THE CANADIAN JOURNAL OF
Neurological Sciences

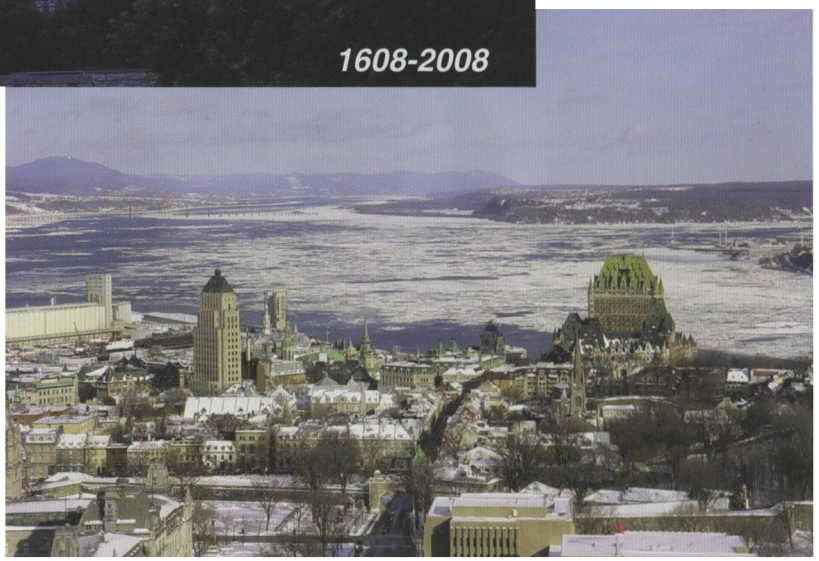
LE JOURNAL CANADIEN DES
Sciences Neurologiques

VOLUME 35 NUMBER 4 SEPTEMBER 2008

Photos courtesy of Dr. Martin Savard, Québec City, QC

This year, all roads lead to Québec City as they mark four fabulous centuries of history! Québec City has come a long way since Samuel de Champlain first landed there 400 years ago.

Cette année, tous les chemins mènent à Québec qui célèbre quatre fabuleux siècles d'histoire! Québec a fait beaucoup de chemin depuis la venue de Samuel de Champlain, il y a 400 ans.



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JOURNAL COVER

We are investigating different options for the cover of the Journal and thought it might be appropriate to include pictures of major Canadian Cities and/or Universities as taken by our readers.

If you are interested in submitting pictures, please send them to maggie-mccallion@cnsfederation.org in high resolution format, (i.e. tif or jpeg). Please also indicate your willingness to provide these pictures free of charge. Picture 'acknowledgement' will be provided.

