Volume 22 Number 2 May 1995

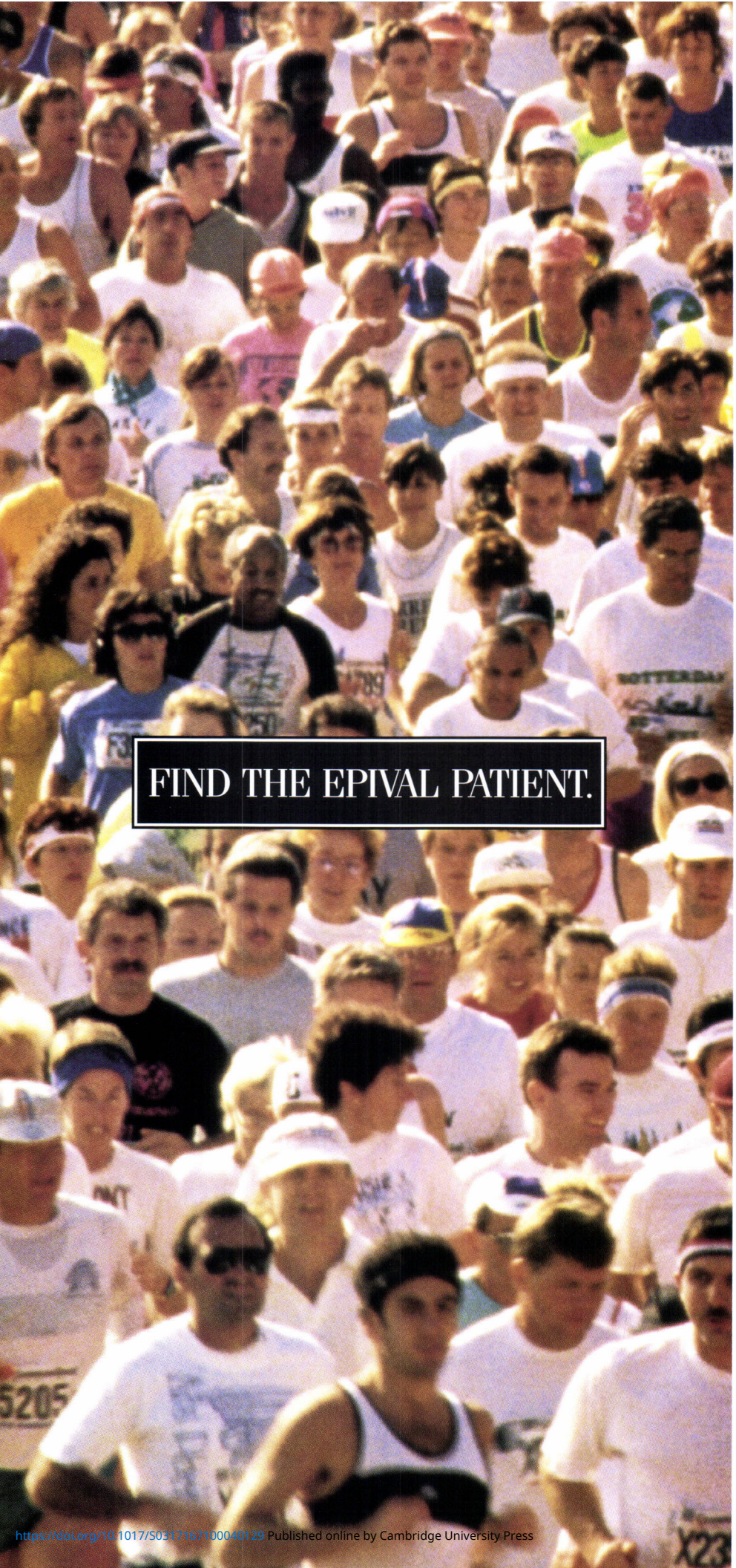
THE CANADIAN JOURNAL OF Neurological Sciences

LE JOURNAL CANADIEN DES Sciences Neurologiques

AN INTERNATIONAL JOURNAL / UN JOURNAL INTERNATIONAL

30th CANADIAN CONGRESS OF NEUROLOGICAL SCIENCES
June 20 - 24, 1995
Victoria,
British Columbia

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



Epival For Control Over Daily Living.

With Epival, epileptic patients can appear "just like anyone else."

Epival has been associated with little effect on learning and cognition.[1] It is effective in primary generalized epilepsy[2–4] as well as in partial seizures that secondarily generalize.[5,6,†] And it is generally well tolerated,[7] causing less GI irritation (nausea, vomiting and indigestion) than valproic acid.[8]

Prescribe Epival — by name only — to help restore your patients' control over daily living.

Because there's more to anticonvulsant therapy than seizure control.

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Epival* (divalproex sodium)

Helps put patients back in control.

[1]For use as sole or adjunctive therapy in the treatment of simple or complex absence seizures, including petit mal and is useful in primary generalized seizures with tonic-clonic manifestations. EPIVAL may also be used adjunctively in patients with multiple seizure types which include either absence or tonic-clonic seizures.

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For brief prescribing information see pages xviii, xix

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Volume 22 Number 1 February 1995

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The official journal of: / La Revue officielle de:

The Canadian Neurological Society
La Société Canadienne de Neurologie

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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.

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.*

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.

