Volume 34 Number 4 November 2007

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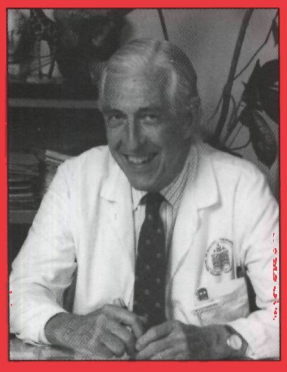
LE JOURNAL CANADIEN DES Sciences Neurologiques

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL



Joe Stratford
1923-2007

Glandular structures consisting of cytokeratin positive cells

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WR Wayne Martin

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Supplement Editor: WJ Becker (See contents pages)

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

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Editor in Chief G. Bryan Young, with approvals from the Editorial Board and the CJNS Board, is pleased to announce that the Journal will be moving to six publications per year in 2008. The Journal will now be published and mailed in March, May, July, September, November and January.

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Neuropathic Pain

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Powerful Pain Relief

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Fast Onset. Sustained Relief.

- Powerful pain reduction (≥50% pain reduction) shown in 48.2% of neuropathic pain patients (DPN or PHN; 24.2% for placebo, $p<0.001$)[2†]
- Rapid neuropathic pain relief shown in patients with PHN as early as Week 1[3,4‡]
- Sustained neuropathic pain relief demonstrated over 3 months[2†]
- Rapid and sustained improvement in pain-related sleep interference observed in patients with PHN[3,4‡]

LYRICA (pregabalin) is an analgesic indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) and postherpetic neuralgia (PHN).

LYRICA is contraindicated in patients who are hypersensitive to pregabalin or to any ingredient in the formulation or component of the container.

The most commonly observed adverse events (twice the rate as that seen with placebo) were dose related for PHN and DPN patients in the recommended dose range of 150 mg/day to 600 mg/day: dizziness (9-37%), somnolence (6.1-24.7%), peripheral edema (6.1-16.2%) and dry mouth (1.9-14.9%).

Dosage reduction is required in patients with renal impairment as LYRICA is primarily eliminated by renal excretion.

Please see Prescribing Information for complete Warnings and Precautions, Dosage and Administration and patient selection criteria.

† A 12-week, multicentre, randomized, double-blind, placebo-controlled study in 338 patients with neuropathic pain (DPN [n=249] or PHN [n=89]), resulting in a significant difference from placebo in the flexible dose range 150-600 mg/day ($p\leq0.05$, weeks 2-3 and $p\leq0.01$, weeks 4-12), and the fixed dose of 600 mg/day ($p\leq0.05$, week 1 and $p\leq0.01$, weeks 2-12).

‡ A 13-week, multicentre, double-blind, placebo-controlled trial in 368 patients with PHN. A significant difference in pain reduction was shown over placebo for all doses: 150 mg/day, 300 mg/day, and 600 mg/day at week 1, $p<0.001$. Sleep interference was improved at all time points (weeks 1 to 13 and endpoint) for the three doses evaluated ($p<0.01$ vs. placebo).

For brief prescribing information see pages A-24 - A-27

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Fast onset. Sustained relief.

Volume 34 Number 4 November 2007

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The Canadian Neurosurgical Society
La Société Canadienne de Neurochirurgie

The Canadian Society of Clinical Neurophysiologists
La Société Canadienne de Neurophysiologie Clinique

The Canadian Association of Child Neurology
L'Association Canadienne de Neurologie Pédiatrique

The permanent secretariat for the four societies and the Canadian Neurological Sciences Federation is at:
Le secrétariat des quatre associations et du Fédération des sciences neurologiques du Canada est situe en permanence à:
7015 Macleod Trail SW, Suite 709, Calgary AB, Canada T2H 2K6.

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La douleur neuropathique
Foudroyé de l'intérieur

Pr LYRICA MD

Un soulagement puissant de la douleur

Puissant.
Effet rapide. Soulagement soutenu.