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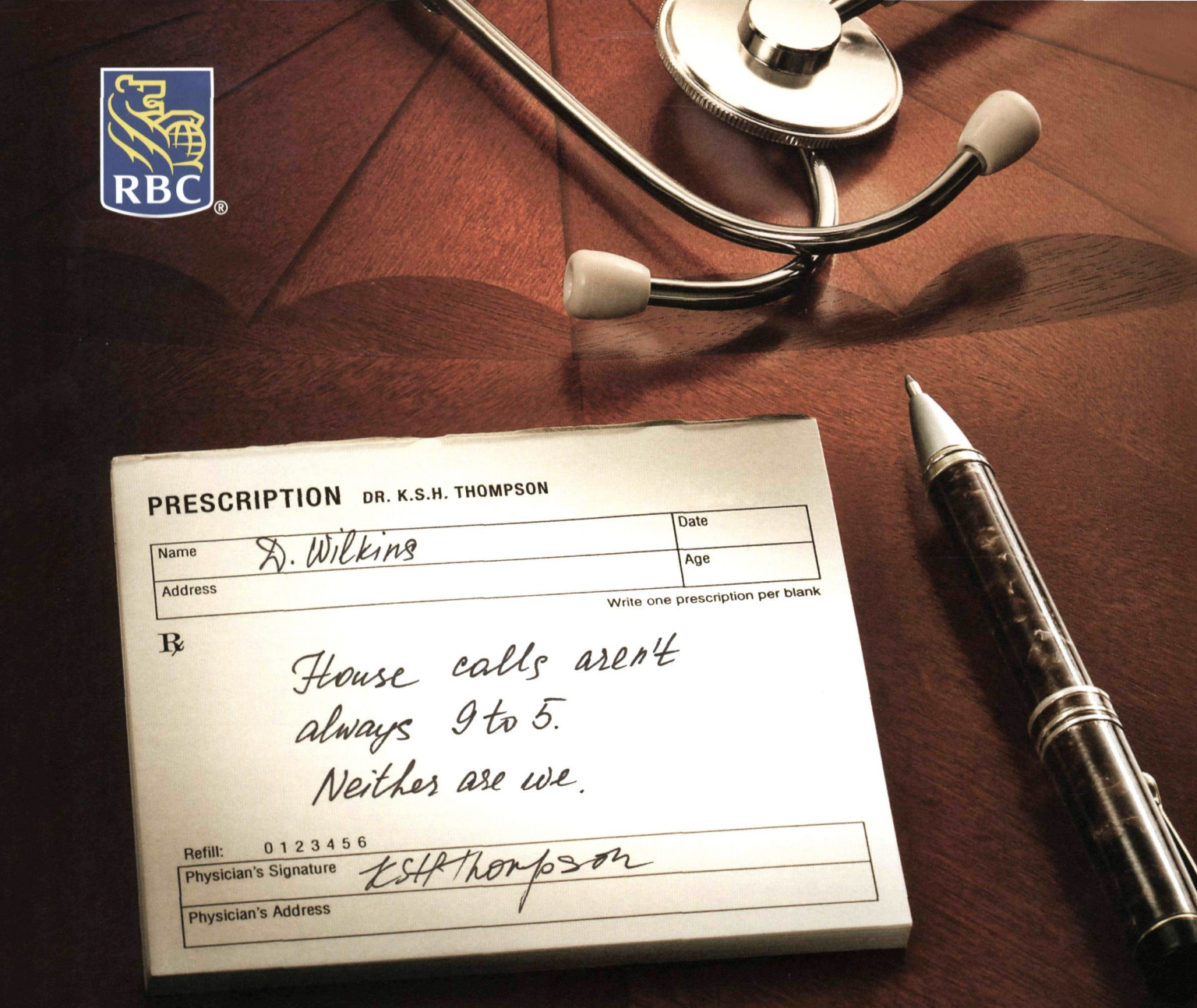

