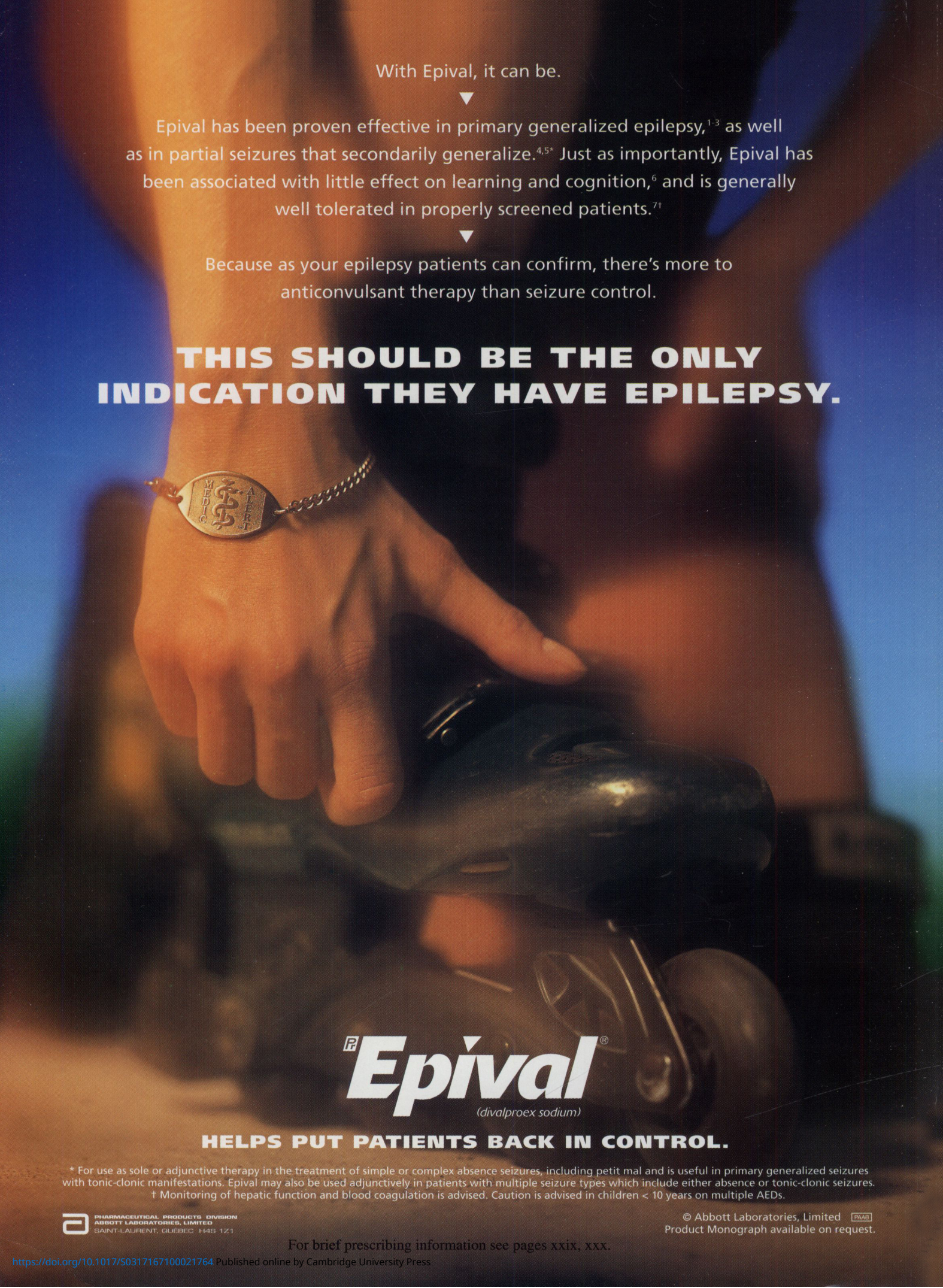
Volume 24 Number 3 August 1997

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL

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



https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

Volume 24 Number 3 August 1997

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

Volume 24 Number 3 August 1997

THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

The official journal of: / La Revue officielle de:

The Canadian Neurological Society
La Société Canadienne de Neurologie

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 Congress of Neurological Sciences is at/
Le secrétariat des quatre associations et du Congrès Canadien des Sciences Neurologiques est situe en permanence à:
810, 906 - 12 Avenue S.W., Calgary, AB Canada T2R 1K7

The Canadian Journal of Neurological Sciences is published quarterly. The annual subscription rate is $65 for members; $75 for non-members in Canada; $85 for USA and elsewhere. Residents, Interns, Pre- and Post-Doctoral Students $32.50 per annum (members); $37.50 per annum (non-members). Single copies $20 each plus postage and handling. All manuscripts and communications should be sent to: Canadian Journal of Neurological Sciences, P.O. Box 4220, Station C, Calgary, AB Canada T2T 5N1. Courier to: 810, 906 - 12th Avenue S.W., Calgary, AB Canada T2R 1K7. Telephone (403) 229-9575; Fax (403) 229-1661. E-mail: cjns@canjneurolsci.org; Web Site: www.canjneurolsci.org

Mailed under Publications Mail registration number 3307. Postage paid at Calgary, Alberta. This journal is indexed by *Index Medicus, Excerpta Medica and Current Contents — Clinical Practice and Life Sciences, Current Awareness in Biological Sciences, Biological Abstracts, Chemical Abstracts, Current Advances in Ecological Sciences, Dent.index, Industrial Medicine, Industrial Science Reviews, INIS Automind, Nutrition Abstracts, Science Citation Index, Weed Abstract.*

Le Journal Canadien des Sciences Neurologiques est publié trimestriellement. L'abonnement annuel est de 65 $ pour les membres; 75 $ pour les non-membres au Canada; 85 $ pour les Etats Unis et ailleurs. Internes, résidents, fellows pré et post doctoral: 32,50 $ par année (membres); 37,50 $ par année (non-membres). Copie simple: 20 $ plus affranchissement et manutention. Toutes les communications et les manuscrits doivent être adressés à Journal Canadien des Sciences Neurologiques, P.O. Box 4220, Station C, Calgary, AB Canada T2T 5N1. Par courrier: 810, 906 - 12th Avenue S.W., Calgary, AB Canada T2R 1K7. Téléphone (403) 229-9575; Fax (403) 229-1661. E-mail cjns@canjneurolsci.org; Web Site: www.canjneurolsci.org

Le Journal est cité et indexé dans *Index Medicus, Excerpta Medica et Current Contents — Clinical Practice et Life Sciences, Current Awareness in Biological Sciences, Biological Abstracts, Chemical Abstracts, Current Advances in Ecological Sciences, Dent.index, Industrial Medicine, Industrial Science Reviews, INIS Automind, Nutrition Abstracts, Science Citation Index, Weed Abstract.*

***Advertising representative/Représentant de publicité*:**
Sally Gregg, Canadian Journal of Neurological Sciences
810, 906 - 12 Ave. S.W., Calgary, AB Canada T2R 1K7
Tel (403) 229-9575 Fax (403) 229-1661
E-mail: cjns@canjneurolsci.org
Web Site: www.canjneurolsci.org

***Printer/Imprimeur*:**
McAra Printing Limited, 105, 2507 - 12th Street N.E.,
Calgary, Alberta T2E 7L5

ISSN 0317 - 1671

Pr SABRIL®

VIGABATRIN

IMPRESSIVE EFFICACY[1] WHEN SABRIL® IS ADDED TO FIRST LINE TREATMENT

- Almost 50% of patients (n=333)†, with mild to moderate partial epilepsy, became seizure-free[2]
- Significant increase in seizure control‡ in 66% of patients[3]
- No negative effects on cognitive function to impair job performance or quality of life[4]

Winner of the 1996 Prix Galien Canada for Innovative Product

† Of the 333 patients who completed > 100 days of treatment (mean dose 2.6 ± 0.5 g/day)

‡ ≥ 50% reduction in seizure frequency; N=31, at doses of 1-2 gm per day, duration of 8 weeks, as part of an initial, open phase study. However in clinical trials, Sabril reduced seizure frequency by 50% or more in approximately half of the patients studied.

Neurological function/visual disturbances should be monitored; used with caution in patients with a history of psychosis, in the elderly, in the renally impaired; there could be occupational hazards due to drowsiness; there may be a possible increase in seizures in some patients.

