Volume 30 Number 3 August 2003

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

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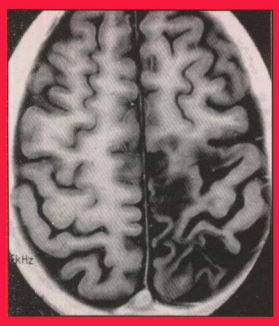
Ants and Neurology

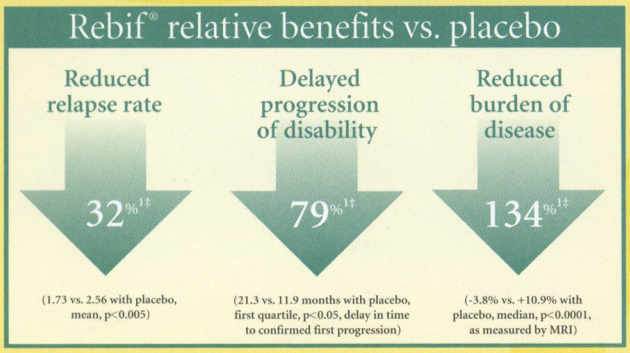


Neuroimaging Highlight

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

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

Picture what Rebif® might do for your MS patients.Δ



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

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

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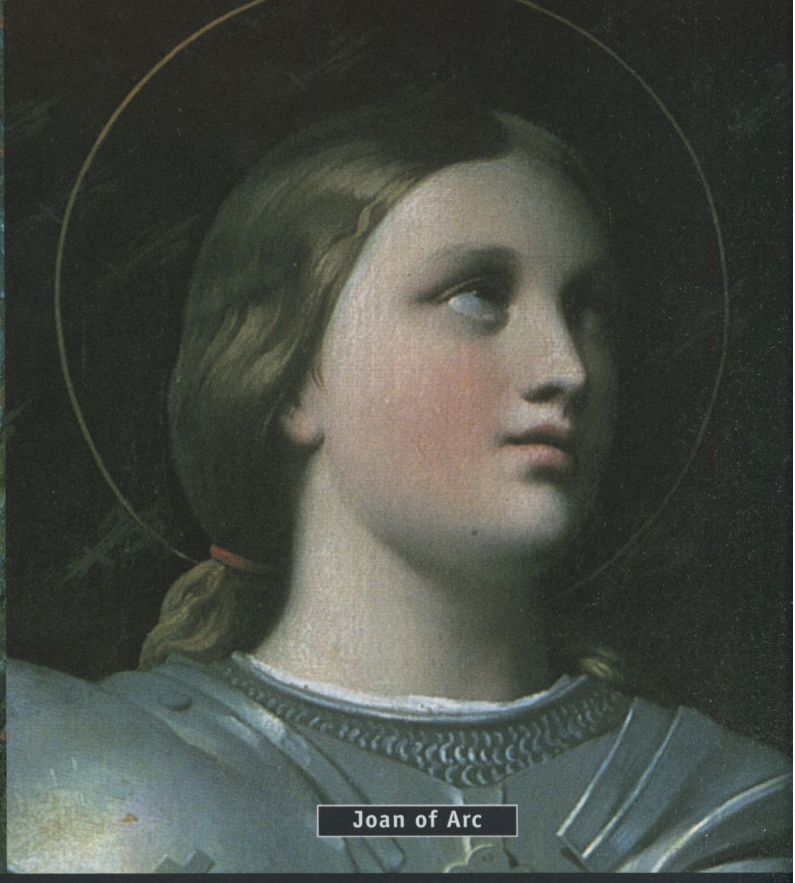
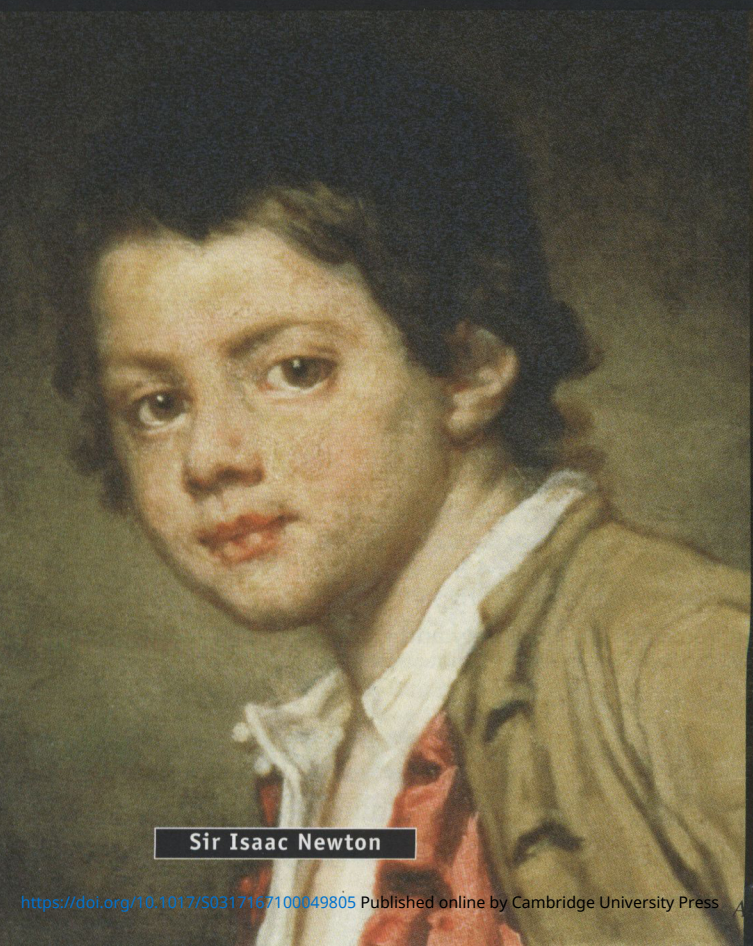
Vincent Van Gogh