- Un soulagement puissant de la douleur neuropathique associée à la NDP et à la NPZ (diminution de la douleur ≥ 50 %) observé chez 48,2 % des patients (24,2 % pour le placebo, $p < 0{,}001$)[2†]
- Un soulagement rapide de la douleur neuropathique associée à la NPZ dès la première semaine[3,4‡]
- Un soulagement soutenu de la douleur neuropathique démontré sur une période de 3 mois[2†]
- Une atténuation rapide et soutenue des perturbations du sommeil causées par la NPZ[3,4‡]

LYRICA (prégabaline) est un analgésique indiqué pour le traitement de la douleur neuropathique associée à la neuropathie diabétique périphérique (NDP) et à la névralgie postzostérienne (NPZ).

LYRICA est contre-indiqué chez les patients qui présentent une hypersensibilité à ce médicament ou à l'un des composants du produit ou du contenant.

Les effets indésirables signalés le plus souvent (fréquence 2 fois plus élevée qu'avec le placebo) chez les patients souffrant de NPZ ou de NDP étaient proportionnels à la dose dans l'intervalle posologique recommandé de 150 mg/jour à 600 mg/jour et ont été les suivants : étourdissements (9,0 - 37,0 %), somnolence (6,1 - 24,7 %), œdème périphérique (6,1 - 16,2 %) et sécheresse buccale (1,9 - 14,9 %).

Comme LYRICA est éliminé principalement par le rein, il faut réduire la dose en présence d'une dysfonction rénale.

Consulter les renseignements thérapeutiques pour obtenir l'information complète sur les mises en garde, les précautions, la posologie, le mode d'administration et les critères de sélection des patients.

† Essai multicentrique d'une durée de 12 semaines, mené à double insu avec placebo après répartition aléatoire de 338 patients souffrant de douleur neuropathique (NDP [n = 249]; NPZ [n = 89]). Une différence significative a été observée par rapport au placebo dans tout l'intervalle posologique flexible de 150 à 600 mg/jour ($p \leq 0{,}05$ pour les semaines 2 et 3 et $p \leq 0{,}01$ pour les semaines 4 à 12) et à la *dose quotidienne fixe de 600 mg ($p \leq 0{,}05$ pour la 1re semaine et $p \leq 0{,}01$ pour les semaines 2 à 12).*

‡ Essai multicentrique d'une durée de 13 semaines, mené à double insu avec placebo auprès de 368 patients souffrant de NPZ. La première semaine, on a observé une différence significative en ce qui a trait au soulagement de la douleur par rapport au placebo à toutes les doses : 150 mg/jour, 300 mg/jour et 600 mg/jour, $p < 0{,}001$. Lors des évaluations prévues (semaines 1 à 13 et fin de l'étude), on a également observé une atténuation des perturbations du sommeil avec les trois doses ($p < 0{,}01$ vs placebo).

Pour documentation voir pages A-24 - A-27

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Vers un monde en meilleure santé

CCPP Membre R&D

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Effet rapide. Soulagement soutenu.

Treat your hypertensive patients with the power of MICARDIS®:

- Powerful 24-hour BP reductions shown, $p<0.0001$ including the early morning hours (6:00 AM-11:59 AM), $p<0.0001$[2†]
- Longest half-life of all AT_1 receptor blockers[3-8§]
- Simple, flexible, once-daily dosing[3¥]

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- The ONTARGET clinical trial program investigates ARB and ACE therapy in more than 31,000 patients.
- ONTARGET investigates MICARDIS® (telmisartan) and ramipril, alone or in combination, in the prevention of cardiovascular morbidity and mortality in patients at high risk for cardiovascular complications.
- Boehringer Ingelheim is committed to cardiovascular protection research.

MICARDIS® is not indicated to reduce cardiovascular or cerebrovascular morbidity and mortality, or to improve renal outcomes.

