering of the dose of ALTACE, has been reported. Such possibility should be considered as part of the differential diagnosis of cough.

Drug Interactions: Concomitant Diuretic Therapy: Hypotension may result but can be minimized by discontinuing diuretic or increasing salt intake prior to ramipril *treatment and/or reducing initial dose.* Agents increasing serum potassium: Use potassium sparing diuretics with caution and monitor frequently. Agents causing renin release: ALTACE antihypertensive effect increased. Lithium: Lithium levels may be increased. Administer lithium with caution and monitor levels frequently. Antacids: The bioavailability of ALTACE and the pharmacokinetics of ramiprilat were not affected. Digoxin: No change in ramipril, ramiprilat or digoxin serum levels. Warfarin: The co-administration of ALTACE with warfarin did not alter the anticoagulant effects. Acenocoumarol: No significant changes. Non-steroidal anti-inflammatory agents (NSAID): The antihypertensive effects of ACE inhibitors may be reduced with concomitant administration of NSAIDs (*e.g. indomethacin*).

ADVERSE REACTIONS: *Essential Hypertension.* Serious adverse events occurring in North American placebo-controlled clinical trials with ramipril monotherapy in hypertension (*n*=972) were: hypotension (0.1%); myocardial infarction (0.3%); cerebrovascular accident (0.1%); edema (0.2%); syncope (0.1%). Among all North American ramipril patients (*n*=1,244), angioedema occurred in patients treated with ramipril and a diuretic (0.1%). The most frequent adverse events occurring in these trials with ALTACE monotherapy in hypertensive patients (*n*=651) were: headache (15.1%); dizziness (3.7%); asthenia (3.7%); chest pain (2.0%); nausea (1.8%); peripheral edema (1.8%); somnolence (1.7%); impotence (1.5%); rash (1.4%); arthritis (1.1%); dyspnea (1.1%). Discontinuation of therapy due to clinical adverse events was required in 5 patients (0.8%). In placebo-controlled trials, an excess of upper respiratory infection and flu syndrome was seen in the ramipril group. As these studies were carried out before the relationship of cough to ACE inhibitors was recognized, some of these events may represent ramipril-induced cough. In a later 1-year study, increased cough was seen in almost 12% of ALTACE patients, with about 4% of these patients requiring discontinuation of treatment. Approximately 1% of patients treated with ALTACE monotherapy in North American controlled clinical trials (*n*=972) have required discontinuation because of cough.

Treatment Following Acute Myocardial Infarction
Adverse events (except laboratory abnormalities) in a controlled clinical trial of post-AMI patients with clinical signs of heart failure considered possibly/probably related to ALTACE and occurring in more than 1% of stabilized patients (n=1,004) were: hypotension (10.7%); increased cough (7.6%); dizziness/vertigo (5.6%); nausea/vomiting (3.8%); angina pectoris (2.9%); postural hypotension (2.2%); syncope (2.1%); heart failure (2.0); severe/resistant heart failure (2.0%); myocardial infarction (1.7%); vomiting (1.6%); headache (1.2%); abnormal kidney function (1.2%); abnormal chest pain (1.1%); diarrhea (1.1%). Isolated cases of death have been reported with the use of ramipril that appear to be related to hypotension (including first dose effects), but many of these are difficult to differentiate from progression of underlying disease (see WARNINGS – Hypotension). Discontinuation of therapy due to adverse reactions was required in 368/1,004 post-AMI patients taking ramipril (36.7%), compared to 401/982 patients receiving placebo (40.8%).

Clinical Laboratory Test Findings: increased creatinine; increases in blood urea nitrogen (BUN); decreases in hemoglobin or hematocrit; hyponatraemia; elevations of liver enzymes, serum bilirubin, uric acid, blood glucose; proteinuria and significant increases in serum potassium.

DOSAGE AND ADMINISTRATION

Essential Hypertension: Dosage of ALTACE (ramipril) must be individualized. Initiation of therapy requires consideration of recent antihypertensive drug treatment, the extent of blood pressure elevation and salt restriction. The dosage of other antihypertensive agents being used with ALTACE may need to be adjusted.