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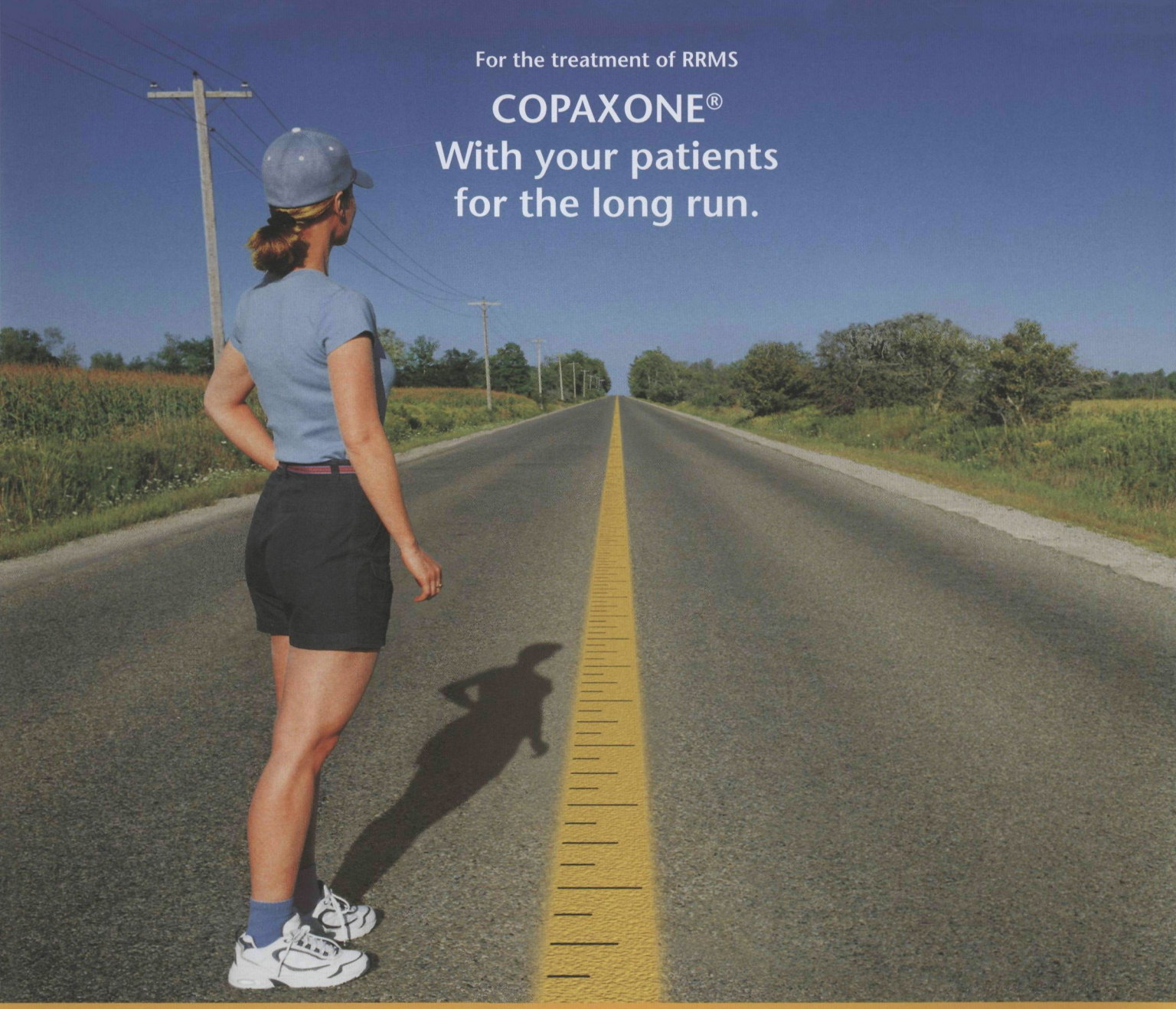

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COPAXONE® is indicated for use in ambulatory patients with Relapsing-Remitting Multiple Sclerosis (RRMS) to reduce the frequency of relapses. The safety and efficacy of COPAXONE® in chronic progressive MS have not been established.

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Reference: 1. COPAXONE® (glatiramer acetate injection) Product Monograph, TEVA Neuroscience

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- Powerful 24-hour BP reductions shown, $p<0.0001$ including the early morning hours (6:00 AM-11:59 AM), $p<0.0001$[2†]
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- The ONTARGET clinical trial program investigates ARB and ACE therapy in more than 31,000 patients.
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- 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® (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.

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%).

If pregnancy is detected, MICARDIS® should be discontinued as soon as possible. In patients who are volume-depleted by diuretic therapy, dietary salt restriction, dialysis, diarrhea or vomiting, symptomatic hypotension may occur after initiation of therapy with MICARDIS®.

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.

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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-20

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LYRICA may be useful in the management of central neuropathic pain (NeP) in adult patients for which it has been issued marketing authorization with conditions to reflect the promising nature of the clinical evidence and the need for a confirmatory study to verify its clinical benefit. Patients should be advised of the nature of the authorization.

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- Pain relief shown in postherpetic neuralgia (PHN) and central NeP as early as week 1 and demonstrated over 3 months[1-3*†]
- Improvement shown in pain-related sleep interference in PHN and central NeP as early as week 1 and demonstrated over 3 months[1-4*†]

Significant improvement in overall status.

