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

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SI Current Issues in the Drug Treatment of Epilepsy

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

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\*Consulter les mises en garde figurant à la monographie avant de prescrire.

Permet d'atteindre et de maintenir une bonne maîtrise des crises tout en offrant une faible incidence d'effets indésirables liés aux concentrations4.



40 CBZ Ordinaire

Tegretol ordinaire et de Tegretol CR chez les enfants (n=25).3

Concentrations plasmatiques diurnes moyennnes de

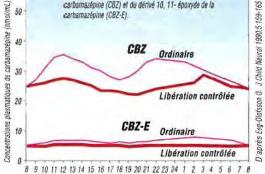
carbamazépine (CBZ) et du dérivé 10, 11- époxyde de la

Courbes des concentrations plasmatiques diurnes de

carbamazépine (CBZ-E)

60

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- Pr Tegretol CR vs Pr Tegretol ordinaire
- Efficacité et tolérabilité équivalentes ou améliorées 6
- Peut réduire considérablement la fréquence des crises
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# For Control Over a Wide Range of Seizure Types, with a Low CNS Side-Effect Profile

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## GENERALLY BETTER TOLERATED<sup>+</sup>

Pooled data from three monotherapy trials show that withdrawals due to

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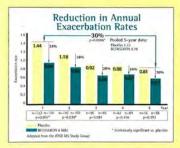
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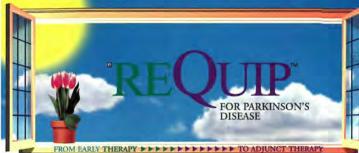
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- No cases of injection site necrosis have been reported for patients on AVONEX<sup>155</sup> therapy.<sup>4</sup>
- Please see product monograph for important patient selection and monitoring information.

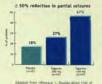


P=0,041; Placebo median ratio 0.50, N=44: Avonex median ratio 0.11, N=44. The exact relationship between MRI findings and clinical status is unknown

## NEW IN EPILEPSY. NOW ON B.C., ALBERTA, SASKATCHEWAI



### ONCE IT TOOK EXCEPTIONAL EFFORT OR EXTRAORDINAR LUCKILY, YOUR PATIENTS CAN NO



#### Improved control over a wide range of seizure types

- . TOPAMAX is indicated as adjunctive therapy for the management of patients with epilepsy who are not satisfactorily controlled with conventional therapy. There is limited information on the use of TOPAMAX in monotherapy at this time.
- High responder rate: 27%(200mg/day, n=45) and 47% (400mg/day, n=45) of patients experienced ≥ 50% reduction in partial seizures(16 week study)1
- · Effective control for patients with secondarily generalized tonic-clonic seizures: 36% of patients experienced a 100% reduction (200-600 mg, n=42, 16 week study)

IOPAMAX build, as adjunctive these of the with refractory

. Unique three-way mechanism of action(Na+ channel blockade, GABA potentiation, glutamate antagonism)2

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## IOVA SCOTIA & QUEBEC FORMULARIES.





## ALENT FOR PEOPLE WITH EPILEPSY TO SUCCEED. NJOY LESS TAXING ALTERNATIVES.

- · Generally well tolerated: Discontinuations due to adverse events were 10.6% at 200-400 mg/day compared to 5.8% in the placebo group (this appeared to increase at dosages above 400 mg/day)?
- · No evidence of serious rash or aplastic anemia?
- Dosage adjustments to primary therapy are generally not required; patients on phenytoin showing clinical signs or symptoms of toxicity should have phenytoin levels monitored"
- Convenient BID dosing

16. with other AEDs, please see prescribing information for complete information on drug interaction A 1.5%(nc) 1715) incidence or kindney stowns have been reported. To even study(or-1200), 43%(15 or ill go Tapiletest retext to controls thesespine "formar adequate hydraction and novid concomitant use with other cathenic ashydrage linkbilters." Findemark Orazon Ortho Inc. 1907

https://doi.org/10.1017/S0317167100034259 Published online by Cambridge University Press -

