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UNIVERSITY OF OTTAWA * FACULTY OF MEDICINE
CHAIR OF NEUROLOGY

The University of Ottawa invites applications for the position of Chairman of the University Division of Neurology.

Suitable applicants must be eligible to practise in Ontario and shall be certified specialists of the Royal College of Physicians and Surgeons of Canada in neurology. Applicants will have demonstrated achievement and experience in clinical and academic neurology. While the position requires a major leadership role in the University/Hospital/community setting, preference will be given to a qualified individual devoted to the pursuit of academic excellence in teaching and research.

Part of the mandate will focus on the development of research in neurology and continuing quality teaching programs at both the undergraduate and postgraduate levels. The University of Ottawa is affiliated with four teaching hospitals providing neurology training programs, namely Children's Hospital of Eastern Ontario, Ottawa Civic Hospital, Ottawa General Hospital and National Defence Medical Center.

The successful candidate will hold a joint appointment as Chairman of the University Division of Neurology and Head of the Hospital Division of Neurology at one of the above-mentioned teaching hospitals.

Salary and fringe benefits are commensurate with qualifications and experience and are in accordance with existing academic scales at the University of Ottawa.

In accordance with Canadian immigration requirements, priority will be given to Canadian Citizens and permanent residents of Canada. Employment equity is University policy.

Applicants are requested to forward their curriculum vitae and the names of three references **PRIOR TO MARCH 31, 1990**, to:

John F. Seely, M.D.
Acting Vice-Dean
Faculty of Medicine
University of Ottawa
451 Smyth Road
Ottawa, Ontario
K1H 8M5

UNIVERSITÉ D'OTTAWA * FACULTÉ DE MÉDECINE
CHAIRE DE NEUROLOGIE

L'Université d'Ottawa ouvre un concours pour le poste de directeur de la division de neurologie. Les candidats qualifiés devront avoir un certificat du Collège royal des médecins et chirurgiens du Canada et être éligibles au permis d'exercer du Collège des médecins et chirurgiens de l'Ontario.

Le candidat choisi sera le responsable de la coordination des programmes d'enseignement aux hôpitaux affiliés soit, l'Hôpital pour enfants de l'Est de l'Ontario, l'Hôpital Civic d'Ottawa, l'Hôpital Général d'Ottawa et le Centre médical de la défense national. Le candidat choisi aura la responsabilité des programmes de formation au niveau prédiplomé et postdoctoral ainsi que du développement des programmes de recherche. Le candidat choisi agira conjointement comme *directeur de la division de neurologie dans un de nos* hôpitaux affiliés.

L'Université et les hôpitaux offrent d'excellentes ressources qui assurent une médecine que qualité et des programmes de formation bien structurés.

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Selon les exigences d'Immigration Canada, cette annonce s'adresse d'abord aux citoyens canadiens et aux résidents permanents du Canada.

Prière de faire parvenir votre curriculum vitae et la liste des références **AVANT LE 31 MARS 1990** à l'attention de :

John F. Seely, M.D.
Vice-doyen intérimaire
Faculté de médecine
Université d'Ottawa
451, chemin Smyth
Ottawa, Ontario
K1H 8M5

NEUROSURGERY CLINICAL AND RESEARCH FELLOW

Full-time position available for one year beginning July 1, 1990, for clinical and research experience in Neurosurgery. The special fields of interest include movement disorders, pain, spinal injuries, posterior fossa and skull base tumours, neuro-oncology and cerebro-vascular disease.

Candidates must already have completed a neurosurgical training program.

Reply with curriculum vitae and name of two references to:

C.H. Tator, Head
Division of Neurosurgery
The Toronto Hospital
399 Bathurst Street
ECW 2-003
Toronto, Ontario
M5T 2S8

SCOTT&WHITE TEXAS A&M UNIVERSITY College of Medicine TEMPLE CAMPUS

The Department of Neurologic Surgery of the Scott and White Institutions and Texas A&M University College of Medicine is seeking applications for senior staff physician faculty in the Sections of Pain/Stereotaxic Surgery or Neurosurgical Oncology. Residency or post residency experience and a defined interest in either subspecialty area together with a broad capability and interest in general neurosurgical disorders is desired. Basic and clinical research opportunities are available commensurate with previous experience. Medical student and resident teaching/daily responsibilities are required. The main campus is located in central Texas, north of Austin in the approximate center of the Dallas/ Ft. Worth, San Antonio, Houston triangle and benefits from easy access to other surrounding universities (Southwestern University, Georgetown; University of Mary Hardin-Baylor, Belton; Baylor University, Waco.)