- Significant improvement demonstrated in patient-reported overall status (Patient Global Impression of Change [PGIC]) in patients with peripheral NeP [diabetic peripheral neuropathy (DPN) or PHN] and central NeP[1-3,5*†‡]

LYRICA (pregabalin) is an analgesic indicated for the management of neuropathic pain (NeP) associated with DPN and 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 (≥5% and 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 (9.0-37.0%), somnolence (6.1-24.7%), peripheral edema (6.1-16.2%), and dry mouth (1.9-14.9%). The most commonly observed adverse events seen in central NeP patients (≥5% and twice the rate as that seen with placebo) in the recommended dose range of 150 mg/day to 600 mg/day were: somnolence (41.4%), dizziness (24.3%), asthenia (15.7%), dry mouth (15.7%), edema (12.9%), constipation (12.9%), amnesia (10.0%), myasthenia (8.6%), amblyopia (8.6%), and thinking abnormal (8.6%). The most commonly observed adverse events in the PHN, DPN, and central NeP patients were usually mild to moderate in intensity. Discontinuation rates due to adverse events for LYRICA and placebo, respectively, were 9% and 4% in DPN, 14% and 7% in PHN and 21% and 13% in central NeP.

Dosage reduction is required in patients with renal impairment (creatinine clearance <60 mL/min) as LYRICA is primarily eliminated by renal excretion.

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

* 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 ($p \leq 0.01$, weeks 1-13). Sleep interference was improved at all time points (weeks 1 to 13 and endpoint) for the three doses evaluated ($p \leq 0.01$ vs. placebo). PGIC was reported as (at least minimally) improved by 51.2%, 47.9% and 67.1% of patients treated with LYRICA doses of 150, 300, and 600 mg/day vs. 35.5% of patients in the placebo group. At study termination, patients in the 150 mg/day ($p=0.02$) and 600 mg/day group ($p=0.003$) were more likely to report global improvement than those in the placebo group.

† Data based on a 12-week, parallel-group, double-blind, flexible-dose, placebo-controlled study. 137 patients with spinal cord injury for ≥1 year and who had a pain score ≥40 mm on the 100-mm visual analog scale (VAS) of the Short-Form-McGill Pain Questionnaire (SF-MPQ) were randomized to LYRICA 150 to 600 mg/day (n=70) or placebo (n=67) BID. Pain scores rated on 11-point numerical scale from 0 (no pain) to 10 (worst possible pain) during the past 24 hours averaged over the last seven days. Pain-related sleep interference scores rated on 11-point numerical scale from 0 (did not interfere) to 10 (completely interferes) during the past 24 hours averaged over the last seven days. A significant difference in pain reduction was demonstrated for the LYRICA group vs. placebo at all time points evaluated ($p \leq 0.001$, weeks 1-7 and endpoint and $p \leq 0.01$, weeks 8-12). Sleep interference was significantly improved at all time points (weeks 1 to 12 and endpoint) vs. placebo ($p \leq 0.01$, weeks 4, 10 and 12 and $p \leq 0.001$ for all other time points evaluated and endpoint). PGIC was reported as (at least minimally) improved by 56.5% and 21.5% of patients in the LYRICA and placebo treatment groups, respectively ($p<0.001$ for overall LYRICA comparison vs. placebo across "improved", "unchanged" and "worse" subgroups).

‡ 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 ($p \leq 0.05$, week 2-3 and $p \leq 0.01$, weeks 4-12), and the fixed dose of 600 mg/day ($p \leq 0.05$, week 1 and $p \leq 0.01$, weeks 2-12). PGIC was reported as very much improved or much improved by 52.0% of the flexible-dose group, 53.6% of the fixed-dose group and 30.5% of the placebo group ($p<0.01$ for overall comparison of both LYRICA treatment groups vs. placebo across "improved", "unchanged" and "worse" subgroups).