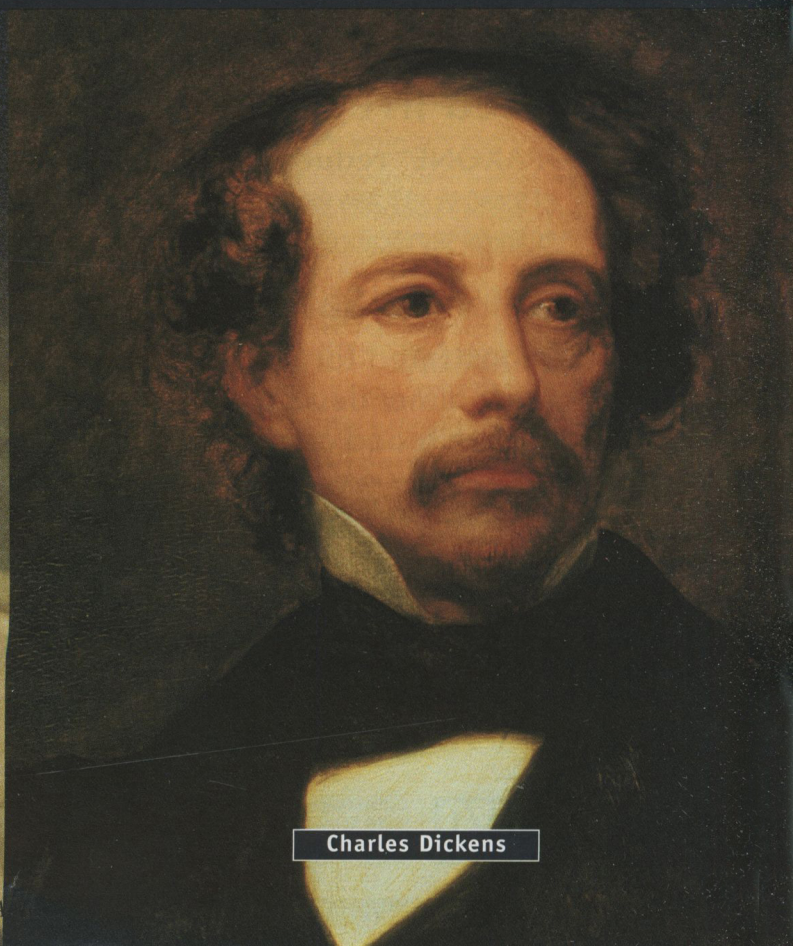


Joan of Arc

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



Sir Isaac Newton



Charles Dickens

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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.