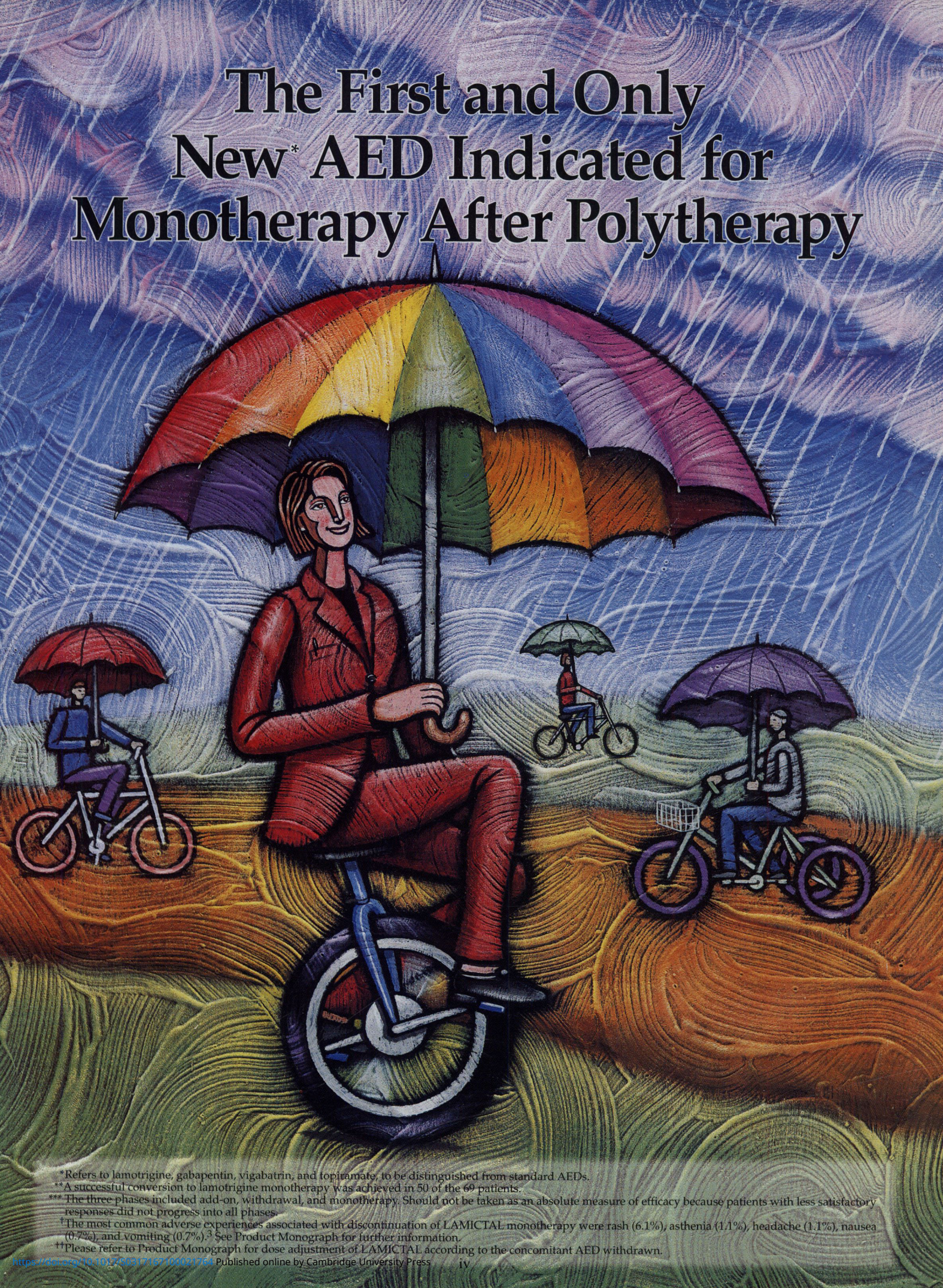
Hoechst Marion Roussel

Hoechst Marion Roussel Canada Inc.,
Laval, Quebec H7L 4A8
A member of the Hoechst Group

Hoechst

For brief prescribing information see page x.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press



*Refers to lamotrigine, gabapentin, vigabatrin, and topiramate, to be distinguished from standard AEDs.
**A successful conversion to lamotrigine monotherapy was achieved in 50 of the 69 patients.
***The three phases included add-on, withdrawal, and monotherapy. Should not be taken as an absolute measure of efficacy because patients with less satisfactory responses did not progress into all phases.
†The most common adverse experiences associated with discontinuation of LAMICTAL monotherapy were rash (6.1%), asthenia (1.1%), headache (1.1%), nausea (0.7%), and vomiting (0.7%).[3] See Product Monograph for further information.
††Please refer to Product Monograph for dose adjustment of LAMICTAL according to the concomitant AED withdrawn.

For Control Over a Wide Range of Seizure Types, with a Low CNS Side-Effect Profile

Effective monotherapy has been largely accepted as the regimen of choice for achieving seizure control with minimal side effects in the management of patients with epilepsy.[1] Now, extending its proven success as adjunctive therapy,[2] LAMICTAL is indicated for monotherapy in adults following withdrawal of concomitant antiepileptic drugs (AEDs).[3]

HIGHLY EFFECTIVE MONOTHERAPY

In one add-on/withdrawal to monotherapy open-label trial, LAMICTAL monotherapy following withdrawal of concomitant AEDs kept 30% (n=50) of the successfully treated patients seizure-free.**[4] In a similarly designed trial, ≥ 40% of the patients were maintained with at least 50% reduction of seizure frequency across all phases of the trial.***[5]

GENERALLY BETTER TOLERATED†

Pooled data from three monotherapy trials show that withdrawals due to CNS-related side effects were 2.5% (n=443) with LAMICTAL monotherapy compared to phenytoin (7.4%; n=95) or carbamazepine (7.7%; n=246).[6] Incidence of somnolence, asthenia, and ataxia were reported less frequently with LAMICTAL compared to carbamazepine and phenytoin. There was no difference in the rate of withdrawal due to skin rash between LAMICTAL (6.1%) and phenytoin (5.3%) or carbamazepine (8.9%).[6] A higher incidence of skin rash has been associated with more rapid initial titration of LAMICTAL or use of concomitant valproic acid.[3]

CONTROL OVER A WIDE RANGE OF SEIZURE TYPES

LAMICTAL add-on polytherapy has been successfully used across a wide range of seizure types.[2] Now, opt to switch with confidence from LAMICTAL polytherapy to LAMICTAL monotherapy,†† particularly when you are concerned with CNS-related side-effects.

Lamotrigine

℗ Lamictal®

FROM POLYTHERAPY TO MONOTHERAPY

GlaxoWellcome

Glaxo Wellcome Inc.

MEMBER PMAC

PAAB CCPP

®Registered trademark of The Wellcome Foundation Limited, Glaxo Wellcome Inc. licensed use. Product Monograph available to healthcare professionals on request.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

For brief prescribing information see pages xxxvii, xxxviii.

2260 32nd Avenue, Lachine, Quebec H8T 3H4

The first treatment for relapsing/remitting multiple sclerosis

T-2 weighted MRI scan (color added). Arrows indicate periventricular lesions.

PAAB PMAC

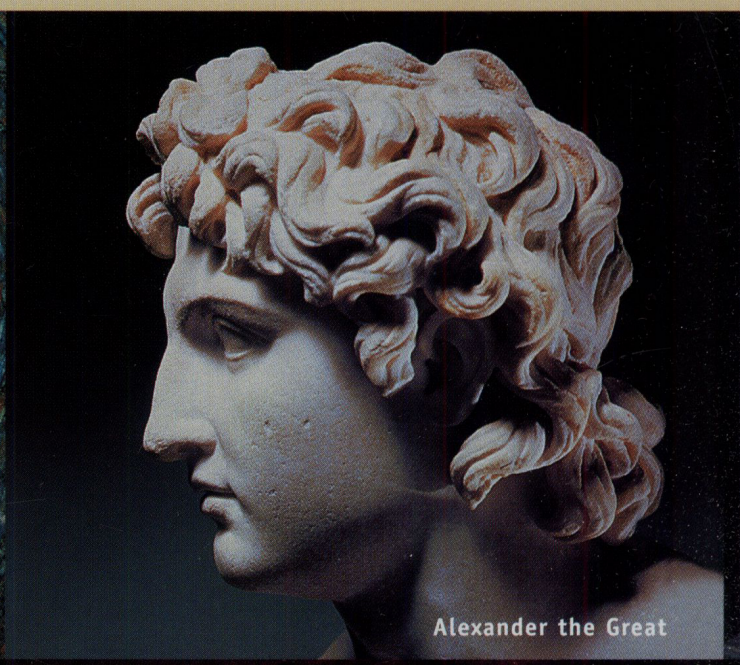
9703590A.00

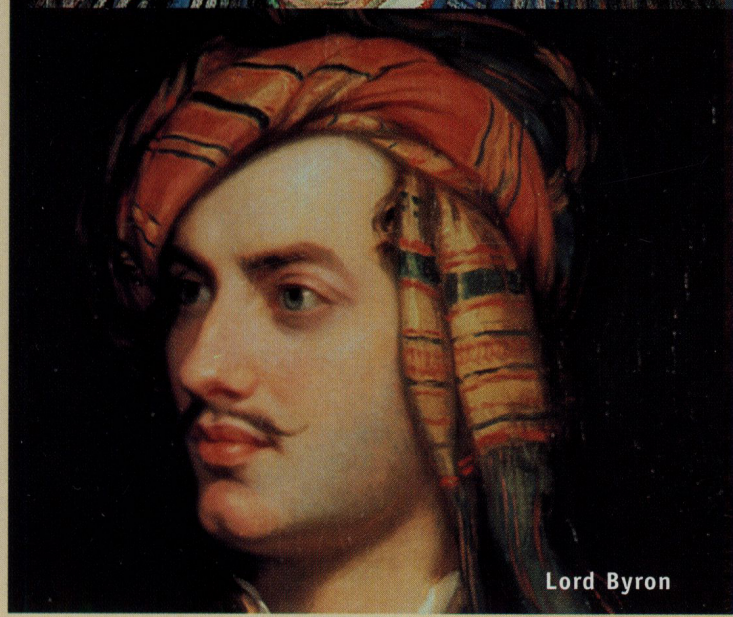
https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

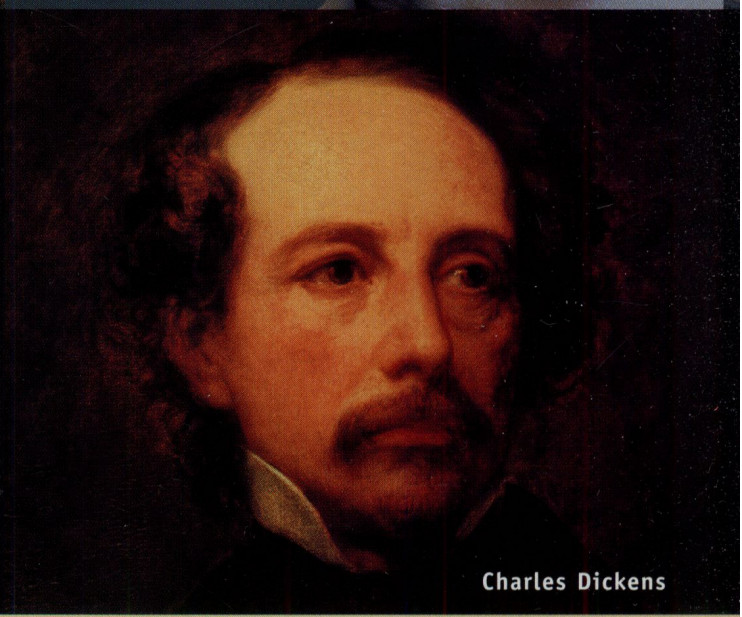
For brief prescribing information see pages xxxix, xl.

NEW IN EPILEPSY

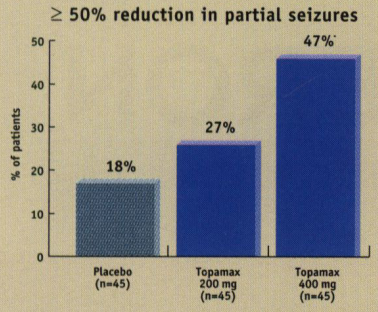

Vincent Van Gogh


Alexander the Great


Lord Byron


Charles Dickens

ONCE IT TOOK EXCEPTIONAL EFFORT OR EXTRAORDINARY LUCKILY, YOUR PATIENTS CAN NOW



Adapted from reference 1. Double-blind trial of placebo vs. TOPAMAX b.i.d. as adjunctive therapy in 181 patients with refractory partial onset epilepsy receiving one or two other AEDs. *p=0.013.