#### Favourable side effect profile (the most common are CNS related)

		TOPAHAX 200-400 mg (n+113)	PLACEBO (n-216)
-	Somolence	30.1	9,7
	Dizziness	28,3	15.3.
	Ataxia	21.2	6,2
	Psychomotor slowing	16.8	2.5
	Speech disorders	16.8	2.3
	Nervousness	15.9	7.4
	Nystagmus	15.0	9,3
	Paresthesia	15.0	- 4,6



Helping patients make more of their lives

## 25 Years Ago in the Canadian Journal of Neurological Sciences

HL-A FREQUENCIES IN PATIENTS WITH MULTIPLE SCLEROSIS

D. W. Paty, H. Mervart, B. Campling, C.G. Rand, C. R. Stiller

SUMMARY: The histocompatibility antigens (HL-A) have been determined in 100 multiple sclerosis (M.S.) patients and 143 randomiy selected controls. In the M.S. group there was a statistically significant increase in the frequeevy of HL-A 7 and w18 with an insignificant increase in HL-A 3. The variance from normal HL-A patterns in the M.S. population may play some role in establishing the substrate for this disease. Studies in experimental animals have shown that susceptibility to autoimmune disease and to virus infaction is linked to the major histocompatibility locus. This has interesting implications for both the "slow virus" and the "autoimmune" theories of the etiology of multiple sclerosis.

Can. J. Neurol. Sci. 1974; 4-211

#### SUPPRESSIVE EFFECTS OF VARIOUS AMINO ACIDS AGAINST OUABAIN-INDUCED SEIZURES IN RATS

Y. Tsukada, N. Inque, J. Donaldson A. Barbeau

SUMMARY: The suppressive effect of various amino acids against ouabain-induced seizures was investigated in young formle rats. The unitine acids were injected in the left lateral verticite 10 minutes prior to the intraventivular administration of Sug. of ouabain. Animals receiving 1.9 x 10-1 M solutions of hypotaurine and of B-alanine were almost completely protected from the ouabain seizures. Administration of L-alanine and of glycine was also effective, although routing and leaping seizures still occurred to some catent. Betain reduced only clonic-tonic and whole body Reaton and extension seizures. In contrast, L-proline exclusively suppressed clonic-tonic and focal clonic seizures. Rats injected with institution acid showed increases in incidence of running and leaping seizures while 1-arginine in high concentrations caused aggravation in clonic-tonic seizures. The EDSO of hypotaurine was 10.11 x 10-2 M for running seizures and 4.63 x 10-2 M for clonic seizures; However, hypotaurine was 14.01 x 10-2 M for running seizures and 4.63 x 10-2 M for clonic-tonic seizures. However, hypotaurine was 14.01 x 10-2 M for running seizures and 4.63 x 10-2 M for clonic-tonic seizures. However, hypotaurine and B-alanine, the inost effective compounds tested in the present studies, provided less protection than turnine proviously examined by us under similar conditions (Zumi et al., 1973)

Can. J. Neurol. Sci. 1974; 4:214

#### ELECTRICAL STIMULATION OF THE HUMAN VISUAL CORTEX Preliminary Report

Andrew Talalla, Leo Bullara, Robert Pudenz

SUMMARY: A feasibility study for the development of a human visual prosthesis has led several workers to observe the effects of electrical simulation of the human visual cortex. Experience with such stimulations of three normal-sighted patients is reported. The results confirm some of the findings of other workers, but do not show that multiple phosphenes were experienced by our patients, using strictly limited parameters of stimulation.

Can. J. Neurol. Sci. 1974; 4:236

IN THE TREATMENT OF ALZHEIMER'S DISEASE

Once-a-day Aricept<sup>•</sup> improves patient function:

For a more *active* day, a *brighter* tomorrow.

The loss of function that comes with Alzheimer's disease has a devastating effect on everyone involved: patient, caregiver and family.<sup>4</sup> Once-a-day Aricept' enhances cognition and improves patient function.<sup>4+</sup> Once-a-day Aricept' (10 mg o.d.) has been shown to significantly improve complex Activities of Daily Living (ADL).<sup>4</sup> A recent Canadian economic evaluation predicts that improvement in patient outcome will result in an overall healthcare cost saving.<sup>4</sup> And once-a-day Aricept' has proven efficacy, dosing simplicity<sup>4</sup> and tolerability<sup>4</sup> in over 54 million patient days of therapy worldwide.<sup>5</sup>

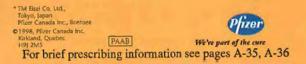
Once-a-day Aricept'. To help your Alzheimer's patients enjoy more active days, and look forward to a brighter tomorrow.