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MICARDIS® Demonstrated Powerful BP Reductions Measured from MORNING to MORNING[1]

Demonstrated significantly greater 24-hour ABPM reduction vs. placebo, $p<0.05$[1#]

MICARDIS® (telmisartan) is indicated for the treatment of mild to moderate essential hypertension and may be used alone or in combination with thiazide diuretics.[3] The most common adverse events vs. placebo were headache (8.0% vs. 15.6%), upper respiratory tract infection (6.5% vs. 4.6%), dizziness (3.6% vs. 4.6%), pain (3.5% vs. 4.3%), fatigue (3.2% vs. 3.3%), back pain (2.7% vs. 0.9%), diarrhea (2.6% vs. 1.0%) and sinusitis (2.2% vs. 1.9%).[3] If pregnancy is detected, MICARDIS® should be discontinued as soon as possible.[3] In patients who are volume-depleted by diuretic therapy, dietary salt restrictions, dialysis, diarrhea or vomiting, symptomatic hypotension may occur after initiation of therapy with MICARDIS®.[3]

6-week, multinational, multicentre, randomized, double-blind, double-dummy, parallel group study comparing MICARDIS® 80 mg and Losartan 50 mg with placebo arm. MICARDIS® 80 mg mean 24-hour SBP vs. placebo = -13.3 mmHg vs. -1.8 mmHg, DBP = -8.4 mmHg vs. -0.8 mmHg, $p<0.05$.

† 14-week, multicentre, prospective, randomized, open-label, blinded-endpoint, parallel group, forced-titration study of MICARDIS® and Altace® in patients with confirmed ambulatory hypertension. Mean 24-hour SBP = -14.8 mmHg vs. -10.7 mmHg, $p<0.0001$ and DBP = -9.9 mmHg vs. -6.7 mmHg, $p<0.0001$. Morning (06:00 AM-11:59 AM) SBP = -14.3 mmHg vs. -9.7 mmHg, $p<0.0001$.

§ Comparative clinical significance is unknown.

¥ Dosing available in MICARDIS® 40 mg, MICARDIS® 80 mg and MICARDIS® PLUS 80/12.5 mg HCTZ.

Boehringer Ingelheim:
Committed to cardio and vascular protection research

>31,000 patients enrolled in the ONTARGET two-part study programme[1,2]

MICARDIS® (telmisartan) is indicated for the treatment of mild to moderate essential hypertension and may be used alone or in combination with thiazide diuretics.

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MICARDIS® is not indicated to reduce cardiovascular or cerebrovascular morbidity and mortality, or to improve renal outcomes.

1. The ONTARGET/TRANSCEND Investigators. Rationale, design, and baseline characteristics of 2 large, simple, randomized trials evaluating telmisartan, ramipril, and their combination in high-risk patients: The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND) trials. *American Heart Journal* 2004;148 vol.1:52-61. 2. Data on file, Boehringer Ingelheim (Canada) Ltd.

Current Ongoing International Cardio and Vascular Trials:

	ONTARGET	TRANSCEND	PRoFESS®
Number of Patients Internationally	25,622[2]	5,926[2]	20,333[2]
Number of Canadian Patients	2,519[2]	426[2]	1,549[2]
Number of International Centres	730[1,2]	730[1,2]	674[2]

ONTARGET Cardiovascular Mortality and Morbidity Trial

- ONTARGET investigates MICARDIS® (telmisartan) and Altace® (ramipril), alone or in combination, in the prevention of cardiovascular morbidity and mortality in patients at high risk for cardiovascular complications.[1]
- Inclusion Criteria:[1]
  - Male or female, age ≥55 years
  - At high risk of developing a CVD event, with a history of one of the following:
    - Coronary artery disease
    - Peripheral arterial occlusive disease (PAOD)
    - Cerebrovascular event
    - Diabetes mellitus with evidence of end-organ disease

TRANSCEND Cardiovascular Mortality and Morbidity Trial

- TRANSCEND investigates MICARDIS® vs. placebo for the prevention of cardiovascular morbidity and mortality in patients at high risk for cardiovascular complications and who are intolerant to angiotensin-converting enzyme inhibitors.[1]

PRoFESS® Stroke Trial

- PRoFESS® investigates patients with known prior ischemic strokes. Patients will receive at random either MICARDIS® or placebo. Both groups will also receive at random either Aggrenox® (ASA/extended-release dipyridamole) or Plavix® (clopidogrel).[2]