Monotherapy: *The recommended initial dosage of ALTACE in patients not on diuretics* is 2.5 mg once daily. Dosage should be adjusted according to blood pressure response, generally, at intervals of at least two weeks. The usual dose range is 2.5 to 10 mg once daily. A daily dose of 20 mg should not be exceeded.

In some patients treated once daily, the antihypertensive effect may diminish towards the end of the dosing interval. This can be evaluated by measuring blood pressure just prior to dosing to determine whether satisfactory control is being maintained for 24 hours. If it is not, either twice daily administration with the same total daily dose, or an increase in dose should be considered. If blood pressure is not controlled with ALTACE alone, a diuretic may be added. After the addition of a diuretic, it may be possible to reduce the dose of ALTACE.

Concomitant Diuretic Therapy: Symptomatic hypotension occasionally may occur following the initial dose of ALTACE and is more likely in patients who are currently being treated with a diuretic. The diuretic should, if possible, be discontinued for two to three days before beginning therapy with ALTACE to reduce the likelihood of hypotension (see WARNINGS). If the diuretic cannot be discontinued, an initial dose of 1.25 mg of ALTACE should be used with careful medical supervision for several hours and until blood pressure has stabilized. The dosage of ALTACE should subsequently be titrated (as described above) to the optimal response.

Use in Renal Impairment: For patients with a creatinine clearance below 40 mL/min/1.73 m^2 (serum creatinine above 2.5 mg/dL), the recommended initial dose is 1.25 mg of ALTACE once daily. Dosage may be titrated upward until blood pressure is controlled or to a maximum total daily dose of 5 mg. In patients with severe renal impairment (creatinine clearance below 10 mL/min/1.73 m^2) the maximum total daily dose of 2.5 mg of ALTACE should not be exceeded.

Treatment Following Acute Myocardial Infarction:
Initiation of therapy requires consideration of concomitant medication and baseline blood pressure and should be instituted under close medical supervision, usually in a hospital, three to ten days following an acute myocardial infarction in haemodynamically stable patients with clinical signs of heart failure. The recommended initial dosage of ALTACE is 2.5 mg given twice a day (b.i.d.), one in the morning and one in the evening. If tolerated, and depending on the patient's response, dosage may be increased by doubling at intervals of one to three days. The maximum daily dose of ALTACE should not exceed 5 mg twice daily (b.i.d). After the initial dose of ALTACE, the patient should be observed under medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. If a patient becomes hypotensive at this dosage, it is recommended that the dosage be lowered to 1.25 mg b.i.d. following effective management of the hypotension. (see WARNINGS – Hypotension).

Patients who have been fluid or salt depleted, or treated with diuretics are at an increased risk of hypotension (see WARNINGS – Hypotension). An excessive fall in blood pressure may occur particularly in the following: after the initial dose of ALTACE; after every first increase of dose of ALTACE; after the first dose of a concomitant diuretic and/or when increasing the dose of the concomitant diuretic. If appropriate, the dose of any concomitant diuretic should be reduced which may diminish the likelihood of hypotension (see PRECAUTIONS – Drug Interactions). Consideration should be given to reducing the initial dose to 1.25 mg of ALTACE in these patients.

Use in Renal Impairment: In patients with impaired renal function (creatinine clearance of 20-50 mL/min/1.73 m^2 body surface area), the initial recommended dosage is generally 1.25 mg of ALTACE once daily. This dosage may be increased with caution up to 1.25 mg of ALTACE twice daily, depending upon clinical response and tolerability.

Insufficient data is available concerning the use of ramipril following acute myocardial infarction in patients with heart failure and severe renal failure. (see ACTION AND CLINICAL PHARMACOLOGY – Pharmacokinetics and Metabolism, PRECAUTIONS – Renal Impairment).

Use in Hepatic Impairment: Insufficient data is available concerning the use of ramipril following acute myocardial infarction in patients with heart failure and hepatic dysfunction. Dose reduction and careful monitoring of these patients is required (see ACTIONS AND CLINICAL PHARMACOLOGY – Pharmacokinetics and Metabolism, PRECAUTIONS – Patients with Impaired Liver Function).