Adverget is indicated for the symptomatic iterating of patients with mild to moderate Alzheimer's disease. Aricept' has not been studied in controlled clinical traits for longer than 6 months. Cognition measures by ADArceg and MMSE Franction measured by CIBIC plus. The most common ider effects observed with Aricept' include diarrhea, mucle cranps, nauses and insomnia; these effects are usually mild and irransient. probying with common diarrhead and an analyze of the second sec

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Hope for a brighter tomorrow



# If only the severity of migraines could be measured...

4

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MIGRAINE SEVERITY METER

https://doi.org/10.1017/S0317167100034219 Published online by Cambridge University Press

# New Amerge from Glaxo Wellcome

A highly selective 5-HT<sub>1</sub> receptor agonist for moderate to severe migraines'

# **Highly Tolerable**

- Overall incidence of adverse events in controlled clinical trials after treatment with AMERGE was similar to placebo1-3 (31% AMERGE 2.5 mg vs. 32% placebo)<sup>2</sup>
- Chest and neck sensations characteristic of the 5-HT<sub>1</sub> agonist class reported in 1.2 - 2.1% of patients1+#
- Tolerability maintained regardless of number of attacks treated<sup>4</sup>

# 5-HT, Efficacy with Long-lasting Migraine Relief

- Significant relief was sustained over 24 hours<sup>21</sup>
- 93% of attacks per patient did not require a second dose for recurrence<sup>4#</sup>
- Efficacy of AMERGE is unaffected by use with beta-blockers, calcium channel blockers, or tricyclic antidepressants<sup>1§</sup>

\*AMERGE is indicated for the acute treatment of migraine attacks with or without aura. AMERGE is contraindicated in patients with hemiplegic, basilar, or ophthalmoplegic migraine. Safety and efficacy have not been established for cluster headache which is present in an older predominantly male population." 'AMERGE 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 (e.g., atherosclerotic disease, congenital heart disease) should not receive AMERGE. AMERGE is also contraindicated in patients with uncontrolled or severe hypertension.

With 2.5 mg naratriptan.

'Headache relief = reduction of moderate or severe pain to mild or no pain.

Percentage does not represent recurrence rate. Headache recurrence equals a return of moderate or severe pain in 4 to 24 hours post dose following initial relief. Appropriate observation of the patient for acute and long term adverse events is advised. "AMERGE" is a registered trademark of Glaxo Group Ltd., Glaxo Wellcome Inc. licensed use.

Consult Product Monograph for complete prescribing information, patient selection, screening and monitoring criteria.

Product monograph available to health care professionals upon request.



Highly tolerable, long-lasting migraine relief Also available in 1 mg tablets

# GlaxoWellcome

Le premier et le seul parmi les nouveaux antiépileptiques indiqué en monothérapie après une polythérapie

## Pour la maîtrise d'un vaste éventail de crises, associée à un profil discret d'effets indésirables liés au SNC

D'une manière générale, une monothérapie efficace a été reconnue comme le traitement. de choix pour obtenir la maîtrise des crises avec le minimum d'effets indésirables chezles patients souffrant d'épilepsie'. Maintenant, renforçant son succes épitouvé comme traitement d'appoint', LAMICTAL est indiqué comme monothérapie chez l'adulte après le retrait d'antiépileptiques administres en concomitance'.