References: 1. Data on file, Pfizer Canada Inc., Study 1008-196. **2.** van Seventer R, Feister HA, Young JP *et al*. Efficacy and tolerability of twice-daily pregabalin for treating pain and related sleep interference in postherpetic neuralgia: a 13-week, randomized trial. *Curr Med Res Opin* 2006; 22(2):375-84. **3.** Siddall PJ *et al*. Pregabalin in central neuropathic pain associated with spinal cord injury: a placebo-controlled trial. *Neurology* 2006; 67:1792-800. **4.** LYRICA Product Monograph, Pfizer Canada Inc., November 8, 2007. **5.** Freynhagen R, Strojek K, Griesing T *et al*. Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomised, double-blind, multicentre, placebo-controlled trial of flexible- and fixed-dose regimens. *Pain* 2005; 115:254-63.

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See prescribing summary on A-29, A-30

LYRICA peut être utile dans le traitement de la douleur neuropathique d'origine centrale chez l'adulte. À ce titre, LYRICA a fait l'objet d'une autorisation de commercialisation conditionnelle sur la base de données cliniques prometteuses et dans l'attente des résultats d'études permettant d'attester ses bienfaits cliniques. Les patients doivent être avisés de la nature de l'autorisation.

NOUVEAU

La prégabaline : le premier et le seul analgésique de première intention approuvé avec conditions pour le traitement de la douleur neuropathique d'origine centrale

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Soulagement efficace de la douleur

Efficacité. Effet rapide. Soulagement soutenu.

- Soulagement de la douleur dans les cas de névralgie postzostérienne (NPZ) et de douleur neuropathique d'origine centrale démontré dèsla 1re semaine et pendant 3 mois[1-3*†]
- Réduction des perturbations du sommeil liées à la douleur dans les cas de NPZ et de douleur neuropathique d'origine centrale dès la 1re semaine et pendant 3 mois[1-4*†]

Amélioration importante de l'état général.

- Amélioration importante démontrée de l'état général tel que perçu par le patient (échelle d'impression globale du patient à propos de l'évolution de son état [PGIC]) dans les cas de douleur neuropathique d'origine périphérique (NDP et NPZ) et de douleur neuropathique d'origine centrale[1-3,5*†‡]

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 observés le plus souvent (chez au moins 5 % des patients et 2 fois plus souvent que dans les groupes témoins) 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 %). Les effets indésirables observés le plus souvent chez les patients atteints de douleur neuropathique d'origine centrale (chez au moins 5 % des patients et 2 fois plus souvent que dans les groupes témoins) dans l'intervalle posologique recommandé de 150 mg/jour à 600 mg/jour et ont été les suivants : somnolence (41,4 %), étourdissements (24,3 %), asthénie (15,7 %), sécheresse buccale (15,7 %), œdème (12,9 %), constipation (12,9 %), amnésie (10,0 %), myasthénie (8,6 %), amblyopie (8,6 %) et anomalies de la pensée (8,6 %). Les effets indésirables signalés le plus souvent chez les patients souffrant de NPZ, de NDP ou de douleur neuropathique d'origine centrale étaient généralement d'intensité légère à modérée. Le taux d'abandons imputables aux effets indésirables chez les patients du groupe LYRICA et du groupe placebo, respectivement, s'élevait à 9 % et à 4 % chez les patients souffrant de NDP, à 14 % et à 7 % chez ceux souffrant de NPZ et à 21 % et à 13 % chez les patients souffrant de douleur neuropathique d'origine centrale.

Comme les reins constituent la principale voie d'élimination de LYRICA, une réduction de la dose s'impose chez les patients présentant un dysfonction-nement rénal (clairance de la créatinine < 60 mL/min).

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

* Essai multicentrique de 13 semaines mené à double insu avec placebo auprès de 368 patients souffrant de NPZ. 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, ($p \leq 0,01$, semaines 1-13). 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 ($p \leq 0,01$ vs placebo). La proportion de patients dont l'état s'était amélioré (au moins très légèrement) selon l'échelle PGIC était de 51,2 %, de 47,9 % et de 67,1 % dans les groupes recevant LYRICA à raison de 150, 300 et 600 mg/jour, respectivement, comparativement à 35,5 % dans le groupe placebo. À la fin de l'étude, les patients qui avaient reçu la dose de 150 mg/jour ou de 600 mg/jour étaient plus susceptibles que ceux du groupe placebo à noter une amélioration globale de leur état ($p = 0,02$ et 0,003 respectivement).