Management of Patients at Increased Risk of Cardiovascular Events: Recommended initial dose: 2.5 mg of ALTACE once daily. Depending on the tolerability, the dose is gradually increased. It is recommended to double the dose after one week of treatment and – after another three weeks – to increase it to *10 mg. Usual maintenance dose: 10 mg of ALTACE daily (see ACTION AND CLINICAL* PHARMACOLOGY, WARNINGS and PRECAUTIONS). Dosage recommendations for special risk groups such as patients with renal or hepatic impairment, or at an increased risk of hypotension (fluid or salt depletion, treated with diuretics) are to be followed as previously described (see WARNINGS and PRECAUTIONS).

DOSAGE FORM

a) Composition
ALTACE (ramipril) capsules 1.25 mg, 2.5 mg, 5.0 mg, and 10.0 mg contain the medicinal ingredient ramipril in quantities of 1.25 mg, 2.5 mg, 5.0 mg, and 10.0 mg respectively. The qualitative formulation for all potencies of ALTACE is: ramipril, pre-gelatinized starch NF (as filler, gliding agent and disintegration agent) and empty gelatin capsules. Empty gelatin capsules for all potencies of ALTACE are composed of gelatin NF and coloring agents specific to each potency (see below).

POTENCY	CAP	BODY
1.25 mg	Yellow iron oxide Titanium dioxide	Titanium dioxide
2.5 mg	Yellow iron oxide FD & C red no. 3 Titanium dioxide	Titanium dioxide
5.0 mg	FD & C blue no. 2 FD & C red no. 3 Titanium dioxide	Titanium dioxide
10.0 mg	FD & C blue no. 2 FD & C red no. 3 Black iron oxide Titanium dioxide	Titanium dioxide

b) Stability and storage recommendations
Store ALTACE (ramipril) in original container at room temperature, below 25°C and not beyond the date indicated on the container.

AVAILABILITY: No. 4 hard gelatin capsules:
- 1.25 mg (white/yellow);
- 2.5 mg (white/orange);
- 5.0 mg (white/red);
- 10.0 mg (white/blue).

ALTACE capsules 1.25 mg, 2.5 mg, 5.0 mg and 10.0 mg are packaged in cartons of 30 (2 x 15 blister-packed) capsules. Bottles of 100 capsules and 500 capsules also available.

Product monograph available upon request.

References:
1. ALTACE Product Monograph. **2.** The Heart Outcomes Prevention Evaluation Study Investigators (HOPE) Trial. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342(3):145-53.

