Something to live for

Parkinson's syndrome is an insidious assault on the lifestyles of more than 58,000 Canadians.

For these individuals, daily, routine habits like knotting a tie, or pinning the hair, are often impossible tasks.

Symmetrel® can help many of these patients gain a better hold on their daily lives, and helps you to control the syndrome.

As initial, or adjunctive therapy, Symmetrel® for Parkinson's syndrome offers:

- few significant side effects, even after long-term use.[1]
- noticeable benefits within 24 hours of start-up dose.[1]
- easy usage with levodopa and anticholinergics.[1]
- simple dosage regimen; simple titration.

SYMMETREL®

(amantadine HCl)

can help in Parkinson's Disease

®TM

PAAB CCPP

For brief prescribing information see page xxiii

Du Pont Pharmaceuticals
Mississauga, Ontario
L5M 2J4

DU PONT CANADA

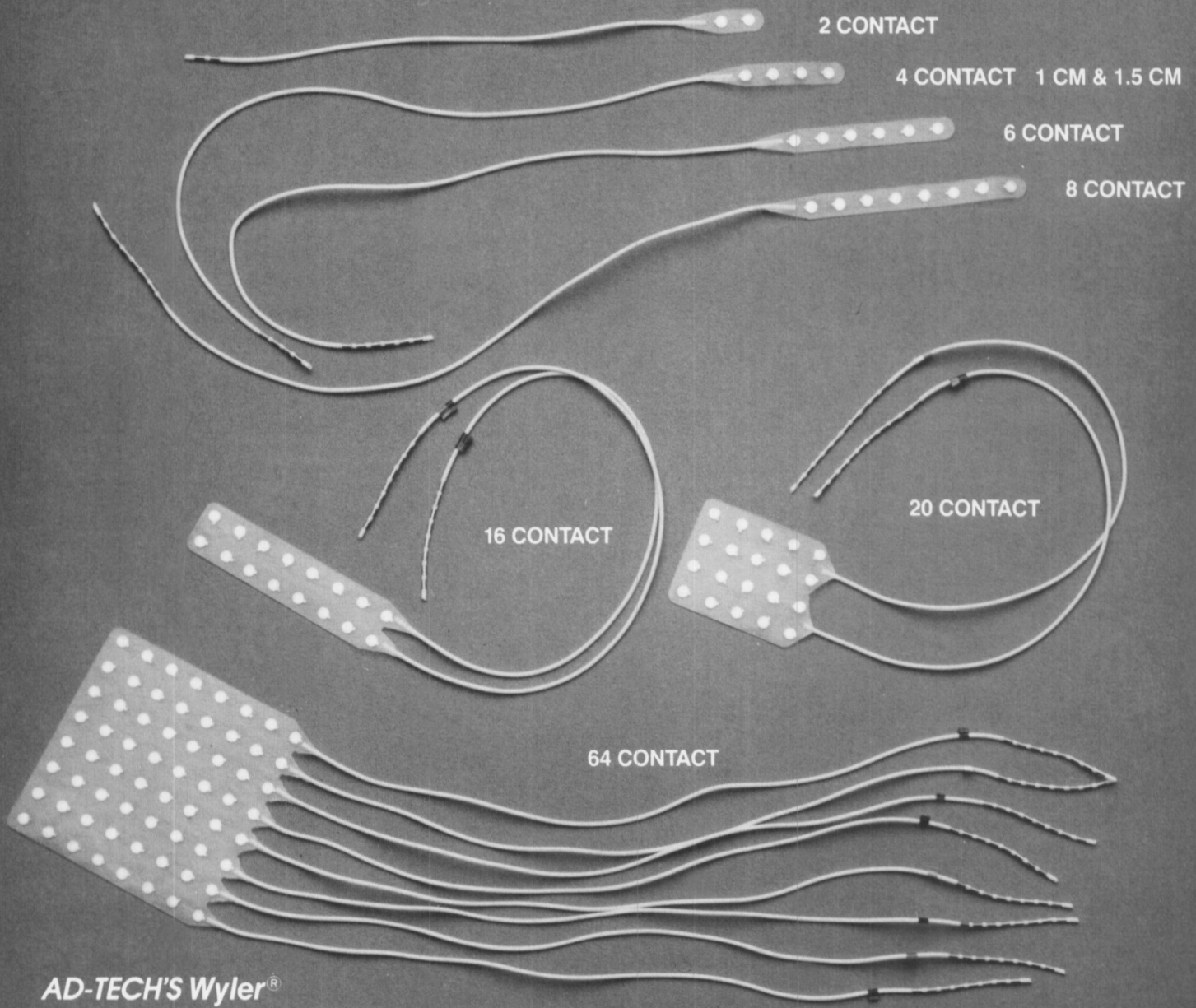
https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press

INTRODUCING

AD-TECH'S Wyler® SUBDURAL ELECTRODES

WITH TECH ATTACH™ CONNECTION SYSTEM

FOR ACCURATE EPILEPSY MONITORING



AD-TECH'S Wyler®
SUBDURAL ELECTRODES ARE THE ONLY ELECTRODES WITH THESE FEATURES

- *MOST FLEXIBLE STRIPS AND ARRAYS*
- *THINNEST STRIPS AND ARRAYS*
- *PERCUTANEOUS REMOVAL (STRIPS)*
- *USE 14 ga. NEEDLE FOR TUNNELING*
- *RADIOPAQUE MARKERS AND WIRE CARRIERS*
- *UNIVERSAL COLOR MARKERS*
- *CUSTOM SIZES AND CONTACT CONFIGURATIONS*
- *STAINLESS STEEL OR PLATINUM*

Patent Pending

IN CANADA
WRITE OR CALL
TEL: (416) 935-1584
FAX: (416) 892-8243

STT MEDICAL

a division of
Sandstrom Trade & Technology Inc.
9 McNicholl Circle, St. Catharines
Ontario, Canada, L2N 7C5

https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press

PARLODEL®
(bromocriptine mesylate)

Because quality of life is the issue

ACTIONS Parlodel (bromocriptine mesylate) is a dopaminomimetic ergot derivate with D_2 type dopamine receptor agonist activity, and has also D_1 dopamine receptor antagonist properties. The dopaminomimetic activity of bromocriptine in the striatum is considered responsible for the clinical benefits seen in selected patients with Parkinson's disease, when low doses of the drug are gradually added to levodopa therapy in patients on long-term treatment who develop late side effects of levodopa or no longer respond to the medication. Excessive dopaminomimetic drive may, however, provoke psychotic and other adverse reactions.

The extreme variability in G.I. tract absorption and the extensive and individually variable first-pass metabolism are responsible for the broad variability in plasma concentrations of bromocriptine and, in part, for the variability in dose response.

INDICATIONS* Parkinson's Disease: Parlodel (bromocriptine mesylate) has been found to be clinically useful as an adjunct to levodopa (usually with a decarboxylase inhibitor), in the symptomatic management of selected patients with Parkinson's disease who experience prominent dyskinesia or wearing off reactions on long-term levodopa therapy.

Patients on long-term treatment who are beginning to deteriorate on levodopa therapy may be controlled by reducing the dose of levodopa and adjusting the frequency and schedule of drug administration. Patients maintained on optimal dosages of levodopa who still experience prominent dyskinesia and/or end-of-dose failure may benefit from the concomitant use of Parlodel, by decreasing the occurrence and/or severity of these manifestations. Since rapid escalation of bromocriptine doses causes severe adverse reactions, it is recommended to combine a slow increase of Parlodel, usually with a concomitant, gradual and limited reduction of levodopa dosage. Continued efficacy of bromocriptine for more than two years has not been established and there is some evidence that its efficacy tends to wane. Evidence available indicates that there is no consistent benefit from bromocriptine in patients who have not responded previously to levodopa, and studies have shown significantly more adverse reactions in bromocriptine-treated patients than in patients treated with levodopa. Parlodel is not recommended in the treatment of newly diagnosed patients or as the sole medication in Parkinson's disease.