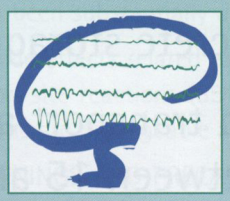
- 73% of patients (n = 52) showed a mean weight decrease of 5.97 lb (Interim analysis. Average duration 60 days)[4]
- 96% of children in clinical trials (≥ one year) who lost weight showed resumption of weight gain in test period**[1]

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.

Pr 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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NOW BETA

"Now my family and I don't have to confront my MS every time I open the fridge door."

—Teresa, MS focus group, April 2002

REFRIGERATION-FREE
storage for a new level of convenience

- New discrete storage flexibility
- Easier to transport and travel with (keep between 15 and 30 °C)

Member R&D PAAB

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NEW REFRIGERATION-FREE STORAGE

TER THAN EVER

Same proven therapy

- Reduces relapse FREQUENCY and SEVERITY in RRMS[1-3]
- Backed by MS Pathways™ of Canada patient management support with toll-free hotline access to MS-specialized registered nurses

BETASERON® (interferon beta-1b) is indicated for the reduction of the frequency of clinical exacerbations in ambulatory patients with relapsing-remitting multiple sclerosis and for the slowing of progression in disability and the reduction of the frequency of clinical exacerbations in patients with secondary-progressive multiple sclerosis.

The safety and efficacy of BETASERON® in primary progressive MS have not been evaluated. Efficacy of treatment for longer than 2 years has not been substantially demonstrated in relapsing-remitting multiple sclerosis (RRMS).

The most common side effects related to BETASERON® in patients with RRMS are: flu-like syndrome (76%), fever (59%), chills (46%), injection-site reactions (85%), myalgia (44%), asthenia (49%) and malaise (15%).[2] Flu-like symptoms and injection-site reactions are manageable and lessen with time.[2]

FOR COMPLETE WARNINGS AND PRECAUTIONS, PLEASE REFER TO THE PRODUCT MONOGRAPH, AVAILABLE TO HEALTH CARE PROFESSIONALS UPON REQUEST.

Pr BETASERON®
INTERFERON BETA-1b

BERLEX

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www.mspathways.ca

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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.

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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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All IGIVs (Immune Globulin Intravenous (Human)) are manufactured differently. Could this impact a product's efficacy or tolerability?

The medical community now expects solid evidence-based medicine through:

- controlled and comparative trial designs
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Bayer believes in taking a New Perspective.

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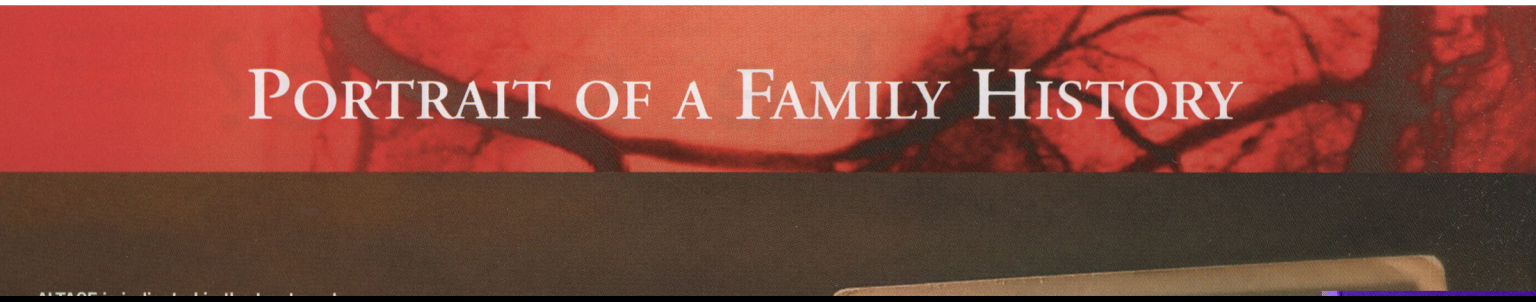
Portrait of a Family History



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BETA

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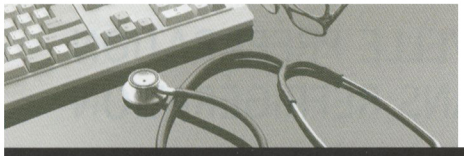

