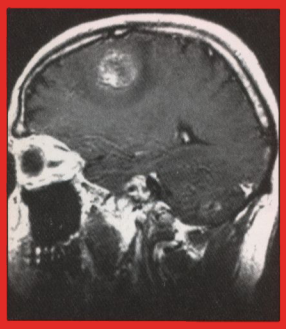
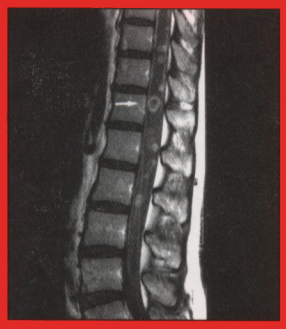
Volume 28 Number 2 May 2001

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

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL



Outpatient Craniotomy



Neuroimaging Highlight

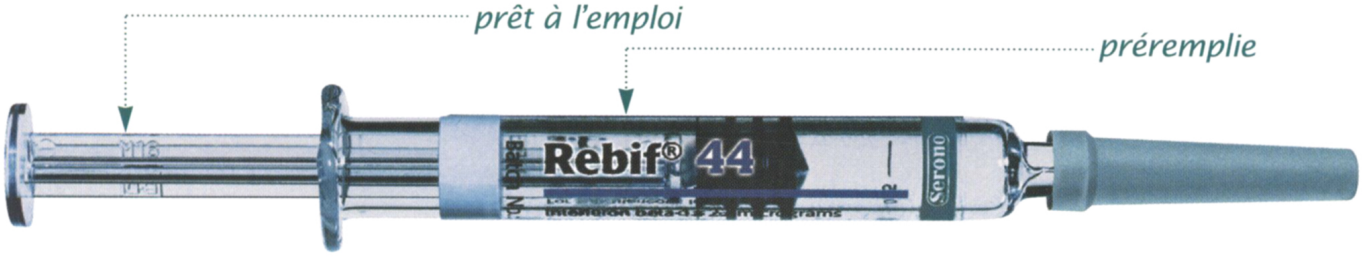
The official Journal of: The Canadian Neurological Society, The Canadian Neurosurgical Society, The Canadian Society of Clinical Neurophysiologists, The Canadian Association of Child Neurology

Rebif®. Efficacité dépendante de la dose dans la SEP rémittente[1]*.

Pas encore

Pr **Rebif®**

Interféron bêta-1a



Les effets secondaires les plus fréquemment observés sont les réactions au point d'injection et les symptômes pseudo-grippaux (asthénie, pyrexie, frissons, arthralgie, myalgie et céphalées). Leur fréquence et leur intensité tend à diminuer avec la poursuite du traitement. Veuillez consulter la monographie du produit pour les renseignements posologiques complets. Les données portant sur l'innocuité et l'efficacité proviennent d'observations sur 2 ans seulement.

* Rebif® est indiqué pour le traitement de la sclérose en plaques rémittente chez des patients dont la cote EDSS se situe entre 0 et 5,0, afin de réduire le nombre et la gravité des poussées cliniques, de ralentir la progression de l'invalidité physique, et de réduire les besoins de corticothérapie et le nombre de séjours à l'hôpital pour le traitement de la sclérose en plaques.

RÉFÉRENCE :

[1] Groupe d'étude PRISMS (Prevention of Relapses and Disability by Interferon ß-1a Subcutaneously in Multiple Sclerosis), 1998. Randomised double-blind placebo-controlled study of Interferon ß-1a in relapsing/remitting multiple sclerosis. *Lancet*, 352:1498-1504

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LE JOURNAL CANADIEN DES Sciences Neurologiques

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THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

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La Société Canadienne de Neurologie

The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

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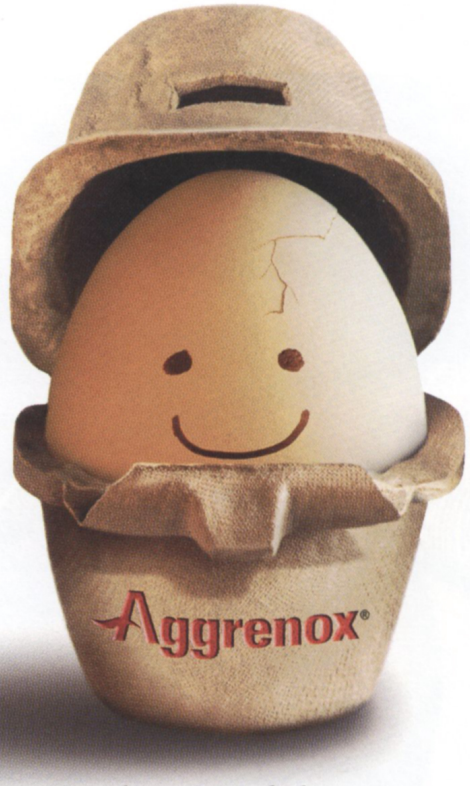
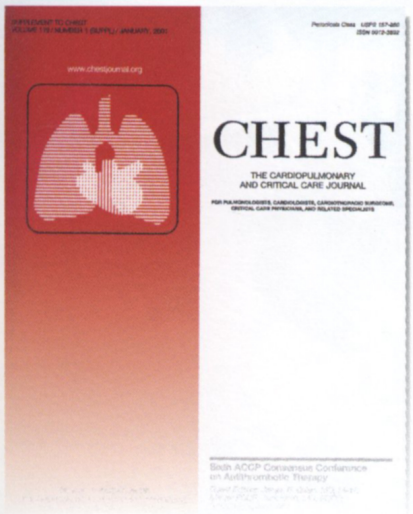
Introducing...

New Aggrenox®



Prevented twice as many strokes vs. ASA[2,3,4]*

New American College of Chest Physician Stroke Guidelines state[1]:



"Aggrenox is more effective than ASA alone for the prevention of [secondary] stroke" (grade 1A evidence)

Consider switching your ASA patients to Aggrenox:

- 22.1% additional stroke protection over ASA (p=0.008)[3†§]
- 36.8% additional stroke protection over placebo (p<0.001)[3]
- Proven safety and tolerability profile[3††] (Most common adverse events vs. ASA alone and vs. placebo: headache 39.2%, 33.8%, 32.9%; nausea 16.0%, 12.7%, 14.1%.)
- One capsule B.I.D.[3]

The overall discontinuation rate for Aggrenox was 27.8%, 23.2% for ASA and 23.7% for placebo.[3]
Aggrenox is indicated for the prevention of stroke in patients who have had a previous stroke or transient ischemic attack (TIA).[3]
Aggrenox is contraindicated in patients with hypersensitivity to dipyridamole, ASA, or any of the other product components. Due to the ASA content, Aggrenox is also contraindicated in patients with known allergy to nonsteroidal anti-inflammatory drug products and in patients with the syndrome of asthma, rhinitis and nasal polyps.[3]
Due to the ASA component, Aggrenox should be avoided in patients with severe hepatic insufficiency or severe renal failure, used with caution in patients with inherited/acquired bleeding disorders or who consume three or more alcoholic drinks every day, and avoided in patients with a history of active peptic ulcer disease.
Aggrenox should not be used in pediatric patients or during the third trimester of pregnancy.[3]
Aggrenox has a vasodilatory effect and should be used with caution in patients with severe coronary artery disease (e.g., unstable angina or recently sustained myocardial infarction).[3]

* For every 1,000 patients treated for two years, Aggrenox prevented 58 strokes vs. only 29 for ASA, compared to placebo.[2,3]

† Percentage of patients experiencing a stroke within two years: Aggrenox 9.5%, ASA 12.5%, placebo 15.2%.[3]

§ Randomised, double-blind, placebo-controlled trial, 6602 patients with history of TIA or ischemic stroke, mean age 66.7 years, 58% male, 42% female.[3]

†† When headache occurred, it was particularly evident in the first month of therapy. 8.9% of patients discontinued due to headache, 66% of these discontinued within the first month.[3]

Full Product Monograph is available upon request.
®Aggrenox is a registered trademark of Boehringer Ingelheim (Canada) Ltd.

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Aggrenox®
ASA/Extended Release Dipyridamole
Helping to maximize stroke protection

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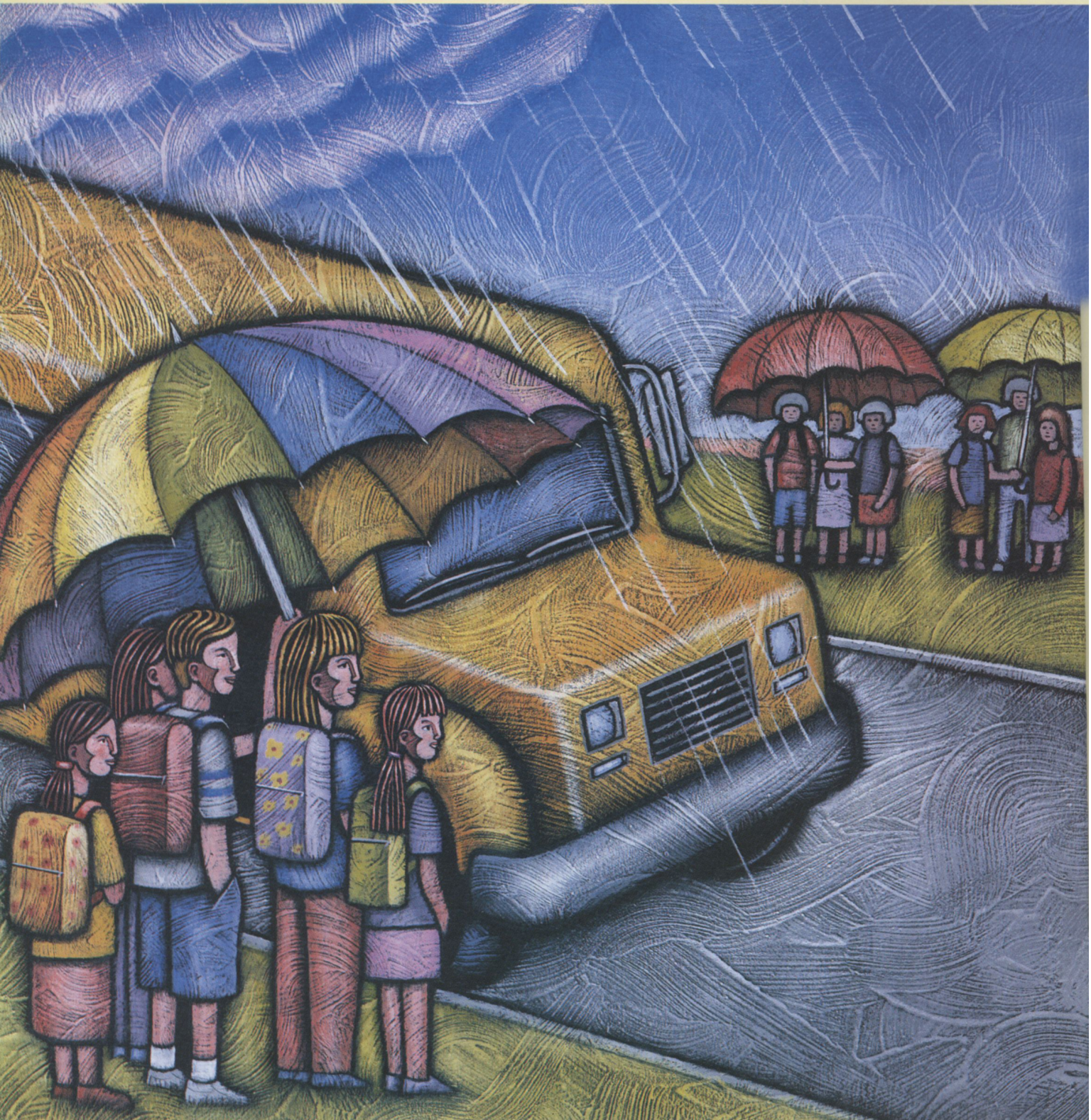
New in Lennox