CONTRAINDICATIONS Other than sensitivity to ergot alkaloids, no absolute contraindications to treatment with Parlodel (bromocriptine mesylate) are known. For procedure during pregnancy see "Use in Pregnancy" under Precautions.

WARNINGS Long-term treatment (6-36 months) with Parlodel in doses of 20 to 100 mg/day has been associated with pulmonary infiltrates, pleural effusion and thickening of the pleura in a few patients. Where Parlodel was discontinued, these changes slowly reverted to normal.

PRECAUTIONS Parlodel (bromocriptine mesylate) may cause hypotension, primarily postural; periodic monitoring of the blood pressure, particularly during the first days of therapy, is advisable. In some patients dizziness (vertigo) may occur with Parlodel; patients should therefore be cautioned against activities requiring rapid and precise responses, such as driving an automobile or operating dangerous machinery, until their response has been determined.

Care should be exercised when administering Parlodel concomitantly with phenothiazines or antihypertensive agents. Due to drug interaction at the receptor site, dosage should be adjusted accordingly.

Alcohol should be avoided during treatment with Parlodel. In some patients, the concomitant use of Parlodel and alcohol has given rise to alcohol intolerance and an increase in the severity and incidence of Parlodel's possible adverse reactions.

Parlodel should always be taken with food. In cases where severe adverse effects, such as nausea, vomiting, vertigo or headaches are severe or persisting, the therapeutic dosage of Parlodel should be reduced to half of one tablet daily (1.25 mg) and increased gradually to that recommended. The dopamine antagonist domperidone may be useful in the control of severe gastrointestinal side effects in parkinsonian patients receiving Parlodel (see Drug Interactions).

As with all medication, Parlodel should be kept safely out of the reach of children.

Use in Pregnancy: If the patient wishes to become pregnant, Parlodel (bromocriptine mesylate) should be stopped as soon as possible after conception is suspected. In this event immunological confirmation should be done immediately. When pregnancy is confirmed, Parlodel, like all other drugs, should be discontinued unless, in the opinion of the treating physician, the possible benefit to the patient outweighs the potential risk to the fetus.

In human studies with Parlodel (reviewed by Turkalj, I.), there were 1410 reported pregnancies, which yielded 1236 live and 5 stillborn infants from women who took Parlodel (bromocriptine mesylate) during early pregnancy. Among the 1241 infants, 43 cases (31 minor and 12 major) of congenital anomalies were reported. The incidence (3.46%) and type of congenital malformations and the incidence of spontaneous abortions (11.13%) in this group of pregnancies does not exceed that generally reported for such occurrences in the population at large.

Use in Parkinson's Disease: Use of Parlodel (bromocriptine mesylate), particularly in high doses, may be associated with mental confusion and mental disturbances. Since patients with Parkinson's disease may manifest varying degrees of dementia, caution should be exercised when treating such patients with Parlodel.

Parlodel administered alone or concomitantly with levodopa may cause visual or auditory hallucinations. These usually resolve with dosage reduction, but discontinuation of Parlodel may be required in some cases. Rarely, after high doses, hallucinations have persisted for several weeks following discontinuation of Parlodel. Caution should be exercised when administering Parlodel to patients with a history of myocardial infarction, particularly if they have a residual atrial, nodal or ventricular arrhythmia.

Symptomatic hypotension can occur and, therefore, caution should be exercised when administering Parlodel, particularly in patients receiving antihypertensive medication. Periodic evaluation of hepatic, hematopoietic, cardiovascular and renal function is recommended.

Drug Interactions: The concomitant use of erythromycin may increase bromocriptine plasma levels.

Domperidone, a dopamine antagonist, may cause increases in serum prolactin. In so doing, domperidone may antagonise the therapeutically relevant prolactin lowering effect of Parlodel. It is possible that the antitumorigenic effect of Parlodel in patients with prolactinomas may be partially blocked by domperidone administration.

ADVERSE REACTIONS The most frequently observed adverse reactions are nausea, vomiting, headache and gastrointestinal side effects such as abdominal pain, diarrhea and constipation. All these effects may be minimized or even prevented by giving small initial doses of bromocriptine and by taking it with food.

Postural hypotension which can, on rare occasions, lead to fainting and "shock-like" syndromes has been reported in sensitive patients. This is most likely to occur during the first few days of Parlodel treatment.

When bromocriptine is added to levodopa therapy, the incidence of adverse reactions may increase. The most common newly appearing adverse reactions in combination therapy were: nausea, abnormal involuntary movements, hallucinations, confusion, "on-off" phenomenon, dizziness, drowsiness, faintness, fainting, vomiting, asthenia, abdominal discomfort, visual disturbance, ataxia, insomnia, depression, hypotension, shortness of breath, constipation and vertigo.

Less common adverse reactions include anorexia, anxiety, blepharospasm, dry mouth, dysphagia, edema of the feet and ankles, erythromelalgia, epileptiform seizures, fatigue, headache, lethargia, mottling of skin, nasal stuffiness, nervousness, nightmares, parethesia, skin rash, urinary frequency, urinary incontinence, urinary retention and rarely signs or symptoms of ergotism such as tingling of fingers, cold feet, numbness, muscle cramps of feet and legs or exacerbation of Raynaud's syndrome.

Abnormalities in laboratory tests may include elevation of blood urea nitrogen, SGOT, SGPT, GGPT, CPK, alkaline phosphatase and uric acid, which are usually transient and not of clinical significance.

The occurrence of adverse reactions may be lessened by temporarily reducing dosage to one-half tablet two or three times daily.

SYMPTOMS AND TREATMENT OF OVERDOSE There have been several reports of acute overdosage with Parlodel (bromocriptine mesylate) in children and adults. No life threatening reactions have occurred. Symptoms reported included nausea, vomiting, dizziness, drowsiness, hypotension, sweating and hallucinations. Management is largely symptomatic; the cardiovascular system should be monitored. Metoclopramide can be used to antagonize the emesis and hallucinations in patients who have taken high doses.

DOSAGE AND ADMINISTRATION Parlodel (bromocriptine mesylate) should always be taken with food.

Although Parlodel (bromocriptine mesylate) has been found clinically useful in decreasing the severity and frequency of "on-off" fluctuations of late levodopa therapy, the decision to use bromocriptine as adjunctive treatment and the selection of dosage must be individualized in each case. A low dose is recommended. The initial dose of Parlodel is one half of a 2.5 mg tablet (1.25 mg) at bedtime with food to establish initial tolerance. Thereafter, the recommended dosage is 2.5 mg daily in two divided doses, with meals, (half a 2.5 mg tablet twice daily). The dosage may be increased very gradually, if necessary, by adding an additional 2.5 mg per day, once every 2 to 4 weeks, to be taken always in divided doses with meals. Increments should usually not exceed 2.5 mg. Clinical assessments are recommended at two week intervals or less during dosage titration, to ensure that the lowest effective dosage is not exceeded. The usual dosage range is from a few milligrams to 40 mg daily in two or three divided doses with meals. The median dose varies with the experience of individual investigators, but can be around 10 mg daily or higher. During initial titration it is recommended that the dosage of levodopa should be maintained, if possible. Subsequently, it might be desirable to combine a slow increase of bromocriptine with a concomitant, limited and gradual reduction of levodopa.

AVAILABILITY

TABLETS each containing 2.5 mg bromocriptine, as mesylate, available in bottles of 100.
CAPSULES each containing 5 mg bromocriptine, as mesylate, available in bottles of 100.

**For information on other approved indications, please consult the Parlodel product monograph, available to physicians and pharmacists on request.*

SANDOZ

Sandoz Canada Inc.
P.O. Box 385
Dorval, Quebec H9R 4P5

See ifc

FULL PRESCRIBING INFORMATION

DILANTIN*

(extended phenytoin sodium capsules USP)

THERAPEUTIC CLASSIFICATION
ANTICONVULSANT

INDICATIONS AND USAGE

Dilantin (phenytoin sodium) is indicated for the control of generalized tonic-clonic and psychomotor (grand mal and temporal lobe) seizures and prevention and treatment of seizures occurring during or following neurosurgery. Phenytoin serum level determinations may be necessary for optimal dosage adjustments (see Dosage and Administration).