† D'après un essai comparatif avec placebo de 12 semaines, mené à double insu avec groupes parallèles et schéma posologique souple. Cent trente-sept (137) patients présentant une lésion de la moelle épinière depuis ≥ 1 an et qui, au début de l'étude, avaient obtenu un score de la douleur d'au moins 40 mm sur 100 mm à l'échelle visuelle analogique du questionnaire *Short-Form-McGill Pain* ont été répartis de façon aléatoire pour recevoir LYRICA à raison de 150 à 600 mg/jour (n = 70) ou un placebo (n = 67) deux fois par jour. Les scores de la douleur ont été établis à partir d'une échelle numérique de 11 points, où 0 désigne l'absence de douleur et 10, la pire douleur possible, au cours d'une période de 24 heures, et représentent la moyenne des sept derniers jours. Les scores des perturbations du sommeil liées à la douleur ont été établis à partir d'une échelle de 11 points, où 0 désigne l'absence de perturbations et 10, une perturbation complète, sur une période de 24 heures, et représentent la moyenne des sept derniers jours. Lors de toutes les évaluations prévues, on a observé une différence significative entre le groupe LYRICA et le groupe placebo en ce qui a trait au soulagement de la douleur ($p \leq 0,001$ pour les semaines 1 à 7 et à la fin de l'étude, et $p \leq 0,01$ pour les semaines 8 à 12) et à la réduction des perturbations du sommeil ($p \leq 0,01$ pour les semaines 4, 10 et 12, et $p \leq 0,001$ pour toutes les autres évaluations et à la fin de l'étude). La proportion de patients dont l'état s'était amélioré (au moins très légèrement) selon l'échelle PGIC était de 56,5 % dans le groupe LYRICA et de 21,5 % dans le groupe placebo ($p < 0,001$ pour la comparaison globale entre LYRICA et le placebo dans les sous-groupes « amélioration », « aucun changement » et « aggravation »).

‡ Essai multicentrique 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). La proportion de patients dont l'état s'était amélioré considérablement ou beaucoup selon l'échelle PGIC était de 52,0 % dans le groupe recevant la dose flexible, de 53,6 % dans le groupe recevant la dose fixe et de 30,5 % dans le groupe placebo ($p < 0,01$ pour la comparaison globale entre les deux groupes LYRICA et le groupe placebo dans les sous-groupes « amélioration », « aucun changement » et « aggravation »).

Références : 1. Données internes, Pfizer Canada Inc., étude 1008-196. **2.** van Seventer R, Feister HA, Young JP *et al.* Efficacy and tolerability of twice-daily pregabalin for treating pain and related sleep interference in postherpetic neuralgia: a 13-week, randomized trial. *Curr Med Res Opin* 2006; 22(2):375-84. **3.** Siddall PJ *et al.* Pregabalin in central neuropathic pain associated with spinal cord injury: a placebo-controlled trial. *Neurology* 2006; 67:1792-800. **4.** Monographie de LYRICA, Pfizer Canada Inc., 8 novembre 2007. **5.** Freynhagen R, Strojek K, Griesing T *et al.* Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomised, double-blind, multicentre, placebo-controlled trial of flexible- and fixed-dose regimens. *Pain* 2005; 115:254-63.