See page A-15

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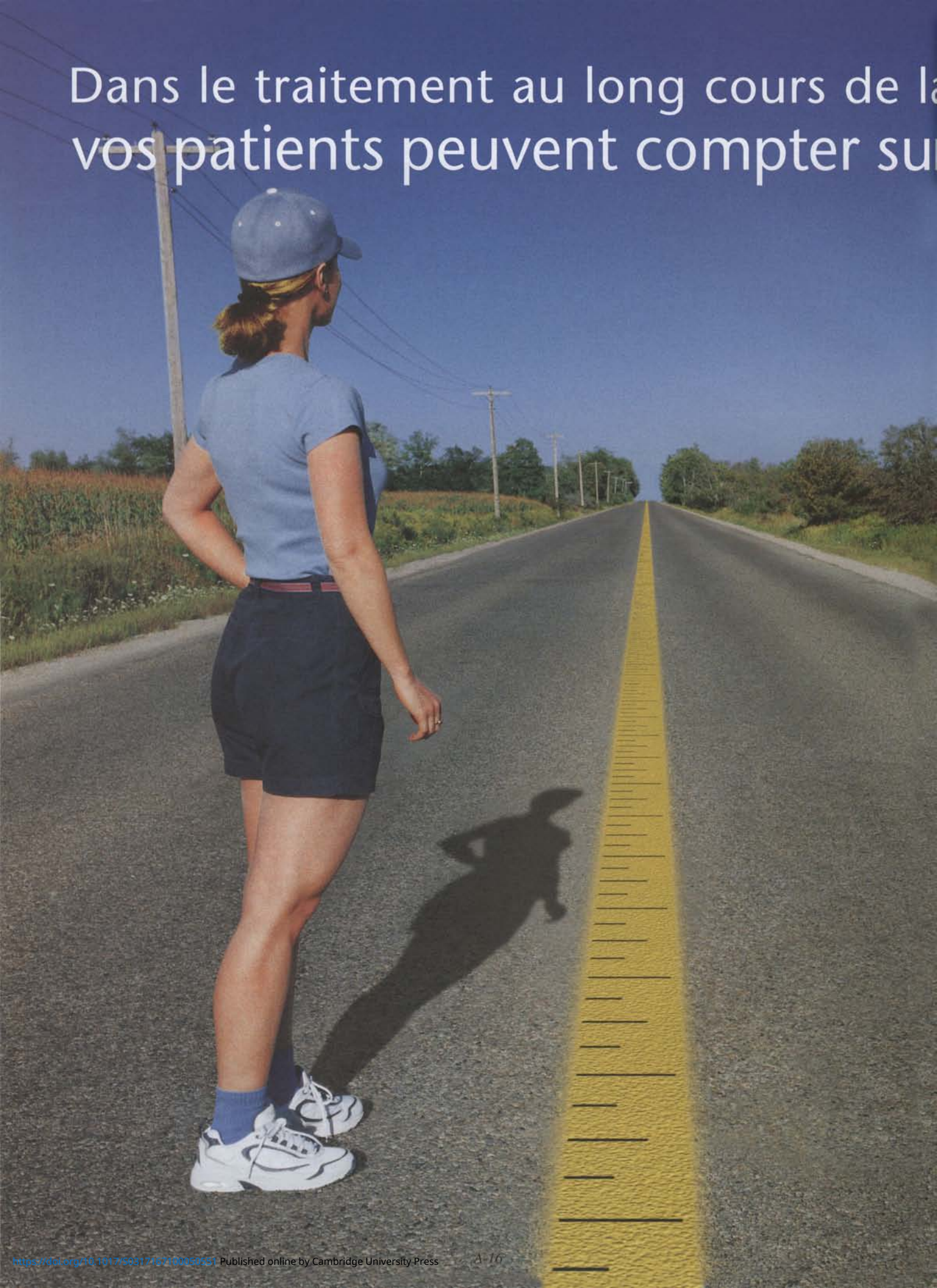
For brief prescribing information see page A-14



SP rémittente, COPAXONE®

Effet démontré sur l'incapacité

- Les patients traités par COPAXONE® ont bénéficié d'une amélioration significative de la variation de la cote EDSS moyenne : 123 % en faveur de l'effet thérapeutique c. le placebo sur deux ans (-0,05 {n = 125} c. +0,21 {n = 126, $p = 0,023$)[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 %).

COPAXONE®
(acétate de glatiramère injectable)

Traitement au long cours de la SP rémittente

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Pour documentation voir pages A-34, A-35, A 52

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.

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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 172 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

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

11th Biennial Canadian Neuro-Oncology Meeting

May 28-30, 2004 • Toronto • Ontario • Canada

CALL FOR ABSTRACTS

ABSTRACT DEADLINE: February 16, 2004

The 2004 Canadian Neuro-Oncology Meeting will be held in Toronto, Ontario on May 28-30, 2004 and will take place at The Residence, 90 Gerrard Street West, Toronto.

The Scientific Committee of the 11th Biennial Canadian Neuro-Oncology Meeting is now inviting abstracts for platform and poster presentation. Abstracts presented at the meeting will be published in the Canadian Journal of Neurological Sciences. The scientific program will encompass basic science, medical neuro-oncology, radiation neuro-oncology, pediatric neuro-oncology and quality of life/epidemiology.

NEWLY ESTABLISHED YOUNG INVESTIGATOR RESEARCH AWARDS

We are pleased to announce the establishment of three new "Young Investigator Awards" for which graduate students, postdoctoral fellows, residents in training and allied health professionals are eligible.

Two awards have been made possible by Schering Canada Inc. and the Canadian Brain Tumour Consortium:

- **Canadian Brain Tumour Consortium Young Investigator Award in Basic Science**
- **Canadian Brain Tumour Consortium Young Investigator Award in Clinical Investigation**

plus

- **The University Health Network Travel Award in Neuro-Oncology: To fund a young investigator to present their work at the World Federation of Neurosurgical Societies: Tumor Section Meeting, Jaipur, India, October 11-13, 2004.**