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)[1]
- Unique three-way mechanism of action(Na+ channel blockade, GABA potentiation, glutamate antagonism)[2]

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

TALENT FOR PEOPLE WITH EPILEPSY TO SUCCEED. ENJOY 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)[2]
- No evidence of serious rash or aplastic anemia[2]
- Dosage adjustments to primary therapy are generally not required; patients on phenytoin showing clinical signs or symptoms of toxicity should have phenytoin levels monitored†[2]
- **Convenient BID dosing**

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

	TOPAMAX 200-400 mg (n=113)	PLACEBO (n=216)
Somnolence	30.1	9.7
Dizziness	28.3	15.3
Ataxia	21.2	6.9
Psychomotor slowing	16.8	2.3
Speech disorders	16.8	2.3
Nervousness	15.9	7.4
Nystagmus	15.0	9.3
Paresthesia	15.0	4.6

†As with other AEDs, please see prescribing information for complete information on drug interactions. A 1.5%(n=1715) incidence of kidney stones has been reported.[2] In one study(n=1200), 83%(15 of 18) of patients elected to continue therapy.[4] Ensure adequate hydration and avoid concomitant use with other carbonic anhydrase inhibitors.[2] *Trademark ©Janssen-Ortho Inc. 1997

JANSSEN-ORTHO Inc.
19 Green Belt Drive
North York, Ontario M3C 1L9

PMAAQ PAAB

TOPAMAX* topiramate

Helping patients make more of their lives

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

For brief prescribing information see pages xxxiii, xxxiv, xxxv.

PRESCRIBING INFORMATION

®SABRIL

VIGABATRIN

Tablets 500 mg

Antiepileptic

ACTION AND CLINICAL PHARMACOLOGY

SABRIL (vigabatrin) is an irreversible inhibitor of gamma-aminobutyric acid transaminase (GABA-T), the enzyme responsible for the catabolism of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the brain. The mechanism of action of vigabatrin is attributed to irreversible enzyme inhibition of GABA-T, and consequent increased levels of the inhibitory neurotransmitter, GABA.

Decreased serum levels of SGOT (ALT) and SGPT (AST) have been observed during treatment with vigabatrin and may be the result of inhibition of these transaminases by vigabatrin. The clinical significance of these findings is unknown.

The duration of effect of vigabatrin is thought to be dependent on the rate of GABA-T resynthesis rather than on the plasma concentration of vigabatrin.

Clinical Trials

In clinical trials, including double-blind, placebo-controlled studies involving 354 patients with drug-resistant complex partial seizures, vigabatrin reduced seizure frequency by 50% or more in approximately half of the patients studied.

In clinical trials involving children, the efficacy of vigabatrin was similar to that seen in adult patients with refractory partial seizures. In one study of 70 children with intractable infantile spasms, approximately 70% of the patients had a greater than 50% reduction in spasms. In this study, long-term response was observed in 75% of the children with symptomatic infantile spasms and 36% of the children with cryptogenic infantile spasms.

Pharmacokinetics

Vigabatrin is rapidly absorbed following oral administration and peak plasma concentrations are reached within two hours. Vigabatrin is widely distributed with an apparent volume of distribution slightly greater than total body water. The primary route of elimination is via the kidney, with little metabolic transformation occurring. Following a single dose, approximately 70% is excreted in the urine as unchanged drug within the first 24 hours post-dose. The plasma elimination half-life is approximately 5-8 hours in young adults and 12-13 hours in the elderly. In renal impairment the elimination is prolonged and the rate of renal clearance is directly related to creatinine clearance (see PRECAUTIONS and DOSAGE AND ADMINISTRATION). Vigabatrin does not induce the hepatic cytochrome P450 system nor is it extensively metabolized or plasma-protein bound. Administration of vigabatrin with food slightly reduces the rate, but not the extent of absorption.

INDICATIONS AND CLINICAL USE

SABRIL (vigabatrin) is indicated for the adjunctive management of epilepsy which is not satisfactorily controlled by conventional therapy.

There is insufficient data on the usefulness of vigabatrin in monotherapy at this time.

Vigabatrin should be used under close monitoring by a neurologist.

CONTRAINDICATIONS

SABRIL (vigabatrin) is contraindicated in pregnancy and lactation (see WARNINGS) and in patients with a known hypersensitivity to vigabatrin or to any components of the product.

WARNINGS

Neurotoxicity in Animals

Rat, Mouse and Dog: Safety studies carried out in the rat, mouse and dog at doses of 30 to 50 mg/kg/day and higher, caused dose-and time-dependent microvacuolation within certain white matter tracts of the brain (the cerebellum, reticular formation and thalamus in rodents and the columns of the fornix and optic tracts in dogs were most affected). The microvacuolation was caused by the separation of the outer lamellar sheath of myelinated fibres, a change characteristic of non-inflammatory intramyelinic edema.

In both the rat and dog (mouse was not tested), the intramyelinic edema was reversible after stopping the administration of vigabatrin; however, in the mouse and rat, residual changes consisting of swollen axons and mineralised microbodies were observed.

Monkey: In monkeys, the oral administration of 300 mg/ kg/day for 16 months produced minimal microvacuolation with equivocal differences between treated and control animals. Low oral absorption of vigabatrin in the monkey resulted in an actual absorbed dose of 75 mg/kg/day. In spite of the poor absorption, cerebrospinal fluid (CSF) levels of vigabatrin in the monkeys were comparable to those seen in rats treated with 300 mg/kg/day; however, GABA levels in the CSF and the brain cortex in treated monkeys were not significantly different from untreated monkeys. This finding may explain the reason for the equivocal effects, since the intramyelinic edema associated with vigabatrin treatment appears to be to increased brain GABA levels.

Evoked Potentials

Evoked potentials in animals: In the dog, studies indicate that intramyelinic edema is associated with increased latencies in somatosensory and visual evoked potentials. Magnetic resonance imaging (MRI) changes also correlated with intramyelinic edema in the fornix, thalamus and hypothalamus.

Evoked potentials in man: No increased evoked potential latencies have been observed in man. Two hundred and twenty-one patients treated for 4-5 months showed no significant evoked potential latency changes at the end of treatment as compared to baseline. MRI results in man did not show the changes observed in dogs who had intramyelinic edema.

Postmortem neuropathological changes seen in 11 patients who were treated with vigabatrin (mean duration of treatment was 28 months, and the longest treatment was 6 years) showed no myelin vacuolation in the white matter that was considered to be outside of the control range.

Although clinical trials have not revealed the type of neurotoxicity seen in animal studies, because of increased CSF GABA levels observed in humans, it is recommended that patients treated with vigabatrin be closely observed for adverse effects on neurological function, with special attention to visual disturbance.

Use in Pregnancy and Lactation: In a teratology study in the rabbit a dose-related incidence, 2% and 9%, of cleft palate was observed at doses of 150 and 200 mg/kg/day, respectively.

In animal reproductive studies neurohistopathology was not performed on the fetuses, therefore it is not known whether micro-vacuolation occurred in utero.The possibility that microvacuolation or other neurotoxicity may occur in human fetuses cannot be discarded.

PRECAUTIONS

Use in Patients with a History of Psychosis Behavioural disturbances such as aggression and psychotic episodes have been reported following initiation of vigabatrin therapy. A history of abnormal behaviour or psychosis appears to be a predisposing factor for such reactions, therefore treatment in such patients should be initiated cautiously at low doses and with frequent monitoring.

Use in the Elderly and in Patients with Renal Impairment Vigabatrin is eliminated via the kidney and caution should be exercised when administering the drug to elderly patients and to patients with renal impairment (see DOSAGE AND ADMINISTRATION).

Use in Patients with Myoclonic Seizures As with other antiepileptic drugs, some patients may experience an increase in seizure frequency with vigabatrin. Patients with myoclonic seizures may be particularly liable to this effect.

Discontinuation of Therapy As with other antiepileptic drugs, abrupt discontinuation may lead to rebound seizures. If a patient is to be withdrawn from vigabatrin treatment, it is recommended that this be done gradually by reducing the dose over a 2 to 4 week period if possible.

Drug Interactions A gradual reduction of about 20% in plasma phenytoin concentration has been observed following add-on therapy with vigabatrin. The mechanism whereby this occurs is unknown. Limited data from clinical trials suggest that increasing the phenytoin dose to compensate may not be necessary.

Occupational Hazards Patients with uncontrolled epilepsy should not drive or handle potentially dangerous machinery. During clinical trials, the most common adverse reactions observed were drowsiness and fatigue. Patients should be advised to refrain from activities requiring mental alertness or physical coordination until they are sure that vigabatrin does not affect them adversely.

ADVERSE REACTIONS

SABRIL (vigabatrin) is generally well tolerated in epileptic patients. Adverse events are mainly CNS-related and probably a secondary consequence of increased GABA levels caused by vigabatrin. The safety of vigabatrin was evaluated in 2081 epileptic patients treated in clinical trials. The relationship of adverse events to vigabatrin therapy was not clearly established as patients were taking other antiepileptic drugs concomitantly. The most frequently reported adverse events were somnolence (12.5%), fatigue (9.2%), and weight gain (5.0%).

The following adverse events were observed in more than 1% of patients:

Adverse Events Reported By More Than 1% of Patients

Body System/ Adverse Event	Number of Patients	Incidence n=2081
Nervous		
somnolence	261	12.5
headache	80	3.8
dizziness	79	3.8
nervousness	56	2.7
depression	52	2.5
memory disturbances	47	2.3
diplopia	46	2.2
aggression	42	2.0
ataxia	39	1.9
vertigo	39	1.9
hyperactivity	37	1.8
vision abnormal	34	1.6
confusion	29	1.4
insomnia	26	1.3
impaired concentration	25	1.2
personality disorder	23	1.1
agitation	21	1.0
Digestive		
abdominal pain	34	1.6
constipation	29	1.4
vomiting	28	1.4
nausea	28	1.4
Body as a Whole		
fatigue	192	9.2
weight gain	104	5.0
asthenia	23	1.1

Adverse events reported with a frequency of less than 1% include: anxiety, emotional lability, behavioural disturbances including psychosis, irritability, tremor, abnormal gait, speech disorder, increased appetite, and dyspepsia.

As with other antiepileptic drugs, some patients may experience an increase in seizure frequency with vigabatrin treatment (see PRECAUTIONS).

Laboratory data indicate that vigabatrin treatment does not lead to renal or hepatic toxicity. Chronic treatment with vigabatrin may be associated with a slight decrease in hemoglobin, which rarely attains clinical significance.

Pediatric Safety Safety data is available in 299 children, aged 2 months to 16 years (1 patient was 18 years of age), participating in clinical trials with vigabatrin. Relationship of adverse events to vigabatrin therapy was not clearly established as children were taking other antiepileptic drugs concomitantly.