*Refers to lamotrigine, gabapentin, vigabatrin, and topiramate, to be distinguished from standard AEDs.
†With the exception of atypical absence seizures.
‡Statistical significance not reported.
§**Rarely, serious skin rashes, including Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell syndrome), have been reported. Although the majority recover following drug withdrawal, some patients experience irreversible scarring and there have been rare cases of associated death.**[2]
¶Frequently reported adverse events were pharyngitis, fever, infection, and rash (p = not significant).[1]
**For detailed information about dosing in adult and pediatric patients with LGS, please refer to the full prescribing information for LAMICTAL.
Dosage of add-on LAMICTAL in Motte *et al*. and Mullens *et al*. studies ranged from 50 to 400 mg/day, after escalation.
DO NOT EXCEED the recommended initial dose and subsequent dose escalations of LAMICTAL. More rapid initial titration has been associated with an increased incidence of serious dermatological reactions.

Product Monograph available to health care professionals upon request.

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Gastaut Syndrome

Lamotrigine

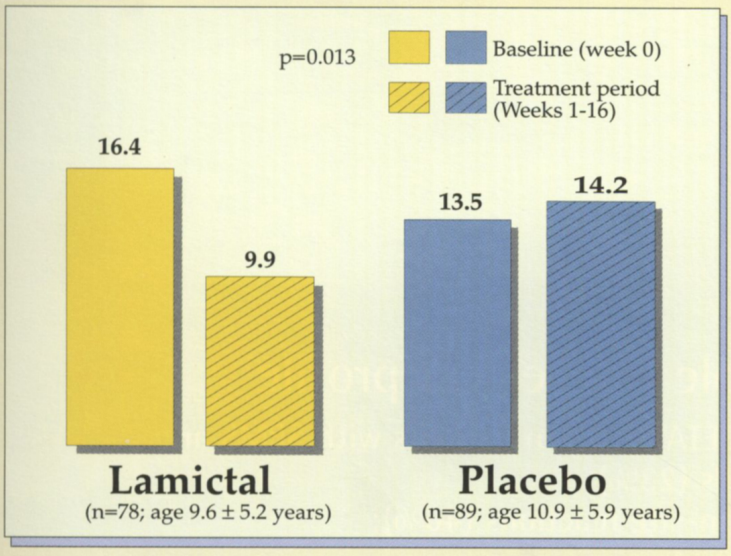
Lamictal®

LAMICTAL is the first and only of the newer* antiepileptic drugs (AED) indicated as adjunctive therapy for pediatric and adult patients with Lennox-Gastaut syndrome (LGS).[1] LAMICTAL is also the first and only of the newer* AEDs indicated for monotherapy after polytherapy in adults.

Significantly superior *control over the wide range of seizure types* associated with Lennox-Gastaut syndrome†

- Add-on LAMICTAL significantly reduced the number of all major seizures, all drop attacks, and all tonic-clonic seizures in patients with LGS.[1]

MEDIAN NUMBER OF ALL MAJOR SEIZURES/WEEK



A double-blind, randomised, placebo-controlled trial in patients from 3 to 25 years of age

Low CNS side-effect profile maintained in patients with Lennox-Gastaut syndrome aged 3-25

- Low withdrawal rate compared to placebo:‡[1,2] group taking LAMICTAL 3.8% (mostly due to rash§) vs. placebo group 7.8% (mostly due to deterioration of seizure control).

- No significant difference in the incidence of adverse events between LAMICTAL and placebo except for cold or viral illness (LAMICTAL 5% vs placebo 0%; p=0.05).¶[1]

Improved neurological function and cognitive skills[2,3]

- A greater proportion of LGS patients (age 3 to 25 years) treated with add-on LAMICTAL (n=79) vs add-on placebo (n=90) had a **clinically significant improvement in neurological findings** across the 16 week treatment period for: behaviour (30.4% vs. 14.4%); speech (11.4% vs. 2.2%); and non-verbal communication (11.4% vs. 7.8%).‡[3]

LAMICTAL offers superior control over the seizure types associated with LGS and a low CNS side-effect profile. You may also improve the neurological function and cognitive skills of your patients.[2,3] Add LAMICTAL** as soon as the diagnosis of LGS is suspected.[4]

GlaxoWellcome
Glaxo Wellcome Inc.

Lamotrigine

Lamictal®

For a Brighter Future

PMAC

PAAB CCPP

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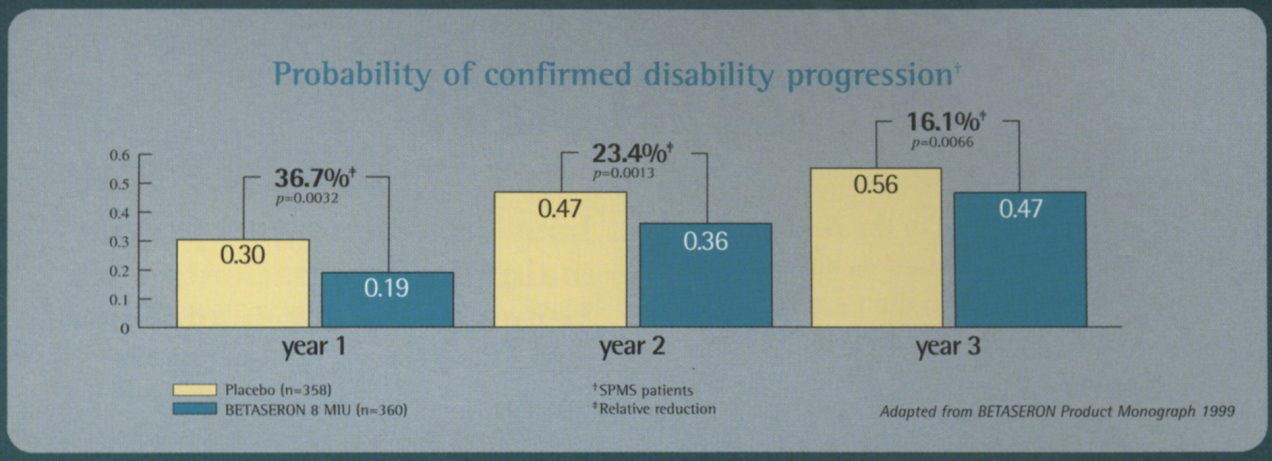
 For brief prescribing information see pages A-56, A-57, A-58, A-59

BETASERON delays disability progression*[1]



BETASERON reduces relapse rate in both relapsing-remitting[2] and secondary progressive MS[1]

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Delays Disability Progression*

Indicated for both RRMS and SPMS

In RRMS and SPMS

Pr BETASERON®

INTERFERON BETA-1b

From Onset Onwards

MULTIPLE SCLEROSIS PATHWAYS™ FOR CANADA

1 800 977-2770

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For brief prescribing information see pages A-43, A-44, A-45

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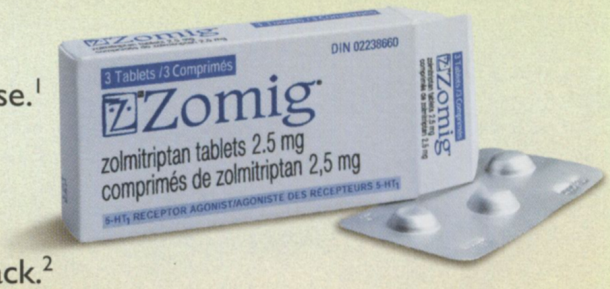
Turn the agony of migraine into the beauty of relief.

Zomig® provides consistent relief.

- Rapid relief within one hour.[1]
- Significant headache response* after a single 2.5 mg dose.[1]
- Consistent efficacy across multiple attacks.[2-4]
- Effective in a wide variety of migraine subtypes.[1†]
- Effective when taken at any time during a migraine attack.[2]
- Treats associated symptoms of photophobia, phonophobia and nausea.[1]
- Proven safety profile in over 5,500 patients treating more than 89,000 attacks.[5,6††]



*Improvement from severe or moderate headache to mild or no pain at two hours.

† Zomig® is indicated for the acute treatment of migraine with or without aura.

Zomig® is not intended for use prophylactically or in hemiplegic, basilar, or ophthalmoplegic migraine. Safety and efficacy have not been established for cluster headache, which is present in an older, predominantly male population.

†† The most common side effects reported with Zomig® compared to placebo were nausea (9% vs. 3.7%), head/face sensations (8.6% vs. 1.7%), dizziness (8.4% vs. 4%) and neck/throat/jaw sensations (7% vs. 3%).

Zomig® is contraindicated in patients with history, symptoms, or signs of ischemic cardiac, cerebrovascular or peripheral vascular syndromes, valvular heart disease or cardiac arrhythmias (especially tachycardias). In addition, patients with other significant underlying cardiovascular disease should not receive Zomig®. Zomig® is also contraindicated in patients with uncontrolled or severe hypertension.

Please see Product Monograph.