Posté sous permis de poste-publications no 3307. Port payé à Calgary, Alberta. Le Journal est cité et indexé dans *Index Medicus, Excerpta Medica et Current Contents — Clinical Practice et Life Sciences.*

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

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

ISSN 0317 - 1671

https://doi.org/10.1017/S0317167100040129 Published online by Cambridge University Press

If one more walks away from

The risk of stroke is greatest within the year following a TIA.[1] So it's worth knowing that a large multicentre trial showed Ticlid prevented non-cardiogenic thromboembolic stroke twice as effectively as ASA.[2] That meant relative to ASA, Ticlid saved three more patients out of every one hundred treated from a potentially crippling or life-threatening stroke.[2]

In long-term prospective randomized trials, only Ticlid has been proven effective in women as well as in men for the prevention of recurrent and initial stroke.[3,4] ASA has not been proven to reduce the rate of recurrent stroke.[5] Nor has ASA been proven to prevent initial stroke in women.[6]

Gastrointestinal complaints such as diarrhea can be limited by taking Ticlid with full meals.[7] A temporary reduction in dose may also resolve this complaint.[3,8]

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TIA patient stroke, it's worth it.

If rash occurs, discontinue therapy and rechallenge. Many rashes will not recur.[7]

In clinical trials there was a 2.4% incidence of neutropenia. Upon immediate discontinuation of therapy, the neutrophil count usually returned to normal within 1 to 3 weeks. White blood cell monitoring is required every two weeks for the first three months starting at baseline.[7]

Ticlid. Possibly the best opportunity a TIA patient has to walk away from stroke.

Turn the page and judge for yourself. Four independent studies attest to the value of Ticlid.

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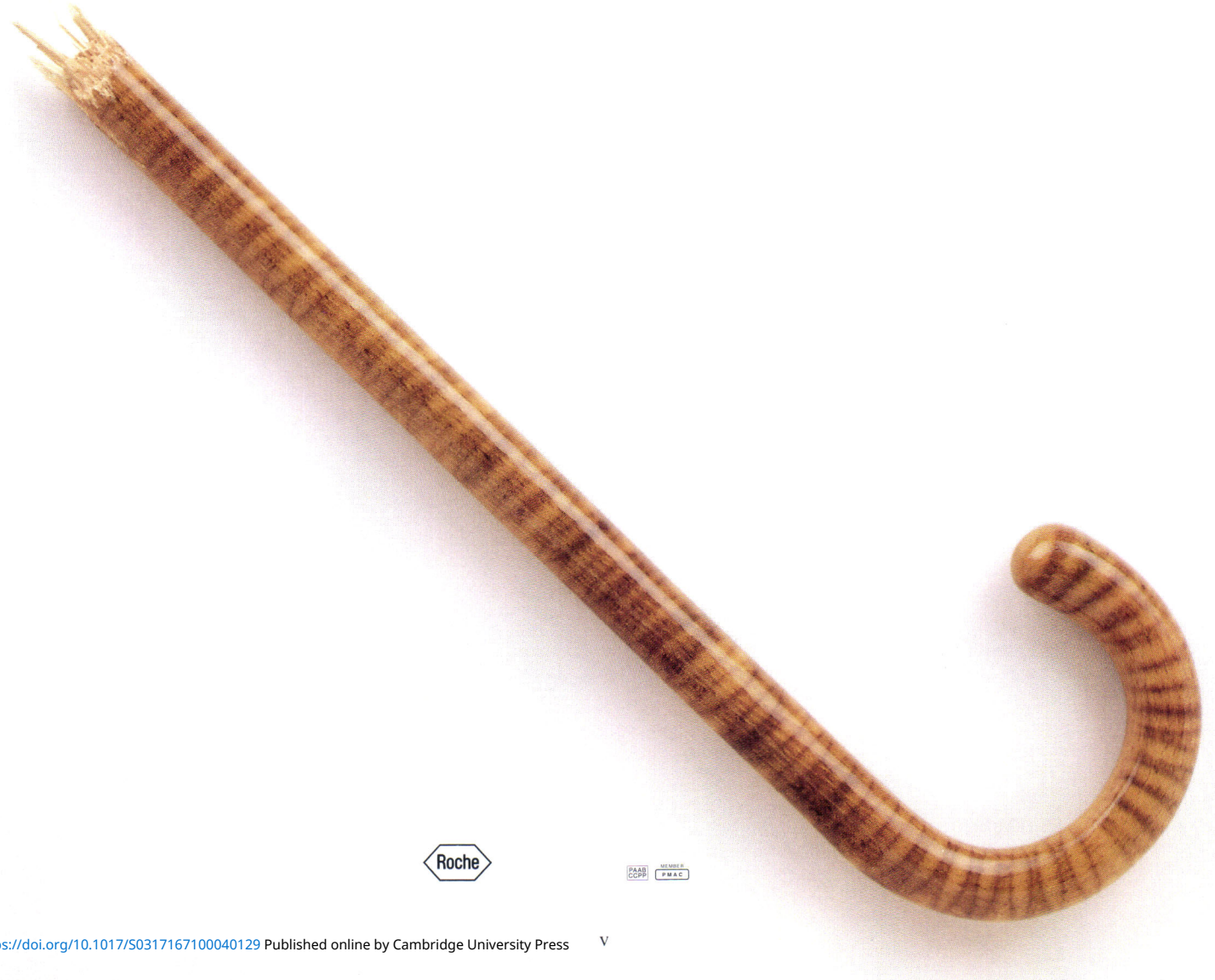
Your patients deserve all the protection they can get.