#### MONOTHÉRAPIE HAUTEMENT EFFICACE

Dans le cadre d'un essai ouvert sur le passage d'un traitement d'appoint à la monothérapie incluant le retrait des antiépileptiques administrés en concomitance, la monotherapie à LAMICTAL a permis à 30 % (n = 50) des patients traités avec succès de rester exempts de crises". Dans un autre essai du même type, ≥40 % des patients ont obtenu une réduction de la fréquence de leurs crises d'au moins 50 % pendant toutes les étapes successives de l'essai

#### GÉNÉRALEMENT MIEUX TOLÉRÉ

have

Selon les données regroupées de trois essais sur la monothérapie, la fréquence des retraits dus aux effets indésirables sur le SNC était de 2,5 % (n = 443) avec la monothérapie à LAMICTAL, par rapport a 7.4 % pour la phénytoine (n = 95) ou a 7,7 % pour la carbamazépine (n = 246)". La fréquence de somnolence, d'asthénie et d'ataxie a été moins élevée pour LAMICTAL que pour la carbamazépine et la phénytoine. On n'a notú aucune différence quant à la fréquence des retraits dus aux éruptions cutanées entre LAMICIAL (6,1 %) et la phénytoine (5,3 %) ou la carbamazépine (8.9 %)". Une fréquence plus élevée d'éruptions cutanées a élé associée à une augmentation posologique plus rapide de la dose initiale de LAMICTAL ou à l'utilisation concomitante d'acide valproïque".

#### MAÎTRISE SUR UN VASTE ÉVENTAIL DE CRISES

LAMICTAL a été utilisé avec succès pour un vaste éventail de crises comme traitement d'appoint dans une polythérapie1. Vous pouvez passer avec confiance de LAMICTAL comme traitement d'appoint en polythérapie à LAMICTAL en monotherapie", en particulier lorsque les effets indésirables lies au SNC sont une consideration importante,

hamotrigme.

https://doi.org/10.1017/S0317167100034259 Published online by Cambridge University Press A.19.

<sup>®</sup>Lamicta DELA POLYTHERAPIE MONOTHÉRAPIE GlaxoWellcome

## 25 Years Ago in the Canadian Journal of Neurological Sciences

## SEX-LINKED HEREDITARY ATAXIC DIPLEGIA, THE BORDERLAND BETWEEN CEREBRAL PALSY AND PELIZSAEUS-MERZBACHER DISEASE

H. G. Dunn, Margaret W. Thompson, Elizabeth Bandler, L. G. Andrews

SUMMARY: After a review of the literature concerning hereditary cases of cerebral palsy, a family is reported in which ataxic diplegia appears to be inherited as a sex-linked and probably recessive condition occuring in 3 males in successive generations. This ataxic diplegia, occurring after an unremarkable perinatal course, is associated with mild to moderate mental retardation, congenital nystagmus and significantly small stature and prevents the acquisition of free walking. Associated extrapyramidal features may gradually become more marked, while the nystagmus may subside. The condition is similar to that described in three previous reports in the literature. No evidence of linkage with other sex-linked disorders has been found,Xga typing showed that recombination between the Xg locus and the locus for hereditary ataxic diplegia has occurred once out of three possible opportunities. In the absence of neuropathological findings or specific biochemical tests, the differential diagnosis from Pelizaeus-Merzbacher disease cannot be made with certainty. The differentiation from other progressive sex-linked neurological disorders is discussed.

Can. J. Neurol. Sci. 1974; 4:226

## SPINAL MYOCLONUS IN ASSOCIATION WITH HERPES ZOSTER INFECTION:

Two Case Reports

G. S. Dhaliwal, D. A. McGreal

SUMMARY: Two cases of segmental spinal myoclonus, attributed to herpes zoster infection, are presented. The findings support the suggestion made by Campbell and Garland (1956) that "subacute myoclonic spinal neuronitis" is of viral origin. Both patients were receiving immuno-suppressive treatment when the myoclonus developed. The value of carbamazepine in therapy is mentioned.

Can. J. Neurol. Sci. 1974; 4:239

## LARGE ELECTROENCEPHALOGRAPHIC RESPONSES AND THEIR RELATIONSHIP TO CLEIDO-CRANIAL DYSPLASIA

## Adrian Upton, Sarah Bundey, Susan Sanders

SUMMARY: We have reported six individuals (five certain heterozygotes for cleido-cranial-dysostosia and one possible heterozygote) who have unusual EEG findings, consisting of very large responses to photic flash stimulation at very low stimulus rates.