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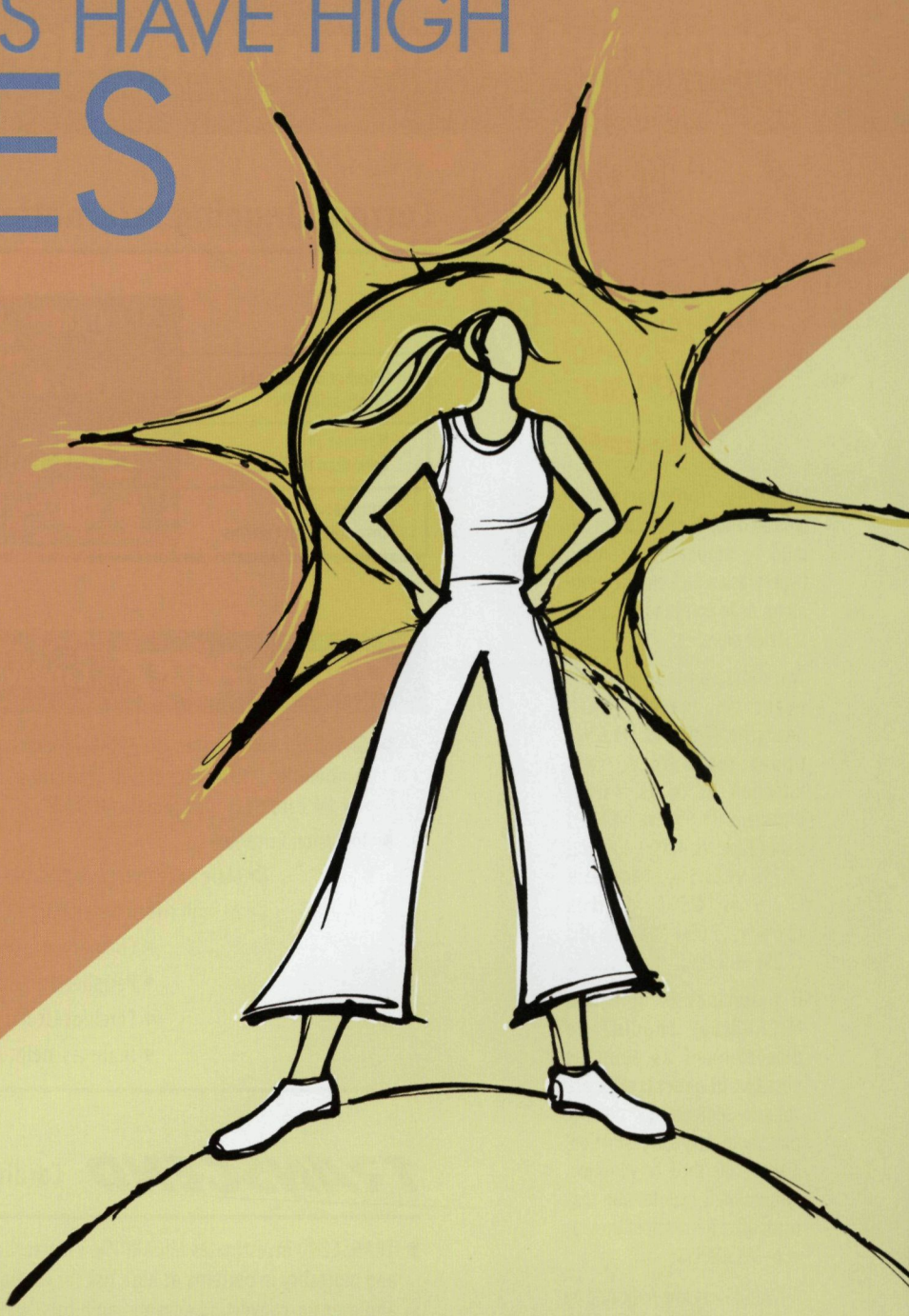
For brief prescribing information see page A-30

MS PATIENTS HAVE HIGH HOPES



TYSABRI is indicated as monotherapy (i.e., single disease-modifying agent) for the treatment of patients with the relapsing-remitting form of multiple sclerosis (MS) to reduce the frequency of clinical exacerbations, to decrease the number and volume of active brain lesions identified on magnetic resonance imaging (MRI) scans and to delay the progression of physical disability. TYSABRI is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, other therapies for multiple sclerosis.[1]

Safety and efficacy in patients with chronic progressive multiple sclerosis, and in geriatric and pediatric patients, have not been established.[1]