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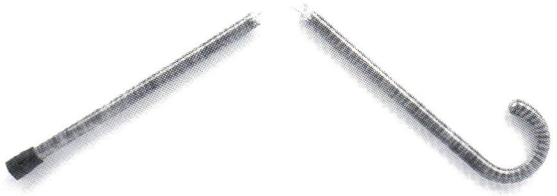

Four major studies establish the superior efficacy of Ticlid.

Ticlopidine Versus Aspirin for Stroke Prevention: On-Treatment Results from the Ticlopidine Aspirin Stroke Study Group

J. D. Easton, Chair, TASS Publications Committee
J Stroke Cerebrovasc Dis. Vol. 3 No. 3. 1993;3:168-176.

Ticlopidine is the newest antiplatelet agent that has been compared with aspirin for stroke prevention. Results from the intent-to-treat analysis of the Ticlopidine Aspirin Stroke Study, a randomized, triple-blind trial, showed ticlopidine to be more effective than aspirin for the prevention of threatened stroke. We present the on-treatment analysis from this study in 3,034 eligible patients receiving either ticlopidine (500 mg daily) or aspirin (1,300 mg daily). Follow-up was for 2-6 years.

During year 1, the high-risk period for stroke in patients with threatened stroke, ticlopidine reduced the risk of stroke over aspirin by 48% ($p = 0.0004$: the event rates were 3.4 and 6.4 respectively). The overall risk for fatal and non fatal stroke was 27% (95% confidence intervals were 6.6 and 42.3), less with ticlopidine than with aspirin. Ticlopidine significantly decreased the risk of fatal and non fatal stroke in both sexes and has a different adverse effect profile than aspirin. More adverse effects, primarily diarrhea and rash, were reported with ticlopidine.

Stroke Prevention in Women: Role of Aspirin Versus Ticlopidine

Linda A. Hershey, M.D., Ph.D., Buffalo, New York
September 1991 *The American Journal of Medicine* Vol. 91;288-292.

Summary and Conclusions: Stroke remains an important health care problem. Although the incidence of stroke and stroke mortality is lower in women than in men, the outcome in terms of major disability, decreased quality of life, economic burdens, and impact on family life is just as real for women as for men. Although aspirin has proven efficacy for preventing initial stroke, it may have limited efficacy in preventing recurrent stroke. Moreover, questions remain about the efficacy of aspirin for stroke prevention in women. There is a need for an alternative to aspirin in stroke prevention therapy.

Ticlopidine has demonstrated efficacy for both initial and recurrent stroke prevention and has been shown to be more effective than aspirin for patients at high risk for a first stroke. It is just as effective for stroke prevention in women as in men. The overall incidence of adverse effects seen with ticlopidine is not significantly different from that seen with aspirin, although careful hematologic monitoring is required with ticlopidine during the first 3 months of use. Both agents are important tools to use in addition to antihypertensive therapy and smoking cessation in stroke prevention.

Ticlopidine Versus Aspirin for the Prevention of Recurrent Stroke
Analysis of Patients With Minor Stroke From the Ticlopidine Aspirin Stroke Study

John W. Harbison. M.D., for the Ticlopidine Aspirin Stroke Study Group
Stroke 1992:1723-1727.

Background and Purpose: Ticlopidine has not been formally compared with aspirin in patients with a completed stroke. We therefore performed an analysis on a subgroup of patients from the Ticlopidine Aspirin Stroke Study (TASS) with a recent minor completed stroke as the qualifying ischemic event.

Methods: This was a multicenter, double-blind, randomized trial of patients with a recent history of cerebral ischemia. Eligible patients had a qualifying minor stroke within 3 months of study entry. All patients received either 650 mg aspirin twice daily or 250 mg ticlopidine twice daily for up to 5.8 years. The primary study end point was the first occurrence of non fatal stroke or death from any cause. A secondary end point was the first occurrence of a fatal or non fatal stroke.

Results: Minor stroke was the qualifying ischemic event in 927 patients (463 received ticlopidine and 464 received aspirin). The cumulative event rate at 1 year for non fatal stroke or death was 6.3% for patients receiving ticlopidine and 10.8% for patients receiving aspirin, a 42% risk reduction in favour of ticlopidine. For fatal or non fatal stroke, the cumulative event rate at 1 year was 4.8% for patients receiving ticlopidine and 7.5% for those receiving aspirin, a risk reduction of 36% for ticlopidine relative to aspirin. The overall risk reductions were 22.1% for non fatal stroke or death and 19.9% for fatal or non fatal stroke. Adverse reactions were reported in 58% of the ticlopidine patients and 51% of the aspirin patients.

Conclusions: The results in this subgroup are consistent with the overall TASS results and show that ticlopidine is somewhat more effective than aspirin for reducing the risk of stroke in patients with a completed minor stroke.

The Canadian American Ticlopidine Study (CATS) in Thromboembolic Stroke

Gent, J., et al. *The Lancet:* Saturday 3 June 1989.