CONTRAINDICATIONS

Dilantin (phenytoin sodium) is contraindicated in those patients who are hypersensitive to phenytoin or other hydantoins.

WARNINGS

Abrupt withdrawal of Dilantin (phenytoin sodium) in epileptic patients may precipitate status epilepticus. When, in the judgement of the clinician, the need for dosage reduction, discontinuation, or substitution of alternative antiepileptic medication arises, this should be done gradually. However, in the event of an allergic or hypersensitivity reaction, rapid substitution of alternative therapy may be necessary. In this case, alternative therapy should be an antiepileptic drug not belonging to the hydantoin chemical class.

There have been a number of reports suggesting a relationship between phenytoin and the development of lymphadenopathy (local or generalized) including benign lymph node hyperplasia, pseudolymphoma, lymphoma, and Hodgkin's Disease. Although a cause and effect relationship has not been established, the occurrence of lymphadenopathy indicates the need to differentiate such a condition from other types of lymph node pathology. Lymph node involvement may occur with or without symptoms and signs resembling serum sickness, e.g. fever, rash and liver involvement.

In all cases of lymphadenopathy, follow-up observation for an extended period is indicated and every effort should be made to achieve seizure control using alternative antiepileptic drugs.

Acute alcoholic intake may increase phenytoin serum levels while chronic alcoholic use may decrease serum levels.

Usage in Pregnancy

A number of reports suggests an association between the use of antiepileptic drugs by women with epilepsy and a higher incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed antiepileptic drugs; less systematic or anecdotal reports suggest a possible similar association with the use of all known antiepileptic drugs.

The reports suggesting a higher incidence of birth defects in children of drug-treated epileptic women cannot be regarded as adequate to prove a definite cause and effect relationship. There are intrinsic methodologic problems in obtaining adequate data on drug teratogenicity in humans; genetic factors or the epileptic condition itself may be more important than drug therapy in leading to birth defects. The great majority of mothers on antiepileptic medication deliver normal infants. It is important to note that antiepileptic drugs should not be discontinued in patients in whom the drug is administered to prevent major seizures, because of the strong possibility of precipitating status epilepticus with attendant hypoxia and threat to life. In individual cases where the severity and frequency of the seizure disorder are such that the removal of medication does not pose a serious threat to the patient, discontinuation of the drug may be considered prior to and during pregnancy, although it cannot be said with any confidence that even minor seizures do not pose some hazard to the developing embryo or fetus. The prescribing physician will wish to weigh these considerations in treating or counseling epileptic women of childbearing potential.

In addition to the reports of the increased incidence of congenital malformations, such as cleft lip/palate and heart malformations in children of women receiving phenytoin and other antiepileptic drugs, there have more recently been reports of a fetal hydantoin syndrome. This consists of prenatal growth deficiency, microcephaly and mental deficiency in children born to mothers who have received phenytoin, barbiturates, alcohol, or trimethadione. However, these features are all interrelated and are frequently associated with intrauterine growth retardation from other causes.

There have been isolated reports of malignancies, including neuroblastoma, in children whose mothers received phenytoin during pregnancy.

An increase in seizure frequency during pregnancy occurs in a high proportion of patients, because of altered phenytoin absorption or metabolism. Periodic measurement of serum phenytoin levels is particularly valuable in the management of a pregnant epileptic patient as a guide to an appropriate adjustment of dosage. However, postpartum restoration of the original dosage will probably be indicated.

Neonatal coagulation defects have been reported within the first 24 hours in babies born to epileptic mothers receiving phenobarbital and/or phenytoin. Vitamin K has been shown to prevent or correct this defect and has been recommended to be given to the mother before delivery and to the neonate after birth.

PRECAUTIONS

General

The liver is the chief site of biotransformation of Dilantin (phenytoin sodium); patients with impaired liver function, elderly patients, or those who are gravely ill may show early signs of toxicity.

A small percentage of individuals who have been treated with phenytoin have been shown to metabolize the drug slowly. Slow metabolism may be due to limited enzyme availability and lack of induction; it appears to be genetically determined.

Phenytoin should be discontinued if a skin rash appears (see "Warnings" section regarding drug discontinuation). If the rash is exfoliative, purpuric, or bullous or if lupus erythematosus or Stevens-Johnson syndrome is suspected, use of this drug should not be resumed and alternative therapy should be considered (see Adverse Reactions). If the rash is of a milder type (measles-like or scarlatiniform), therapy may be resumed after the rash has completely disappeared. If the rash recurs upon reinstitution of therapy, further phenytoin medication is contraindicated.

Hyperglycemia, resulting from the drug's inhibitory effects on insulin release, has been reported. Phenytoin may also raise the serum glucose level in diabetic patients.

Osteomalacia has been associated with phenytoin therapy and is considered to be due to phenytoin's interference with Vitamin D metabolism.

Phenytoin is not indicated for seizures due to hypoglycemic or other metabolic causes. Appropriate diagnostic procedures should be performed as indicated.

Phenytoin is not effective for absence (petit mal) seizures. If tonic-clonic (grand mal) and absence (petit mal) seizures are present, combined drug therapy is needed.

Serum levels of phenytoin sustained above the optimal range may produce confusional states referred to as "delirium", "psychosis", or "encephalopathy", or rarely, irreversible cerebellar dysfunction. Accordingly, at the first sign of acute toxicity, plasma level determinations are recommended. Dose reduction of phenytoin therapy is indicated if plasma levels are excessive; if symptoms persist, termination is recommended (see Warnings).

Information for Patients

Patients taking phenytoin should be advised of the importance of adhering strictly to the prescribed dosage regimen, and of informing the physician of any clinical condition in which it is not possible to take the drug orally as prescribed, e.g. surgery, etc.

Patients should also be cautioned on the use of other drugs or alcoholic beverages without first seeking the physician's advice.

Patients should be instructed to call their physician if skin rash develops.

The importance of good dental hygiene should be stressed in order to minimize the development of gingival hyperplasia and its complications.

Do not use capsules which are discoloured.

Laboratory Tests

Phenytoin serum level determinations may be necessary to achieve optimal dosage adjustments.

Drug Interactions

There are many drugs which may increase or decrease phenytoin levels or which phenytoin may affect. The most commonly occurring drug interactions are listed below:

1. Drugs which may increase phenytoin serum levels include: chloramphenicol, dicumarol, disulfiram, tolbutamide, isoniazid, phenylbutazone, acute alcohol intake, salicylates, chlordiazepoxide, phenothiazines, diazepam, estrogens, ethosuximide, halothane, methylphenidate, sulfonamides, cimetidine, trazodone.
2. Drugs which may decrease phenytoin levels include: carbamazepine, chronic alcohol abuse, reserpine. Ingestion times of phenytoin and antacid preparations containing calcium should be staggered in patients with low serum phenytoin levels to prevent absorption problems.
3. Drugs which may either increase or decrease phenytoin serum levels include: phenobarbital, valproic acid, and sodium valproate. Similarly, the effect of phenytoin on phenobarbital, valproic acid and sodium valproate serum levels is unpredictable.
4. Although not a true drug interaction, tricyclic antidepressants may precipitate seizures in susceptible patients and phenytoin dosage may need to be adjusted.
5. Drugs whose efficacy is impaired by phenytoin include: corticosteroids, coumarin anticoagulants, oral contraceptives, quinidine, vitamin D, digitoxin, rifampin, doxycycline, estrogens, furosemide.

Serum level determinations are especially helpful when possible drug interactions are suspected.

Drug/Laboratory Test Interactions

Phenytoin may cause decreased serum levels of protein-bound iodine (PBI). It may also produce lower than normal values for dexamethasone or metyrapone tests. Phenytoin may cause increased seurm levels of glucose, alkaline phosphatase, and gamma glutamyl transpeptidase (GGT).

Nursing Mothers

Infant breast-feeding is not recommended for women taking this drug because phenytoin appears to be secreted in low concentrations in human milk.