The most frequent adverse event observed in children was "hyperactivity" (reported as hyperkinesia 7.7%, agitation 2.3%, excitation 0.3% or restlessness 0.7%), which was observed in 11.0% of children, an incidence higher than that seen in adults. Other commonly reported adverse events were somnolence (8.0%) and weight gain (3.0%).

The following adverse events were reported in children with a frequency greater than 1%:

Adverse Events Reported By More Than 1% of Pediatric Patients

Body System/ Adverse Event	Number of Patients	Incidence n=299
Nervous		
somnolence	24	8.0
hyperkinesia	23	7.7
aggression	8	2.7
insomnia	8	2.7
agitation	7	2.3
ataxia	7	2.3
emotional lability	3	1.0
headache	3	1.0
increased seizures	3	1.0
Digestive		
vomiting	6	2.0
nausea	3	1.0
increased saliva	3	1.0
Body as a Whole		
weight gain	9	3.0
fatigue	8	2.7
hypotonia	3	1.0

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no specific antidote. The usual supportive measures should be employed.

Two cases of SABRIL (vigabatrin) overdose have been reported. In the first case, the patient accidentally took a dose of 14 g daily for 3 days and transient vertigo and tremor were reported. In the second case, an 18-year old female took 30 g of vigabatrin and 250 mg of chlorazepate in a suicide attempt. The patient was admitted to hospital in a state of coma which lasted four days; however, the coma was considered to be due to the chlorazepate rather than vigabatrin. The patient recovered without sequelae.

DOSAGE AND ADMINISTRATION

SABRIL (vigabatrin) is intended for oral administration once or twice daily and may be taken with or without food. Sabril should be added to the patient's current antiepileptic therapy.

Instructions to the patient on the use of SABRIL are provided in the INFORMATION FOR THE CONSUMER section.

Adults The recommended starting dose is 1 g/day, although patients with severe seizure manifestations may require a starting dose of up to 2 g/day. The daily dose may be increased or decreased in increments of 0.5 g depending on clinical response and tolerability. The optimal dose range is between 2-4 g/day. Increasing the dose beyond 4 g/day does not usually result in improved efficacy and may increase the occurrence of adverse reactions.

Children The recommended starting dose in children is 40 mg/kg/day, increasing to 80 - 100 mg/kg/day depending on response. Therapy may be started at 0.5 g/day, and raised by increments of 0.5 g/day weekly depending on clinical response and tolerability.

Elderly and Renally Impaired Patients Vigabatrin is almost exclusively eliminated via the kidney and, therefore, caution should be exercised when administering the drug to the elderly, and more particularly to patients with creatinine clearance less than 60 mL/min. It is recommended that such patients be started on a lower dose of vigabatrin and observed closely for adverse events such as sedation and confusion.

Bodyweight	Daily Dose	No. Tablets/Day
10 - 15 kg	0.5 – 1 g/day	1 – 2 tablets/day
16 - 30 kg	1 – 1.5 g/day	2 – 3 tablets/day
31 - 50 kg	1.5 – 3 g/day	3 – 6 tablets/day
> 50 kg	2 – 4 g/day	4 – 8 tablets/day

AVAILABILITY OF DOSAGE FORMS

Tablets

Each SABRIL (vigabatrin) 500 mg tablet is white to off-white film-coated, oval biconvex, and imprinted "SABRIL" on one side. SABRIL is available in HDPE bottles containing 100 tablets.

Product Monograph available on request.

References:

1 Grant SM, Heel RC, A Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Potential in Epilepsy and Disorders of Motor Control. Drugs. Adis International: June 1991, Vol. 41 No. 6, pg. 889-926.

2 Arzimanoglou AA, Dumas C, Chirardi L et al. Multicentre clinical evaluation of vigabatrin (Sabril) in mild to moderate partial epilepsies. Epilepsia 1995;36(S3)

3 Reynolds BH, Ring HA Farr IN et al. Open, double-blind and long term study of vigabatrin in long term epilepsy. Epilepsia 1991;32:(4):530-538.

4 Doddrill CB, Arnett JL, Sommerville KW, Sussman NM. Effects of differing dosages of vigabatrin (Sabril) on cognitive abilities and quality of life in epilepsy. Epilepsia 1995;36(2):164-173.

PAAB PMAC SABR96016E

Hoechst Marion Roussel

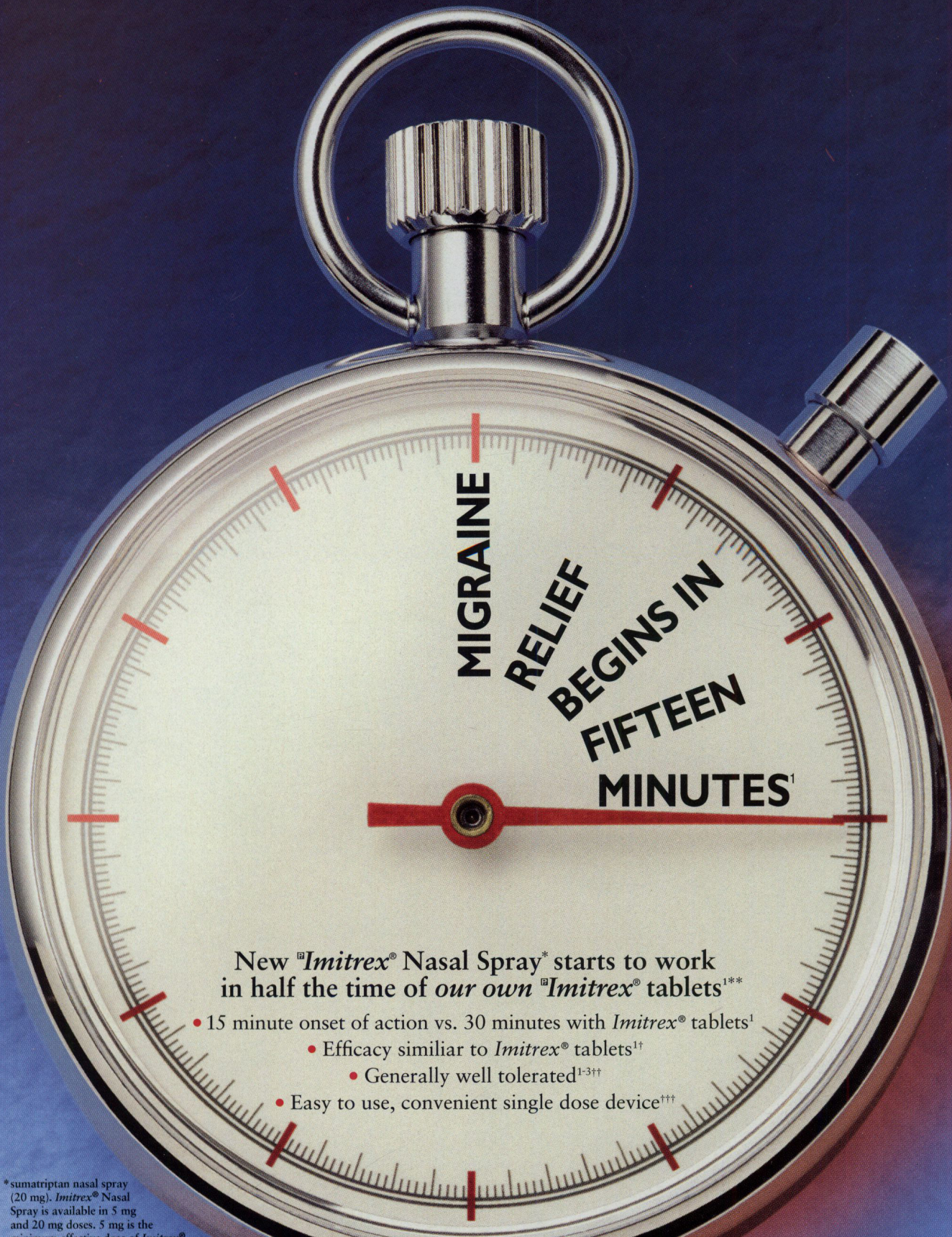
Hoechst Marion Roussel Canada Inc.,
Laval, Quebec H7L 4A8
A member of the Hoechst Group

Hoechst

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

Pour documentation voir page x.

https://doi.org/10.1017/S0317167100021764



New ℗*Imitrex*® Nasal Spray* starts to work in half the time of *our own* ℗*Imitrex*® tablets[1]**

- 15 minute onset of action vs. 30 minutes with *Imitrex*® tablets[1]
- Efficacy similiar to *Imitrex*® tablets[1†]
- Generally well tolerated[1-3††]
- Easy to use, convenient single dose device[†††]

*sumatriptan nasal spray (20 mg). *Imitrex*® Nasal Spray is available in 5 mg and 20 mg doses. 5 mg is the minimum effective dose of *Imitrex*® Nasal Spray. Optimal rates of headache relief are achieved with the 20 mg dose.[1]

**sumatriptan succinate (100 mg tablets)

†*Imitrex*® is a selective 5-HT_1 receptor agonist. *Imitrex*® is indicated for the relief of migraine attacks with or without aura. Contraindicated in patients with ischaemic heart disease, angina pectoris including Prinzmetal angina (coronary vasospasm), previous myocardial infarction and uncontrolled hypertension. There is no experience in patients with recent cerebrovascular accidents or cardiac arrhythmias (especially tachycardias). Therefore the use of *Imitrex*® in these patients is not recommended. For patient selection, please consult the Product Monograph of *Imitrex*® for detailed safety information.[1]

††Adverse event profile similar to placebo – except for a higher incidence of taste disturbance.[1-3]

†††No priming, one spray into one nostril.