The Canadian American Ticlopidine Study (CATS) is a randomised, double-blind placebo-controlled trial to assess the effect of ticlopidine (250 mg twice daily) in reducing the rate of subsequent occurrence of stroke, myocardial infarction, or vascular death in patients who have had a recent thromboembolic stroke. Twenty-five centres entered 1,072 patients into the study between 1 week and 4 months after their qualifying stroke. The patients were treated and followed up to 3 years (mean 24 months). In the efficacy analysis, the event rate per year for stroke, myocardial infarction or vascular death, considered together, was 15.3% in the placebo group and 10.8% in the ticlopidine group, representing a relative risk reduction with ticlopidine of 30.2% (95% confidence interval 7.5-48.3%; p=0.006). Ticlopidine was beneficial for both men and women (relative risk reductions 28.1%, p=0.037, and 34.2%, p=0.045, respectively). Analysis by intention-to-treat gave a smaller estimate of risk reduction (23.2%, p=0.020) for stroke, myocardial infarction, or vascular death. Adverse experiences associated with ticlopidine included neutropenia (severe in about 1% of cases) and skin rash and diarrhea (severe in 2% of cases each); all were reversible.

This study provides evidence of a beneficial effect of ticlopidine in both men and women with a recent thromboembolic stroke.

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P Ticlid®

ticlopidine hydrochloride 250 mg tablets

THERAPEUTIC CLASSIFICATION Inhibitor of Platelet Function

ACTION Ticlid (ticlopidine hydrochloride) is an inhibitor of platelet aggregation. It causes a time and dose-dependent inhibition of platelet aggregation and release of platelet factors, as well as a prolongation of bleeding time. The drug has no significant *in-vitro* activity.

The exact mechanism of action is not fully characterized, but does not involve inhibition of the prostacyclin/thromboxane pathways or platelet cAMP.

Ticlid interferes with platelet membrane function by inhibiting ADP-induced platelet-fibrinogen binding and subsequent platelet-platelet interactions. The effect of Ticlid on platelet function is irreversible.

Template bleeding time is usually prolonged by two to five-fold of baseline values with the therapeutic dose of Ticlid.

Upon discontinuation of Ticlid dosing, bleeding time and other platelet function tests return to normal within one week in the majority of patients.

The correlation between ticlopidine hydrochloride plasma levels and activity is still under investigation. Much of the following data was obtained from older patients corresponding to the age of patients participating in clinical trials (mean age: 63 years).

After oral administration of the therapeutic dose of Ticlid, rapid absorption occurs, with peak plasma levels occurring at approximately 2 hours after dosing. Absorption is at least 80% complete. Administration of Ticlid after meals results in an increased (20%) level of ticlopidine hydrochloride in plasma.

Steady state plasma levels of ticlopidine hydrochloride in plasma are obtained after approximately 14 days of dosing at 250 mg BID. The terminal elimination half-life is 4-5 days. However, inhibition of platelet aggregation is not correlated with plasma drug levels.

Ticlopidine hydrochloride binds reversibly (98%) to plasma proteins, mainly to serum albumin and lipoproteins in a non-saturable manner.

Ticlopidine hydrochloride is metabolized extensively by the liver; no intact ticlopidine hydrochloride is detected in the urine. Unmetabolized ticlopidine hydrochloride is a minor component in plasma after a single dose, but at steady state, ticlopidine hydrochloride is the major component.

Impaired hepatic function resulted in higher than normal plasma levels of unchanged ticlopidine hydrochloride after single doses or after multiple doses.

Inhibition of platelet aggregation is detected within 2 days of administration with 250 mg BID. Maximum platelet aggregation inhibition is achieved 8 to 11 days following dosing with 250 mg BID.

INDICATIONS AND CLINICAL USE Ticlid (ticlopidine hydrochloride) tablets are indicated for reduction of the risk of first or recurrent stroke for patients who have experienced at least one of the following events: Complete Thromboembolic Stroke, Minor Stroke, Reversible Ischemic Neurological Deficit (RIND), or Transient Ischemic Attack (TIA) including Transient Monocular Blindness (TMB).

Considerations in the selection of stroke prevention therapy should include the patient's current medical status and history, and their ability to comply with the required blood monitoring instructions concerning the use of ticlopidine.

CONTRAINDICATIONS Ticlid (ticlopidine hydrochloride) is contraindicated in the following conditions: 1. Known hypersensitivity to drug or its excipients. 2. Presence of haematopoietic disorders (such as neutropenia and/or thrombocytopenia). 3. Presence of haemostatic disorder. 4. Conditions associated with active bleeding, such as bleeding peptic ulcer or intracranial bleeding. 5. Severe liver dysfunction.

WARNINGS The following warnings were developed from clinical trial experience with over 2000 patients with cerebrovascular disease who were treated with ticlopidine for as long as 5.8 years.

Neutropenia and Thrombocytopenia: About 2.4% of ticlopidine-treated patients in clinical trials developed neutropenia (defined as an absolute neutrophil count (ANC) below 1.2×10^9 cells/L). The incidence of severe neutropenia (ANC<0.45×10^9 cells/L) was 0.8%. Severe neutropenia occurs during the first 3-12 weeks of therapy, and may develop quickly over a few days. The bone marrow shows a reduction in myeloid precursors. The condition may be life-threatening. It is usually reversible, and the recovery occurs within 1-3 weeks after discontinuation of the drug but may take longer, on occasion.

In clinical trials, thrombocytopenia (defined as a platelet count of $<0.8 \times 10^{11}$ cells/L) has been observed in 0.4% of ticlopidine patients. The incidence of thrombocytopenia in patients on ASA or placebo was 0.3% or 0.4% respectively. The thrombocytopenia may occur as an isolated finding or in combination with neutropenia. Thrombocytopenia occurs during the first 3-12 weeks of therapy, and recovery usually occurs after drug discontinuation.