Such visual responses are extremely rare and have not been seen before in the experience of an EEG department over 12 years and they were not seen in 98 control subjects. It is likely that these responses are an irregular manifestation of the gene for cleido-cranial-dysplasia, and that the responses are independent of skull deformity. One importance of these responses is their demonstration in neurologically normal individuals for previously such large responses have only been reported in association with neurolipidosis. They may have neurophysiological significance in that they may reflect an unusual balance between inhibitory and excitatory mechanisms in the nervous system.

Can. J. Neurol. Sic. 1974; 4: 242

## POLARTERITIS NODOSA COMPLICATED BY A MULTIPLE SCLEROSIS LIKE SYNDROME

## H. Waisburg, K. L. Meloff, R. Buncic

SUMMARY: A case is presented of a 16-year-old boy with angiographically proven polyarteritis nodosa who developed a multiple sclerosis like syndrome affecting the brain stem and cerebrum. His serum demyelinated nerve in tissue culture. The case is reviewed in detail and the mechanism of myelotoxicity is discussed.

Can. J. Neurol. Sci. 1974; 4:250

# A Renewed Opportunity

## PARKINSON'S DISEASE

A world in which the therapeutic options are limited

For those who have it, treat it, live with it; managing their Parkinson's cisease can be quite instrating. Yet there are moments that can be most rewarding. Motor function improves, the number of "off" hours decreases, rigidity subsides, gait improves. Their levoldpa seems to be working... at least for today! Then there are times when nothing seems to help. Even their medication seems to be causing problems. It seems holeeles... Today, however, there is another way to renew their hope. Even after its discovery more than fifteen years ago, Permax (pergolide mesylate) is still considered the most potent dopamine agonist available for the treatment of Parkinson's disease!" With its unique mode of action, i.e. stimulating both D1 and D2 dopamine receptors, Permax has demonstrated (n=376) statistically significant improvement in virtually all those numerous parameters of parkinsonian function, including bradykinesia, rigidity, gait, dexterity, etc. Equally important, these benefits were achieved with significantly less levodopa ... 24.7% (p <.001), and by starting Permax at low, doses "Adverse reactions were, for the most part, mild, reversible, and not of major clinical significance.""

Successful treatment with Permax can last for up to 3-5 years<sup>48</sup> and renewed improvement has been demonstrated when Permax was given to patients (n=10) in whom the beneficial effect of bromocriptine had waned, "whereas the reverse was not true in a separate, non-comparable study (n=11) when bromocriptine was given to Parkinson's patients in whom Permax had waned."

So, when given an opportunity to manage Parkinson's disease, there may be a way of renewing hope.



For brief prescribing information see page A-54

DRAXIS

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dge University

Turn the agony of migraine into the beauty of relief.

## Introducing Zomig.

Consistent migraine relief that patients can depend on time after time.

ZOMIG<sup>®</sup> is a new oral 5-HT<sub>1</sub> agonist indicated for the acute treatment of migraine.<sup>1</sup>

ZOMIG<sup>®</sup> offers consistent efficacy with significant headache response<sup>®</sup> rates at 2 hours following a single 2.5 mg dose.<sup>33</sup> In addition, efficacy is maintained across multiple migraine attacks and within different migraine subtypes.<sup>45</sup>

> ZOMIG<sup>®</sup> has a proven safety and tolerability profile with studies in over 3,000 patients treating more than 34,000 attacks.<sup>47</sup>

For consistent migraine relief, prescribe ZOMIG<sup>®</sup> 2.5 mg.

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Consistent migraine relief. https://doi.org/10.1017/50317167100034259 Published online by Cambridge University Press

## DU NOUVEAU EN ÉPILEPSIE. MAINTENANT REMBOURSE PAR LES FORMULAII



### NAGUÈRE ENCORE, LA RÉUSSITE EXIGEAIT D'UN ÉPILEPTIO HEUREUSEMENT POUR VOS PATIENTS, IL EXIS

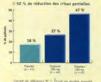


Exhibit de ofference N° Li Eluce en deube avergét avec placebo conte TOPAHAN (LLC, contre turisement d'appoint, portant sur l'El patients attaints d'apólissis patiente véhactaine et recevant une ou deux actes Contrôle amélioré d'une plus grande variété de types de crises.