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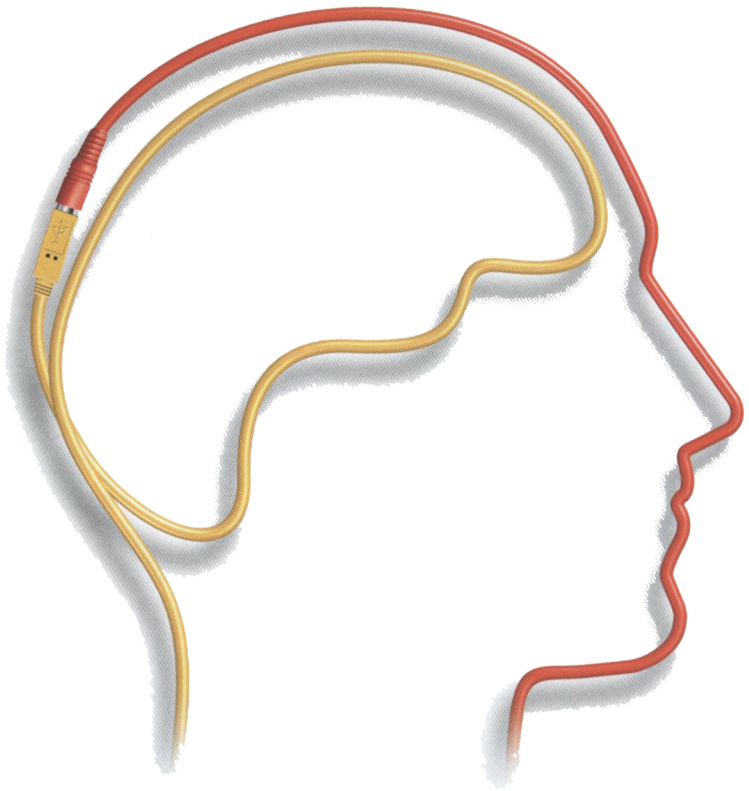

Generally well tolerated

- Favourable side effect profile
- Adverse events not dose dependent[2]
- Low discontinuation or dosage reduction (Keppra 14.3% vs placebo 11.7%) due to adverse events†

Efficacy and manageability right from the start

- Starting dose of 1000 mg/day (500 mg bid) shown to be effective and may be adjusted to a maximum of 3000 mg/day if required
- No blood level monitoring required
- No drug/drug interactions‡ with other AEDs, warfarin, digoxin or between Keppra 500 mg bid and a combination oral contraceptive (0.03 mg ethinyl estradiol and 0.15 mg levonorgestrel)§

§ Note: Pharmacokinetic interaction studies with contraceptives have not been conducted covering the full recommended dosage range of Keppra. Physicians should advise their female patients to be alert to any irregular vaginal bleeding or spotting and report any occurrences.