All patients should have a white blood cell count with a differential and platelet count performed every 2 weeks starting at baseline, before treatment is initiated, to the end of the third month of therapy with Ticlid. When the neutrophil count shows a declining trend or the neutrophil numbers have fallen below 30% of the baseline, the values should be confirmed. If the presence of neutropenia (ANC $<1.2 \times 10^9$ cells/L) or thrombocytopenia ($<0.8 \times 10^{11}$ cells/L), are confirmed, the drug should be discontinued. Because of the long plasma half-life of Ticlid, it is recommended that any patient who discontinues Ticlid for any reason within the first 90 days have an additional CBC with white cell differential count obtained two weeks after discontinuation of therapy. (See PRECAUTIONS.)

Rarely, cases of pancytopenia, aplastic anemia or thrombocytopenia, have been reported. Most cases were reversible, but some of them have been fatal. Thrombocytopenia may occur in isolation or together with neutropenia. Thrombotic thrombocytopenic purpura (TTP) has been reported, therefore careful attention to diagnosis should be made to guide treatment, platelet transfusion may be harmful in these patients.

Hemorrhagic Complications: Prolongation of bleeding time occurs in subjects treated with Ticlid. Purpura and a few cases of more serious hemorrhagic events such as hematemesis, melena, hemothorax and intracranial bleeding have been reported. Patients must be instructed to watch for signs of bleeding disorders and to report any abnormality to their physician immediately. Ticlid therapy has to be stopped by the patient if a physician is not immediately available for consultation.

Anticoagulant Drugs: Should be avoided as tolerance and safety of simultaneous administration with Ticlid has not been established.

Hepatic Abnormalities: Most patients receiving ticlopidine hydrochloride showed some increase of their alkaline phosphatase values above their baseline and in one-third the increase exceeded the upper reference range. In 6% the value was greater than twice the upper reference range. These increases in alkaline phosphatase were nonprogressive and asymptomatic. In clinical trials, two cases (0.1%) of cholestatic jaundice accompanied by elevated transaminases alkaline phosphatase, and bilirubin levels above 43 µmol/L have been observed. Both patients recovered promptly upon drug discontinuation.

Pregnancy: The safety of Ticlid in pregnancy has not been established. It should not be used in pregnant patients.

Pediatric Use: Safety in children has not been studied. Do not use in pediatric patients.

PRECAUTIONS

Selection of Patients: Ticlid should be used only for the established indications (see INDICATIONS) and should not be given to patients with haematopoietic disorders, haemostatic disorders, patients suffering from conditions associated with active bleeding (see CONTRAINDICATIONS) and patients anticipating elective surgery. In clinical trials elderly patients tolerated the drug well, but safety in children and pregnant women has not been established.

Clinical Monitoring: All patients have to be carefully monitored for clinical signs and symptoms of adverse drug reactions (see ADVERSE REACTIONS). The signs and symptoms possibly related to neutropenia (fever, chills, sore throat, ulcerations in oral cavity), thrombocytopenia and abnormal hemostasis (prolonged or unusual bleeding, bruising, purpura, dark stool), jaundice (including dark urine, light coloured stool) and allergic reactions should be explained to the patients who should be advised to stop medication and consult their physician immediately if any of these occur.

Laboratory Monitoring: All patients should have a white blood cell count with a differential and a platelet count performed every 2 weeks starting at baseline, before treatment is initiated, to the end of the third month of therapy with Ticlid. When the neutrophil count shows a declining trend or the neutrophil numbers have fallen below 30% of the baseline, the value should be confirmed. If the presence of neutropenia (ANC $<1.2 \times 10^9$ cells/L) or thrombocytopenia ($< 0.8 \times 10^{11}$ cells/L) are confirmed, the drug should be discontinued. Because of the long plasma half-life of Ticlid, it is recommended that any patient who discontinues Ticlid for any reason within the first 90 days have an additional CBC with white cell differential obtained two weeks after discontinuation of therapy (see WARNINGS). Thereafter, the WBC counts need only be repeated for symptoms or signs suggestive of neutropenia. Liver function tests should be conducted during therapy with Ticlid (ticlopidine hydrochloride) in response to signs and symptoms suggestive of hepatic dysfunction.

Elective Surgery: Ticlid should be discontinued 10 to 14 days prior to elective surgery or dental extraction and bleeding time and thrombocyte count performed before the procedure if clinically indicated.

Emergency Surgery: Prolonged bleeding during surgery may be a problem in ticlopidine-treated patients. Transfusions of fresh platelets would be expected to improve haemostasis in such patients, but there are no data from clinical trials to confirm this expectation. There are data from clinical pharmacology trials that indicate treatment with glucocorticosteroids can normalize bleeding time in ticlopidine-treated subjects, but there is no experience with ticlopidine-treated surgical patients to show that such treatment improves haemostasis.

Specific Precautions: Liver: Ticlid is contraindicated in patients with severe liver dysfunction or cholestatic jaundice. Mild increase of alkaline phosphatase may be seen for the duration of the treatment and is inconsequential in the majority of patients (see WARNINGS and CONTRAINDICATIONS).

Kidneys: Ticlid has been well tolerated in patients with moderately decreased renal function. In severe renal disease, caution and close monitoring are recommended.

Gastrointestinal System: Conditions associated with active bleeding, such as bleeding ulcers, constitute contraindication for Ticlid. Clinical judgement and monitoring of stool for occult blood are required for patients with a history of ulcerative lesions. Trauma: Ticlid should be discontinued temporarily until the danger of abnormal bleeding is eliminated. A single fatal case of intracranial bleeding following head trauma has been reported. The extent to which Ticlid may have contributed to the severity of the bleeding is unknown.