GlaxoWellcome

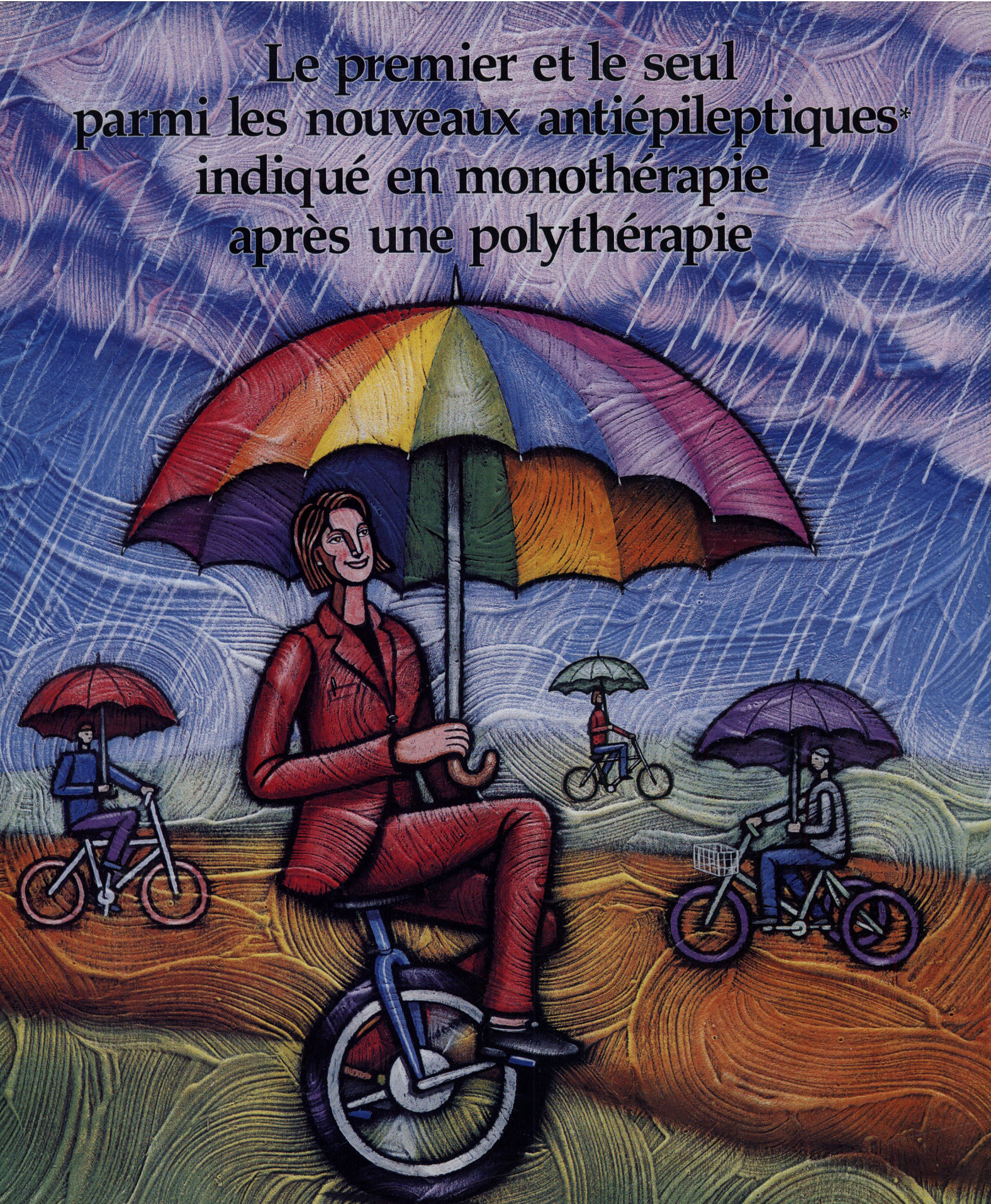
PAAB CCPP

℗IMITREX®
SUMATRIPTAN NASAL SPRAY
A faster way back.™

Single dose device.

For brief prescribing information see pages xiv, xxxv.

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



*C'est-à-dire la lamotrigine, la gabapentine, la vigabatrine et le topiramate, qui se distinguent des antiépileptiques traditionnels.
** Un passage réussi à la lamotrigine en monothérapie a été obtenu chez 50 patients sur 69.
*** L'essai comprenait trois phases : traitement d'appoint, retrait des autres antiépileptiques et monothérapie. Ne doit pas être considéré comme une mesure absolue de l'efficacité parce que les patients n'ont pas terminé toutes les phases de l'essai lorsque leur réponse n'était pas satisfaisante.
† Les effets indésirables le plus fréquemment associés à un arrêt de la monothérapie à LAMICTAL ont été les éruptions cutanées (6,1 %), l'asthénie (1,1 %), la céphalée (1,1 %), la nausée (0,7 %) et les vomissements (0,7 %)[2]. Pour de plus amples renseignements, consulter la monographie de LAMICTAL.
†† Veuillez consulter la monographie pour ce qui est de l'ajustement posologique de LAMICTAL lors du retrait des antiépileptiques administrés en concomitance.

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 chez les patients souffrant d'épilepsie[1]. Maintenant, renforçant son succès éprouvé comme traitement d'appoint[2], LAMICTAL est indiqué comme monothérapie chez l'adulte après le retrait d'antiépileptiques administrés en concomitance[3].

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 monothérapie à LAMICTAL a permis à 30 % (n = 50) des patients traités avec succès de rester exempts de crises[**4]. 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[***5].

GÉNÉRALEMENT MIEUX TOLÉRÉ[†]

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 à 7,4 % pour la phénytoïne (n = 95) ou à 7,7 % pour la carbamazépine (n = 246)[6]. La fréquence de somnolence, d'asthénie et d'ataxie a été moins élevée pour LAMICTAL que pour la carbamazépine et la phénytoïne. On n'a noté aucune différence quant à la fréquence des retraits dus aux éruptions cutanées entre LAMICTAL (6,1 %) et la phénytoïne (5,3 %) ou la carbamazépine (8,9 %)[6]. Une fréquence plus élevée d'éruptions cutanées a été associée à une augmentation posologique plus rapide de la dose initiale de LAMICTAL ou à l'utilisation concomitante d'acide valproïque[3].

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 polythérapie[2]. Vous pouvez passer avec confiance de LAMICTAL comme traitement d'appoint en polythérapie à LAMICTAL en monothérapie[††], en particulier lorsque les effets indésirables liés au SNC sont une considération importante.

lamotrigine

Lamictal®

DE LA POLYTHÉRAPIE À LA

MONOTHÉRAPIE

MEMBRE ACIM

GlaxoWellcome

Glaxo Wellcome Inc.
Bureau d'affaires du Québec

PAAB CCPP

® Marque déposée de The Wellcome Foundation Limited, utilisée sous licence par Glaxo Wellcome Inc.

Monographie du produit fournie sur demande aux professionnels de la santé.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

Pour documentation voir pages xxxvii, xxxviii.

Pr MIGRANAL*

(dihydroergotamine mesylate nasal spray)

4 mg/mL Nasal Spray

THERAPEUTIC CLASSIFICATION: Migraine Therapy

PHARMACOLOGICAL CLASSIFICATION: 5-HT_1 Receptor Agonist

ACTIONS AND CLINICAL PHARMACOLOGY: Dihydroergotamine displays agonist activity at the 5-HT_{1D} receptor, which, by reducing 5-HT neuronal function and/or contracting elements of the cranial vasculature and/or suppressing neurogenic inflammation, is believed to underlie its anti-migraine efficacy. It also displays affinity for the 5-HT_{1C} receptor and antagonistic activity at the 5-HT_2 subtype. Dihydroergotamine displays blocking actions at alpha adrenoreceptors, with a direct stimulating effect on the smooth muscle of peripheral blood vessels. Its tonic effect on capacitance vessels (veins) is particularly pronounced, compared to its effects on resistance vessels (arterioles). Dihydroergotamine differs from ergotamine by being more potent with respect to its adrenergic blocking actions and less potent with respect to its capacity to produce arterial vasoconstriction, but it maintains a marked venoconstrictor effect. Dihydroergotamine reduces the incidence and degree of nausea, photophobia, and phonophobia. Intranasally administered dihydroergotamine is rapidly absorbed in a dose-independent manner (t_{max} = approximately 45 minutes). Significant relief of migraine begins within approximately 30 minutes following administration of MIGRANAL (dihydroergotamine mesylate nasal spray). Once pain is relieved, the incidence of return of pain within 24 hours is low. The bioavailability of dihydroergotamine administered intranasally is 43%. Dihydroergotamine is 93% bound to plasma proteins and has a steady-state volume of distribution of about 800 L. The parent drug constitutes 70 to 80% of plasma concentrations of drug-related materials. The nasal spray form of dihydroergotamine, like most parenteral dose routes, is not subject to first-pass hepatic metabolism. The total body clearance is about 1.5 L/min., reflecting mainly a hepatic clearance. Plasma elimination of dihydroergotamine is biphasic with a mean terminal half-life of 10 hours. The major route of excretion is via the bile in the feces. After intranasal administration, the urinary recovery of parent drug amounts to about 2% of the dose.

INDICATIONS AND CLINICAL USE: MIGRANAL (dihydroergotamine mesylate nasal spray) is indicated for the treatment of migraine headaches, with or without aura, in adults. MIGRANAL is not indicated for prophylactic therapy or for the management of hemiplegic or basilar migraine.

CONTRAINDICATIONS: MIGRANAL (dihydroergotamine mesylate nasal spray) is contraindicated in patients who have previously shown hypersensitivity to ergot alkaloids, or to any of the components of MIGRANAL. MIGRANAL is contraindicated in patients having conditions predisposing to vasospastic reactions such as known peripheral arterial disease, coronary heart disease (in particular unstable or vasospastic angina), septic conditions and shock, vascular surgery, obliterative vascular disease, inadequately controlled hypertension, and severely impaired hepatic function. Dihydroergotamine possesses oxytocic properties and, therefore, should not be administered during pregnancy. It is likely that dihydroergotamine is excreted in breast milk. MIGRANAL is therefore contraindicated for nursing mothers.