For further information, please send curriculum vitae and references to:

Mitchell Smigiel, M.D., Chairman, Neurologic Surgery
Scott and White, Texas A&M University
College of Medicine
2401 South 31st Street, Temple, TX 76508

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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 (slowed 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. Kramer G., Besser R., Katzmann K., Theisohn M. Slow release carbamazepine in the treatment of epilepsy: Akt. Neurol. 1985; 12: 70-74 2. Data on file 3. Product Monograph 4. Hoppener RJ, Kuryer A, Meijer JWA, Hulsman J. Correlation between daily fluctuations of carbamazepine serum levels and intermittent side effects. Epilepsia 1980, 21: 341-350 5. Diurnal fluctuations in free and total steadstate plasma levels of carbamazepine and correlation with intermittent side effects. Epilepsia 1984; 25 (4): 476-481 6. Aldenkamp AP, Alpherts WCJ, Moerland MC, Ohevenger N, Van Parys JAP. Controlled release carbamazepine: cognitive side effects in patients with epilepsy. Epilepsia 1987, 28: 507-514

Product Monograph supplied upon request.

PAAB CCPP

Geigy Mississauga, Ontario L5N 2W5

G-88056E

See page v

℞LIORESAL®

(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

℞SYMMETREL® (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.

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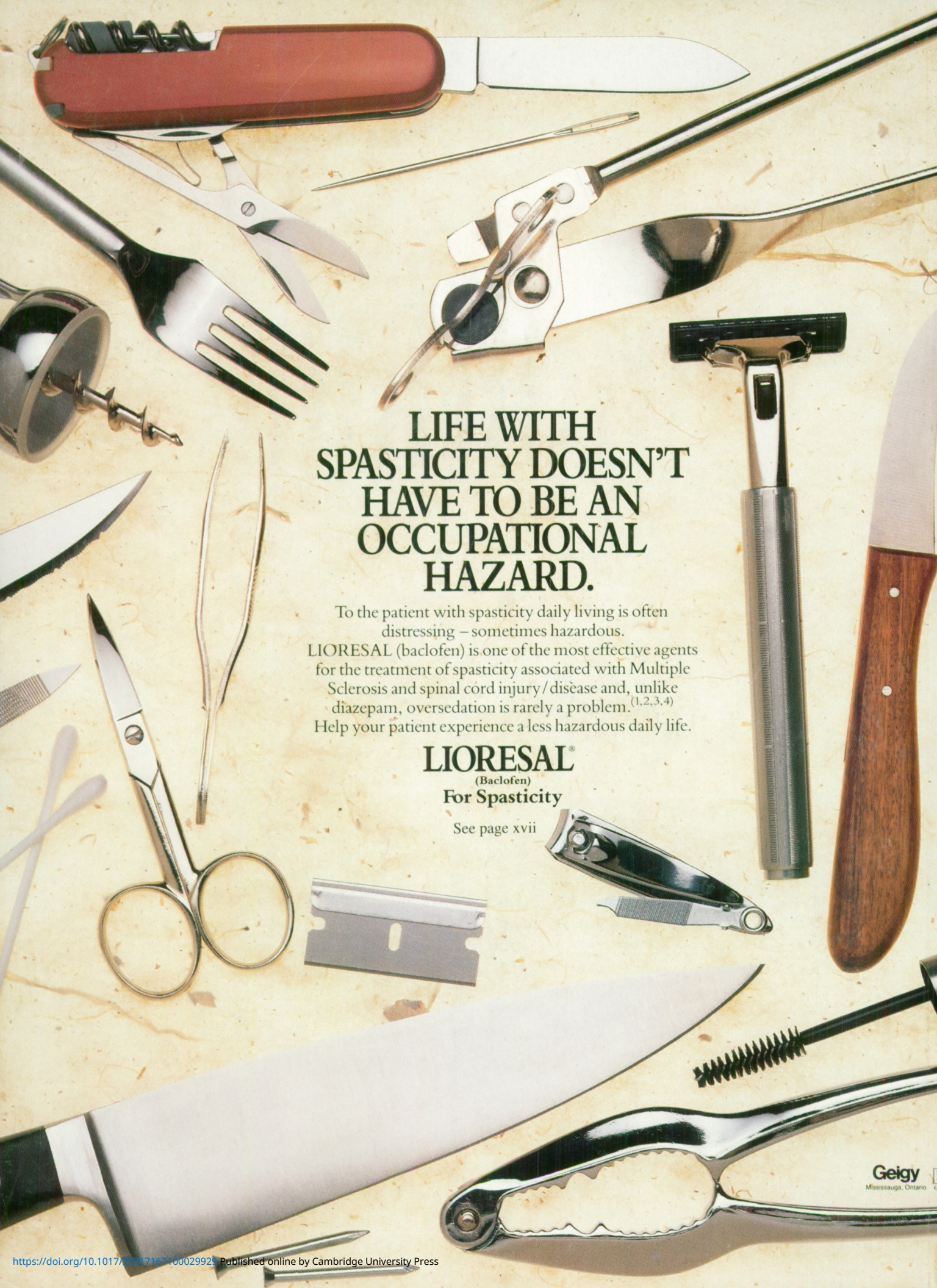

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