Pregnancy

See WARNINGS section.

Carcinogenesis

See WARNINGS section.

ADVERSE REACTIONS

Central Nervous System:

The most common manifestations encountered with Dilantin (phenytoin sodium) therapy are referable to this system and are usually dose-related. These include nystagmus, ataxia, slurred speech, decreased coordination and mental confusion. Dizziness, insomnia, transient nervousness, motor twitchings, and headaches have also been observed. There have also been rare reports of phenytoin induced dyskinesias, including chorea, dystonia, tremor and asterixis, similar to those induced by phenothiazine and other neuroleptic drugs.

A predominantly sensory peripheral potyneuropathy has been observed in patients receiving long-term phenytoin therapy.

Gastrointestinal System:

Nausea, vomiting, and constipation.

Integumentary System:

Dermatological manifestations sometimes accompanied by fever have included scarlatiniform or morbilliform rashes. A morbilliform rash (measles-like) is the most common; other types of dermatitis are seen more rarely. Other more serious forms which may be fatal have included bullous, exfoliative or purpuric dermatitis, lupus erythematosus, and Stevens-Johnson syndrome (see Precautions).

Hemopoietic System:

Hemopoietic complications, some fatal, have occasionally been reported in association with administration of phenytoin. These have included thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, and pancytopenia with or without bone marrow suppression. While macrocytosis and megaloblastic anemia have occurred, these conditions usually respond to folic acid therapy. Lymphadenopathy including benign lymph node hyperplasia, pseudolymphoma, lymphoma, and Hodgkin's Disease have been reported (see Warnings).

Connective Tissue System:

Coarsening of the facial features, enlargement of the lips, gingival hyperplasia, hypertrichosis and Peyronie's Disease.

Other:

Systemic lupus erythematosus, periarteritis nodosa, toxic hepatitis, liver damage, and immunoglobulin abnormalities may occur.

OVERDOSAGE

The lethal dose of Dilantin (phenytoin sodium) in children is not known. The lethal dose in adults is estimated to be 2 to 5 grams. The initial symptoms are nystagmus, ataxia, and dysarthria. Other signs are tremor, hyperflexia, lethargy, slurred speech, nausea, vomiting. The patient may become comatose and hypotensive. Death is due to respiratory and circulatory depression.

There are marked variations among individuals with respect to phenytoin plasma levels where toxicity may occur. Nystagmus, on lateral gaze, usually appears at 20 mcg/mL, ataxia at 30 mcg/mL, dysarthria and lethargy appear when the plasma concentration is over 40 mcg/mL, but as high a concentration as 50 mcg/mL has been reported without evidence of toxicity. As much as 25 times the therapeutic dose has been taken to result in a serum concentration over 100 mcg/mL with complete recovery.

Treatment

Treatment is nonspecific since there is no known antidote.

The adequacy of the respiratory and circulatory systems should be carefully observed and appropriate supportive measures employed. Hemodialysis can be considered since phenytoin is not completely bound to plasma proteins. Total exchange transfusion has been used in the treatment of severe intoxication in children.

In acute overdosage the possibility of other CNS depressants, including alcohol, should be borne in mind.

DOSAGE AND ADMINISTRATION

Serum concentrations should be monitored when switching a patient from the sodium salt to the free acid form.

Dilantin Capsules, Dilantin Parenteral, and Dilantin with Phenobarbital are formulated with the sodium salt of phenytoin. The free acid form of phenytoin is used in Dilantin-30 Pediatric and Dilantin-125 Suspensions and Dilantin Infatabs. Because there is approximately an 8% increase in drug content with the free acid form than the sodium salt, dosage adjustments and serum level monitoring may be necessary when switching from a product formulated with the free acid to a product formulated with the sodium salt and vice versa.

General

Dosage should be individualized to provide maximum benefit. In some cases, serum blood level determinations may be necessary for optimal dosage adjustments — the clinically effective serum level is usually 10 - 20 mcg/mL. Serum blood level determinations are especially helpful when possible drug interactions are suspected. With recommended dosage, a period of seven to ten days may be required to achieve therapeutic blood levels with Dilantin.

Adult Dose:

Patients who have received no previous treatment may be started on one 100 mg extended phenytoin sodium capsule three times daily, and the dose then adjusted to suit individual requirements. For most adults, the satisfactory maintenance dosage will be three to four capsules (300-400 mg) daily. An increase to six capsules daily may be made, if necessary.

Pediatric Dose:

Initially, 5 mg/kg/day in two or three equally divided doses, with subsequent dosage individualized to a maximum of 300 mg daily. A recommended daily maintenance dosage is usually 4 to 8 mg/kg. Children over 6 years old may require the minimum adult dose (300 mg/day). Pediatric dosage forms available include a 30 mg extended phenytoin sodium capsule, a 50 mg palatably flavoured Infatab, or an oral suspension form containing 30 mg of Dilantin in each 5 mL.

Alternative Dose:

Once-a-day dosage for adults with 300 mg of extended phenytoin sodium capsules may be considered if seizure control is established with divided doses of three 100 mg capsules daily. Studies comparing divided doses of 300 mg with a single daily dose of this quantity indicated that absorption, peak plasma levels, biologic half-life, difference between peak and minimum values, and urinary recovery were equivalent. Once-a-day dosage offers a convenience to the individual patient or to nursing personnel for institutionalized patients, and is intended only to be used for patients requiring this amount of drug daily. A major problem in motivating noncompliant patients may also be lessened when the patient can take all of his medication once-a-day. However, patients should be cautioned not to inadvertently miss a dose. Only extended phenytoin sodium capsules are recommended for once-a-day dosing.

HOW SUPPLIED

DILANTIN CAPSULES: (EXTENDED PHENYTOIN SODIUM CAPSULES USP):

Each white capsule with pale pink cap contains: phenytoin sodium 30 mg. Bottles of 100 and 500.

Each white capsule with orange cap contains: phenytoin sodium 100 mg. Bottles of 100 and 1,000.

Also available as:

Dilantin Injection:

Ready mixed 2 and 5 mL ampoules containing phenytoin sodium 50 mg/mL with propylene glycol 40% and alcohol 10% in water for injection. Adjusted to pH 12. 2 mL ampoules are available in packages of 10 and 5 mL ampoules in packages of 5.

Dilantin with Phenobarbital Capsules:

Each white capsule with garnet cap contains: phenytoin sodium 100 mg and phenobarbital 15 mg. Bottles of 100 and 500.

Each white capsule with black cap contains: phenytoin sodium 100 mg and phenobarbital 30 mg. Bottles of 100.

Dilantin Infatabs:

Each flavoured, triangular shaped, grooved tablet contains: phenytoin 50 mg. Bottles of 100.

Dilantin Suspensions:

Each 5 mL of flavoured, coloured suspension contains: phenytoin 30 mg (red, Dilantin-30) or 125 mg (orange, Dilantin-125). Bottles of 250 mL.

Store at room temperature below 30°C (86°F). Protect from light and moisture.

Product Monograph available on request.

PARKE-DAVIS

Scarborough, Ontario M1L 2N3

*T.M. Warner-Lambert Company, Parke-Davis Division, Warner-Lambert Canada Inc. auth.user.

See ibc

ℙLIORESAL®

(baclofen)
Muscle relaxant
Antispastic agent

INDICATIONS AND CLINICAL USES

Alleviation of signs and symptoms of spasticity resulting from multiple sclerosis. Spina cord injuries and other spinal cord diseases.

CONTRAINDICATIONS

Hypersensitivity to LIORESAL.

WARNINGS

Abrupt Drug Withdrawal: Except for serious adverse reactions, the dose should be reduced slowly when the drug is discontinued to prevent visual and auditory hallucinations, confusion, anxiety with tachycardia and sweating, and worsening of spasticity.

Impaired Renal Function: Caution is advised in these patients and reduction in dosage may be necessary.

Stroke: Has not been of benefit and patients have shown poor tolerability to the drug.