* 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

For brief prescribing information see pages A-35, A-36

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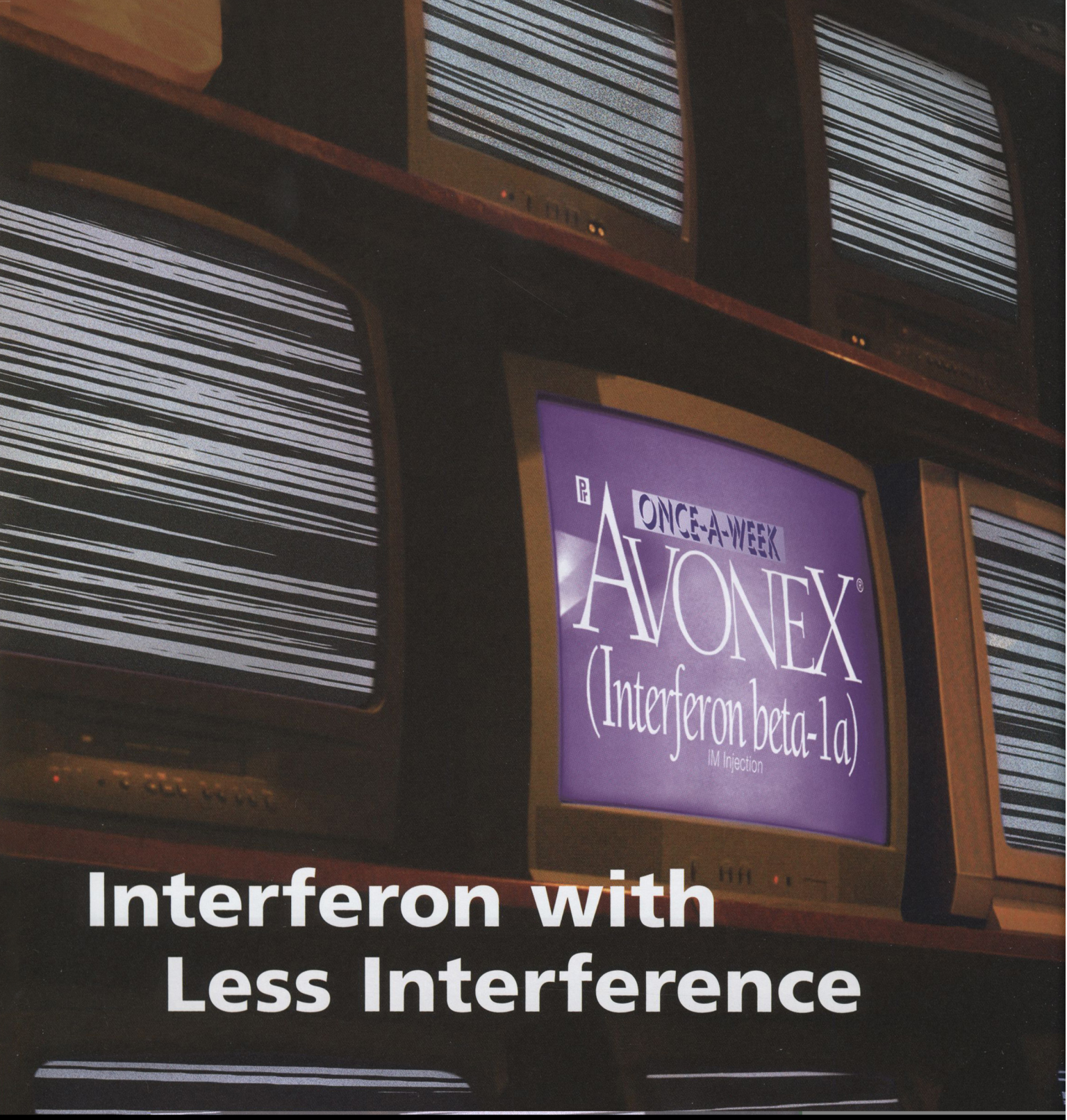

Interferon with Less Interference

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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).[@,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.

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.
@ 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.
Biogen Canada is a trademark of Biogen, Inc. AVONEX is a registered trademark of Biogen, Inc.
Rebif is a registered trademark of Serono Canada Inc. Betaseron is a registered trademark of Berlex Canada Inc.

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The CCNS website has a new look and new features. Check out the home page for a new feature on "Pioneers in Canadian Neurology". Visit the site to get the latest information on the annual scientific meeting, and register online. Planning a CME event? Look up the comprehensive Maintenance of Certification section. Not a member? Visit the "Become a Member" section, read about member benefits and download an application form. Are you a resident or Fellow? Visit the "Residents and Fellows" section for information just for you.

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The CCNS website has a new section just for members. Watch for your password in the mail to enter the Members' Centre, which will also provide password access to the *Canadian Journal of Neurological Sciences* (CJNS) online.

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ARICEPT 5 years OF EXCELLENT EFFICACY

For living with Alzheimer's disease.

Aricept* is indicated for the symptomatic treatment of mild-to-moderate dementia of the Alzheimer's type, and does not change the underlying course of the disease. With appropriate dose escalation, 5 mg/d, 10 mg/d and placebo were shown to have comparable adverse events, the most common being diarrhea, nausea, insomnia, fatigue, vomiting, muscle cramps and anorexia. These are usually mild and transient, resolving with continued treatment without need for dose modification.

Make Aricept* your standard of care.

Pfizer NEUROSCIENCE

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Once-a-day Aricept* donepezil HCl 5 & 10 mg tablets

