

# The Canadian Journal of Neurological Sciences

# Le Journal Canadien des Sciences Neurologiques



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**XXVIIIth Canadian Congress of  
Neurological Sciences  
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## **The Official Journal of**

The Canadian Neurological Society  
The Canadian Neurosurgical Society  
The Canadian Society of Clinical Neurophysiologists  
The Canadian Association for Child Neurology

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In clinical trials, there was a 2.4% incidence of neutropenia (0.8% severe). Upon immediate discontinuation of therapy, the neutrophil count usually returned to normal within one to three weeks.<sup>2,3</sup>

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**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).

**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  $1.2 \times 10^9$  cells/L). The incidence of severe neutropenia (ANC  $< 0.45 \times 10^9$  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 is reversible, and recovery usually occurs within 1-3 weeks after discontinuation of the drug. 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 count and platelet count performed every 2 weeks during the first 3 months of therapy. The incidence of neutropenia or thrombocytopenia after three months of therapy is not appreciably higher than the background levels observed in control groups, and continued periodic monitoring is not warranted. However, for the duration of ticlopidine therapy, any signs or symptoms suggestive of neutropenia or thrombocytopenia should be promptly investigated with complete blood counts and platelet counts.

**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, hemorthorax 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 43µmol/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**

**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 WBC count with differential and platelet count performed every 2 weeks during the first 3 months of therapy. 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 hemostasis 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 hemostasis.

**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.

**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 (see WARNINGS)
Acetylsalicylic acid (ASA)	Potential of ASA's effect on collagen-induced platelet aggregation (see WARNINGS).
Antipyrine and products metabolized by hepatic microsomal enzymes	30% increase in 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	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)	ASA (n=1527)	Placebo (n=536)		Ticlid (n=2048)	ASA (n=1527)	Placebo (n=536)
	Incidence	Incidence	Incidence		Incidence	Incidence	Incidence
<b>Event</b>							
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)
C/P 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, thrombocytopenic 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.

**DOSE 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, microcrystalline 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 2-week Patient Starter Packs 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. Adapted from Feinberg W. Antithrombotic therapy in stroke and transient ischemic attacks. *American Family Physician* 1989;40(Suppl):S35-95. 2. Hass WK et al. Ticlopidine Aspirin Stroke Study (TASS). A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. *N Eng J Med* 1989;321:501-7. 3. Gent M et al. The Canadian American Ticlopidine Study (CATS) in thromboembolic stroke. *The Lancet* 1989 Jun;1215-20. 4. Ticlopidine Aspirin Stroke Study (TASS). Data on file, Syntex Inc., Vol.52, Oct 1989. 5. Compendium of Pharmaceuticals and Specialties, 1992. 6. Ticlid product monograph.

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See pages iv, v




In Meniere's Disease

**P**

# SERC<sup>®</sup>

(betahistine hydrochloride tablets)

- 
- Acts to restore microcirculation of the inner ear<sup>1</sup>
  - Can reduce the frequency of vertigo attacks<sup>2</sup>
  - Non-sedating, generally well tolerated<sup>3</sup>
  - Proven effective over long term use<sup>4</sup>

## EFFECTIVE MANAGEMENT OF RECURRENT VERTIGO



SOLVAY  
KINGSWOOD Inc.

PAAB  
CCPP

For brief prescribing information see page xxi



# IF YOU'RE LO EFFECTIVE MIGRAI YOU'VE JUST S

A recent clinical study published in *The Canadian Journal of Neurological Sciences* makes it clear; Sibelium is very effective in preventing migraine attacks.<sup>1</sup> In fact, the percentage reduction in attack frequency with Sibelium was twice that of propranolol.<sup>1</sup>

In the most common type of migraine, migraine without aura, 73% of patients responded to Sibelium,

compared with 44% to propranolol ( $p=0.035$ ).<sup>1</sup> Several studies have also shown Sibelium reduces the severity of migraine and many patients have become attack-free.<sup>2-5</sup>

Sibelium had fewer side effects and was better tolerated than propranolol.<sup>1</sup> There were no unwanted effects on cardiovascular function with Sibelium, whereas propranolol significantly

 **JANSSEN**  
PHARMACEUTICA  
Mississauga, Ontario

MEMBER  
PMAC PAAB  
COPE  
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# LOOKING FOR THE PROPHYLAXIS, TRUCK GOLD.

reduced blood pressure and heart rate.<sup>1</sup>

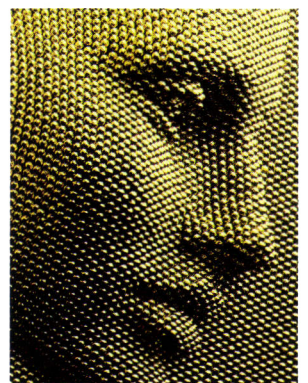
Now you know what you may have already suspected. For patients who...<sup>6</sup>