For more information about Zomig® please contact AstraZeneca Customer Relations by phone at 1-800-668-6000 or fax at (905) 896-4745.

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Zomig®
zolmitriptan tablets 2.5 mg

Consistent migraine relief.

AstraZeneca PMAB

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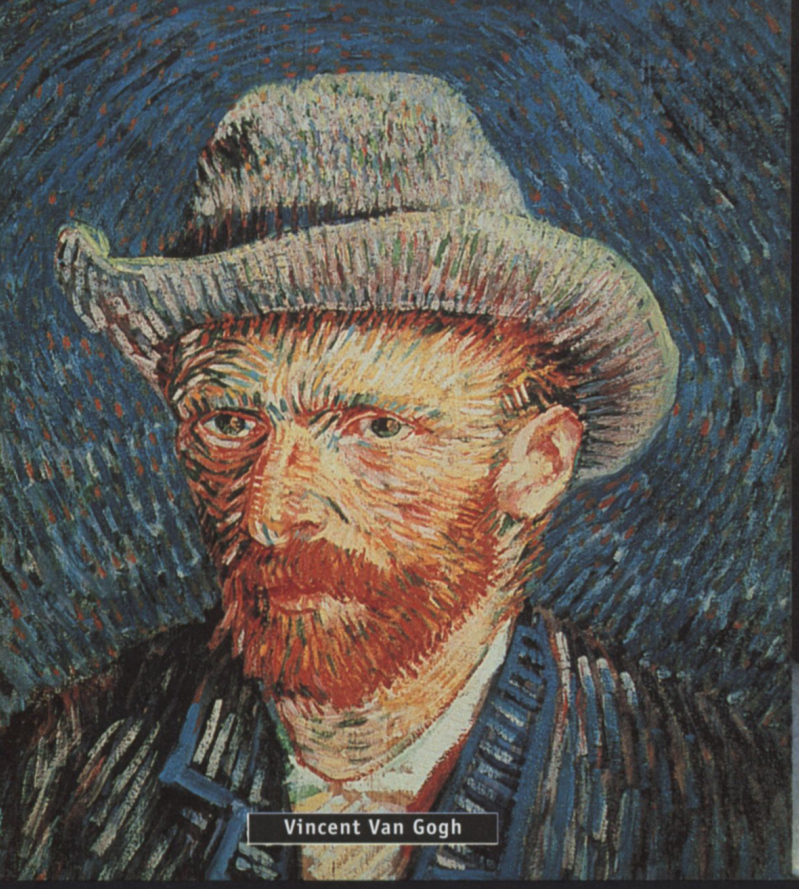
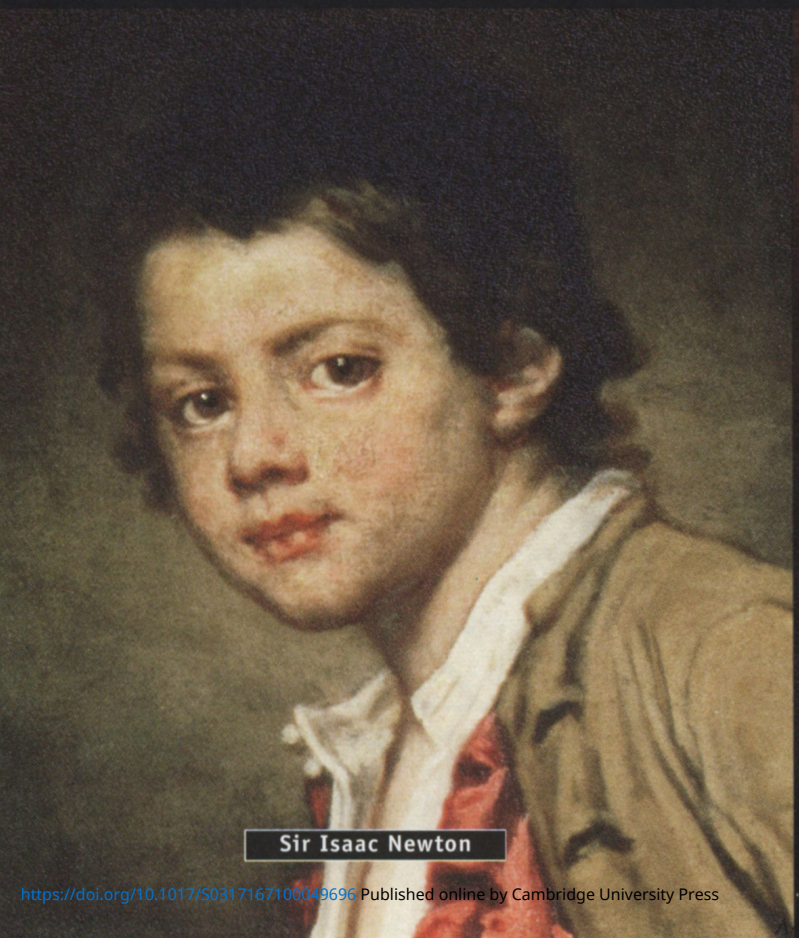
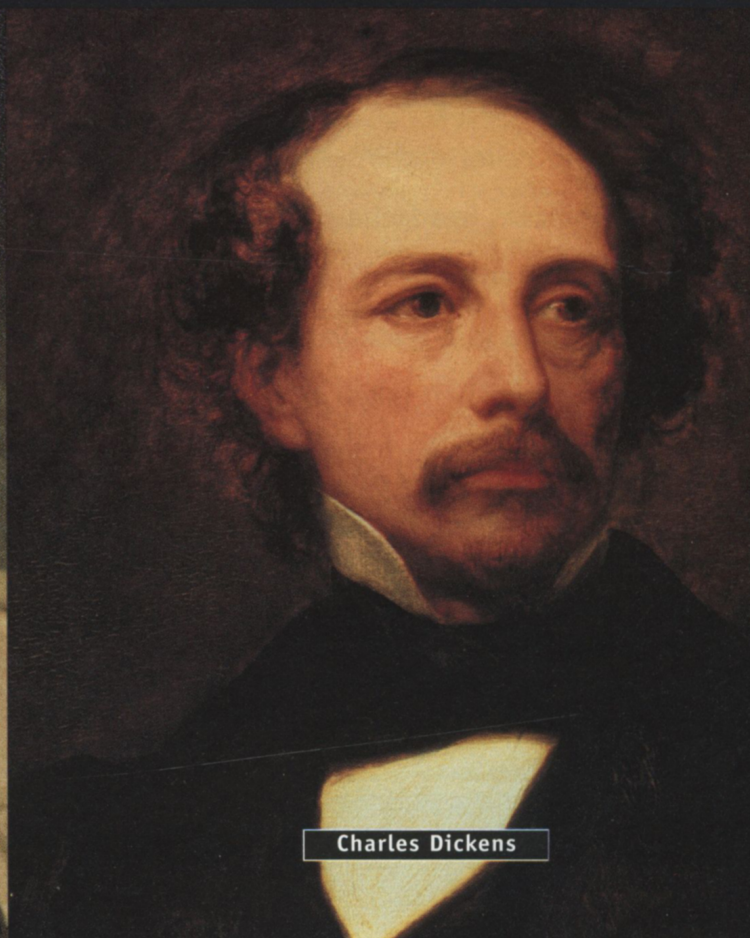


YESTERDAY, PEOPLE WITH EPILEPSY HAD TO BE EXTRAORDINARY TO SUCCEED.





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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.*[1]

† 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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For brief prescribing information see pages A-41, A-42

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AS IN MS, SOME THINGS ARE NOT ALWAYS OBVIOUS.

Danger can lurk behind the face of an apparently healthy MS patient.

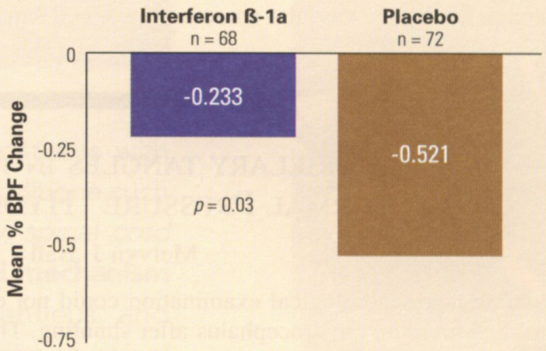
Progressive brain atrophy begins early in the course of MS and is likely irreversible.[1] Cognitive disturbances begin early in the MS process, but are often subtle and easily overlooked by patient and clinician alike.[2-4]

AVONEX® has shown a 55% reduction in brain atrophy progression.[5]

The use of AVONEX® can help patients with relapsing forms of MS maintain both physical AND mental function longer. In a clinical trial, patients treated with AVONEX® showed a 55% reduction in brain atrophy progression versus placebo, during the second year of treatment.*[5] AVONEX® is proven to slow the progression of physical disability - patients treated with AVONEX® showed a 37% reduction in the risk of disability progression and a 32% reduction in annual exacerbation rate over two years.†[6] AVONEX® also demonstrated a significant MRI effect showing an 89% reduction in gadolinium-enhanced lesions in patients with enhancement at baseline.◊[7]

Change in Brain Parenchymal Fraction[5]

(Adapted from Rudick et al.)



Change in brain parenchymal fraction (BPF) according to treatment arm in the interferon ß-1a clinical trial. Significantly less brain atrophy in interferon ß-1a patients during the second year.

Once-a-Week AVONEX® is generally well tolerated.[6]

The once-a-week intramuscular dosing regimen with AVONEX®, means few opportunities for injection-related side effects to disrupt patient's lifestyle.[6] The most common side effects associated with treatment are flu-like symptoms and usually resolve within 24 hours after injection.[6,8] Incidence of side effects decrease over time with continued treatment for most people.[8] Please see product monograph for important patient selection and monitoring information.

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

Helping people with relapsing forms of MS get on with their lives.

* It remains to be determined whether brain atrophy during the relapsing-remitting stage of MS will predict long-term disability progression better than clinical features in the majority of patients. Additional prospective studies are needed to determine the biologic factors associated with atrophy progression, the clinical significance of BPF change during the relapsing-remitting disease stage, and the impact and time course of therapeutic intervention.

† Kaplan-Meier estimate of percentage progressing at two years for placebo patients: 34.9% (n=143); AVONEX®-treated patients: 21.9% (n=158);(p=0.02). Placebo annual exacerbation rate: 0.90 (n=87); AVONEX® annual exacerbation rate: 0.61(n=85);(p=0.002).