Pregnancy and Lactation: Not recommended as safety has not been established. High doses in rats and rabbits are associated with an increase of abdominal hernias and ossification defects in the fetuses.

PRECAUTIONS

Not recommended in children under 12 as safety has not been established.

Because sedation may occur, caution patients regarding the operation of automobiles or dangerous machinery, activities made hazardous by decreased alertness, and use of alcohol and other CNS depressants.

Use with caution in spasticity that is utilized to sustain upright posture and balance in locomotion, or whenever spasticity is utilized to obtain increased function, epilepsy or history of convulsive disorders (clinical state and EEG should be monitored), peptic ulceration, severe psychiatric disorders, elderly patients with cerebrovascular disorders, and patients receiving antihypertensive therapy.

ADVERSE REACTIONS

Most common adverse reactions are transient drowsiness; dizziness, weakness and fatigue. Others reported:

Neuropsychiatric: Headache, insomnia, euphoria, excitement, depression, confusion, hallucinations, paresthesia, muscle pain, tinnitus, slurred speech, coordination disorder, tremor, rigidity, dystonia, ataxia, blurred vision, nystagmus, strabismus, miosis, mydriasis, diplopia, dysarthria, epileptic seizures.

Cardiovascular: Hypotension, dyspnea, palpitation, chest pain, syncope.

Gastrointestinal: Nausea, constipation, dry mouth, anorexia, taste disorder, abdominal pain, vomiting, diarrhea, and positive test for occult blood in stool.

Genitourinary: Urinary frequency, enuresis, urinary retention, dysuria, impotence, inability to ejaculate, nocturia, hematuria.

Other: Rash, pruritus, ankle edema, excessive perspiration, weight gain, nasal congestion.

Some of the CNS and genitourinary symptoms reported may be related to the underlying disease rather than to drug therapy.

The following laboratory tests have been found to be abnormal in a few patients receiving LIORESAL: SGOT, alkaline phosphatase and blood sugar (all elevated).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Signs and Symptoms: Vomiting, muscular hypotonia, hypotension, drowsiness, accommodation disorders, coma, respiratory depression, and seizures.

Co-administration of alcohol, diazepam, tricyclic anti-depressants, etc., may aggravate the symptoms.

Treatment: Treatment is symptomatic. In the alert patient, empty the stomach (induce emesis followed by lavage). In the obtunded patient, secure the airway with a cuffed endotracheal tube before beginning lavage (do not induce emesis).

Maintain adequate respiratory exchange; do not use respiratory stimulants. Muscular hypotonia may involve the respiratory muscles and require assisted respiration. Maintain high urinary output. Dialysis is indicated in severe poisoning associated with renal failure.

DOSAGE AND ADMINISTRATION

Optimal dosage of LIORESAL requires individual titration. Start therapy at a low dosage and increase gradually until optimum effect is achieved (usually 40-80 mg daily).

The following dosage titration schedule is suggested:

5 mg t.i.d. for 3 days
10 mg t.i.d. for 3 days
15 mg t.i.d. for 3 days
20 mg t.i.d. for 3 days

Total daily dose should not exceed a maximum of 20 mg q.i.d.

The lowest dose compatible with an optimal response is recommended. If benefits are not evident after a reasonable trial period, patients should be slowly withdrawn from the drug (see Warnings).

AVAILABILITY

LIORESAL (baclofen) 10 mg tablets: White to off-white flat-faced, oval tablets with GEIGY monogram on one side and the identification code 23 below the monogram. Fully bisected on the reverse side.

LIORESAL D.S. 20 mg tablet: White to off-white capsule-shaped, biconvex tablets. Engraved GEIGY on one side and GW with bisect on the other.

Available in bottles of 100 tablets.

Product Monograph supplied on request.

References:

1. Cartlidge, N.E.F., Hudgson, P., Weightman, D.: A comparison of baclofen and diazepam in the treatment of spasticity. J Neurol. Sci. 23: 17-24 (1974).
2. Young, R., Delwaide, P.: Spasticity. New England Journal of Medicine 304: 28-33 & 96-99 (1981).
3. From, A., Heltberg, A.: A double blind trial with baclofen and diazepam in spasticity due to multiple sclerosis. Acta Neurol. Scandinav. 51: 158-166, (1975).

see obc

Geigy
Mississauga, Ontario
L5N 2W5

PAAB CCPP

ℙSYMMETREL® (Amantadine HCl) Antiparkinsonian Agent

INDICATIONS: The treatment of Parkinson's syndrome and in the short-term management of drug-induced extrapyramidal symptoms.

CONTRAINDICATIONS: Patients with known hypersensitivity to the drug.

WARNINGS: Patients with a history of epilepsy or other "seizures" should be observed closely for possible untoward central nervous system effects. Patients with a history of congestive heart failure or peripheral edema should be followed closely as there are patients who developed congestive heart failure while receiving SYMMETREL®.

Safety of use in pregnancy has not been established. SYMMETREL® should not be used in women of childbearing potential, unless the expected benefit to the patient outweighs the possible risk to the fetus.

SYMMETREL® is secreted in the milk and should not be administered to nursing mothers.

PRECAUTIONS: The dose may need careful adjustment in patients with renal impairment, congestive heart failure, peripheral edema or orthostatic hypotension. Since SYMMETREL® is not metabolized and is mainly excreted in the urine, it may accumulate when renal function is inadequate.

Care should be exercised when administering to patients with liver disease, a history of recurrent eczematoid rash, psychosis, or severe psychoneurosis not controlled by chemotherapeutic agents. Careful observation is required when administered concurrently with central nervous system stimulants.

Patients with Parkinson's syndrome improving on SYMMETREL® should resume normal activities gradually and cautiously, consistent with other medical considerations, such as the presence of osteoporosis or phlebothrombosis. Patients receiving SYMMETREL® who note central nervous system effects or blurring of vision should be cautioned against driving or working in situations where alertness is important.

SYMMETREL® should not be discontinued abruptly since a few patients with Parkinson's syndrome experienced a parkinsonian crisis, ie., sudden marked clinical deterioration, when this medication was suddenly stopped.

The dose of anticholinergic drugs or of SYMMETREL® should be reduced if atropine-like effects appear when these drugs are used concurrently.

ADVERSE REACTIONS: Adverse reactions have occurred in patients while receiving SYMMETREL® alone or in combination with anticholinergic antiparkinson drugs and/or levodopa.

Important adverse reactions are orthostatic hypotensive episodes, congestive heart failure, depression, psychosis and urinary retention; and rarely convulsions, reversible leukopenia and neutropenia, and abnormal liver function test results.

Adverse reactions of less importance are: anorexia, anxiety, ataxia, confusion, hallucinations, constipation, dizziness (light-headedness), dry mouth, headache, insomnia, livedo reticularis, nausea, peripheral edema, drowsiness, dyspnea, fatigue, hyperkinesia, irritability, nightmares, rash, slurred speech, visual disturbance, vomiting and weakness; and very rarely eczematoid dermatitis and oculogyric episodes. Some side effects were transient and disappeared even with continued administration of the drug.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: Limited data are available concerning clinical effects and management of SYMMETREL® overdosage. An elderly patient with Parkinson's syndrome who took an overdose of 2.8 g of SYMMETREL® in a suicidal attempt, developed acute toxic psychosis, urinary retention, and a mixed acid-base disturbance. The toxic psychosis was manifested by disorientation, confusion, visual hallucinations and aggressive behaviour. Convulsions did not occur, possibly because the patient had been receiving phenytoin prior to the acute ingestion of SYMMETREL®.

There is no specific antidote. For acute overdosing, general supportive measures should be employed, along with immediate gastric lavage or induction of emesis. Fluids should be forced, and if necessary, given I.V. The pH of the urine has been reported to influence the excretion rate of SYMMETREL®. Since the excretion rate of SYMMETREL® increases rapidly when the urine is acidic, the administration of urine acidifying fluids may increase the elimination of the drug from the body. Blood pressure, pulse, respiration and temperature should be monitored. The patient should be observed for possible development of arrhythmias, hypotension, hyperactivity, and convulsions; if required, appropriate therapy should be administered. Blood electrolytes, urine pH and urinary output should be monitored. If there is no record of recent voiding, catheterization should be done. The possibility of multiple drug ingestion by the patient should be considered.