INSTRUCTIONS FOR SUBMISSION OF ABSTRACT

1. Submit an electronic abstract (not exceeding 200 words) and use 12-point typeface in Word format only. Submit by February 16, 2004 to sandi.amaral@uhn.on.ca
2. The web does not support special characters and these must be spelled out in full (e.g., alpha, beta, greater than and equal to, etc.)
3. The abstract title must be in LOWER CASE LETTERS except for the first word and abbreviations, and followed by the authors' initials, family name(s), city and province(s). The presenting author MUST be asterisked.
   Example: J. Smith, E. Clarke* (anywhere, Ontario), A. Brown (Elsewhere, Newfoundland).
4. Type the abstract body in a program on your own computer so that you can retain a copy for your records and submit the abstract in Word format.
5. Spell out special or unusual abbreviations in full words.
6. An individual may present more than one abstract. Abstracts submitted for presentation in poster or platform session will be reviewed by the Scientific Program Committee. Notification of acceptance and schedule information will be sent via email by April 1, 2004.

IMPORTANT DATES:

ABSTRACT DEADLINE: February 16, 2004

EARLY REGISTRATION DEADLINE: April 15, 2004

Contact: Ms. Sandi Amaral, c/o 11th Biennial Canadian Neuro-Oncology Meeting, Division of Neurosurgery, Toronto Western Hospital, 399 Bathurst Street, West Wing 4-427, Toronto, Ontario, Canada M5T 2S8
T: (416) 603-5503 / F: (416) 603-5298 / Email: sandi.amaral@uhn.on.ca

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The Crolla Family Brain Tumour Research Centre

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IF YOU STARTED PATIENTS ON REQUIP®, WOULD THE FUTURE LOOK DIFFERENT?

Interim 6-month results from a 5-year multicentre study show ReQuip® demonstrated similar efficacy to L-dopa in the control of early† Parkinson's disease.[1Ω] Yet ReQuip® has demonstrated a low propensity to produce dyskinesias.[2††] Maybe it's time to rethink Parkinson's. And start early Parkinson's patients on ReQuip® alone.

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. Three year and five year active-comparator controlled clinical trials have been conducted.

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.[†††]

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.

† Hoehn and Yahr stages I-II.

Ω A 6-month interim analysis of a 5-year, double-blinded, randomized, multicentre study of patients with early Parkinson's disease. *n*=268:179 patients received ropinirole and 89 received L-dopa. The mean daily dose was 9.7 mg and 464.0 mg respectively. There was no difference in Clinical Global Improvement scale in patients with Hoehn and Yahr stages I-II although L-dopa showed improvement in a greater proportion of patients with more severe disease. The proportion of responders was 58% in the L-dopa group and 48% in the ropinirole group; this was not of statistical significance.

†† In Early therapy, the respective incidences of dyskinesia in patients receiving ropinirole was 1.2% and in patients receiving L-dopa was 11.2%. Meta analysis, *n*=515, 17 months.

††† Please consult the Warnings section of the Prescribing Information.

Pr REQUIP® ropinirole

Rethinking Parkinson's.

PAAB Member R&D

gsk GlaxoSmithKline

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For brief prescribing information see pages A-50, A-51

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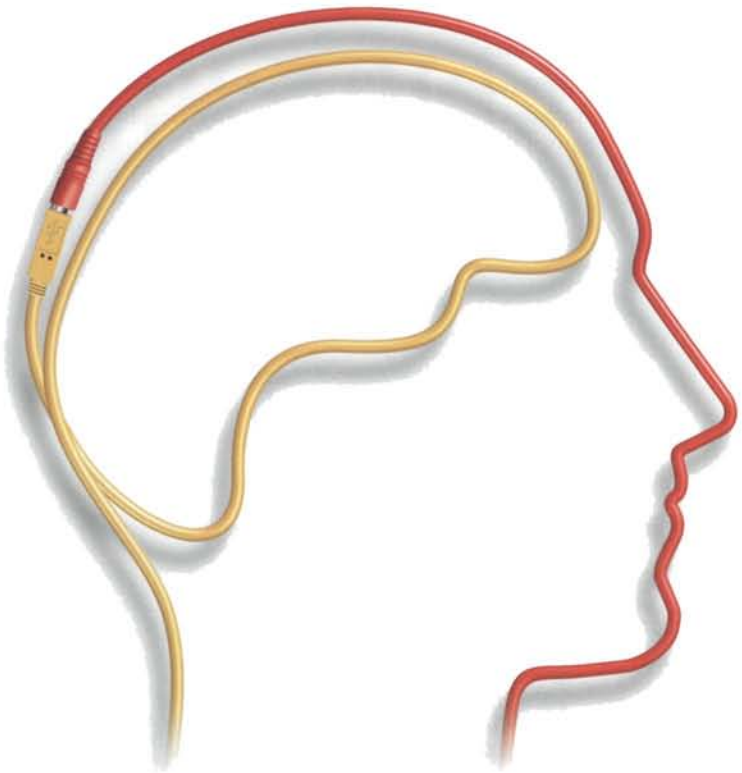
to control