◊ The exact relationship between MRI findings and clinical status is unknown (n=44).

AVONEX® is indicated for the treatment of relapsing forms of MS.

PAAB

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For brief prescribing information see pages A-61, A-62, A-63

25 Years Ago in the Canadian Journal of Neurological Sciences

The Possible Local Synthesis of Antibodies to Herpes Simplex Virus in Normal Cerebrospinal Fluid

Anthony Science Russell

SUMMARY: We have used the technique of antibody mediated cell dependent immune lysis to examine paired samples of serum and CSF for antibody to herpes simplex virus. The 40 patients studied had no inflammatory disease of the nervous system, yet 20 of the CSF specimens did have antiviral antibody. This is an extremely sensitive technique for the detection of at least one type of antiviral antibody and "*in vitro*" is a very effective way of killing virus infected cells. There is no correlation between the level of antiviral antibody in the CSF with total protein content, but the high CSF:serum antibody ratio in some subjects who are particularly susceptible to recurrent herpes infection raises the possibility that local stimulation and production of this antibody may occur.

Can. J. Neurol. Sci. 1976;4:219

A Theory of the Mechanism of Cerebral Vasospasm and its Reversal, the Role of Calcium and Cyclic AMP

Eric W. Peterson and Richard Leblanc

SUMMARY: It is proposed that the basic mechanism of vasospasm which sometimes follows subarachnoid hemorrhage is dependent on increased free intracellular calcium ion produced by spasmogens from closely applied extravasated blood. Relaxation of this spasm occurs when the intracellular cyclic AMP levels are raised, resulting in sequestration of calcium ion by the vascular smooth muscle cell sarcoplasmic reticulum.

Can. J. Neurol. Sci. 1976;4:223

Neurofibrillary tangles in the Dementia of "Normal Pressure" Hydrocephalus

Melvyn J. Ball

SUMMARY: Routine neuropathological examination could not explain the dramatic improvement exhibited by one patient with "normal pressure" hydrocephalus after shunting. The improved patient contrasted remarkably with the unchanged condition of four others also shunted successfully. The five brains were analyzed by quantitative morphometry to determine the degree of neurofibrillary tangle formation in mesial temporal neurons. The density of tangle-bearing nerve cells in the four unimproved cases was markedly greater than in age-matched control brains from nineteen normal subjects, and fell in the same range as that of eight dements with neuropathologically confirmed Alzheimer's disease. The density of the one who recovered was within normal limits.

The duration of dementia before shunting, and the total duration of dementia in these five patients rank in the same order as their degree of neurofibrillary formation. Furthermore, a positive linear correlation exists between the Tangle Indices and the total duration of dementia. The data suggest that early diagnosis may improve the chances of reversing the dementia of normal pressure hydrocephalus before histological alterations prove too severe.

Can. J. Neurol. Sci. 1976;4:227

Continued on page A-20

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Nouveau dans le syndr

*Lamotrigine, gabapentine, vigabatrine et topiramate (à distinguer des antiépileptiques standards).
†À l'exception des absences épileptiques atypiques.
‡Signification statistique non indiquée.
§**Dans de rares cas, des éruptions cutanées graves, y compris le syndrome de Stevens-Johnson et l'épidermolyse nécrosante suraiguë (syndrome de Lyell), ont été signalées. Bien que la plupart des patients se soient rétablis après le retrait du médicament, certains patients ont éprouvé des séquelles irréversibles et il y a eu de rares cas de décès associés.**
¶Les effets indésirables fréquemment signalés sont la pharyngite, la fièvre, les infections et les éruptions cutanées (p = non significatif).
Pour obtenir des précisions sur la posologie de LAMICTAL chez l'adulte ou chez l'enfant atteints du syndrome de Lennox-Gastaut, consulter les renseignements thérapeutiques détaillés sur ce produit. La posologie de LAMICTAL comme traitement d'appoint qui a été utilisée dans les études de Motte et al. et de Mullens et al. était de 50 à 400 mg par jour, après augmentation graduelle de la dose initiale. **NE PAS DÉPASSER la dose initiale de LAMICTAL ni l'augmentation posologique graduelle qui sont recommandées. Un ajustement plus rapide de la dose initiale a été associé à une fréquence accrue de réactions dermatologiques graves.

me de Lennox-Gastaut

lamotrigine

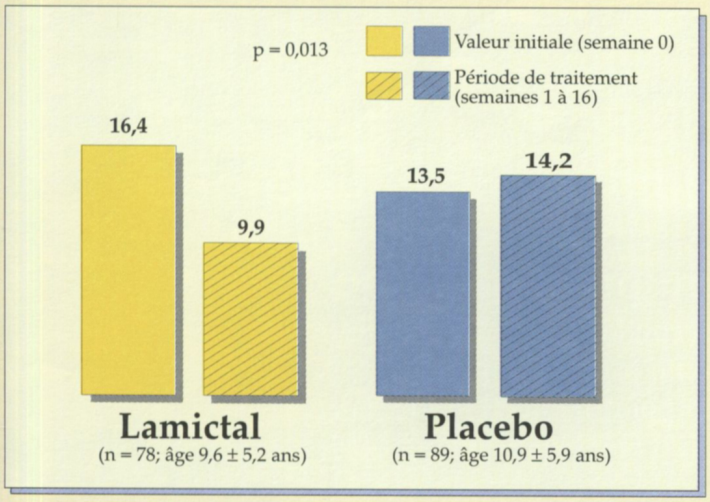
Lamictal®

LAMICTAL est le premier et le seul parmi les nouveaux antiépileptiques* qui soit indiqué comme traitement d'appoint chez les enfants et les adultes atteints du syndrome de Lennox-Gastaut (SLG)[1]. LAMICTAL est également le premier et le seul parmi les antiépileptiques récents* qui soit indiqué comme monothérapie après polythérapie chez l'adulte.

Une supériorité significative pour *maîtriser les divers types de crises* liées au syndrome de Lennox-Gastaut†

- L'adjonction de LAMICTAL réduit, de façon significative, le nombre de crises majeures, les effondrements épileptiques et les crises tonico-cloniques chez les patients atteints de SLG[1].

NOMBRE MÉDIAN
DES CRISES MAJEURES/SEMAINE



Essai à double insu, à répartition aléatoire et à contrôle placebo chez des patients de 3 à 25 ans

Maintien d'un *faible profil d'effets indésirables touchant le SNC* chez les patients de 3 à 25 ans atteints du syndrome de Lennox-Gastaut

- Faible taux d'abandons comparativement au placebo‡[1,2] : 3,8 % pour le groupe LAMICTAL (principalement reliés aux éruptions cutanées§) contre 7,8 % pour le groupe placebo (principalement reliés à une détérioration de la maîtrise des crises).
- Aucune différence significative dans la fréquence des effets indésirables entre LAMICTAL et le placebo, sauf pour le rhume ou des maladies virales (LAMICTAL, 5 % contre placebo, 0 %; p = 0,05)¶[1].

Amélioration de la fonction neurologique et des facultés cognitives[2,3]

- Une plus forte proportion de patients (de 3 à 25 ans) atteints de SLG, traités à l'aide de LAMICTAL comme traitement d'appoint (n = 79) c. un placebo d'appoint (n = 90), ont connu une **amélioration cliniquement significative des symptômes neurologiques** durant la période de traitement de 16 semaines : comportement (30,4 % c. 14,4 %), parole (11,4 % c. 2,2 %) et communication non verbale (11,4 % c. 7,8 %)‡[3].

LAMICTAL offre une plus grand maîtrise des divers types de crises liées au SLG, avec faible profil d'effets indésirables touchant le SNC. Vous pouvez aussi améliorer la fonction neurologique et les facultés cognitives de vos patients[2,3]. Ajoutez LAMICTAL** dès que l'on soupçonne un SLG[4].

GlaxoWellcome
Glaxo Wellcome Inc.

lamotrigine
Lamictal®
L'avenir en tête

ACIM
CCPP
PAAB

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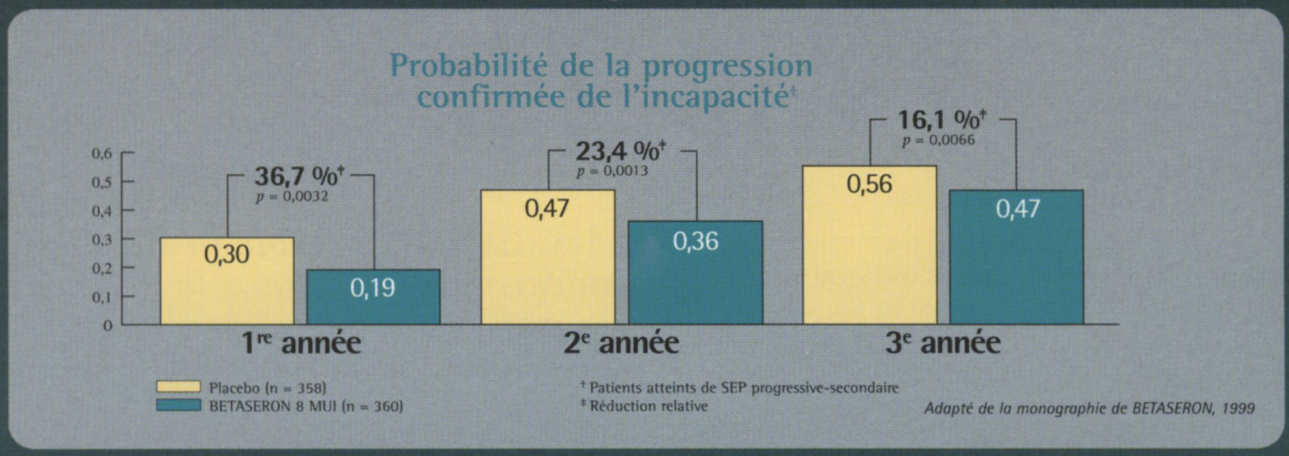
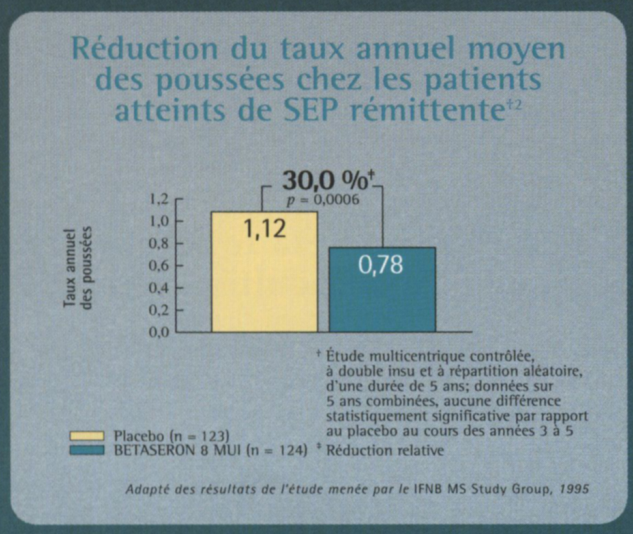
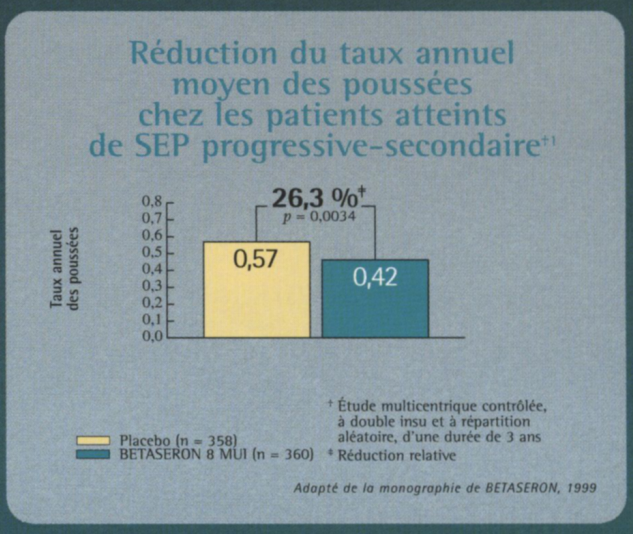
Pour documentation voir pages A-56, A-57, A-58, A-59