DOSAGE AND ADMINISTRATION: Parkinson's Syndrome: Initial dose is 100 mg daily for patients with serious associated medical illnesses or who are receiving high doses of other antiparkinson drugs. After one to several weeks at 100 mg once daily, the dose may be increased to 100 mg twice daily. When SYMMETREL® and levodopa are initiated concurrently, SYMMETREL® should be held constant at 100 mg daily or twice daily while the daily dose of levodopa is gradually increased to optimal dose. When used alone, the usual dose of SYMMETREL® is 100 mg twice a day.

Patients whose responses are not optimal with SYMMETREL® at 200 mg daily may benefit from an increase to 300 mg daily in divided doses. Patients who experience a fall-off of effectiveness may regain benefit by increasing the dose to 300 mg daily; such patients should be supervised closely by their physicians.

DOSAGE FORMS: Capsules: (bottles of 100) - each red, soft gelatin capsule contains 100 mg of amantadine HCl. **Syrup:** (500 mL) - each 5 mL (1 teaspoonful) of clear colorless syrup contains 50 mg of amantadine HCl.

References:

1. Schwab RS, Poskanzer DC, England AC Jr., Young RR: Amantadine in Parkinson's disease. JAMA 1972;227:7.

Product monograph available on request.

®TM

PAAB CCPP

DU PONT CANADA

Du Pont Pharmaceuticals
Mississauga, Ontario
L5M 2J4

See page xvi

Brief Prescribing Information

Ⓟ Tegretol® (carbamazepine)

TEGRETOL® 200 mg
TEGRETOL® CHEWTABS™ 100 mg and 200 mg
TEGRETOL® CR 200 mg and 400 mg

Action

TEGRETOL (carbamazepine) has anticonvulsant properties which have been found useful in the treatment of psychomotor epilepsy and, as an adjunct in the treatment of partial epilepsies, when administered in conjunction with other anticonvulsant drugs to prevent the possible generalization of the epileptic discharge. A mild psychotropic effect has been observed in some patients, which seems related to the effect of the carbamazepine in psychomotor or temporal lobe epilepsy.

TEGRETOL relieves or diminishes the pain associated with trigeminal neuralgia often within 24 to 48 hours.

Like other tricyclic compounds, TEGRETOL has a moderate anticholinergic action which is responsible for some of its side effects. A tolerance may develop to the action of TEGRETOL after a few months of treatment and should be watched for.

TEGRETOL may suppress ventricular automaticity due to its membrane-depressant effect similar to that of quinidine and procainamide, associated with suppression of phase 4 depolarization of the heart muscle fibre. A number of investigators have reported a deterioration of EEG abnormalities with regard to focal alterations and a higher incidence of records with nil beta activity, during carbamazepine-combined treatment.

The absorption of carbamazepine in man is relatively slow. When taken in a single oral dose, TEGRETOL (carbamazepine tablets) and TEGRETOL CHEWTABS (carbamazepine chewable tablets) yield peak plasma concentrations of unchanged carbamazepine within 4-24 hours. With respect to the quantity of carbamazepine absorbed, there is no clinically relevant difference between the various dosage forms. When TEGRETOL CR (carbamazepine controlled release tablets) are administered repeatedly, they yield a lower average maximal concentration of carbamazepine in the plasma, without a reduction in the average minimal concentration. This tends to result in a lower incidence of intermittent concentration-dependent adverse drug reactions. It also ensures that the plasma concentrations remain largely stable throughout the day, thereby making it possible to manage with a twice-daily dosage.

Carbamazepine becomes bound to serum proteins to the extent of 70-80%. The concentration of unchanged substance in the saliva reflects the non-protein-bound portion present in the serum (20-30%).

The elimination half-life of unchanged carbamazepine in the plasma averages approximately 36 hours following a single oral dose, whereas after repeated administration, which leads to autoinduction of hepatic enzymes, it averages only 16-24 hours, depending on the duration of the medication. In patients receiving concomitant treatment with other enzyme-inducing anti-epileptic agents, half-life values averaging 9-10 hours have been found.

Only 2-3% of the dose, whether given singly or repeatedly, is excreted in the urine in unchanged form. The primary metabolite is the pharmacologically active 10, 11-epoxide.

In man, the main urinary metabolite of carbamazepine is the trans-diol derivative originating from the 10, 11-epoxide; a small portion of the epoxide is converted into 9-hydroxymethyl-10-carbamoyl-acridan. Other important biotransformation products are various monohydroxylated compounds, as well as the N-glucuronide of carbamazepine.

The therapeutic range for the steady-state plasma concentration of carbamazepine generally lies between 4-10 mcg/ml.

Indications and Clinical Use

A. Trigeminal Neuralgia:

TEGRETOL (carbamazepine) is indicated for the symptomatic relief of pain of trigeminal neuralgia only during periods of exacerbation of true or primary trigeminal neuralgia (tic douloureux). It should not be used preventively during periods of remission. In some patients, TEGRETOL has relieved glossopharyngeal neuralgia. For patients who fail to respond to TEGRETOL, or who are sensitive to the drug, recourse to other accepted measures must be considered.

TEGRETOL is not a simple analgesic and should not be used to relieve trivial facial pains or headaches.

B. TEGRETOL has been found useful in:

1. the management of psychomotor (temporal lobe) epilepsy and,
2. as an adjunct, in some patients with secondary or partial epilepsy with complex symptomatology or secondarily generalized seizures, when administered in combination with other antiepileptic medication.
3. as an alternative medication in patients with generalized tonic-clonic seizures who are experiencing marked side effects or fail to respond to other anticonvulsant drugs.

TEGRETOL is not effective in controlling petit mal, minor motor, myoclonic and predominantly unilateral seizures, and does not prevent the generalization of epileptic discharge. Moreover, recent information suggests that exacerbation of seizures may occasionally occur in patients with atypical absences.

Contraindications

TEGRETOL (carbamazepine) should not be administered to patients with a history of hepatic disease or serious blood disorder.

TEGRETOL should not be administered immediately before, in conjunction with, or immediately after a monoamine oxidase inhibitor. When it seems desirable to administer TEGRETOL to a patient who has been receiving an MAO inhibitor, there should be as long a drug-free interval as the clinical condition allows, but in no case should this be less than 14 days. Then the dosage of TEGRETOL should be low initially, and increased very gradually.

TEGRETOL should not be administered to patients presenting atrioventricular heart block. *(See Sections on Action and Precautions).*

Safe use in pregnancy has not been established. Therefore, TEGRETOL should not be administered during the first 3 months of pregnancy. TEGRETOL should not be given to women of child-bearing potential unless, in the opinion of the physician, the expected benefits to the patient outweigh the possible risk to the fetus *(See Reproductive Studies)*. Because of demonstrated toxicity in nursing animals TEGRETOL should not be administered to nursing mothers.

TEGRETOL should not be administered to patients with known hypersensitivity to carbamazepine or to any of the tricyclic compounds, such as amitriptyline, trimipramine, imipramine, or their analogues or metabolites, because of the similarity in chemical structure.

Warnings

Although reported infrequently, serious adverse effects have been observed during the use of TEGRETOL (carbamazepine). Agranulocytosis and aplastic anemia have occurred in a few instances with a fatal outcome. Leucopenia, thrombocytopenia, hepatocellular and cholestatic jaundice, and hepatitis have also been reported. It is, therefore, important that TEGRETOL should be used carefully and close clinical and frequent laboratory supervision should be maintained throughout treatment in order to detect as early as possible signs and symptoms of a possible blood dyscrasia.

Long-term toxicity studies in rats indicated a potential carcinogenic risk *(See Section on "Toxicology")*. Therefore, the possible risk of drug use must be weighed against the potential benefits before prescribing carbamazepine to individual patients.