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.

* 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.

NEW Pr Keppra® levetiracetam

CONNECTING EXCELLENT PROFILES IN EFFICACY AND TOLERABILITY

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

25 Years Ago in the Canadian Journal of Neurological Sciences

Seven Cases of Gilles de la Tourette's Syndrome: Partial Relief with Clonazepam: A Pilot Study

M. Gonce and A. Barbeau

Summary: The histories of seven consecutive case of Gilles de la Tourette's syndrome are presented to exemplify the range of clinical manifestations in this disease and to collate preliminary results with the new benzodiazepine, clonazepam, as a possible adjuvant therapy of this disorder. Controlled trials with clonazepam alone and in association with haloperidol are now justified. Five of our seven patients had a positive family history of tics, and two a confirmed family history of gout. Because clonazepam improves myoclonia and tics and because its mechanism of action possibly involves serotonin, we thought it worthwhile to study simultaneously the relative roles of serotonin and dopamine metabolism in the production of tics, and their relationship to possible defects in purine metabolism in Gilles de la Tourette's syndrome.

Can. J. Neurol. Sci. 1977;4:279

Platelet Dopamine Uptake in Huntington's Chorea and Gilles de la Tourette's Syndrome: Effect of Haloperidol

Roger F. Butterworth, Michel Gonce and André Barbeau

Summary: Uptake of ^{14}C-dopamine by human platelets has been studied in two diseases, namely Gilles de la Tourette's syndrome and Huntington's chorea, in which abnormal metabolism of dopamine has been implicated. Platelets from untreated Huntington's chorea patients showed a small increase in Km and Vmax.; platelets from patients in all other groups showed an uptake identical with the controls. Haloperidol (10^{-5}M) was also shown to be a strong non-competitive inhibitor of ^{14}C-DA uptake by platelets. This property is probably unrelated to the drug's action in ameliorating the symptoms of Huntington's chorea which is likely related to the increase in cholinergic neuronal activity produced by neuroleptic blockade of dopamine receptors.

Can. J. Neurol. Sci. 1977;4:285

Chroma-Memo-Flow Technique for Rapid Sequential Analysis of Regional Cerebral Blood Flow (rCBF) Responses

Jørn Overgaard

SUMMARY: This is the first report of a method of sequential regional cerebral blood flow (rCBF) analysis, called Croma-Memo-Flow. This technique is a computerized modification of the initial slope method of regional cerebral blood flow (rCBF init.), allowing temporal resolution of the flow pattern by calculation of the slopes of sequential segments of the initial 1-2 minutes of the Xenon-133 washout curve. The same theoretical analysis applies to this method as to the rCBF init. method. Each flow calculation is based on the slope of a discrete 16 second segment of the initial washout; and each second the segment is advanced by one second. A new flow calculation is made each second and is displayed as a color coded map on a TV screen. Each map is labelled, indicating the time in seconds following Xenon injection, and sequential rCBF changes during the clearance period can be immediately visualized. This allows for almost instantaneous analysis and display of rapid or transient rCBF responses to activation and deactivation of the cerebral cortices.