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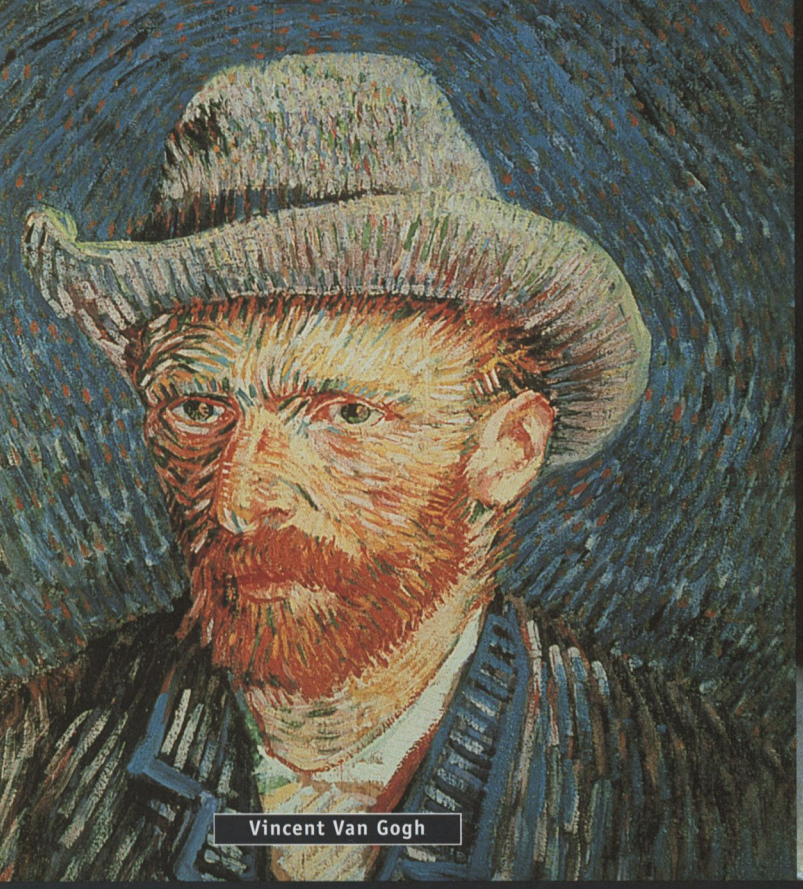
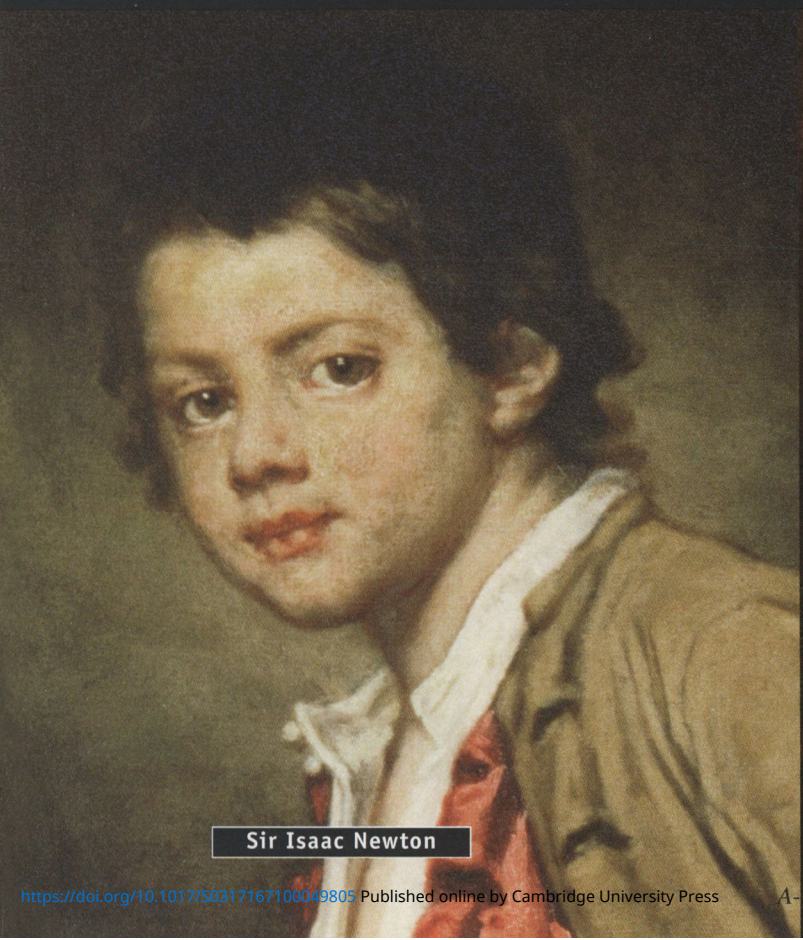
For brief prescribing information see page A-42