WARNINGS: Dihydroergotamine could cause vasospastic reactions, including angina, although it seems to do so less frequently than ergotamine. This action appears to be dose-related. These reactions are manifested by intense arterial vasoconstriction, producing signs and symptoms of peripheral vascular ischemia (e.g., muscle pains, numbness, coldness and pallor or cyanosis of the digits), angina or unusual syndromes, such as mesenteric ischemia. Consequently, MIGRANAL (dihydroergotamine mesylate nasal spray) should be discontinued immediately if signs or symptoms of vasoconstriction develop. The solution used in MIGRANAL was especially developed for intranasal administration and **must not be injected.**

PRECAUTIONS: ***Pediatric Use:*** Safety and effectiveness of MIGRANAL (dihydroergotamine mesylate nasal spray) in children have not been established. ***Use in Elderly:*** Experience with the use of MIGRANAL in patients aged over 65 years is limited. ***Drug Interactions:*** The concomitant use of oral contraceptives by female patients does not appear to influence the disposition of MIGRANAL (dihydroergotamine mesylate nasal spray). MIGRANAL should not be used with vasoconstrictors because the combination may cause a further elevation of blood pressure. Concurrent use of vasoconstrictor agents including ergotamine, sumatriptan and nicotine may enhance the risk of vasoconstriction. Twenty four hours should elapse before taking sumatriptan following administration of MIGRANAL. This will avoid additive vasospastic effects. Conversely, MIGRANAL can be taken six hours following the administration of sumatriptan. Although there have been reports that propranolol may potentiate the vasoconstrictive action of ergotamine by synergism upon ß-blockade, the results of a limited clinical study (n=8) did not indicate a safety problem associated with the administration of MIGRANAL in subjects already receiving propranolol. The concomitant use of macrolide antibiotics such as erythromycin, troleandomycin or josamycin with MIGRANAL should be avoided since these antibiotics may increase the plasma level of dihydroergotamine. ***Nursing Mothers:*** It is likely that dihydroergotamine is excreted in human milk, although it is not known at which concentration, while it is known that ergotamine is excreted in breast milk and may cause vomiting, diarrhea, weak pulse and unstable blood pressure in breast-fed infants. Because of the potential for these serious adverse events in breast-fed infants, nursing mothers should not use MIGRANAL (dihydroergotamine mesylate nasal spray). ***Information for the Patient:*** Currently available data have not demonstrated drug abuse and psychological dependence with MIGRANAL (dihydroergotamine mesylate nasal spray). However, due to the chronicity of migraines, patients should be advised not to exceed recommended dosages. Patients should be advised to report immediately to the physician any of the following: numbness or tingling in the fingers and toes, muscle pain in the arms and legs, weakness in the legs, pain in the chest, temporary speeding or slowing of the heart rate, swelling, or itching. Patients should be advised of the importance of priming the applicator (pump 4 times) prior to administration to ensure correct dosage. No more than four sprays (2.0 mg) of MIGRANAL should be administered for any single migraine headache attack. No more than eight sprays (4.0 mg) of MIGRANAL should be administered during any 24 hour period. The maximum weekly dosage is 24 sprays (12.0 mg) of MIGRANAL (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS: The most commonly reported adverse events associated with the use of MIGRANAL (dihydroergotamine mesylate nasal spray) in placebo-controlled, double-blind studies for the treatment of migraine headaches, and not reported at an equivalent incidence by placebo-treated patients, were rhinitis, nausea, taste disturbance and application site reaction. In clinical trials these events were transient and self-limiting, and generally did not result in patient drop-out. The following table lists the adverse events experienced at incidences greater than 1%.

Adverse Events Reported in Double-Blind Placebo-Controlled Studies for the Treatment of Migraine Headaches (Reported at Incidences ≥ 1%)

Adverse Reactions According to Body System	Rate of Occurrence (%) MIGRANAL (N=642)	Rate of Occurrence (%) Placebo (N=632)
Central Nervous System		
Dizziness	2	2
Somnolence	2	1
Fatigue	1	1
Confusion	1	<1
Nervousness	1	<1
Asthenia	1	<1
Gastrointestinal System		
Nausea	9	4
Taste disturbance	7	1
Vomiting	4	2
Diarrhea	2	<1
Dysphagia	1	0
Respiratory System		
Rhinitis[1]	25	7
Application site reaction	4	1
Pharyngitis	3	1
Nasal discharge	1	<1
Sinusitis	1	<1
Musculo-skeletal System		
Myalgia	1	<1
Stiffness	1	0
Autonomic Nervous System		
Hot flushes	1	<1
Sweating increased	1	0
Dry mouth	1	1

[1] Rhinitis includes reports of nasal/nose congestion, nose dryness, nose edema, rhinitis, rhinorrhea and excessive sneezing.

In a few patients who have taken oral dihydroergotamine continuously over years, development of fibrotic changes, in particular of the pleura and the retroperitoneum, has been observed. Chest tightness/pain was seen in earlier studies although the incidence was less than 1% and a causal relationship was not established. In rare cases, vascular spasms may occur, particularly in the lower extremities. If signs of vascular spasms are observed, MIGRANAL should be discontinued and treatment with a peripheral vasodilator initiated (see SYMPTOMS AND TREATMENT OF OVERDOSAGE).

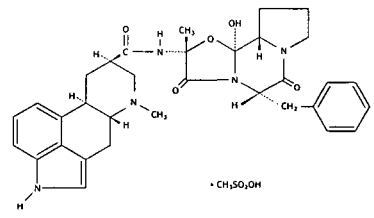
SYMPTOMS AND TREATMENT OF OVERDOSAGE: There have been no reports of acute overdosage with MIGRANAL (dihydroergotamine mesylate nasal spray). The symptoms of an acute oral dihydroergotamine overdose are similar to those of an ergotamine overdose, although there is less pronounced nausea and vomiting with dihydroergotamine. These symptoms include the following: peripheral signs and symptoms of vasospasm (e.g. numbness, tingling, pain and cyanosis of the extremities associated with diminished or absent peripheral pulses); respiratory depression; an increase and/or decrease in blood pressure usually in that order; confusion, delirium, convulsions and coma; and/or some degree of nausea, vomiting and abdominal pain. The treatment of an overdosage is symptomatic under close monitoring of the cardiovascular and respiratory systems. Treatment includes discontinuation of the drug, local application of warmth to the affected area and nursing care to prevent tissue damage; in case of severe vasospasms, vasodilators should be administered (e.g. sodium nitroprusside, phentolamine or dihydralazine). In the case of coronary constriction, appropriate treatment such as nitroglycerin should be initiated.

DOSAGE AND ADMINISTRATION: Prior to administration of MIGRANAL (dihydroergotamine mesylate nasal spray) the nasal spray applicator must be primed (pumped 4 times). In order to let the drug be absorbed through the skin in the nose, **patients should not inhale deeply** through the nose while spraying or immediately after spraying. For best results, treatment should be initiated at the first symptom or sign of an attack. However, MIGRANAL can be used at any stage of a migraine attack. At the first sign or symptoms of a migraine headache, or as early as possible after the onset of headache pain, one spray (0.5 mg) of MIGRANAL (dihydroergotamine mesylate nasal spray) should be administered into each nostril. If the condition has not sufficiently improved approximately fifteen minutes later, an additional spray (0.5 mg) of MIGRANAL should be administered to each nostril. The usual dosage required to obtain optimal efficacy is a total dosage of four sprays (2.0 mg) of MIGRANAL. MIGRANAL is exclusively indicated for the symptomatic treatment of migraine attacks. **MIGRANAL should not be used as a prophylactic therapy.** Significant relief of migraine begins within approximately 30 minutes following nasal administration of MIGRANAL. No more than four sprays (2.0 mg) should be administered for any single migraine attack. An interval of at least 6-8 hours should be observed before treating another migraine attack with MIGRANAL or any drug containing dihydroergotamine or ergotamine. No more than eight sprays (4.0 mg) (corresponding to the use of 2 ampoules) should be administered during any 24 hour period. The maximum weekly dosage is 24 sprays (12.0 mg) of MIGRANAL. MIGRANAL does not need to be administered with an antiemetic, as is recommended with the parenteral form of dihydroergotamine mesylate, since the administration of the nasal spray form is not associated with nausea and vomiting to the same extent as the parenteral form. Once pain is relieved, the incidence of pain return within 24 hours is low. **Once the nasal spray applicator has been prepared, it must be discarded with any remaining drug after 8 hours.**

PHARMACEUTICAL INFORMATION

Trade Name: MIGRANAL; ***Common Name:*** 9-10-Dihydro-12'-hydroxy-2'-methyl-5' α (phenylmethyl) ergotaman -3', 6', 18-trione monomethane sulfonate

Structural Formula:



Molecular Formula: $C_{33}H_{37}N_5O_5 \cdot CH_4SO_3$; ***Molecular Weight:*** 679.8; ***Description:*** White or off-white, fine, crystalline, hygroscopic powder. Moderately soluble in water. ***pK_a in ethanol-water (1:1):*** 6.35 ± 0.05. ***pH in solution:*** 4.4 - 5.4. Dihydroergotamine mesylate melts with strong decomposition between 220°C and 240°C. ***Composition of MIGRANAL:*** Each ampoule of MIGRANAL contains 4.0 mg dihydroergotamine mesylate USP as well as the following non-medicinal ingredients: anhydrous caffeine, carbon dioxide, anhydrous dextrose, and water. ***Storage Requirements:*** MIGRANAL should be stored at room temperature (15°C to 25°C).

AVAILABILITY OF DOSAGE FORM: MIGRANAL (dihydroergotamine mesylate nasal spray) is available as a clear, colourless to faintly yellow solution, in 1 mL amber glass ampoules. MIGRANAL is provided as a package of three units, each unit consisting of one ampoule with a plastic breaker sleeve and a nasal spray applicator.

References:

1. Migranal Product Monograph 1996, Sandoz Canada Inc.
2. Gallagher RM, Ventura D, DiSerio FJ et al. Arch of Neurol 1996 (in press).
3. Ziegler D, Ford R, Kriegler J et al. Neurology 1994;44:447-453.

Product Monograph available on request.