- suffer 3 or more attacks per month,
- have unusually severe or prolonged attacks, or
- find acute therapy ineffective,

...Sibelium is worth its weight in gold.

once-a-day  
**SIBELIUM**  
flunarizine

**PREVENTION MAY BE THE BEST CURE.**



THE *Stable* PARKINSON'S PATIENT



# SHE DOESN'T KNOW HOW BAD IT COULD GET.

All she knows is that her condition may deteriorate, even with levodopa treatment — She's been told she could, most likely, develop swings in mobility and immobility — Yet, although the causes of these motor fluctuations aren't completely understood, it has been demonstrated that they can be attenuated by treatment regimens that produce steady plasma levels of levodopa.

  
**SINEMET<sup>®</sup> CR**  
(levodopa/carbidopa) CONTROLLED-RELEASE



TREAT TODAY WITH TOMORROW IN MIND

For brief prescribing information see pages xxii, xxiii

Available on all provincial drug formularies (ODB non-formulary list)  
(xi)

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and Du Pont Merck Pharma, R.U. SCR-92-CDN-0032-JA

P A A B



**Be Part of a  
Miracle!**

## **TRANSPLANTATION**

A proven, effective treatment for end-stage organ disease.

Through transplants, hundreds of Canadians have a chance of a normal, productive life.

But many others don't get that chance. They die waiting for donated kidneys, hearts, lungs and livers.

Ask the families of brain-injured patients about organ donation. It doesn't conflict with the interests of these patients. It can give the families a chance to change pain and death into life and hope.

### **Remember TRANSPLANTS WORK**

MORE Ont.	1-800-263-2833
PORT B.C.	1-800-663-6189
HOPE Alb.	(403) 492-1970
METRO Que.	(514) 876-6768
OPEN Newf.	(709) 737-6600
OPT-NB N.B.	(506) 648-6111
HSC Man.	(204) 787-2379