BETASERON retarde la progression de l'incapacité*[1]



BETASERON réduit le taux de poussées dans la SEP rémittente[2] et dans la SEP progressive-secondaire[1]

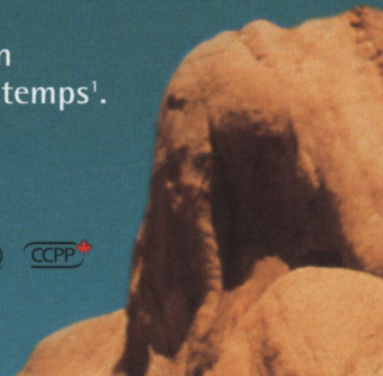




Effets indésirables pouvant être pris en charge[1]

Chez les patients atteints de SEP progressive-secondaire, les effets indésirables les plus fréquents de BETASERON sont : syndrome pseudo-grippal (61 %), fièvre (40 %), frissons (23 %), inflammation au point d'injection (48 %), réactions au point d'injection (46 %), myalgie (23 %), hypertonie (41 %) et éruption cutanée (20 %)[1].

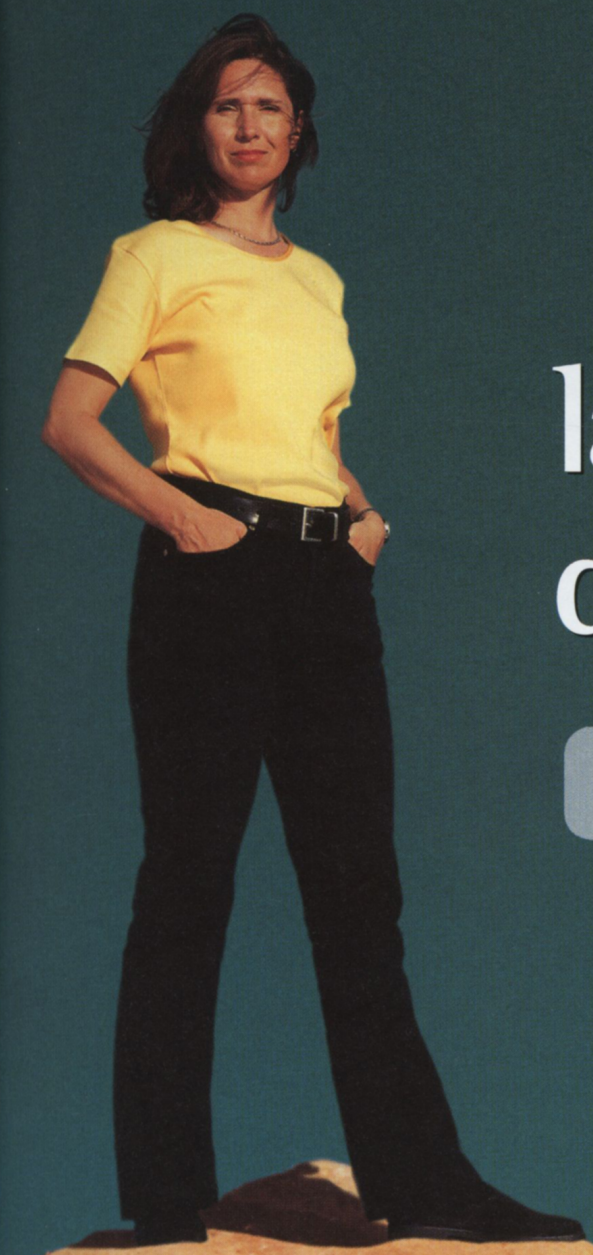
Les symptômes pseudo-grippaux et les réactions au point d'injection peuvent être pris en charge et diminuent de façon marquée avec le temps[1].



*Il a été démontré que BETASERON retarde la progression de l'incapacité chez les patients atteints de SEP progressive-secondaire[1].
L'efficacité et l'innocuité de BETASERON dans la SEP progressive-primaire n'ont pas été évaluées.
On ne dispose pas de données probantes sur l'efficacité du traitement dans la SEP rémittente au-delà de deux ans, ni de données sur l'efficacité et l'innocuité du traitement dans la SEP progressive-secondaire au-delà de trois ans.

VEUILLEZ CONSULTER LA MONOGRAPHIE DE PRODUIT POUR OBTENIR LA LISTE COMPLÈTE DES MISES EN GARDE ET DES PRÉCAUTIONS.
MONOGRAPHIE DE PRODUIT OFFERTE SUR DEMANDE AUX PROFESSIONNELS DE LA SANTÉ.

Membre R&D CCPP



Retarde la progression de l'incapacité*

Indiqué dans la SEP rémittente et la SEP progressive-secondaire

Dans la SEP rémittente et la SEP progressive-secondaire

Pr BETASERON®

INTERFÉRON BÊTA-1b

Dès le tout début

SCLÉROSE EN PLAQUES
ACCÈS MC
POUR LE CANADA

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Pour documentation voir pages A-43, A-44, A-45

25 Years Ago in the Canadian Journal of Neurological Sciences

Some Neurophysiological Effects of Cerebellar Stimulation in Man

Adrian R.M. Upton and Irving S. Cooper

SUMMARY: This paper presents the results of neurophysiological studies of the effects of cerebellar stimulation on H reflexes, late reflexes, blind reflexes, evoked potentials and EEG patterns in 18 human subjects (male 13, female 5, age 25.8±10.0, epileptic 9, cerebral palsy 9).

In addition to the effects of cerebellar stimulation on the H reflex studies on soleus we assessed V_1 and V_2 "late" responses (Upton et al, 1971), cortical somatosensory evoked potentials (SSEP) after median nerve stimulation, and visual evoked response (VER) after flash stimulation. Experiments were extended to assess recovery curves of all the potentials and we examined the effects of changes on the rate or voltage of cerebellar stimulation.

Cerebellar stimulation was inhibitory to all the responses except the visual evoked potentials. Serial studies in five patients produced consistent results. Preoperative and postoperative results were compared in two patients with no significant difference in the results in the absence of cerebellar stimulation.

Ipsilateral cerebellar stimulation (CS) had the greatest inhibitory effects on H, V_1 and V_2 responses in the arm and leg, whereas contralateral CS produced the greatest effects on cortical SSEPs. There was a greater bilateral effect on SSEPs and reflex responses after right CS than left CS and this may be the first indication of "dominance" in the cerebellar hemispheres. Cerebellar stimulation in patients on diphenylhydantoin produced minimal effects on SSEPs and this observation has led to further studies in patients taking diphenylhydantoin.

Recovery of amplitude of the reflex and cortical responses took eight to 30 minutes after one minute of cerebellar stimulation. Serial CS of one minute on and one minute off produced increasing inhibition of SSEPs and reflexes for up to five stimulations. Recovery after cessation of cerebellar stimulation was associated with rebound excitation in six patients, the rebound being noted in the amplitude of H reflexes and SSEPs as well as in the frequency of paroxysmal spike and wave discharges in the EEG.

The correlation of the results of such quantitative neurophysiological tests with clinical improvement may allow prediction of clinical results after cerebellar stimulation. These techniques have already been used to measure the threshold of stimulation and may allow optimal stimulation characteristics to be assessed. The prolonged neurophysiological effects of stimulation may allow the use of maximum effective intervals between optimal epochs of stimulation so that any cerebellar damage can be minimized.

Can. J. Neurol. Sci. 1976;4:237

The Reactivity of Canine Cerebral Arteries to O_2 and CO_2 in Vitro

P. Steinbok, M.J. Kendall, R.J. Clarke and S.J. Peerless

SUMMARY: The responses of canine middle cerebral arteries to change in pCO_2 and pO_2 were tested *in vitro*. It was found that there was no response to changes in pCO_2 from 38.1 mmHg to 26.6 mmHg, but there was some constriction of vessels with lowering of the pCO_2 below 26.6 mmHg and there was minimal dilatation of the vessels when the pCO_2 was increased from 38.1 mmHg to 87.2 mmHg. There was no response to changes in pO_2 from more than 500 mmHg to 59.6 mmHg, but when pO_2 was lowered below 50 mmHg there was a sudden, massive constriction of the arteries tested. It is postulated that this constriction is due to build-up of a substance (substances) during a period of hypoxia (pO_2 <50 mmHg). The significance of the results obtained are discussed.