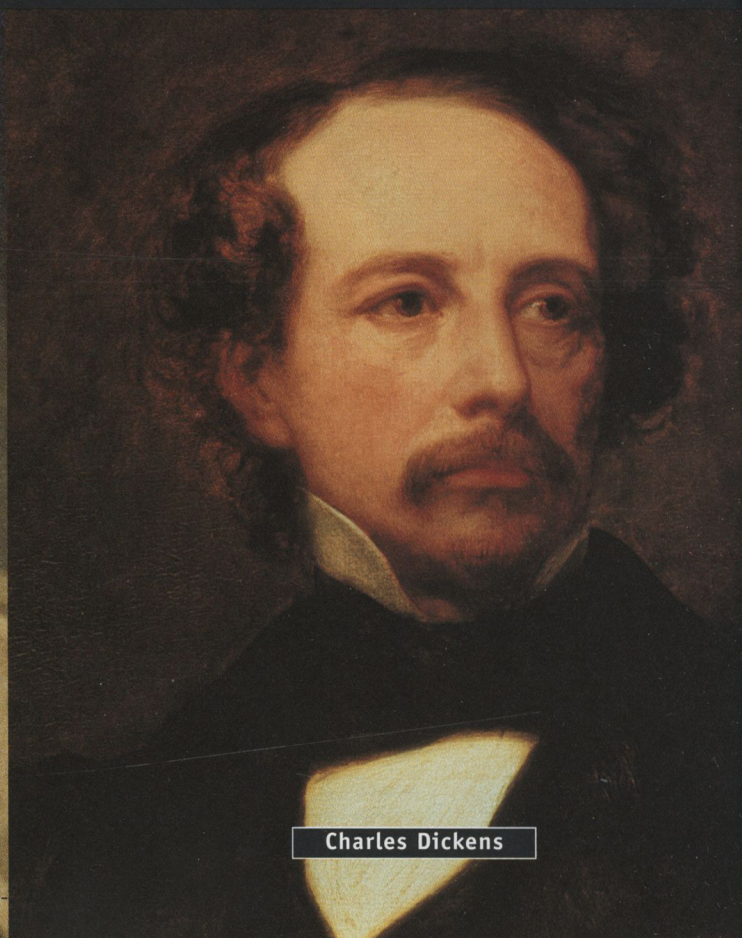
Vincent Van Gogh

Jeanne d'Arc

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



Sir Isaac Newton



Charles Dickens

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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]

IL EST POSSIBLE QUE LES PATIENTS ADULTES SUBISSENT UNE PERTE DE POIDS.

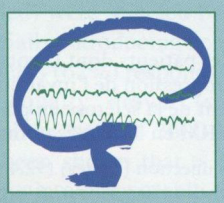
- 73 % (n = 52) des patients ont subi une perte de poids de 5,97 lb en moyenne (Analyse provisoire. Durée moyenne de 60 jours)[4]
- 96 % des enfants traités dans le cadre des essais cliniques pendant au moins un an et ayant subi une perte de poids ont repris du poids au cours de la période d'exécution des essais**[1]

AUJOURD'HUI, IL Y A TOPAMAX.

UNE POSOLOGIE BIQUOTIDIENNE POUR TENIR COMPTE DU PATIENT.

- Le traitement par TOPAMAX peut être commencé et ajusté selon la réponse clinique quel que soit le traitement anticonvulsivant en cours
- Les comprimés sont inscrits au formulaire††

MAINTENANT OFFERT EN CAPSULES À SAUPOUDRER



TOPAMAX* topiramate

MAINTENANT INDIQUÉ CHEZ L'ENFANT

POUR AIDER LES PATIENTS À MIEUX PROFITER DE LA VIE

Comprimés et capsules à saupoudrer Pr TOPAMAX (topiramate) : indiqués comme traitement adjuvant chez les patients (adultes et enfants âgés de deux ans ou plus) atteints d'épilepsie dont l'état n'est pas maîtrisé de façon satisfaisante avec le traitement traditionnel. Les renseignements sur l'emploi du topiramate en monothérapie sont encore limités[1].*