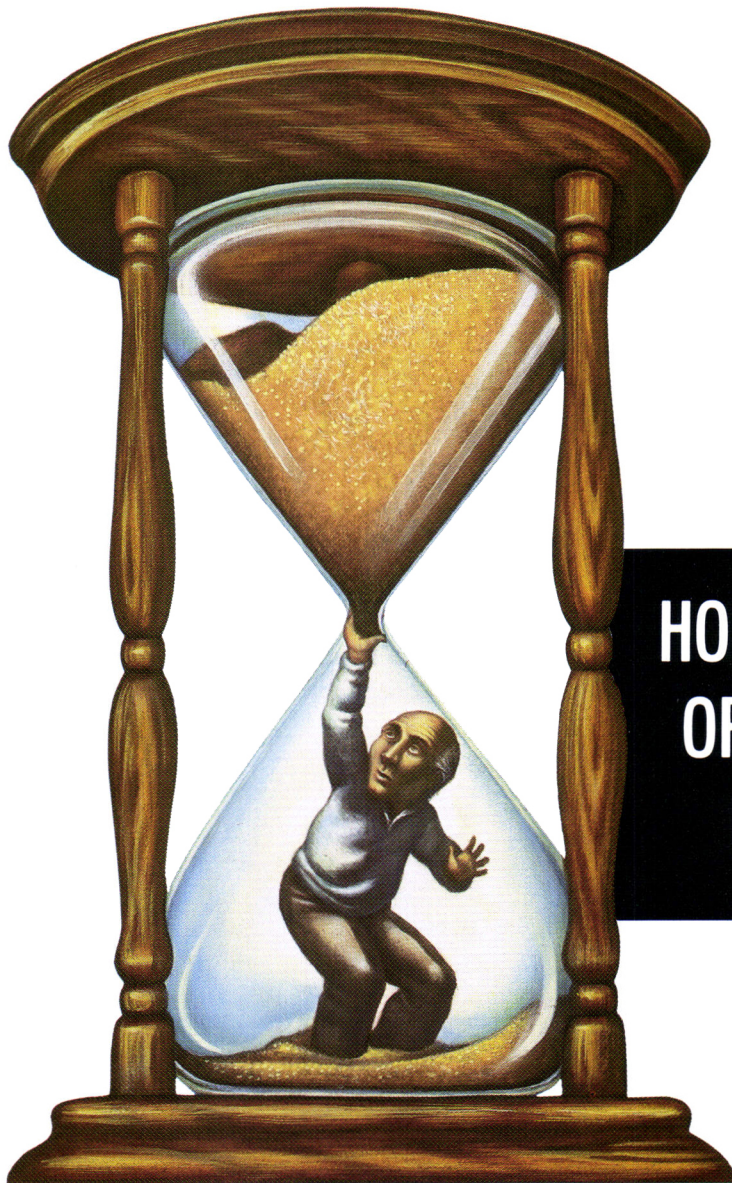
OD-91-04-1639E

ROY T.  
Kidney Transplant  
June 26, 1989

## NOW ELDEPRYL IS INDICATED FOR FIRST LINE THERAPY.

Now you can do more than deal with the disability of Parkinson's disease. You can delay it with Eldepryl first line. □ In newly diagnosed patients, Eldepryl can significantly retard the worsening of symptoms<sup>2,3</sup> and delay the need for levodopa therapy.<sup>2,4,5</sup> □ In fact, Eldepryl can delay the onset of disability and thereby prolong functional life by as much

as one year.<sup>1,4</sup> □ As well, Eldepryl appears to have a remarkable safety profile. It has been generally well-tolerated with few side effects.<sup>4,6,7</sup> □ So when you see patients with Parkinson's disease, prescribe



**HOLD BACK THE DISABILITY  
OF PARKINSON'S DISEASE  
FOR AN EXTRA YEAR.<sup>1</sup>**

Eldepryl first line. It's their first line of defence against the progression of disability.

**ELDEPRYL<sup>®</sup> FIRST LINE**  
selegiline hydrochloride

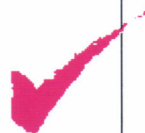
**DELAYS THE PROGRESSION OF DISABILITY.**

**PAAB**

For brief prescribing information see page xxiv

(xiii)

# Botulinum toxin information



**Physicians that are  
injecting**



**Reimbursement**



**Training seminars**



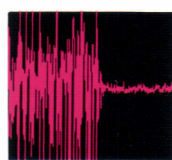
**Patient support groups**



**Safety/efficacy profile**

## Call 1-800-44-BOTOX

This number provides you with the latest information  
on botulinum toxin and its use. Call today.



**Botulinum Toxin  
Type A**





## 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<sup>1,2,3,4</sup>. Contrairement aux médicaments tels la phénytoïne, Tegretol CR permet à de nombreux patients de penser clairement et de donner le meilleur d'eux-mêmes<sup>1,2,3,4</sup>.

### *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<sup>5,6</sup>.

### *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.*

**Gelgy** Mississauga, Ontario L5N 2W5

PAAB  
CCPP MEMBRE  
ACIM G-92111F

For brief prescribing information see pages xx, xxi

Good news for patients taking oral contraceptives: Epival does not appear to be associated with O.C. failure.<sup>1</sup>



## Epival: For their epilepsy... and their lifestyles

A significant benefit for the newly diagnosed child with absence: Epival not only controls most patients with absence<sup>5</sup>, but is also effective against primary generalized seizures with tonic-clonic manifestations.<sup>4,8</sup>



Proven efficacy in a broad range of primary generalized seizures<sup>4,5</sup>

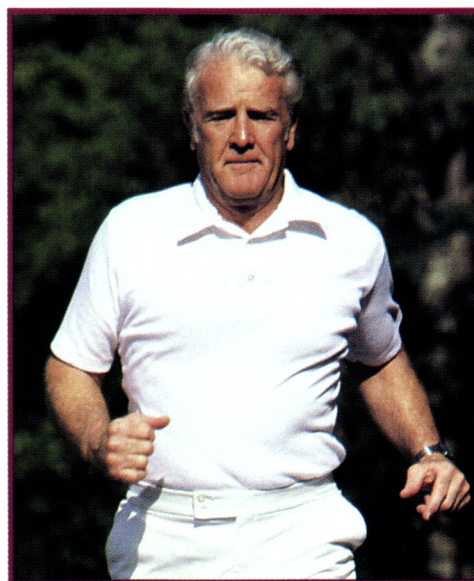
Little effect on learning and cognition<sup>3</sup>

Relatively few clinically substantiated drug interactions<sup>2,9</sup>

Wide therapeutic range<sup>6</sup> for easy titration

Most patients (85%) unable to tolerate other forms of valproic acid were able to take Epival<sup>7</sup>

A dual benefit for the elderly: Epival has relatively few clinically substantiated drug interactions<sup>2,9</sup> and is rarely associated with ataxia or dyskinesias.<sup>3</sup>



**Epival**<sup>\*</sup>  
divalproex sodium  
A drug of choice in  
primary generalized seizures

<sup>\*</sup>TM Abbott Laboratories, Limited

 PHARMACEUTICAL PRODUCTS DIVISION  
ABBOTT LABORATORIES, LIMITED  
MONTRÉAL, CANADA