Precautions

Monitoring of Hematological and Other Adverse Reactions:

Complete blood studies, including platelet counts, and evaluation of hepatic and renal function and urinalysis should be carried out before treatment is instituted. Careful clinical and laboratory supervision should be maintained throughout treatment, including frequent performance of complete blood counts, in order to detect any early signs or symptoms of blood dyscrasia. Should any signs or symptoms or abnormal laboratory findings suggestive of blood dyscrasia or liver disorder occur, TEGRETOL (carbamazepine) should be immediately discontinued until the case is carefully reassessed.

Non-progressive or fluctuating asymptomatic leucopenia, which is encountered, does not generally call for the withdrawal of TEGRETOL. However, treatment with TEGRETOL should be discontinued if the patient develops leucopenia which is progressive or accompanied by clinical manifestations, e.g. fever or sore throat.

Urinary Retention and Increased Intraocular Pressure:

Because of its anticholinergic action, TEGRETOL should be given cautiously, if at all, to patients with increased intraocular pressure or urinary retention. Such patients should be followed closely while taking the drug.

Occurrence of Behavioural Disorders:

Because it is closely related to the other tricyclic drugs, there is some possibility that TEGRETOL might activate a latent psychosis, or, in elderly patients, produce agitation or confusion, especially when combined with other drugs. Caution should also be exercised in alcoholics.

Use in Patients with Cardiovascular Disorders:

TEGRETOL should be used cautiously in patients with a history of coronary artery disease, organic heart disease, or congestive failure. If a defective conductive system is suspected, an ECG should be performed before administering TEGRETOL, in order to exclude patients with atrioventricular block.

Driving and Operating Hazardous Machinery:

Because dizziness and drowsiness are possible side effects of TEGRETOL, patients should be warned about the possible hazards of operating machinery or driving automobiles.

Drug Interactions:

Induction of hepatic enzymes in response to TEGRETOL may have the effect of diminishing the activity of certain drugs that are metabolized in the liver. This should be considered when administering TEGRETOL concomitantly with other anti-epileptic agents and drugs such as theophylline.

Concomitant administration of TEGRETOL with verapamil, diltiazem, erythromycin, troleandomycin, cimetidine, propoxyphene or isoniazid, has been reported to result in elevated plasma levels of carbamazepine. Since an increase in the blood levels of carbamazepine may result in unwanted effects (e.g. dizziness, headache, ataxia, diplopia and nystagmus may occur), the dosage of carbamazepine should be adapted accordingly and blood levels monitored.

The concomitant administration of carbamazepine and lithium may increase the risk of neurotoxic side effects.

In patients receiving oral anticoagulant medication, the dosage of the anticoagulant should be readapted to clinical requirements whenever treatment with TEGRETOL is initiated or withdrawn.

TEGRETOL, like other anticonvulsants, may adversely affect the reliability of oral contraceptives. Patients should accordingly be advised to use some alternative, non-hormonal method of contraception.

TEGRETOL, like other psycho-active drugs, may reduce the patient's alcohol tolerance; it is therefore advisable to abstain from alcohol consumption during treatment.

TEGRETOL should not be administered in conjunction with an MAO inhibitor. *(See Section on Contraindications).*

Adverse Reactions

The reactions which have been most frequently reported with TEGRETOL (carbamazepine) are drowsiness, unsteadiness on the feet, vertigo, dizziness, gastrointestinal disturbances, and nausea. These reactions usually occur only during the initial phase of therapy. They have rarely necessitated discontinuing TEGRETOL therapy, and can be minimized by initiating treatment at a low dosage.

The more serious adverse reactions observed are the hematologic, hepatic, cardiovascular and dermatologic reactions, which require discontinuation of therapy. If treatment with TEGRETOL has to be withdrawn abruptly, the change-over to another anti-epileptic drug should be effected under cover of diazepam.

The following adverse reactions have been reported:

Hematologic – Transitory leucopenia, eosinophilia, hyponatremia, leucocytosis, thrombocytopenic purpura, agranulocytosis, macrocytic anemia and aplastic anemia. In a few instances, deaths have occurred.

Hepatic – During the long-term administration of TEGRETOL, abnormalities in liver function tests, cholestatic and hepatocellular jaundice, and hepatitis have been reported.

Dermatologic – The following reactions occurred during treatment with TEGRETOL: skin sensitivity reactions and rashes, erythematous rashes, pruritic eruptions, urticaria, photosensitivity, pigmentary changes, neurodermatitis and in rare cases Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, alopecia, diaphoresis, erythema multiforme, erythema nodosum, and aggravation of disseminated lupus erythematosus.

Neurologic – The reactions reported as occurring during treatment with TEGRETOL include vertigo, somnolence, ataxia, confusion, headache, fatigue, blurred vision, visual hallucinations, transient diplopia and oculomotor disturbances, speech disturbances, abnormal involuntary movements and increase in motor seizures. In addition, peripheral neuritis and paresthesia, depression with agitation, talkativeness, nystagmus, hyperacusis, and tinnitus have been reported but only very rarely. There have been some reports of paralysis and other symptoms of cerebral arterial insufficiency but no conclusive relationship to the administration of TEGRETOL could be established.

Cardiovascular – Thromboembolism, recurrence of thrombophlebitis in patients with a prior history of thrombophlebitis, primary thrombophlebitis, congestive heart failure, aggravation of hypertension, Stokes-Adams in patients with AV block, hypotension, syncope and collapse, edema, aggravation of coronary artery disease. Some of these complications (including myocardial infarction and arrhythmia) have been associated with other tricyclic compounds.

Genitourinary – Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, azotemia, renal failure, and impotence. Elevation of BUN, albuminuria and glycosuria also have been observed.

Respiratory – Pulmonary hypersensitivity characterized by fever, dyspnea, pneumonitis or pneumonia.

Gastrointestinal – Disturbances associated with TEGRETOL therapy have included nausea, vomiting, gastric or abdominal discomfort, diarrhea or constipation, anorexia and dryness of the mouth and throat, glossitis and stomatitis.

Ophthalmic – There is no conclusive evidence that TEGRETOL produces pathological changes in the cornea, lens or retina. However, it should be recognized that many phenothiazines and related drugs have been shown to cause eye changes. By analogy, periodic eye examinations, including slit-lamp fundoscopy and tonometry, are recommended.

Other reactions reported during treatment with TEGRETOL include fever and chills, aching joints and muscles, leg cramps, conjunctivitis, and adenopathy or lymphadenopathy.

Symptoms and Treatment of Overdosage

Symptoms of Overdosage:

The symptoms of overdosage include dizziness, ataxia, drowsiness, stupor, nausea, vomiting, restlessness, agitation, disorientation; tremor, involuntary movements, opisthotonos, abnormal reflexes (stowed or hyperactive); mydriasis, nystagmus; flushing, cyanosis, and urinary retention. Hypotension or hypertension may develop. Coma may ensue. EEG and ECG changes may occur. The laboratory findings in isolated instances of overdosage have included leukocytosis, reduced leukocyte count, glycosuria and acetonuria.

Treatment of Overdosage:

There is no known specific antidote to TEGRETOL (carbamazepine). Experience with accidental TEGRETOL overdosage is limited. Since TEGRETOL is chemically related to the tricyclic antidepressants, reference to treatment of TOFRANIL (imipramine) overdosage is relevant.

It is recommended that emesis be induced, and that gastric lavage be performed. Vital signs should be watched and symptomatic treatment should be administered as required. Hyperirritability may be controlled by the administration of parenteral diazepam or barbiturates. However, barbiturates should not be used if drugs that inhibit monoamine oxidase have also been taken by the patient, either in overdosage or in recent therapy (within two weeks).

Barbiturates may also induce respiratory depression, particularly in children. It is therefore advisable to have equipment available for artificial ventilation and resuscitation when barbiturates are employed. Paraldehyde may be used to counteract muscular hypertonus without producing respiratory depression.

Shock (circulatory collapse) should be treated with supportive measures, including intravenous fluids, oxygen, and corticosteroids.