*Registered trademark

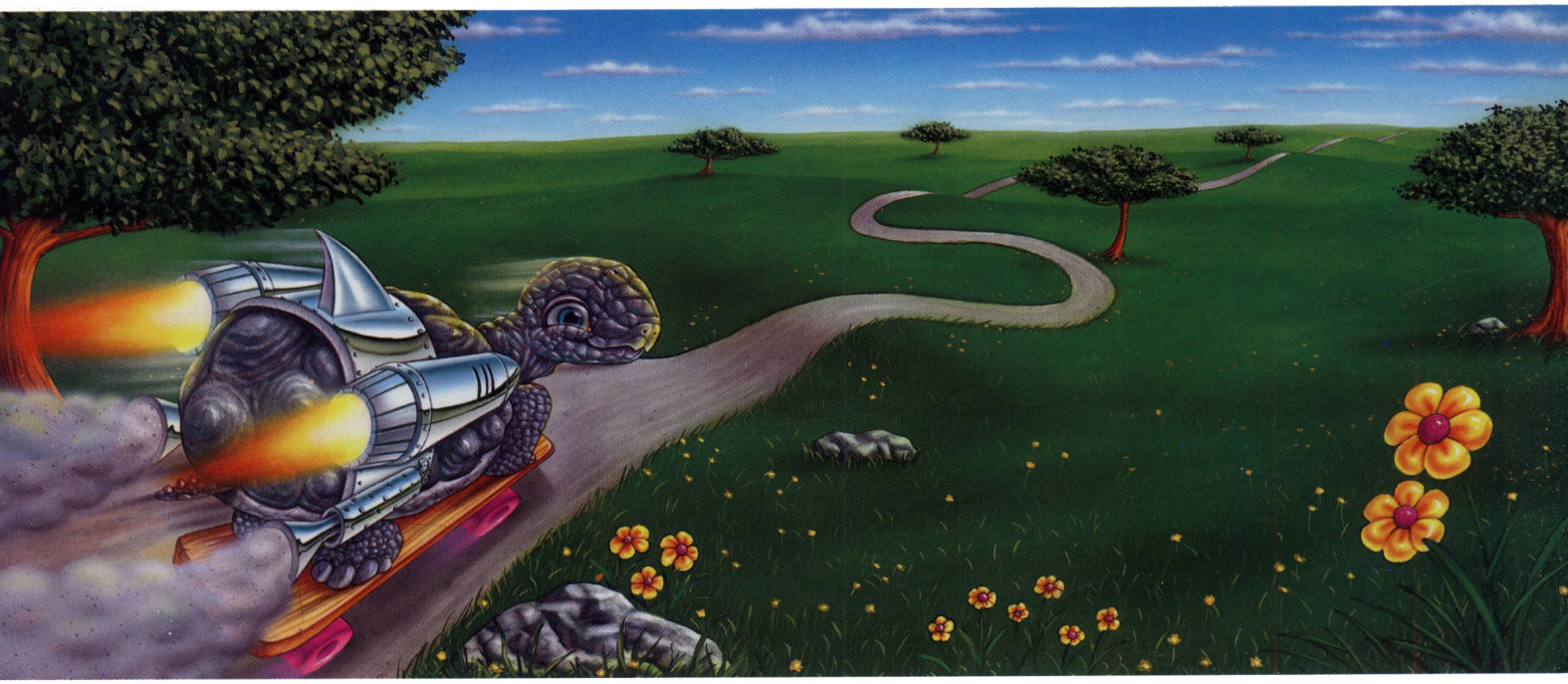
October 1996

SANDOZ SANDOZ CANADA INC. Dorval, Québec H9R 4P5

PAAB MEMBER PMAC

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

Voici MIGRANAL en vaporisateur nasal



Un agoniste des récepteurs 5-HT$_1$ qui agit rapidement et qui offre un soulagement durable de la migraine

Agoniste des récepteurs 5-HT$_1$
- MIGRANAL soulage la migraine et les symptômes connexes[1].
- L'administration par voie nasale permet de contourner le tractus gastro-intestinal.

Pour un soulagement rapide
- On peut prendre MIGRANAL à n'importe quel stade de la migraine[1,◊].
- La réponse clinique commence à se manifester en moins de 30 minutes[1].
- Jusqu'à 70 % des migraines sont soulagées 4 heures après l'administration de MIGRANAL (n = 105)[2,†].

Pour un soulagement durable††
- Longue demi-vie : 10 heures[1]
- Pas de réapparition de la migraine chez 85 % des répondeurs au cours des 24 heures suivant l'administration de MIGRANAL (n = 73)[2]
- Par conséquent, MIGRANAL peut permettre d'éviter le renouvellement fréquent de la dose, la prise de médicaments d'urgence, ainsi que les coûts qui s'y rattachent.

Généralement bien toléré lors des essais cliniques[1]
- Les effets indésirables les plus courants étaient transitoires, spontanément résolutifs et peut-être imputables à la voie d'administration[2,3]. La rhinite (incidence de 25 %) comprend : rhinite, rhinorrhée, congestion nasale, sécheresse et oedème de la muqueuse nasale et éternuements en rafale. Parmi les autres effets secondaires observés, mentionnons les nausées (9 %), les perturbations gustatives (7 %) et les vomissements (4 %).

◊ Pour de meilleurs résultats, entreprendre le traitement dès les premiers signes ou symptômes d'une crise migraineuse.

† Soulagement = disparition complète ou atténuation de la douleur modérée ou grave

†† Jusqu'à 24 heures avec une seule dose de 2 mg

MIGRANAL est contre-indiqué chez les patients prédisposés aux réactions angiospastiques. Veuillez consulter les renseignements posologiques pour obtenir plus de détails.

P MIGRANAL*

(mésylate de dihydroergotamine en vaporisateur nasal)

Soulagement rapide et durable de la migraine

CCPP MEMBRE ACIM

*Marque déposée

MIG-96-10-3531F

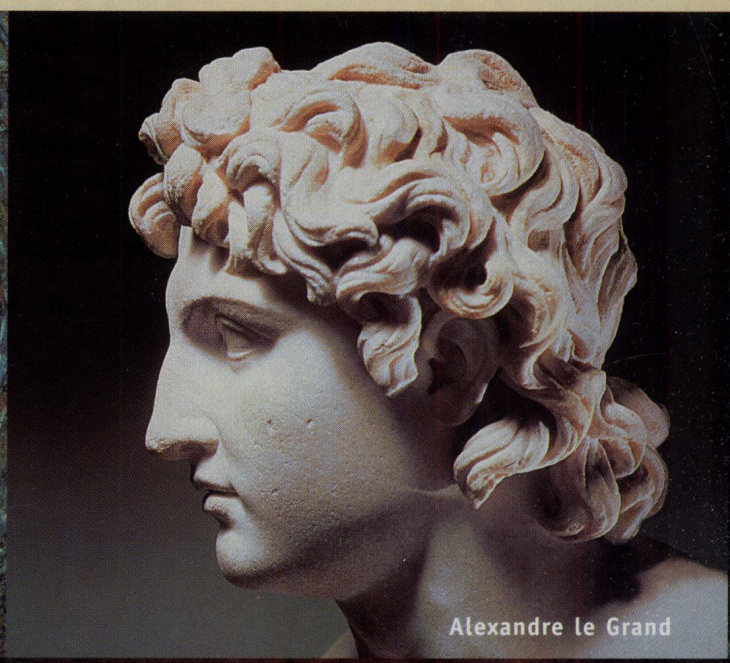
SANDOZ

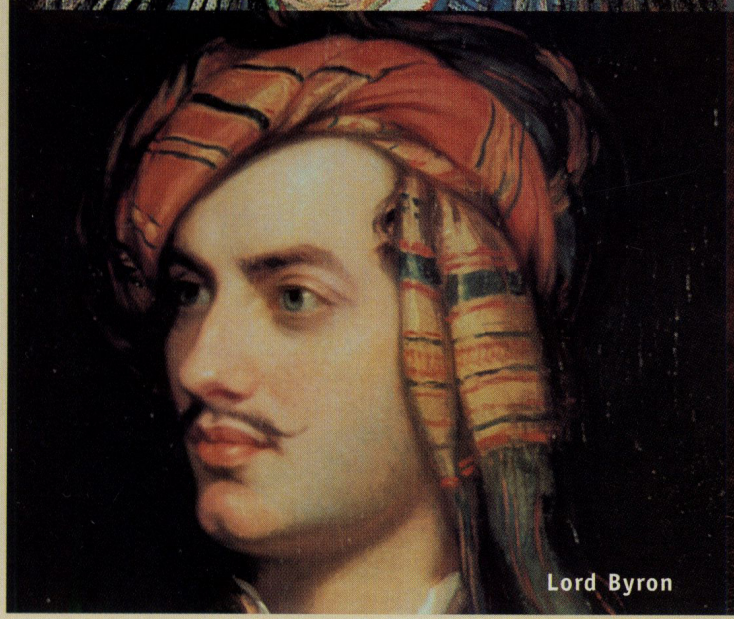
SANDOZ CANADA INC.
Dorval (Québec) H9R 4P5

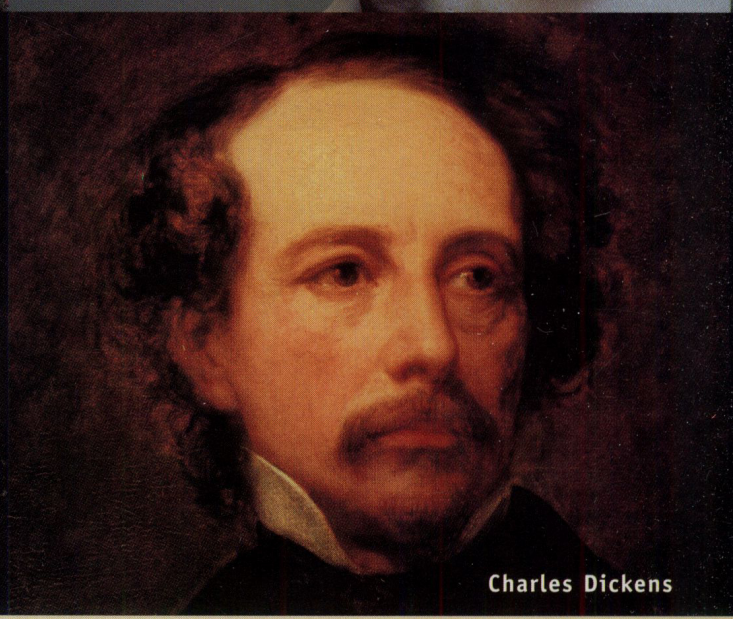
https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

DU NOUVEAU À PROPOS DE L'ÉPILEPSIE

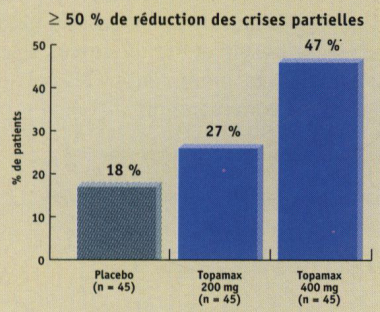

Vincent Van Gogh


Alexandre le Grand


Lord Byron


Charles Dickens

NAGUÈRE ENCORE, LA RÉUSSITE EXIGEAIT D'UN ÉPILEPTIQUE HEUREUSEMENT POUR VOS PATIENTS, IL EXISTE



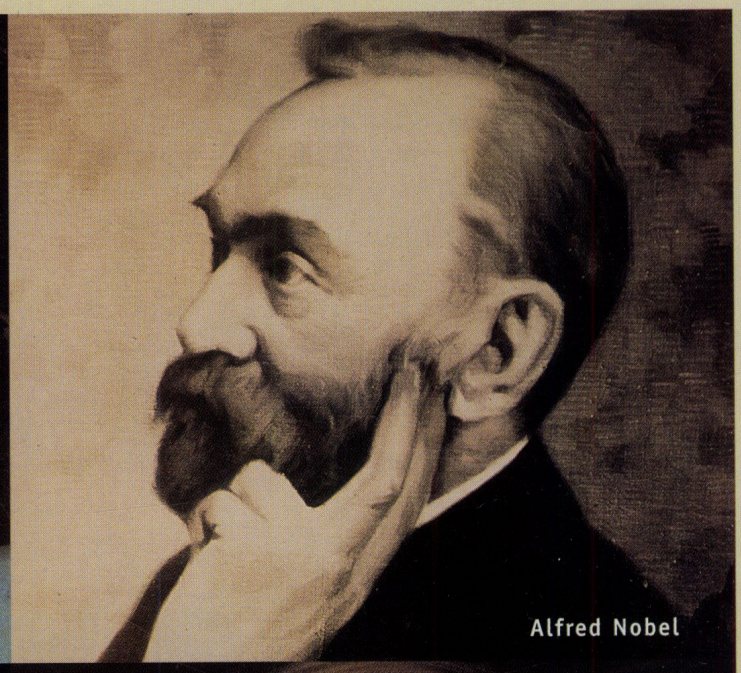
Extrait de référence N° 1. Étude en double aveugle avec placebo contre TOPAMAX b.i.d. comme traitement d'appoint, portant sur 181 patients atteints d'épilepsie partielle réfractaire et recevant une ou deux autres médications antiépileptiques. *p = 0,013.