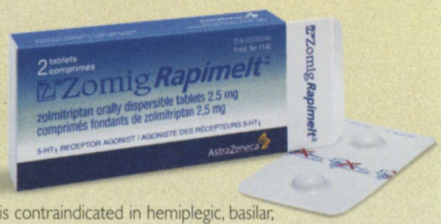
Can. J. Neurol. Sci. 1976;4:255

Introducing Zomig Rapimelt™

A new twist in migraine relief

- Can be taken anytime, anywhere.[1,2*]
- Excellent choice for patients experiencing nausea and unable to drink water.
- Dissolves on the tongue.
- Effective migraine relief† demonstrated as early as 30 minutes.[1]
- **Orange** flavoured, orally dispersible tablets.
- Side effect profile consistent with Zomig® 2.5 mg tablet.[2††]

Available in packages of 2 or 6 orally dispersible tablets 2.5 mg



* Zomig® is indicated for the acute treatment of migraine with or without aura. Zomig® is not intended for use prophylactically and is contraindicated in hemiplegic, basilar, or ophthalmoplegic migraine. Safety and efficacy have not been established for cluster headache, which is present in an older, predominantly male population.

†† The most common side effects reported with Zomig® compared to placebo were nausea (9% vs. 3.7%), head/face sensations (8.6% vs. 1.7%), dizziness (8.4% vs. 4%) and neck/throat/jaw sensations (7% vs. 3%).[2]

† Improvement in headache pain (a 1 point drop in headache intensity, 22% vs. 15%, p=0.0385). Double-blind, placebo-controlled, parallel group. Adapted from Purdy A et al.[1] n=470

Zomig® is contraindicated in patients with history, symptoms or signs of ischemic, cardiac, cerebrovascular or peripheral vascular syndromes, valvular heart disease or cardiac arrhythmias (especially tachycardias). In addition, patients with other significant underlying cardiovascular disease, cerebrovascular syndromes or peripheral vascular disease should not receive Zomig®. Zomig® is also contraindicated in patients with uncontrolled or severe hypertension.

Zomig® should not be used within 24 hours of treatment with another 5-HT_1 agonist, or an ergotamine-containing or ergot-type medication like dihydroergotamine or methysergide.

Concurrent administration of MAO inhibitors or use of zolmitriptan within 2 weeks of discontinuation of MAO inhibitor therapy is contraindicated.

AstraZeneca

Zomig Rapimelt™

zolmitriptan orally dispersible tablets 2.5 mg

Convenient migraine relief

PAAB Member R&D

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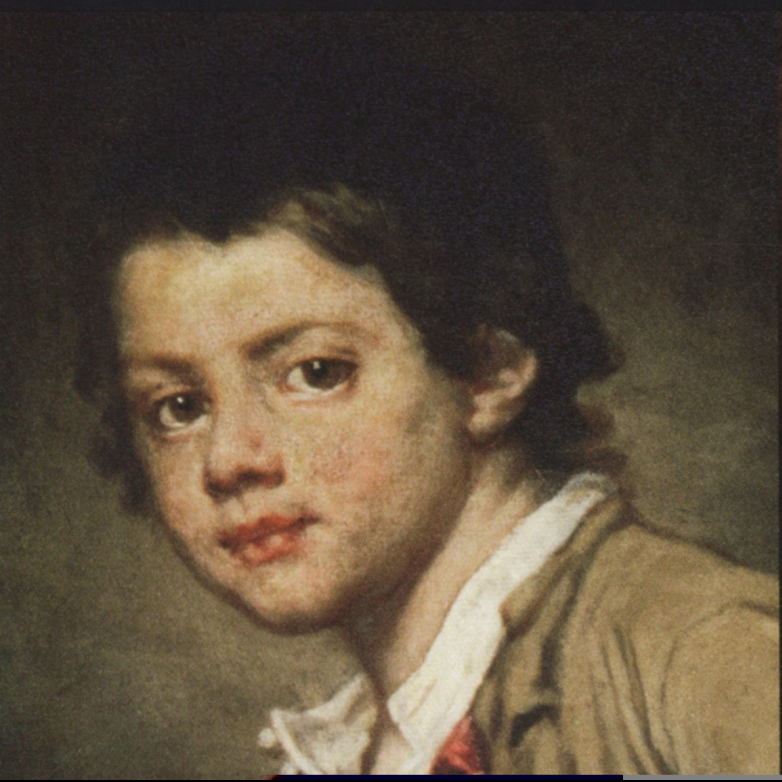
For brief prescribing information see pages A-47, A-48

Vincent Van Gogh

Jeanne d'Arc

AUPARAVANT, LES PERSONNES ÉPILEPTIQUES DEVAIENT SE MONTRER EXCEPTIONNELLES POUR RÉUSSIR.



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EFFICACE CONTRE UN GRAND NOMBRE DE TYPES DE CRISES.

- TOPAMAX est efficace contre les crises partielles initiales, les crises tonico-cloniques primaires généralisées et les crises associées au syndrome de Lennox-Gastaut[1]
- Des résultats souhaitables avec absence totale de crises chez 19 % des adultes† et 22 % des enfants‡ atteints de crises partielles initiales[2,3]

AUCUN SIGNE D'EFFETS SECONDAIRES CAPABLES DE MENACER LE PRONOSTIC VITAL.

- Comme pour la plupart des antiépileptiques, les effets secondaires le plus fréquemment signalés relèvent du SNC et sont généralement légers à modérés et de nature passagère[§1]

https://doi.org/10.1017/S0317167100049696

SINCE 1997, COPAXONE® HAS BEEN AVAILABLE TO HELP MEET YOUR NEEDS AND THOSE OF YOUR RRMS PATIENTS.

For the reduction of relapse frequency in ambulatory patients with relapsing-remitting multiple sclerosis...

COPAXONE® is an excellent choice for early treatment.

COPAXONE® has a side effect profile that compares to placebo and is an excellent choice to start with.

In clinical trials, only 8% of 844 patients discontinued treatment due to an adverse event.[1] The most commonly observed adverse events associated with the use of COPAXONE® in controlled clinical trials which occurred at a higher frequency than placebo were[1]:

Adverse Event	Non-interferon COPAXONE®[1]	Placebo
Injection Site Reactions†	2.4% - 66.4%	0.0% - 36.5%
Asthenia	64.8%	61.9%
Hypertonia	35.2%	29.4%
Vasodilatation	27.2%	11.1%
Back Pain	26.4%	22.2%
Chest Pain	26.4%	10.3%
Arthralgia	24.8%	17.5%
Nausea	23.2%	17.5%
Pain (Neck)	12.8%	7.1%
Infection (Vaginal Moniliasis)	12.8%	7.1%
Agitation (Anxiety)	5.6%	3.2%

† Depending on reaction.

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COPAXONE® is an excellent choice for the long-term (2 years), too.

COPAXONE® is supported by long-term evidence of up to 2 years and efficacy that's been demonstrated in 6 clinical studies.[2-7] A correlation between a reduction in attack frequency and a decreased risk of future disability remains to be established. The safety and efficacy of COPAXONE® beyond two years have not been adequately studied in placebo-controlled trials.

COPAXONE® is an antigenic substance and thus, it is possible detrimental host responses can occur with its use.

Only COPAXONE® has Shared Solutions™.

Shared Solutions™ helps support patients through early treatment and in the long-term (January 1999-March 2000 data).†† With Shared Solutions™, 93% of COPAXONE® patients stayed on therapy.[8]

††n=1377

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(glatiramer acetate for injection)

EFFICACY BACKED BY EVIDENCE

Product Monograph available on request. PAAB

TEVA MARION™
Dedicated to enhancing the management of multiple sclerosis.

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For brief prescribing information see pages A-49, A-50

Neurology / neurosurgery physician or resident?

If so, you should become a member of one of these:

- **Canadian Neurological Society**
- **Canadian Neurosurgical Society**
- **Canadian Society of Clinical Neurophysiologists**
- **Canadian Association of Child Neurologists**

Membership Benefits

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- The Canadian Journal of Neurological Sciences
- Newsletters and Communications
- Manpower Information
- Education Opportunities
- Professional Development Initiatives
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Further Information

For further information, or to join one of the CCNS societies, please call the secretariat office or complete the form on the website www.ccns.org.

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Tel: (403) 229-9544; Fax: (403) 229-1661; E-mail: brains@ccns.org; Web: www.ccns.org

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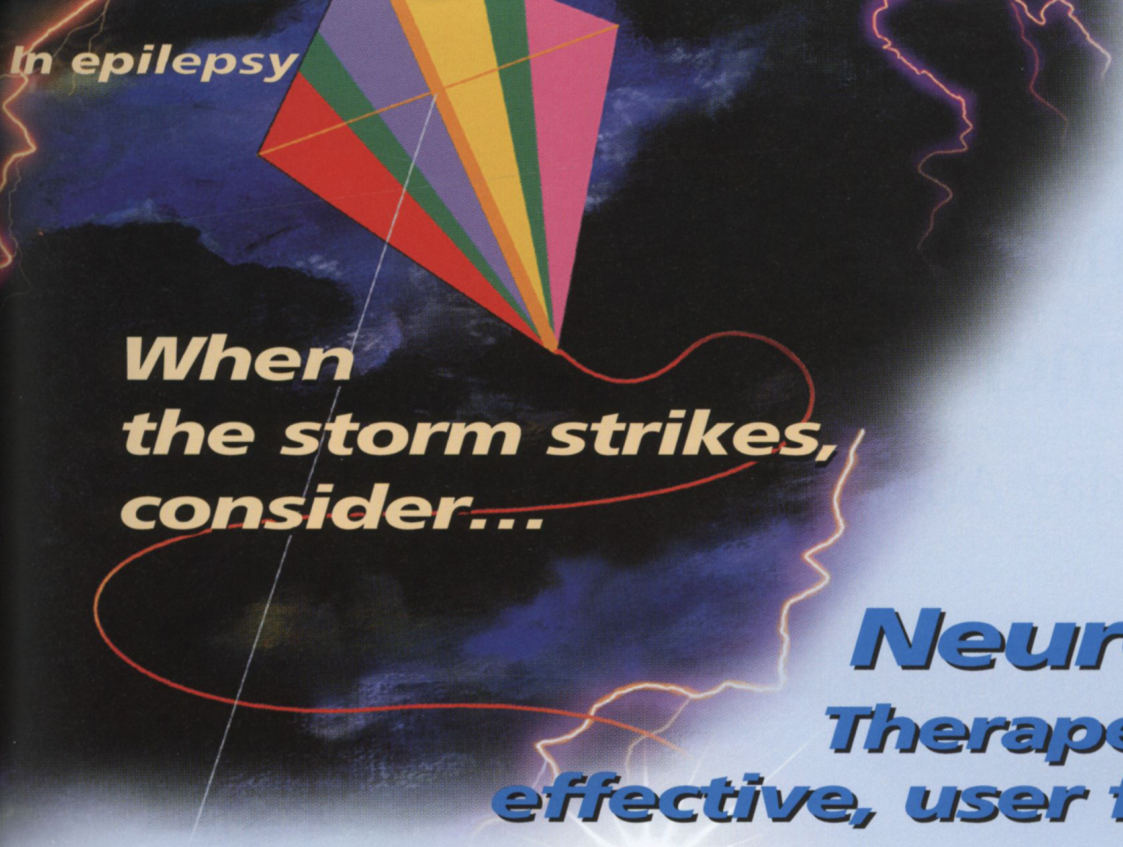

When the storm strikes, consider...