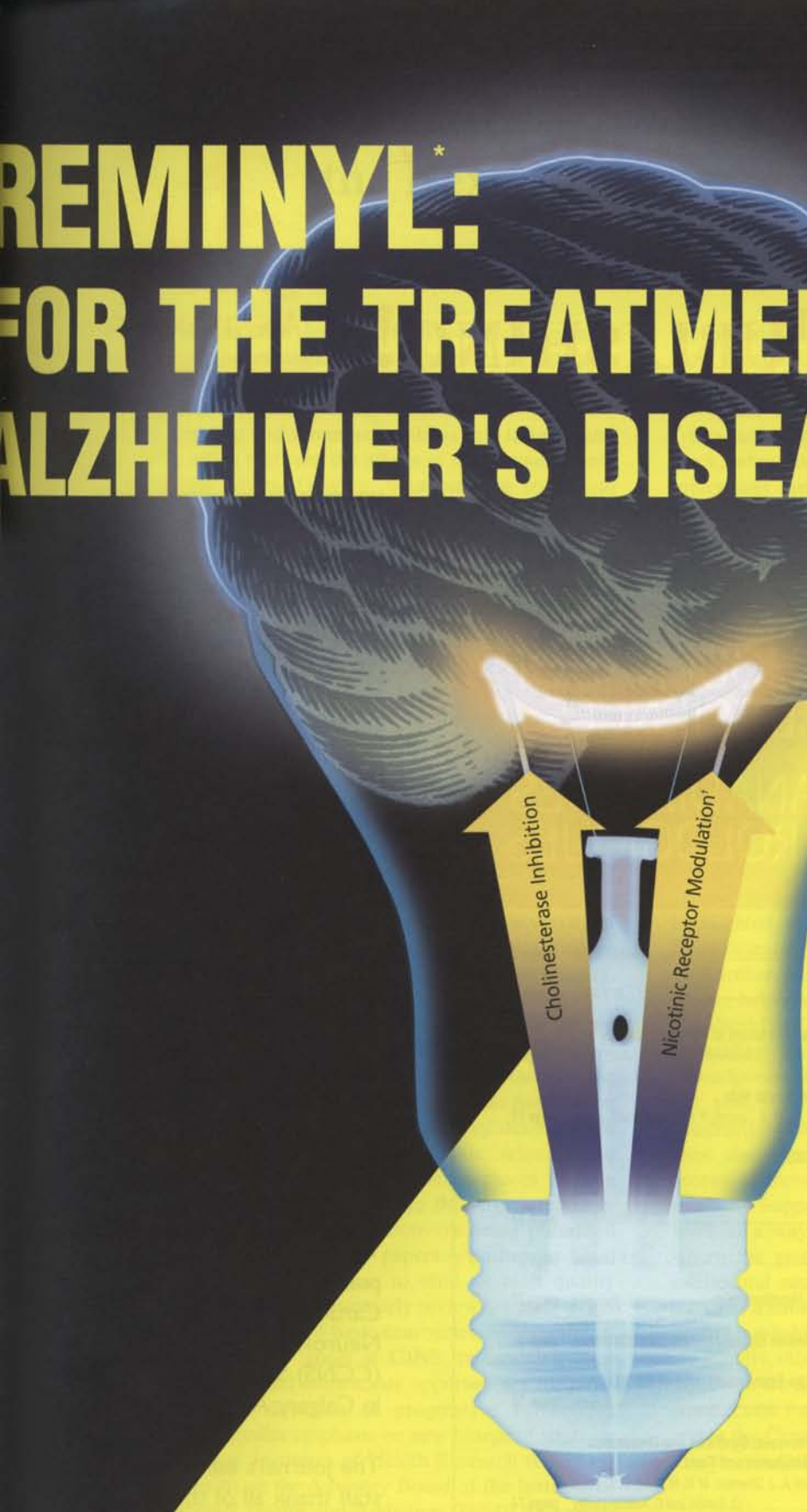
The data is stored in a 35 channel memory for deliberate replay, photography, and analysis.

Functional tests may be applied during the initial washout period and both the magnitude and chronological relationships of the evoked regional cerebrovascular responses observed. A clinical study is presented to illustrate the possibilities of applying the technique to assess cortical reactivity.