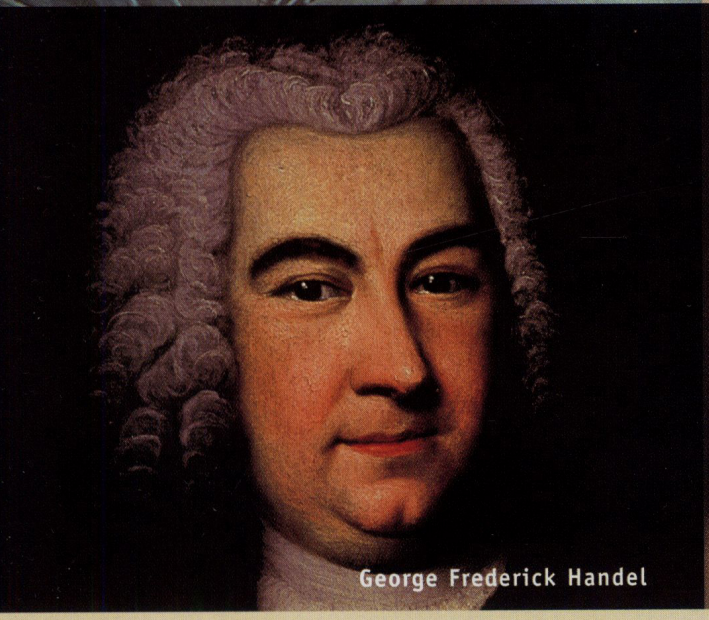
Contrôle amélioré d'une plus grande variété de types de crises.

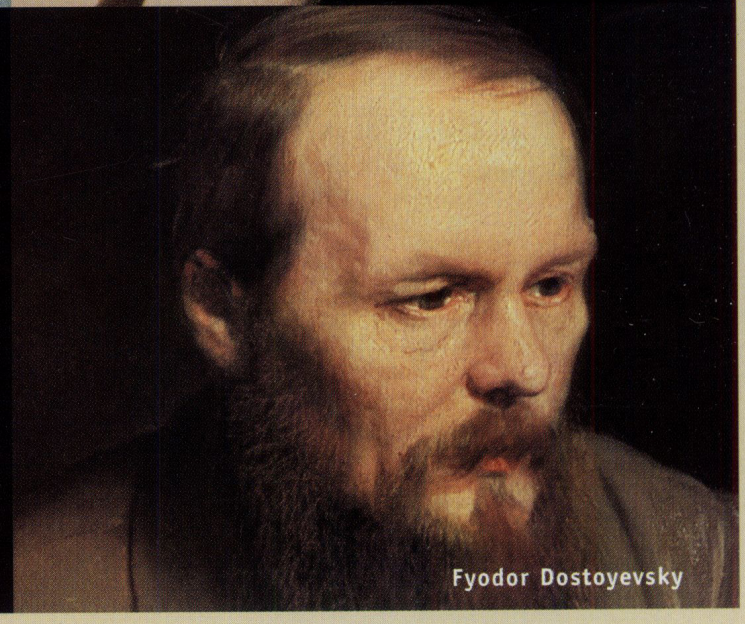
- TOPAMAX est indiqué comme traitement d'appoint pour toutes les épilepsies réfractaires aux traitements conventionnels. À l'heure actuelle, les données sur l'utilisation de TOPAMAX comme traitement unique demeurent limitées.
- Taux élevé de répondants : 27 % (200 mg/jour, n = 45) et 47 % (400 mg/jour, n = 45) des patients ont manifesté une réduction des crises d'épilepsie partielle ≥ 50 % (étude d'une durée de 16 semaines)[1]
- 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)[1]
- Triple mécanisme d'action unique : blocage des canaux sodiques, activation de l'acide gamma-aminobutyrique, antagonisme du glutamate)[2]

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press


Jeanne d'Arc


Alfred Nobel


George Frederick Handel


Fyodor Dostoyevsky

DES EFFORTS EXCEPTIONNELS OU UN TALENT EXTRAORDINAIRE. MAINTENANT 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 mg)[2]
- Aucune preuve d'éruption cutanée sérieuse ni d'anémie aplasique[2]
- Il n'est généralement pas nécessaire de changer le dosage des médications principales; les patients prenant de la phénytoïne et manifestant des signes ou symptômes de toxicité devraient faire contrôler leurs niveaux de phénytoïne[†2]
- **Dosage commode BID**

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

	TOPAMAX 200-400 mg (n = 113)	PLACEBO (n = 216)
Somnolence	30,1	9,7
Étourdissements	28,3	15,3
Ataxie	21,2	6,9
Ralentissement psychomoteur	16,8	2,3
Troubles de la parole	16,8	2,3
Nervosité	15,9	7,4
Nystagmus	15,0	9,3
Paresthésie	15,0	4,6

TOPAMAX®
topiramate

Aide vos patients à mieux tirer parti de leur vie

†Comme pour les autres traitements antiépileptiques, veuillez vous reporter aux renseignements thérapeutiques pour plus de détails concernant les interactions médicamenteuses. On a rapporté l'occurence de 1,5 % (n = 1715) de calculs rénaux[2]. Dans une étude (n = 1200), 83 % des patients (15 sur 18) ont choisi de continuer le traitement[4]. Assurer un taux d'hydratation adéquat et éviter l'utilisation parallèle d'autres inhibiteurs de l'anhydrase carbonique[2].

Pour documentation voir pages xxxiii, xxxiv, xxxv.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

Pour documentation voir pages xxii, xxxvi.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

For brief prescribing information see pages xxxi, xxxii.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

THE CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES

33rd Meeting of the Canadian Congress of Neurological Sciences
June 16-20, 1998
Montreal, Quebec, Canada

Next year's meeting will highlight the 50th Anniversary of the Canadian Neurological Society founded by Wilder Penfield which consisted of members who were both neurologists and neurosurgeons. To commemorate this event, we are planning historical static displays in addition to the scientific posters.

Preliminary Scientific Program Topics

Neurobiology Review Course
Disorders of the Thoracic Spine
Neurogenetics
Alzheimer's Disease
Multiple Sclerosis
Headache
Motor Neuron Disease
Vascular Malformations
Sleep Disorders
Pediatric Surgery
New Technologies Applied to Child Neurology
Debates, Plenary Sessions, Poster and Platform Sessions
Epilepsy Management
Coma and Impaired Consciousness
Movement Disorder Video Session
Neonatal Neurology
Cerebral Ischemia
Tremors
Brain Tumours

1997 NORTH AMERICAN STROKE MEETING

October 16-18, 1997
Montreal, Quebec, Canada

The Canadian Stroke Society, the National Stroke Association and the Mexican Academy of Neurology wish to invite you to Montreal for the 1997 North American Stroke Meeting. The perspective of our stroke meeting is clinically oriented which brings together many areas of expertise including neurology, neurosurgery, vascular surgery, neuroepidemiology, nursing and rehabilitative medicine. All areas of presentation reflect state of the art topics as they relate to patient care.

Scientific Program

Impact of Clinical Trials
Cerebral Angioplasty
Acute Cerebral Ischemia
Managing Stroke Patients Across the Continuum of Care
Management of Hemorrhagic Strokes
Organized Stroke Care
Long Term Prevention of Stroke
Nutrition and Swallowing After Stroke
Nursing Research and Stroke
Thrombolysis in Acute Stroke
Ultrasound in Cerebrovascular Disease
Platform and Poster Sessions
Exhibits

On Friday, October 17, 1997 at 1:30 p.m., the first Henry J. Barnett Research Scholarship in cerebrovascular disease will be presented by the Heart and Stroke Foundation of Canada.

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

PARKINSON'S DISEASE

A world in which the therapeutic options are limited[1]

For those who have it, treat it, live with it; managing their Parkinson's disease can be quite frustrating. Yet there are moments that can be most rewarding. Motor function improves, the number of "off" hours decreases, rigidity subsides, gait improves. Their levodopa 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 hopeless...

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.[1-3] With its unique mode of action, i.e. stimulating both D_1 and D_2 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."[3]*

Successful treatment with Permax can last for up to 3-5 years[4,5] and renewed improvement has been demonstrated when Permax was given to patients (n=10) in whom the beneficial effect of bromocriptine had waned,[4] 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.[6]

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

℞ PERMAX®
pergolide mesylate

DRAXIS

Draxis Health Inc.
Mississauga, Ontario

PAAB

* Rapid escalation of pergolide dosage may cause severe adverse reactions. Therefore a slow increase combined with a concomitant gradual and limited reduction of levodopa is recommended. See ADVERSE REACTIONS section in Prescribing Information

https://doi.org/10.1017/S0317167100021764 Published online by Cambridge University Press

For brief prescribing information see page xlii.

in

EPILEPSY

treatment goal is complete control

Impressive degree of complete seizure control[1]

Frisium is a "remarkably effective and [generally] safe add-on anti-epileptic drug"[1]

Effective in all seizure types, in adults and children alike[2]

Once-daily dosage, preferably at bedtime†

WIDE-RANGE

Pr Frisium® (clobazam)

Once a Day†

† Daily dose can be divided for some patients

Frisium is indicated as adjunctive therapy in epileptic patients not adequately stabilized with their current anticonvulsant therapy. As with all benzodiazepines, patients (particularly geriatrics) should be cautioned accordingly. Most frequent adverse effects (> 1%) include drowsiness, dizziness, fatigue, ataxia, weight gain, nervousness, behaviour disorder, hostility and blurred vision.

Hoechst Marion Roussel

Hoechst Marion Roussel Canada Inc.,
Laval, Quebec H7L 4A8
A member of the Hoechst Group

Hoechst

®Reg. trade mark of Hoechst AG, Germany PAAB PMAC FRI 96012 E

For brief prescribing information see page xli.