Efficacy and safety of TYSABRI for a treatment duration beyond 2 years has not been determined.[1]

TYSABRI should be used by physicians who have sufficient knowledge of multiple sclerosis and who have familiarized themselves with the efficacy/safety profile of TYSABRI.[1]

TYSABRI is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container; patients who have or have had progressive multifocal leukoencephalopathy (PML); patients who are immunocompromised, including those immunocompromised due to immunosuppressant or antineoplastic therapies, or immunodeficiencies (HIV, leukemias, lymphomas, etc.).[1]

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GIVE THEM STRENGTH TO HELP REACH THEM

The strength of TYSABRI has demonstrated powerful benefits in clinical trials.

Over 2 years TYSABRI vs. placebo (n = 627 vs. n = 315)[1]:

- **68% reduction in annualized relapse rate ($p < 0.001$) (0.24 vs. 0.73)**
- **42% reduction in the risk of disability progression (EDSS increase sustained for 12 weeks) ($p < 0.001$)† (17% vs. 29%)**
- **Significant improvement in all MRI endpoints ($p < 0.001$)‡**
- **Significant slowing of brain atrophy in the second year of treatment (BPF) ($p = 0.004$)§**
- **Significant improvement in cognitive function (PASAT3) ($p = 0.005$)¶**

TYSABRI is a selective adhesion molecule inhibitor.

* Comparative clinical significance has not been established.

† Disability progression defined as a ≥ 1.0 point increase from baseline EDSS of ≥ 1.0 or a ≥ 1.5 point increase from baseline EDSS of 0.

‡ Reduction in mean number of Gd-enhancing lesions vs. placebo (0.1 vs. 1.2), reduction in mean number of new or newly enlarging T2-hyperintense lesions vs. placebo (1.9 vs. 11.0), percentage of patients free of either type of lesion vs. placebo (Gd-enhancing 97% vs. 72%, T2-hyperintense 57% vs. 15%) and median change in volume of T2-hyperintense lesions vs. placebo (-9.4% vs. 8.8%).

§ TYSABRI 0.24% vs. placebo 0.43% reduction in brain volume measured by Brain Parenchymal Function.

¶ Paced Auditory Serial Addition Test 3.

Treatment with TYSABRI has been associated with an increased risk of progressive multifocal leukoencephalopathy (PML). PML can cause disability or death. Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. TYSABRI dosing should be withheld immediately at the first sign or symptom suggestive of PML.[1]

Patients who are prescribed TYSABRI should enroll in the Tysabri Care Program.™[1]

The most common serious adverse drug reactions were infections (3.2% vs. 2.6% placebo), acute hypersensitivity reactions (1.1% vs. 0.3%), depression (1.0% vs. 1.0%) and cholelithiasis (1.0% vs. 0.3%).[1]

REFERENCE:

1. TYSABRI Product Monograph, 2006.

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NEW EVERY 4-WEEKS TYSABRI™ (natalizumab)