Drug Interactions: The following table outlines the agents which have been concomitantly administered with ticlopidine hydrochloride and the observed interaction (if any):

AGENTS	OBSERVED INTERACTION
Acetylsalicylic acid (ASA)	Potentiation of ASA's effect on collagen-induced platelet aggregation (see WARNINGS).
Antipyrine and products metabolized by hepatic microsomal enzymes	30% increase in $t^1/_2$ of antipyrine. Dose of products metabolized by hepatic microsomal enzymes to be adjusted when starting or stopping concomitant therapy with ticlopidine hydrochloride.
Theophylline	$t^1/_2$ of theophylline increased from 8.6 to 12.2 hr along with a comparable reduction in its total plasma clearance.
Digoxin	Approximately 15% reduction in digoxin plasma levels (little or no change in digoxin's efficacy expected).
Cimetidine	Chronic administration of cimetidine induced a 50% reduction in clearance of a single dose of ticlopidine hydrochloride.
Antacids	20% decrease in ticlopidine plasma level when administered after antacids.
Phenobarbital	No interaction reported.

Other Concomitant Therapy: Although specific interaction studies were not performed, in clinical studies, Ticlid was used concomitantly with beta blockers, calcium channel blockers, diuretics, and nonsteroidal anti-inflammatory drugs (however see WARNINGS) without evidence of clinically significant adverse interactions.

ADVERSE REACTIONS Most adverse effects are mild, transient and occur early in the course of treatment.

In controlled clinical trials of 1 to 5 years duration, discontinuation of Ticlid (ticlopidine hydrochloride) due to one or more adverse effects was required in 20.9% of patients. In these same trials, ASA and placebo led to discontinuation in 14.5% and 6.7% of patients respectively. The incidence rates of adverse reactions listed in the following table were derived from multicenter, controlled clinical trials comparing ticlopidine HCl, placebo, and ASA over study periods of up to 5 years. The rates are based on adverse reactions considered probably drug-related by the investigator. Adverse experiences occurring in greater than one percent of patients treated with Ticlid in controlled clinical trials are shown in the Table below.

PERCENT OF PATIENTS IN CONTROLLED STUDIES

	Ticlid (n=2048) Incidence	ASA (n=1527) Incidence	Placebo (n=536) Incidence		Ticlid (n=2048) Incidence	ASA (n=1527) Incidence	Placebo (n=536) Incidence
Event							
Diarrhea	12.5(6.3)*	5.2(1.8)	4.5(1.7)	Nausea	7.0(2.6)	6.2(1.9)	1.7(0.9)
Dyspepsia	7.0(1.1)	9.0(2.0)	0.9(0.2)	Rash	5.1(3.4)	1.5(0.8)	0.6(0.9)
GI Pain	3.7(1.9)	5.6(2.7)	1.3(0.4)	Neutropenia	2.4(1.3)	0.8(0.1)	1.4(0.4)
Purpura	2.2(0.2)	1.6(0.1)	0.0(0.0)	Vomiting	1.9(1.4)	1.4(0.9)	0.9(0.4)
Flatulence	1.5(0.1)	1.4(0.3)	0.0(0.0)	Pruritus	1.3(0.8)	0.3(0.1)	0.0(0.0)
Dizziness	1.1(0.4)	0.5(0.4)	0.0(0.0)	Anorexia	1.0(0.4)	0.5(0.4)	0.0(0.0)

* Percent of patients (in parentheses) discontinuing clinical trials due to event.

The incidence of thrombocytopenia in these controlled studies was 0.4% in the Ticlid and placebo groups of patients and 0.3% in the ASA patient population.

The following rare events have been reported and their relationship to Ticlid is uncertain.

Pancytopenia, hemolytic anemia with reticulocytosis, thromobcytopenic thrombotic purpura, jaundice, allergic pneumonitis, systemic lupus (positive ANA), peripheral neuropathy, vasculitis, serum sickness, arthropathy, hepatitis, nephrotic syndrome, myositis, and hyponatremia.

Gastrointestinal: Ticlid therapy has been associated with a variety of gastrointestinal complaints including diarrhea and nausea. The majority of cases are mild and transient in nature and occur within 3 months of initiation of therapy. Typically, events are resolved within 1-2 weeks without discontinuation of therapy. If the effect is severe or persistent, therapy should be discontinued.

Hemorrhagic: Ticlid has been associated with a number of bleeding complications such as ecchymosis, epistaxis, hematuria, conjunctival hemorrhage, gastrointestinal bleeding, and postoperative bleeding.

Intracerebral bleeding was rare in clinical trials with Ticlid, and was no more than that seen with comparator agents (ASA, placebo).

Rash: Ticlopidine hydrochloride has been associated with a maculopapular or urticarial rash (often with pruritus). Rash usually occurs within 3 months of initiation of therapy, with a mean time to onset of 11 days. If drug is discontinued, recovery should occur within several days. Many rashes do not recur on drug rechallenge. There have been rare reports of more severe rashes.

Altered Laboratory Findings: Hematological: Neutropenia and rarely thrombocytopenia have been associated with Ticlid administration (see WARNINGS).