Neurontin: Therapeutically effective, user friendly†

Uncomplicated pharmacokinetics profile‡[1,2]

"...[Neurontin] is remarkably user friendly in that it is not metabolized by the liver, is not protein bound, is excreted unchanged in the urine... has no significant drug interactions."[2]

Generally well-tolerated§[1,3]

- Safety and tolerability of gabapentin were assessed as excellent or good for 78.5% of patients receiving gabapentin as adjunctive therapy (n=281)*[3]

An excellent drug interaction profile[1,4]

- No cytochrome P450 drug interactions reported[1]
- No clinically significant interactions with other AEDs or other frequently used concomitant medications[1,4]

Sample of commonly used medications	Interactions with Neurontin[1,4]
Ibuprofen	No interaction noted
Morphine	
Carbamazepine	
Amitriptyline	
Lovastatin	
Antacids	Some††

Dose responsive efficacy¥[5]

- Patients receiving increased doses of up to 3,600 mg/day reported greater benefits (n=1,055)[5]

NEURONTIN* (gabapentin)
USER FRIENDLY EFFICACY

Please refer to full prescribing information.

† Indicated for use in adjunctive epilepsy management in patients not satisfactorily controlled by conventional therapy.
‡ Clinical significance unknown.
§ The most commonly observed adverse events not seen at an equivalent frequency in placebo-treated patients, were somnolence, dizziness, ataxia, fatigue, nystagmus and tremor.
* 16-week, open-label, multi-centre assessement of the efficacy, safety and tolerability of gabapentin (900-3600 mg/day) as adjunctive therapy in patients with inadequately controlled partial seizures.[3,5]
¥ Data from clinical trials suggest that doses higher than 1200 mg/day may have increased efficacy in some patients, up to a maximum daily recommended dose of 2400 mg; however, higher doses may also increase the incidence of adverse events. The usual effective maintenance dose is 900 to 1200 mg/day.
†† Co-administration not recommended with aluminum and magnesium based antacids.

Reference: **1.** Neurontin Product Monograph, July 2000. **2.** Sandler M. New Options in epilepsy. *Patient Care Canada* July 1995: vol 6(6):49-55. **3.** McLean MJ *et al*. Safety and Tolerability of Gabapentin as Adjunctive Therapy in a Large, Multicentre Study. *Epilepsia* 1999;40:965–972. **4.** Compendium of Pharmaceuticals and Specialties, Thirty-fourth edition, 1999. **5.** Morrell MJ. Dosing to Efficacy and Perspectives on Seizure Control: Epilepsy: STEPS Trial. *Epilepsia* 1999.

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PAAB Member R&D

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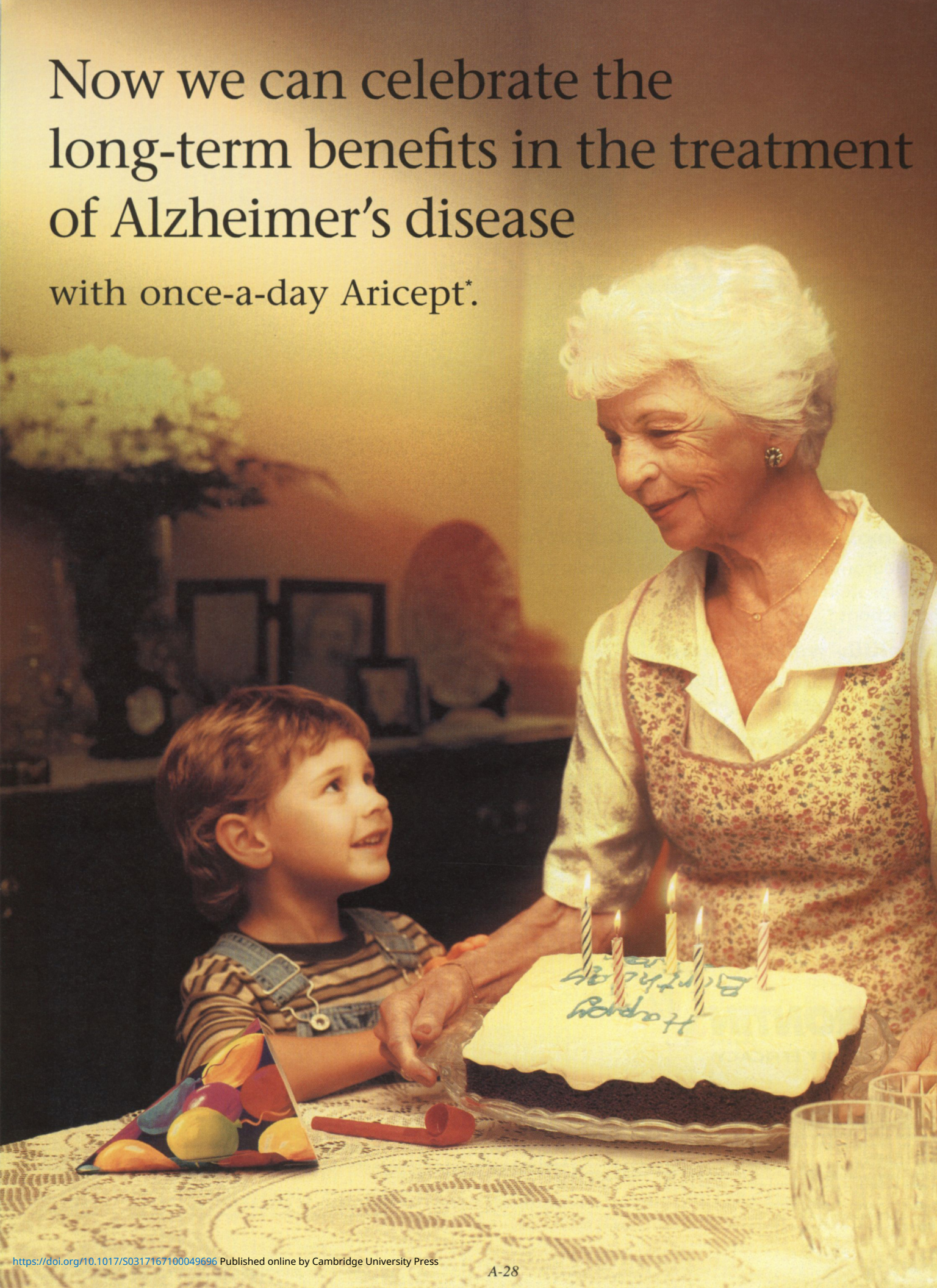

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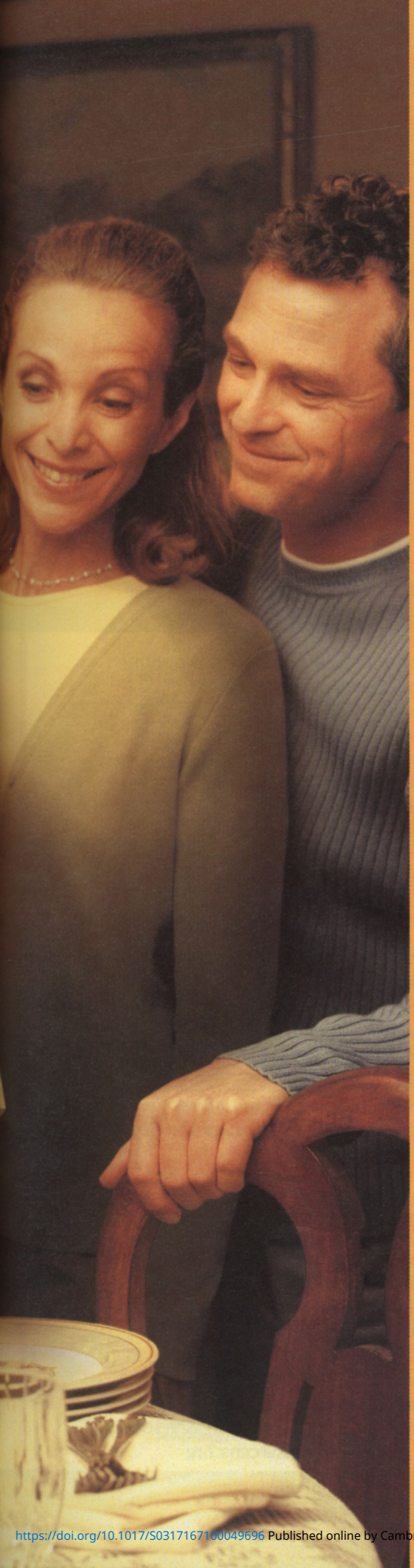

Celebrate another birthday, another holiday, another family gathering. Because Aricept* has been shown to result in improvement or stabilization in 80% of Alzheimer's disease patients over six months of treatment[1‡] and our new long-term data is even more cause for making Aricept* your standard of care.[2]

After one year, placebo-controlled studies demonstrated that Aricept*-treated patients showed significantly less decline in their cognition, global functioning and Activities of Daily Living.[3,4§¶]

After almost 2 years, Aricept*-treated patients showed significantly less decline in their cognition and global functioning in comparison to data expected from untreated patients.[5††]

After 3 years, Aricept*-treated patients continued to show treatment benefits on cognition and global functioning compared to data expected from untreated patients.[6‡‡]

Aricept* has demonstrated long-term safety and tolerability profiles.[3-6] With appropriate dose escalation, 10 mg/day dose, 5 mg/day dose and placebo were shown to have comparable adverse events.[1†]

With Aricept*, patients may now be able to maintain their autonomy—for a longer time. Now that's cause for celebration.

Aricept* does not change the underlying course of the disease. Aricept* is indicated for the symptomatic treatment of patients with mild-to-moderate dementia of the Alzheimer's type.