Strength you can believe in

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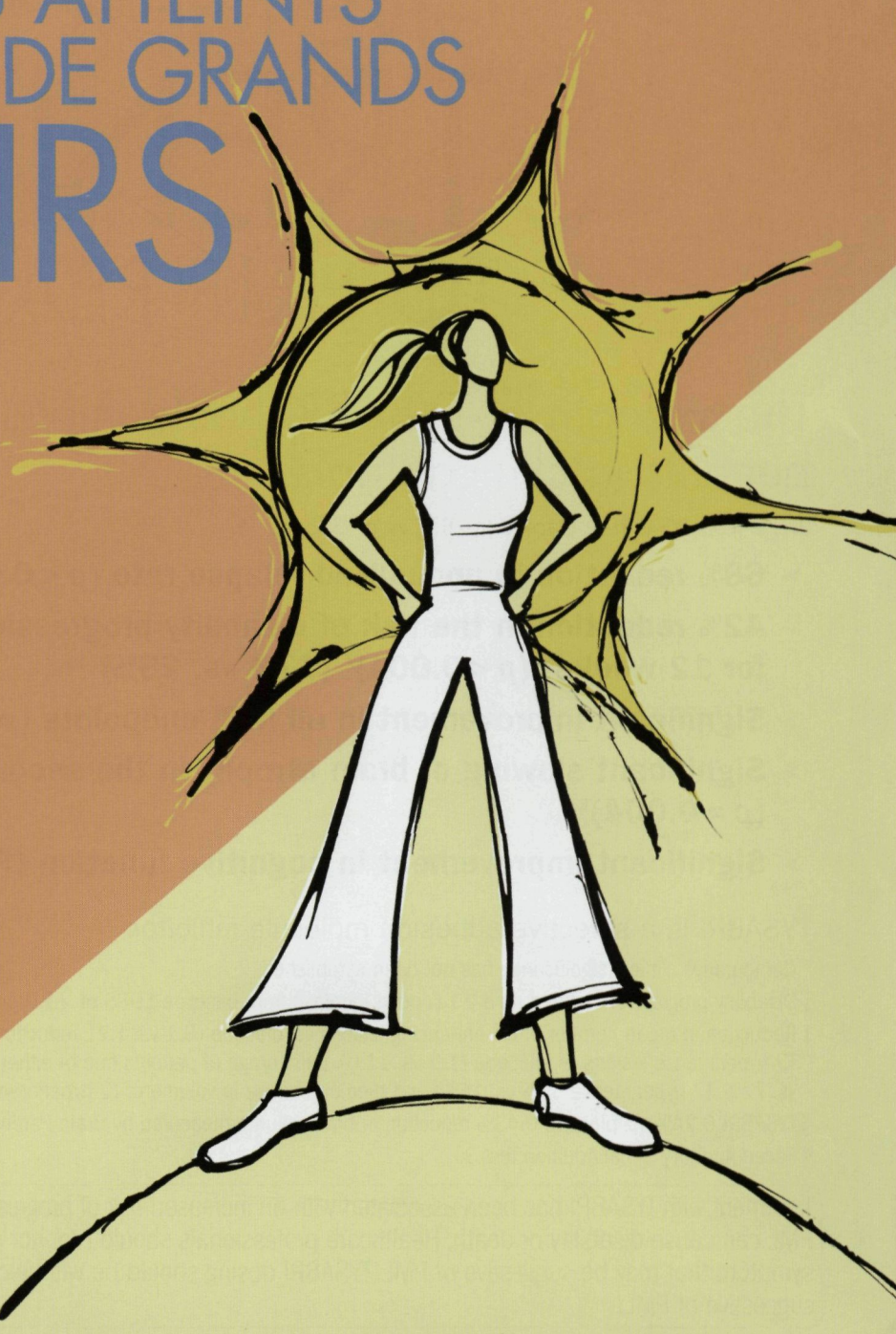
For brief prescribing information see pages A-22, A-23

LES PATIENTS ATTEINTS DE SEP ONT DE GRANDS ESPOIRS



TYSABRI est indiqué en monothérapie (c'est-à-dire comme agent d'un traitement de fond utilisé seul) pour le traitement de la forme rémittente de la sclérose en plaques (SEP) afin de diminuer la fréquence des poussées cliniques, de réduire le nombre et le volume des lésions cérébrales actives décelées aux examens d'imagerie par résonance magnétique (IRM) et de ralentir la progression de l'incapacité. TYSABRI est généralement recommandé chez les patients atteints de SEP qui ne répondent pas bien aux autres traitements de la SEP ou ne peuvent les tolérer[1].

On n'a pas établi l'innocuité ni l'efficacité du produit chez les patients atteints de sclérose en plaques chronique progressive, ni chez les patients en pédiatrie et en gériatrie[1].

On n'a pas déterminé l'innocuité ni l'efficacité de TYSABRI dans un traitement durant plus de deux ans[1].

Seuls les médecins qui connaissent suffisamment la sclérose en plaques et qui se sont familiarisés avec l'efficacité et l'innocuité du médicament peuvent utiliser TYSABRI[1].

TYSABRI est contre-indiqué chez les patients qui présentent une hypersensibilité à ce médicament, à l'un des composants du produit ou du contenant; chez les patients qui sont, ou ont déjà été, atteints de leucoencéphalopathie multifocale progressive (LMP); chez les patients immunodéprimés, y compris ceux qui le sont par suite de l'administration d'immunosuppresseurs ou d'agents antinéoplasiques et ceux qui sont atteints d'immunodéficience (infection par le VIH, leucémies, lymphomes, etc.)[1].