Liver: Ticlid therapy has been associated with elevations of alkaline phosphatase (See WARNINGS). Maximal changes occur within 1-4 months of therapy initiation. No further progressive increases are seen with continuous therapy. Occasionally patients developed deviations in bilirubin and SGOT.

Cholesterol: Chronic Ticlid therapy has been associated with increased serum cholesterol and triglycerides. Serum levels of HDL-C, LDL-C, VLDL-C, and triglycerides are increased 8-10% after 1-4 months of therapy. No further progressive elevations are seen with continuous therapy. The ratios of the lipoprotein subfractions are unchanged. The effect is not correlated with age, sex, alcohol use, or diabetes.

SYMPTOMS AND TREATMENT OF OVERDOSAGE One case of deliberate overdosage with Ticlid (ticlopidine hydrochloride) has been reported in a foreign postmarketing surveillance program. A 38-year-old male took a single 6000 mg dose of Ticlid (equivalent to 24 standard 250 mg tablets). The only abnormalities reported were increased bleeding time and increased SGPT. No special therapy was instituted and the patient recovered without sequelae. Based on animal studies, overdosage may result in severe gastrointestinal intolerance.

In the case of excessive bleeding after injury or surgery, standard supportive measures should be carried out if indicated, including gastric lavage, platelet transfusion and use of corticosteroids.

DOSAGE AND ADMINISTRATION The recommended dose of Ticlid (ticlopidine hydrochloride) is 250 mg twice daily with food. Ticlid should be taken with meals to minimize gastrointestinal intolerance.

PHARMACEUTICAL INFORMATION

(i) Drug Substance

Description: Ticlopidine hydrochloride is a white crystalline solid. It is freely soluble in water and self buffers to a pH of 3.6. It also dissolves freely in methanol, is sparingly soluble in buffer solutions above pH 6.0, methylene chloride and ethanol, and is slightly soluble in acetone.

(ii) Composition: Ticlopidine hydrochloride tablets are provided, as white film coated tablets containing ticlopidine hydrochloride, citric acid, povidone, micro-crystalline cellulose, corn starch, stearic acid powder, magnesium stearate and water. The coating suspension consists of hydroxypropyl methylcellulose, titanium dioxide and polyethylene glycol. The ink for printing contains D&C yellow #10 aluminum lake and FD&C blue #1 aluminum lake.

(iii) Stability and Storage Recommendations: Store at room temperature. Ticlid tablets should be dispensed in light resistant containers. Blister packs should not be exposed to light.

AVAILABILITY Ticlid 250 mg tablets are oval white film coated tablets printed using green ink with Ticlid above half an arrow on one side, "250" above half an arrow on the other side. The tablets are available in a fold-over card of 28 tablets (2 blisters of 14 tablets). They are also available in boxes of 56 (4 x 14) tablets and 168 (12 x 14) tablets.

For the first 3 months of therapy, only request or dispense the 14 days supply of tablets (see PRECAUTIONS).

Product Monograph available to Health Professionals on request.

REFERENCES 1. Adams HP, Gordon DL. Epidemiology of and stroke-preventive strategies for atherothromboembolic brain infarction in the elderly. *Clinics in Geriatic Medicine* 1991;7(3):401-416. **2.** Ticlopidine Aspirin Stroke Study (TASS), Data on file, Vol.52, Oct 1989 Syntex Inc.,1989. **3.** Hass WK, Easton DJ, Adams HP. A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. *New Engl J Med* 1989;321:501-527. **4.** Gent M, Easton DJ, Hachinski VC et al. The Canadian American Ticlopidine Study (CATS) in Thromboembolic Stroke. *The Lancet* 1989; June:1215-1220. **5.** Entrophen product monograph, 1994. **6.** Hershey LA. stroke prevention in women: Role of aspirin versus Ticlopidine. *The American Journal of Medicine* 1991;91:288-92. **7.** Ticlid product monograph, 1993. **8.** Harbison JW. Ticlopidine versus aspirin for the prevention of recurrent Stroke: analysis of patients with minor stroke from the Ticlopidine Aspirin Stroke Study. *Stroke* 1992;1723-7.

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New!

Lamotrigine

Lamictal*

A Broad-Spectrum Antiepileptic With A Low CNS Side-Effect Profile

https://doi.org/10.1017/S0317167100040129 Published online by Cambridge University Press

Many patients with epilepsy – across the broad spectrum of seizure types – are unsatisfactorily controlled with current therapies.[1]

Now there's LAMICTAL, a novel antiepileptic drug (AED). LAMICTAL has activity across a broad range of seizure types with a low CNS side-effect profile,[2-5] therefore more of your refractory patients will feel better on LAMICTAL.

LAMICTAL offers broad-spectrum activity in the management of seizures such as tonic/clonic and partial seizures, as well as atonic, tonic and myoclonic seizures, typical absence and atypical absence.[1,2,6,7] In fact, LAMICTAL has been shown to render up to 65% of patients either seizure-free[2-4,6] or reduce seizure frequency[1,4,6-11] and reduce severity.[1,4,6,9,10]

LAMICTAL has demonstrated a more favourable CNS side-effect profile in healthy volunteers compared to phenytoin.[12] Incidence of somnolence was 13% for LAMICTAL compared to 12% for placebo in pooled results of four double-blind, placebo-controlled studies.[5] Moreover, the majority of patients taking LAMICTAL will not experience unwanted CNS-related side effects.[3†]

LAMICTAL is chemically unrelated to all other AEDs in current use. It is believed to act presynaptically, to inhibit the release of excitatory amino-acid neurotransmitters, primarily glutamate, thus reducing excessive stimulation.[1,13]

LAMICTAL has activity across a broad spectrum of seizure types. You can now offer your patients proven tolerability with a low CNS side-effect profile. When faced with refractory patients, choose LAMICTAL – in 25-, 100- or 150-mg strengths – as your first add-on therapy.[‡]

Prescribe New

Lamotrigine

℞ **Lamictal***

BURROUGHS WELLCOME INC.
KIRKLAND, QUÉ.