†Une étude ouverte d'une durée de 20 semaines (n = 450 adultes). Posologie optimale : 300 à 350 mg/jour (moyenne : 288 mg/jour).
‡Étude ouverte portant sur des enfants (n = 72) traités pendant au moins 3 mois. Posologie moyenne : 10 mg/kg/jour.
§Manifestations indésirables liées au SNC : Somnolence (30,1 %), étourdissements (28,3 %), ataxie (21,2 %), troubles de la parole (16,8 %), ralentissement psychomoteur (16,8 %), nystagmus (15 %), paresthésie (15 %), nervosité (15,9 %), difficulté à se concentrer/troubles de l'attention (8 %), confusion (9,7 %), dépression (8 %), anorexie (5,3 %), problèmes de langage (6,2 %) et troubles de l'humeur (3,5 %). Une évaluation de 1 446 adultes et 303 enfants a indiqué que ces deux groupes semblent présenter des profils de manifestations indésirables similaires.
**Les effets à long terme d'une perte de poids chez les enfants ne sont pas connus.
††Médicament à usage limité : Ontario, Nouvelle-Écosse, Nouveau-Brunswick, Î.-P.-É. Remboursement intégral : Québec, Saskatchewan, Colombie-Britannique, Alberta, Manitoba.
Veuillez vous reporter aux Renseignements thérapeutiques sur TOPAMAX pour les détails thérapeutiques complets.

RÉFÉRENCES : **1.** Monographie des comprimés et capsules à saupoudrer TOPAMAX* (topiramate), 11 mai 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, Etterman 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.

JANSSEN-ORTHO Inc.
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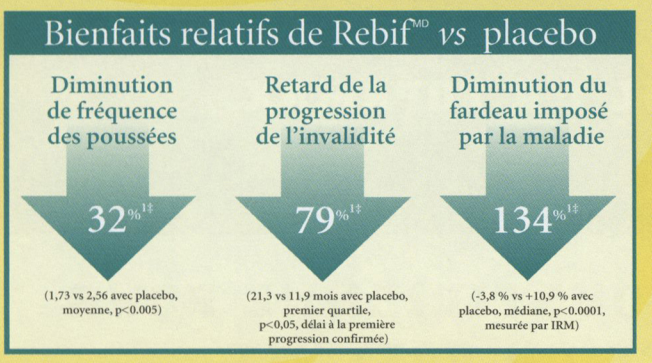
Pour documentation voir pages A-31, A-32

Visualisez ce que Rebif[MD] peut faire pour vos patients atteints de SEP[Δ].



Résultats de la dose de 44 mcg trois fois par semaine après 2 ans[1].

Au cours de deux études pivots incluant un total de 628 patients, Rebif a démontré une efficacité significative pour les trois paramètres principaux (poussées, progression de l'invalidité et IRM)[1,2].

Sa capacité de modifier le cours de la maladie[2] a fait non seulement de Rebif un bon médicament de première ligne pour la SEP rémittente, mais également le médicament dominant de sa catégorie[3].

Rebif est généralement bien toléré. Les effets indésirables les plus fréquents sont souvent traitables et diminuent en fréquence et en gravité avec le temps[2†].

Rebif modifie l'évolution naturelle de la SEP rémittente[2].

Rebif[MD] 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. Son efficacité a été confirmée au moyen d'évaluations IRM en T_1 marquées au Gd et d'évaluations IRM en T_2 (fardeau imposé par la maladie)[2].

† Les effets indésirables rapportés le plus souvent sont les suivants : réactions au point d'injection (toutes) (92,4 % *vs* 38,5 % pour le placebo), infections des voies respiratoires supérieures (74,5 % *vs* 85,6 % pour le placebo), céphalée (70,1 % *vs* 62,6 % pour le placebo), syndrome pseudo-grippal (58,7 % *vs* 51,3 % pour le placebo), fatigue (41,3 % *vs* 35,8 % pour le placebo) et fièvre (27,7 % *vs* 15,5 % pour le placebo). Les preuves d'innocuité et d'efficacité sont obtenues de l'étude de 2 ans seulement. Veuillez consulter la monographie du produit pour les renseignements d'ordonnance[2].

‡ Étude randomisée, à double insu, contrôlée par placebo. Groupe Rebif 44 mcg 3 fois/semaine (n = 184), groupe Rebif 22 mcg 3 fois/semaine (n = 189), groupe placebo (n = 187)[1].

Δ Le cas hypothétique peut ne pas représenter les résultats obtenus dans la population générale.

CCPP

Pr Rebif[MD] interféron bêta-1a

serono

POUR DE MULTIPLES RAISONS.

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Pour documentation voir pages A-27, A-28