DONNEZ-LEUR DE LA PUISSANCE POUR LES AIDER À LES ATTEINDRE

La puissance de TYSABRI a permis de montrer de grands bienfaits dans les essais cliniques.

Deux ans avec TYSABRI vs placebo (n = 627 vs n = 315)[1] :

- **Réduction de 68 % du nombre de poussées par année ($p < 0,001$) (0,24 vs 0,73)**
- **Réduction de 42 % du risque de progression de l'incapacité (augmentation de la cote EDSS soutenue pendant 12 semaines) ($p < 0,001$)† (17 % vs 29 %)**
- **Amélioration significative de tous les paramètres de l'IRM ($p < 0,001$)‡**
- **Ralentissement significatif de l'atrophie cérébrale durant la deuxième année de traitement (FPC) ($p = 0,004$)§**
- **Amélioration significative de la fonction cognitive (PASAT3) ($p = 0,005$)¶**

TYSABRI est un inhibiteur sélectif de la molécule d'adhésion.

* La portée clinique comparative n'a pas été établie.

† La progression de l'incapacité se définit par l'augmentation de ≥ 1,0 point de la cote EDSS par rapport à des valeurs de départ de ≥ 1,0 ou par l'augmentation de ≥ 1,5 point par rapport à une valeur de départ de 0.

‡ Réduction du nombre moyen de lésions qui prennent le gadolinium vs placebo (0,1 vs 1,2), réduction du nombre moyen de lésions hyperintenses en T2, nouvelles ou nouvellement en progression, vs placebo (1,9 vs 11,0), pourcentage de patients ne présentant pas ces types de lésions vs placebo (prenant le gadolinium 97 % vs 72 %, hyperintenses en T2 57 % vs 15 %) et changement médian du volume des lésions hyperintenses en T2 vs placebo (– 9,4 % vs 8,8 %).

§ Réduction de 0,24 % avec TYSABRI vs de 0,43 % avec le placebo du volume du cerveau mesuré d'après la fonction parenchymateuse du cerveau.

¶ Test d'additions en série en réponse à des directives vocales (*Paced Auditory Serial Addition Test 3*).

On a associé le traitement par TYSABRI à une augmentation du risque de leucoencéphalopathie multifocale progressive (LMP). La LMP peut entraîner une incapacité ou le décès. Les professionnels de la santé doivent surveiller les patients qui prennent TYSABRI au cas où de nouveaux signes ou symptômes signaleraient l'apparition de la LMP. Il faut interrompre l'administration de TYSABRI dès l'apparition du premier signe ou symptôme qui laisse croire à une LMP[1].

Les patients à qui on a prescrit TYSABRI doivent adhérer au Programme de soins Tysabri[MC1].

Les effets indésirables graves le plus souvent signalés étaient les suivants : infections (3,2 % vs 2,6 % placebo), réactions aiguës d'hypersensibilité (1,1 % vs 0,3 %), dépression (1,0 % vs 1,0 %) et cholélithiase (1,0 % vs 0,3 %)[1].

RÉFÉRENCE :
1. Monographie de TYSABRI, 2006.

biogen idec[MC] élan CCPP

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FÉDÉRATION DES SCIENCES NEUROLOGIQUES DU CANADA

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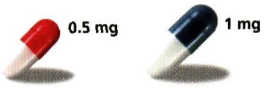
Reference: 1. Cesamet Product Monograph, September 2004.



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La Fédération des sciences neurologiques du Canada est heureuse de reconnaître nos commanditaires pour l'annéee 2007. Ces organisations forment un partenariat avec la FSNC pour déterminer les causes des maladies et des lésions du système nerveux, pour leur trouver un traitement, et pour s'occuper des patients qui ont ces maladies et lésions. Parallèlement à l'aide financière qu'elles apportent au Journal canadien des sciences neurologiques et à d'autres initiatives que la FSNC aide tout au long de l'année, ces organisations octroient gracieusement des subventions sans condition à but éducatif au congrès annuel qui a lieu cette année à Edmonton, Alberta, du 19 au 22 juin 2007.*

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