*Trade Mark

PAAB CCPP

†Withdrawal rates (≥ 0.6%): dizziness 2.4%, headache 1.3%, nausea 1.3%, blurred vision 1.1%, rash 1.1%, diplopia 0.7%, ataxia 0.6%. If there is any unexplained rash, fever, flu-like symptoms or worsening of seizure control, then hepatic, renal and clotting parameters should be monitored. ‡ As with most other AEDs, before prescribing LAMICTAL, refer to Product Monograph for possible drug interactions with other AEDs.

For brief prescribing information see pages xxiv, xxv.

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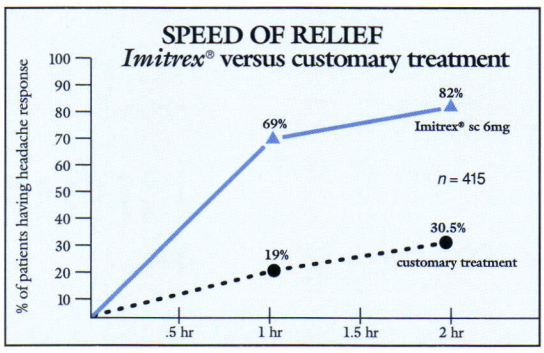
Sooner or later, every migra
again. Imitrex® believes

A patient who complains about migraine is also complaining about a disrupted life. Indeed, research shows that in at least 31% of attacks, migraine sufferers cannot continue with their daily activities.[1]

That's where *Imitrex*® comes in. For most patients, *Imitrex*® can bring complete relief between 90 minutes and 2 hours, versus up to 9 hours for the usual treatments.*[2,3] *Imitrex*® treats all the symptoms of migraine.**[3-5]



Adapted from *Cephalalgia*: Schoenen 1994.[2]

Unlike conventional remedies, it has not been shown to cause medication-induced headache.[3,6-8] Its adverse events are generally well tolerated, quickly resolved and usually non-threatening when explained to the patient.***[3,7,9] *Imitrex*® may be more expensive, but over 250,000 Canadian patients continue to choose it for migraine relief.[10]

The successful use of *Imitrex*® is most likely in patients who understand its common

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ine sufferer will feel normal it should be sooner.

side effects, and who know when the drug should be used.***[11] *Imitrex*® should be taken at the start of a debilitating attack, and may also be used after the failure of conventional treatments (except ergotamine-containing preparations).[3]

Most patients have attacks that limit normal function.[1,12] So give your patients† the option of using *Imitrex*®. It's a proven route to a fast recovery.[2]

For more information about *Imitrex*®, please call 1-800-268-0324.

℗ IMITREX®

SUMATRIPTAN SUCCINATE

1994 Winner of the Prix Galien

A faster way back.

Glaxo
Glaxo Canada Inc.

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CCPP

*Customary treatments include simple analgesics, combination analgesics, ergot derivatives, NSAIDs, narcotics, antiemetics, others.[2] **Head pain, nausea, vomiting, photophobia and phonophobia.[3] ***Fatigue, dizziness, nausea and vomiting have been reported. These side effects are usually mild to moderate in intensity, transient and resolve within 45 minutes of s.c. administration and within two hours of oral administration. *Imitrex*® has been associated with transient chest pain and tightness which may mimic angina pectoris. Only in very rare cases have the symptoms been associated with ischaemic ECG changes. If chest symptoms persist, patient should immediately consult physician.[3] †Contraindicated in patients with ischaemic heart disease, angina pectoris including Prinzmetal angina, previous myocardial infarction and uncontrolled hypertension.[3] *Imitrex*® is a selective 5-HT_1-like receptor agonist.[3]

For brief prescribing information see page xxvi.

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On peut facilement reconnaître le jeune patient épileptique traité au Tegretol® CR.

Excellent contrôle des crises

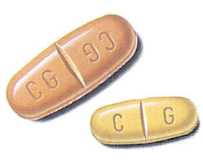
℗ Tegretol® CR (carbamazépine à libération contrôlée) maîtrise les crises chez de nombreux patients, causant peu d'impact sur la fonction cognitive[1,2]. Tegretol CR permet à de nombreux patients de penser clairement et de donner le meilleur d'eux-mêmes[1,2].

Taux sanguins uniformes

Tegretol CR cause moins de «hauts et de bas» dans les taux sanguins que le Tegretol conventionnel. Les effets secondaires sont ainsi réduits et le modèle de fonction cognitive est plus stable[3,4].

Posologie b.i.d. commode

Lorsque vous instituez ou remplacez un traitement, pensez au Tegretol CR. Il est présenté en comprimés à 200 mg et 400 mg facilement divisibles pour une plus grande souplesse d'administration et améliorer l'observance du patient.



TEGRETOL® CR.

Aide les épileptiques à réaliser leur plein potentiel.

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For brief prescribing information see page xvii.

For brief prescribing information see pages xxii, xxiii.

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