† Most common adverse clinical events with Aricept*: diarrhea, nausea, insomnia, fatigue, vomiting, muscle cramps and anorexia. These events are usually mild and transient, resolving with continued Aricept* treatment without need for dose modification.

‡ In a 24-week, double-blind, placebo-controlled study, 473 mild-to-moderate AD patients were randomized to receive Aricept* 5 mg/day, 10 mg/day or placebo. The mean difference for Aricept*-treated patients (10 mg/day) vs. placebo was –2.87±0.63 (p<0.0001) units in ADAS-cog, 0.47±0.11 (p<0.0001) units in CIBIC-plus, and 0.59±0.17 (p=0.0007) units in CDR-SB.

§ In a 52-week, multicentre, double-blind, placebo-controlled study, 286 mild-to-moderate AD patients were randomized to receive Aricept* 5 mg/day for 28 days, followed by 10 mg/day, as per clinician's judgement, or placebo. At study endpoint, significant treatment differences were observed in MMSE in Aricept*-treated patients with mild AD (1.50; p=0.049) and moderate AD (2.11; p=0.002).

¶ In a 54-week, multicentre, double-blind, placebo-controlled study, 431 mild-to-moderate AD patients were randomized to receive Aricept* 5 mg/day for 28 days, followed by 10 mg/day, or placebo. At study endpoint, significant differences were observed in favour of Aricept* in IADL and ADL (p=0.001 and 0.007), and MMSE (1.21; p=0.0005). CDR-SB was also improved.

†† In an interim analysis (at 98 weeks of treatment) of a 192-week, multicentre, non-randomized, open-label extension study in which 133 mild-to-moderate AD patients continued to receive Aricept* (up to 10 mg/day) after a 14-week, double-blind, placebo-controlled study. Differences with placebo were observed in cognitive and global functioning as measured by the ADAS-cog and CDR-SB.

‡‡ In a 162-week, multicentre, open-label extension study, 579 patients who had previously completed a randomized, double-blind, placebo-controlled study (n=818) with Aricept* were treated with Aricept* 5 mg which could be increased to 10 mg between weeks 6 and 24, as per clinician's judgement. At study endpoint, ADAS-cog declined 15.57 points (95% CI, 12,19.2) vs. the estimated decline of 6-12 points per year in untreated patients.

Product Monograph available upon request.

Now on several provincial formularies.§§

Once-a-day

Aricept*

donepezil HCl 5 & 10 mg tablets

Hope for a brighter tomorrow

* TM Eisai Co. Ltd., Tokyo, Japan
Pfizer Canada Inc., licensee

PAAB Member R&D

Pfizer CNS

Life is our life's work

§§ In Saskatchewan, Quebec, Alberta, Manitoba and Ontario. Please see individual formularies for special-, exceptional-, and limited-use drug status. For more information on coverage criteria, please call 1-800-510-6141.

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CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

CONGRÈS CANADIEN DES SCIENCES NEUROLOGIQUES

The Canadian Congress of Neurological Sciences is a non-profit organization dedicated to the advancement of knowledge, patient care, and collegiality among health care professionals and research scientists working in all branches of neurological sciences.

The Canadian Congress of Neurological Sciences (CCNS) is an affiliation of national societies for neurology, neurosurgery, and related disciplines which share a common interest in the functions and disorders of the human nervous system and which work together to achieve the following goals:

- To improve the well being of persons suffering from disorders of the nervous system.
- To provide a national forum for communication of information regarding disorders of the nervous system.
- To provide educational programs to meet the continuing professional development needs of the members of the constituent societies.
- To encourage fundamental and applied research aimed at advancing knowledge related to the functions of the nervous system and its disorders.
- To work with other organizations to promote increased public awareness and understanding of neurologic disorders.

Constituent Societies

The Canadian Congress of Neurological Sciences is comprised of four societies:

- Canadian Neurological Society
- Canadian Neurosurgical Society
- Canadian Society of Clinical Neurophysiologists
- Canadian Association of Child Neurologists

For further information contact: The Canadian Congress of Neurological Sciences, or see the web site www.ccns.org

Activities

The Canadian Congress of Neurological Sciences has its office in Calgary. The CCNS acts as a secretariat to the societies and undertakes many other activities on behalf of the members.

- CME Programs
- National and international event planning
- Professional Development projects
- Fellowship and Research Proposals
- Needs Assessment
- Exam Management
- Practice Guidelines Development
- Manpower Surveys
- Newsletter and Communications
- MOCOMP Assessment
- Promotion

Membership Benefits

- Annual Membership Directory
- The Canadian Journal of Neurological Sciences
- Newsletters and Communications
- Manpower information
- Education Opportunities
- Professional Development Initiatives
- Information and Services through the Secretariat
- Advocacy

Further Information

For further information, or to join one of the CCNS societies, please call the secretariat office or complete the form on the website www.ccns.org.

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Calgary, AB T2H 2K6 Canada
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E-mail: brains@ccns.org
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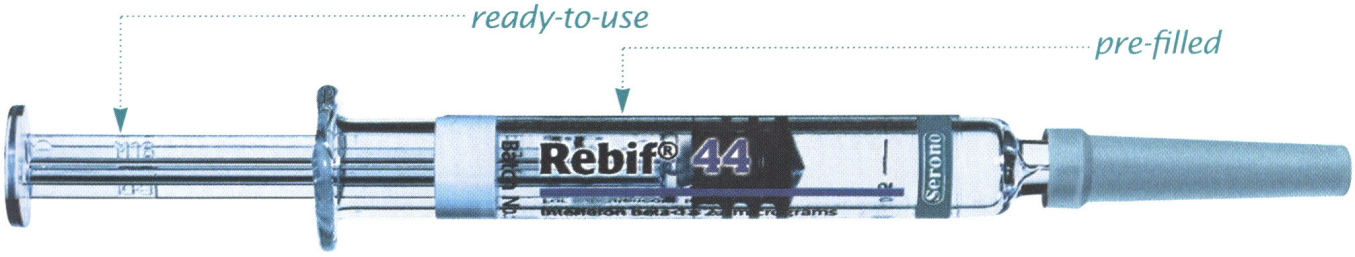
Rebif®. Dose-dependent Efficacy in Relapsing MS[1]*.

Pr Rebif®

Interferon beta-1a



The most common reported adverse events are injection-site reactions and flu-like symptoms – e.g., asthenia, pyrexia, chills, arthralgia, myalgia, and headache. These tend to decrease in frequency and severity with continued treatment. Please see product monograph for full prescribing information. Evidence of safety and efficacy derived from 2-year data only.

* 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.

REFERENCES:

[1] PRISMS (Prevention of Relapses and Disability by Interferon ß-1a Subcutaneously in Multiple Sclerosis) Study Group (1998). Randomised double-blind placebo-controlled study of interferon ß-1a in relapsing/remitting multiple sclerosis. Lancet 352:1498-1504

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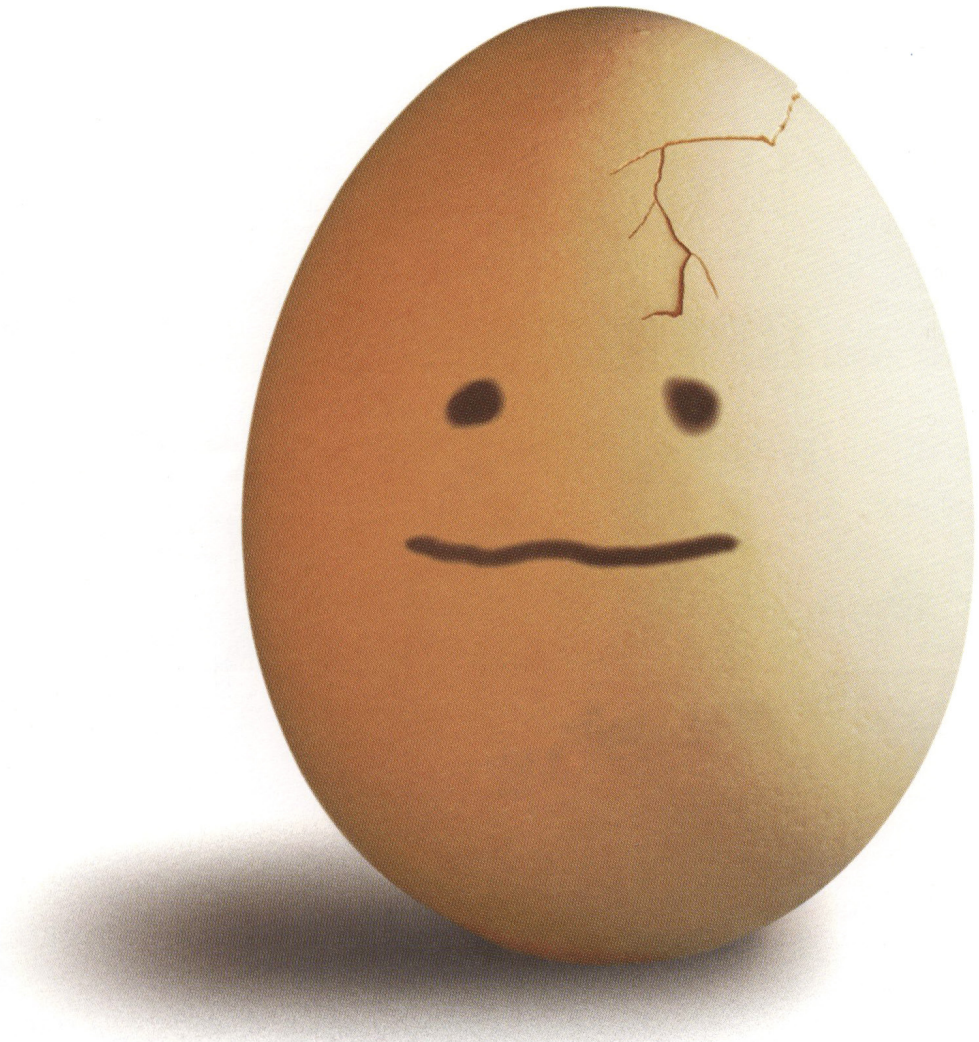
Are you using ASA alone for the prevention of a second stroke?



"Every patient who has experienced an atherothrombotic … stroke or TIA and has no contraindication should receive an antiplatelet agent regularly …"

- Sixth ACCP Consensus Conference on Antithrombotic Therapy[1]

Reassess your options...

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