It is recommended that the electrocardiogram be monitored, particularly in children, to detect any cardiac arrhythmias or conduction defects.

Dosage and Administration

Use in Epilepsy (See Indications):

A low initial daily dosage of TEGRETOL (carbamazepine) with a gradual increase in dosage is advised. Dosage should be adjusted to the needs of the individual patient.

TEGRETOL tablets and CHEWTABS should be taken in 2 to 4 divided doses daily, with meals whenever possible.

The controlled release characteristics of TEGRETOL CR reduce the daily fluctuations of plasma carbamazepine. TEGRETOL CR tablets (either whole or, if so prescribed, only half a tablet) should be swallowed unchewed with a little liquid during or after a meal. These controlled release tablets should be prescribed as a twice-daily dosage. If necessary, three divided doses may be prescribed.

Adults and Children Over 12 Years of Age:

Initially, 100 to 200 mg once or twice a day depending on the severity of the case and previous therapeutic history. The initial dosage is progressively increased, in divided doses, until the best response is obtained. The usual optimal dosage is 800 to 1200 mg daily. In rare instances some adult patients have received 1600 mg. As soon as disappearance of seizures has been obtained and maintained, dosage should be reduced very gradually until a minimum effective dose is reached.

Children 6-12 Years of Age:

Initially, 100 mg in divided doses on the first day. Increase gradually by adding 100 mg per day until the best response is obtained. Dosage should generally not exceed 1000 mg daily. As soon as disappearance of seizures has been obtained and maintained, dosage should be reduced very gradually until a minimum effective dose is reached.

Use in Trigeminal Neuralgia:

The initial daily dosage should be small; 200 mg taken in 2 doses of 100 mg each is recommended. The total daily dosage can be increased by 200 mg/day until relief of pain is obtained. This is usually achieved at dosage between 200 and 800 mg daily, but occasionally up to 1200 mg/day may be necessary. As soon as relief of pain has been obtained and maintained, progressive reduction in dosage should be attempted until a minimal effective dosage is reached. Because trigeminal neuralgia is characterized by periods of remission, attempts should be made to reduce or discontinue the use of TEGRETOL at intervals of not more than 3 months, depending upon the individual clinical course.

Prophylactic use of the drug in trigeminal neuralgia is not recommended.

Availability

TEGRETOL Tablets 200 mg: Each white, round, flat, bevelled-edge double-scored tablet engraved GEIGY on one side contains 200 mg carbamazepine. Available in bottles of 100 and 500 tablets.

TEGRETOL CHEWTABS 100 mg: Pale pink, round, flat, bevelled-edge tablets with distinct red spots. GEIGY engraved on one side and MR on the other. Fully bisected between the M and R. Each chewable tablet contains 100 mg carbamazepine. Available in bottles of 100 CHEWTABS.

TEGRETOL CHEWTABS 200 mg: Pale pink, oval biconvex tablets with distinct red spots. GEIGY engraved on one side and PU engraved on the other. Fully bisected between the P and U. Each chewable tablet contains 200 mg carbamazepine. Available in bottles of 100 CHEWTABS.

TEGRETOL CR 200 mg: Beige-orange, capsule-shaped, slightly biconvex tablet, engraved CG/CG on one side and HC/HC on the other. Fully bisected on both sides. Each controlled release tablet contains 200 mg carbamazepine. Available in bottles of 100 tablets.

TEGRETOL CR 400 mg: Brownish-orange, capsule-shaped, slightly biconvex tablet, engraved CG/CG on one side and ENE/ENE on the other. Fully bisected on both sides. Each controlled release tablet contains 400 mg carbamazepine. Available in bottles of 100 tablets.

Protect from heat and humidity.

References:

1. Data on File – CIBA-GEIGY Canada Ltd.
2. Arvidsson J. Eeg-Olofsson O. The diurnal variation of carbamazepine and carbamazepine-10. 11- Epoxide in plasma and saliva in children with epilepsy using convenient and slow release (CR) formulation of Tegretol. Acta Neurol Scand 1981; Suppl 88:64:1-202.

Geigy
Mississauga, Ontario
L5N 2W5

PAAB CCPP G-850331

December 1987

see page.xii

PEDIATRIC NEUROLOGIST

MEMORIAL UNIVERSITY OF NEWFOUNDLAND FACULTY OF MEDICINE

The Discipline of Pediatrics of the Faculty of Medicine at Memorial University of Newfoundland and the Dr. Charles A. Janeway Child Health Centre, St. John's, Newfoundland, are seeking a Pediatric Neurologist for a full-time faculty and hospital appointment. This appointment carries with it a faculty rank appropriate to the training and experience of the accepted candidate.

Memorial University has a fully accredited training program for Certification in Pediatrics. Trainees in Adult Neurology also rotate to the Pediatric Neurology service for part of their training.

In accordance with Canadian Immigration regulations, preference will be given to Canadian citizens and permanent residents.

Please apply, with a curriculum vitae and the names of three referees to:

Dr. Albert J. Davis
Professor and Chairman
Discipline of Pediatrics
Faculty of Medicine
Memorial University of Newfoundland
St. John's, Newfoundland
Canada A1B 3V6

UNIVERSITY OF TORONTO

CENTRE FOR RESEARCH IN NEURODEGENERATIVE DISEASES

Applications are invited for a position in research into the etiology and mechanisms of amyotrophic lateral sclerosis (motor neuron) disease. Applicants must have a Ph.D. or M.D. and have a strong background in molecular biology, molecular genetics and gene regulation. Start up funds will be provided. Successful candidates must initiate independent and original research programs.

The Centre is located in the core of the University/Hospital complex in close proximity to more than 150 neuroscientists.

Send a curriculum vitae and names of references to Dr. D.R. McLachlan, Centre for Research in Neurodegenerative Diseases, University of Toronto, Rm. 3318, Medical Sciences Bldg., 1 King's College Circle, Toronto, Canada, M5S 1A8. Application deadline: June 30, 1990.

The University of Toronto encourages both men and women to apply for positions. In accordance with Canadian immigration requirements, this advertisement is directed to Canadian citizens and permanent residents.

MACLACHLAN STROKE RESEARCH FELLOW

Full-time clinical research associated with Acute Stroke Unit in the Department of Neurosciences, Stroke Research Unit, and associated Neurobehavioural Unit. Post includes training and research in Carotid and Transcranial Doppler Laboratory, Neuroimaging, and in disorders of speech and behavioural changes related to stroke.

Position starts July 1, 1991. Preference for 2 years' tenure.

Apply: Dr. J.W. Norris or Dr. S.E. Black
Stroke Research Unit
Sunnybrook Health Science Centre
2075 Bayview Avenue
Toronto, Canada M4N 3M5
(416) 480-4287

THE UNIVERSITY OF CALGARY

HEAD, DEPARTMENT OF CLINICAL NEUROSCIENCES

The University of Calgary Faculty of Medicine, and the Foothills Hospital, invite applications and nominations for the position of Head of the Department of Clinical Neurosciences. This is a growing multidisciplinary department which includes representation from neurology, neurosurgery and related fields. The University of Calgary is accredited for residency training in adult and paediatric neurology and in neurosurgery.

We are searching for an outstanding academic neurologist or neurosurgeon with proven administrative leadership and research experience. The successful candidate will relate to the practising community and the affiliated teaching hospitals, and to the Neurosciences Research Group in the Faculty of Medicine.

In accordance with Canadian immigration requirements, priority will be given to Canadian citizens and permanent residents of Canada. The University of Calgary has an Employment Equity Program and encourages applications from all qualified candidates, including women, aboriginal people, visible minorities, and people with disabilities.

Applications and nominations, including a curriculum vitae, a statement of research interests and academic goals, and the names of three referees should be forwarded by May 31, 1990, to:

Dr. M. Watanabe
Dean, Faculty of Medicine
The University of Calgary
3330 Hospital Drive N.W.
Calgary, Alberta T2N 4N1

https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press

See page ii

See page xi

https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press

https://doi.org/10.1017/S0317167100030286 Published online by Cambridge University Press