Pfizer

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Pr LYRICA MD PRÉGABALINE

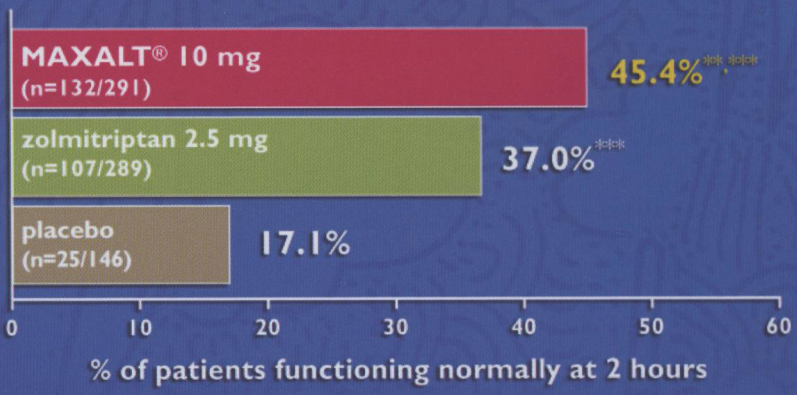
Effet rapide. Soulagement soutenu.

Veuillez consulter les renseignements thérapeutiques à la page A29, A30

MAXALT® RPD: The most dispensed non-tablet formulation migraine drug in Canada[1]

Help Them Face the Day

23% more patients experienced return to normal function at 2 hours with PrMAXALT® 10 mg tablet than with zolmitriptan 2.5 mg.[2,*]



Adapted from Pascual J et al

No statistically significant difference in headache relief was seen at the 2-hour endpoint.[2]

MAXALT® (rizatriptan benzoate) is indicated for the acute treatment of migraine attacks with or without aura in adults. MAXALT® is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic, ophthalmoplegic or basilar migraine. Safety and effectiveness of MAXALT® have not been established for cluster headache, which is present in an older, predominantly male population.

MAXALT® 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 diseases should not receive MAXALT®. MAXALT® is also contraindicated in patients with uncontrolled or severe hypertension. MAXALT® is contraindicated in co-administration with monoamine oxidase (MAO) inhibitors within 2 weeks after discontinuation of treatment, and within 24 hours of administration of 5-HT_1 agonists and ergot-type medications. For a complete list of contraindications, please consult the Product Monograph.

The recommended single adult dose is 5 mg. The maximum recommended single dose is 10 mg.

The most common adverse events during treatment with MAXALT® (rizatriptan benzoate) tablets 10 mg were dizziness (8.9%), somnolence (8.4%), asthenia/fatigue (6.9%), nausea (5.7%) and pain/pressure sensation (1.8-3.1%). The most common adverse events during treatment with MAXALT RPD® (rizatriptan benzoate) wafers 10 mg were dizziness (8.6%), nausea (7.0%), dry mouth (6.0%), somnolence (5.3%), asthenia/fatigue (3.6%), and pain/pressure sensation (chest, 1.7%; neck/throat/jaw, 2.0%; upper limb, 2.0%).

MAXALT RPD® wafers contain phenylalanine (a component of aspartame).

*Return to normal function: An assessment of functional disability on a four-point scale (0=normal, 1=mildly impaired, 2=severely impaired, 3=unable to do activities, requires bed-rest).[2] A randomized, double-blind, placebo-controlled outpatient study comparing the clinical profiles of rizatriptan 10 mg tablets and zolmitriptan 2.5 mg tablets for the acute treatment of a single migraine attack. A total of 882 men and women who met the IHS criteria for migraine with or without aura were enrolled. Patients had to have had a six-month history of migraine and usually experienced one to eight attacks per month.[2]

**$p<0.05$ vs zolmitriptan

***$p<0.001$ vs placebo

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BEFORE PRESCRIBING, PLEASE CONSULT THE ENCLOSED PRESCRIBING INFORMATION FOR WARNINGS, PRECAUTIONS, ADVERSE EVENTS AND IMPORTANT PATIENT SELECTION CRITERIA.

Reference: 1. Brogan Inc. Geographic Prescription Monitor (GPM®) December 2006 to November 2007. **2.** Pascual J et al. Comparison of rizatriptan 10 mg vs zolmitriptan 2.5 mg in the acute treatment of migraine. Cephalalgia 2000;20:455-61.

PrMaxalt RPD®
(rizatriptan benzoate)

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See prescribing summary on pages A-24 to A-26

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