- TOPAMAX est indiqué comme traitement d'appoint pour toutes les épilepsies réfractaires aux traitements conventionnels. À l'heure actuelle, les données sur l'utilisation de TOPAMAX comme traitement unique demeurent limitées.
- Taux élevé de répondants : 27 % (200 mg/jour, n = 45) et 47 % (400 mg/jour, n = 45) des patients ont manifesté une réduction des crises d'épilepsie partielle ≥ 50 % (étude d'une durée de 16 semaines)'
- Contrôle efficace pour les patients souffrant de cirses toniques-cloniques secondaires généralisées: 36 % des patients ont manifesté une réduction de 100 % (200-600 mg, n = 42, étude portant sur 16 semaines)<sup>5</sup>
- Triple mécanisme d'action unique: blocage des canaux sodiques, activation de l'acide gamma-aminobutyrique, antagonisme du glutamate)?
  0024259 Publiched oplique bu Camphidae University.

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## E LA C.-B., L'ALBERTA, LA SASKATCHEWAN, LA NOUVELLE-ÉCOSSE ET DU QUÉBEC.





## ES EFFORTS EXCEPTIONNELS OU UN TALENT EXTRAORDINAIRE. AINTENANT DES SOLUTIONS PLUS ACCESSIBLES.

- · Généralement bien toléré : les interruptions entraînées par des réactions adverses étaient de 10,6 % pour les doses journalières de 200 à 400 mg, comparé à 5,8 % pour le groupe placebo (cela semblerait augmenter pour les doses journalières supérieures à 400 mol?
- Aucune preuve d'éruption cutanée sérieuse ni d'anémie aplasique!
- Il n'est généralement pas nécessaire de changer le dosage des médications principales; les patients prenant de la phénytoine et manifestant des signes ou symptômes de toxicité devraient faire contrôler leurs niveaux de phénytoïne"
- Dosage commode BID

https://doi.org/10.1017/S0317167100034259 Published online050 Cambridge University Press

Profil favorable des effets secondaires (les plus courants affectent (e SNC)

	TOPAMAX 200-400 mg (n = 113)	PLACEBO (n = 216)
Somolence	30.1	9.7
Itsudicoments	28.5	13.3
Attale	21.2	8.5
Rainitistement psychomote	ur 15.8	2,3
froubles de la parpie	18.8	2.3
Newcolté	15.9	7,4
Nystagmes	15.0	8.3
Paresthes'e	35.0	4.6



Aide vos patients à mieux tirer parti de leur vie

## Introducing Rebif. The 1st Relapsing & Remitting MS Treatment to Significantly Improve All 3 Major Outcomes

Seours more son of several

REDUCES NUMBER AND SEVERITY OF RELAYSES

REDUCES MRI DISEASE ACTIVITY AND SUBDEN

The largest and most comprehensive RRMS clinical study ever undertaken, PRISMS<sup>1</sup>, confirms "Rebif" (Interferon Beta-1a for injection) ...

REBIE

#### Reduces progression of disability

The time to confirmed progression was significantly increased by 78% and 54% at both the 44 mcg and 22 mcg doses respectively versus placebo.

#### **Reduces the** number and severity of relapses The likelihood of

remaining relapse-free at 2 years increased by 75% with the 22 mca dose and by 119% with the 44 mcg dose."

#### **Reduces MRI** disease activity and burden

Compared to placebo, Rebif'significantly reduced the number of active lesions per patient per MRI scan by 78% and 67% (at the 44 and 22 mcg doses respectively) in 560 patients. This reduction was seen early and persisted throughout the 2 year study period."

#### Flexible dosing for optimal response

Available in readyto-use liquid pre-filled syringes for subcutaneous injection.

RE.

The most commonly reported adverse events are injection-site reactions and fluilike symptoms e.g., asthenia, pyrecia, chills, myalgia, headache and anthraigia. These tend to decrease in frequency and sevenity with continued treatment. Please see Product Monograph for further Information on patient selection 12-year clinical trial involving 560 patients given 44 mcg and 22 mcg doles of Rebif three times per week. Evidence of efficacy is derived from 2-year triats only.

http://www.internet.com/action/a Press