Can. J. Neurol. Sci. 1978;5: 1

REMINYL*: FOR THE TREATMENT OF ALZHEIMER'S DISEASE

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



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

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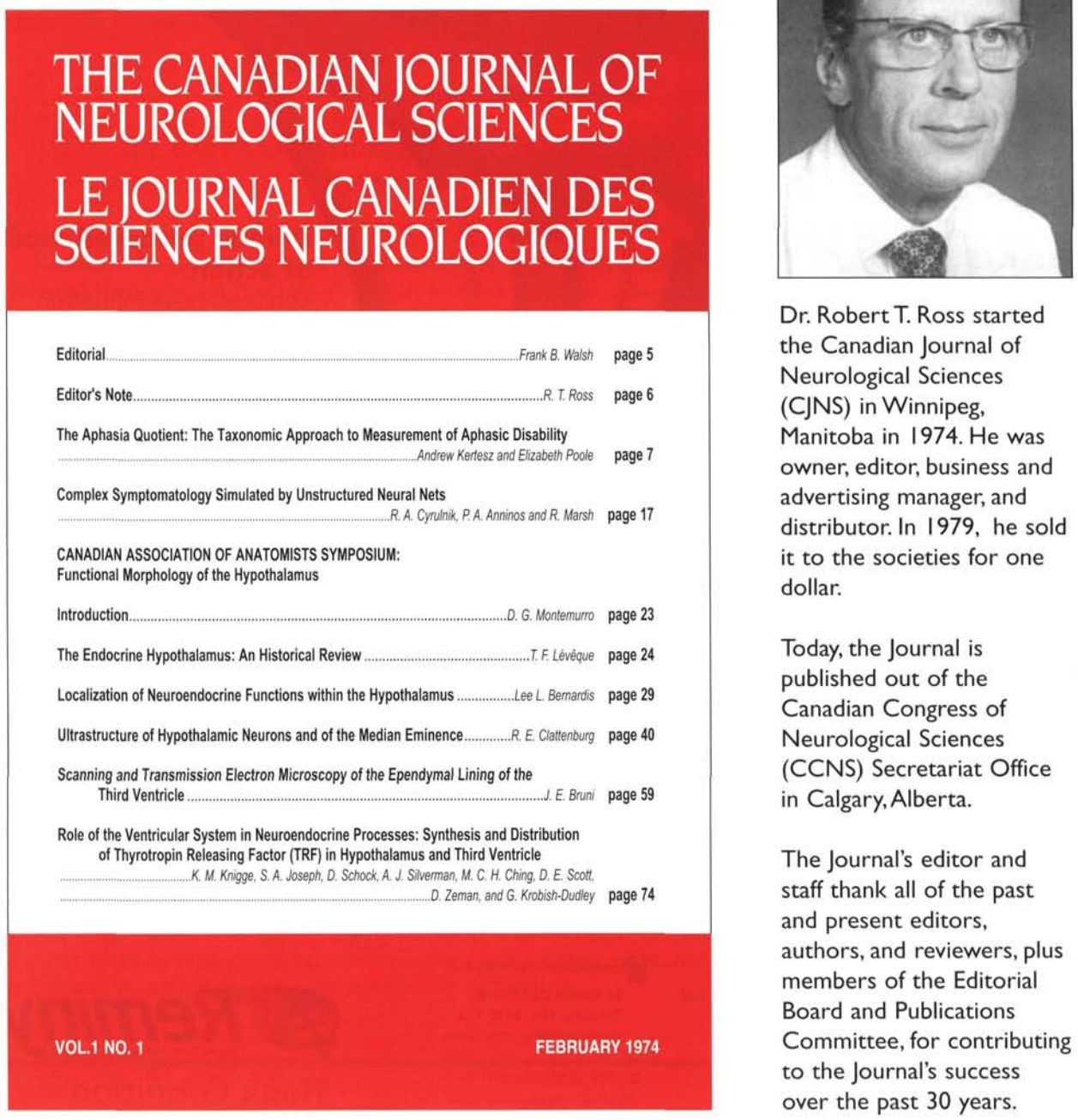
First Journal Cover, 1974



THE CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES

VOL.1 NO. 1 FEBRUARY 1974

Dr. Robert T. Ross started the Canadian Journal of Neurological Sciences (CJNS) in Winnipeg, Manitoba in 1974. He was owner, editor, business and advertising manager, and distributor. In 1979, he sold it to the societies for one dollar.

Today, the Journal is published out of the Canadian Congress of Neurological Sciences (CCNS) Secretariat Office in Calgary, Alberta.

The Journal's editor and staff thank all of the past and present editors, authors, and reviewers, plus members of the Editorial Board and Publications Committee, for contributing to the Journal's success over the past 30 years.