https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press

℞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 pages x, xi

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.

®TM

PAAB CCPP

DU PONT CANADA

Du Pont Pharmaceuticals
Mississauga, Ontario
L5M 2J4

See page vii

https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press

Intermediate Prescribing Information

P Tegretol® 200 mg tablets
(carbamazepine)

P Tegretol® Chewtabs™ 100 mg and 200 mg
(carbamazepine chewable tablets)

For Symptomatic Relief of Trigeminal Neuralgia Anticonvulsant

Action:
TEGRETOL (carbamazepine) has anticonvulsant properties which have been found useful in the treatment of psychomotor and other 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.

Indications and Clinical Use

A. Trigeminal Neuralgia:
For the symptomatic relief of pain of trigeminal neuralgia only during periods of exacerbation of true or primary trigeminal neuralgia (tic douloureux). Do not use 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:
1) in 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 ineffective in controlling petit mal, minor motor, myoclonic and predominantly unilateral seizures, and does not prevent the generalization of epileptic discharge.

Warnings

Although reported infrequently, serious adverse effects have been observed during the use of TEGRETOL. Agranulocytosis and aplastic anemia have occurred in a few instances with a fatal outcome. Leucopenia, thrombocytopenia and hepatocellular and cholestatic jaundice 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. Therefore, the possible risk of drug use must be weighed against the potential benefits before prescribing carbamazepine to individual patients.

Contraindications
Hepatic disease, serious blood disorder, less than 14 days either before or after monoamine oxidase inhibitor (then the dosage of TEGRETOL should be low initially, and increased very gradually), atrioventricular heart block, hypersensitivity to tricyclic compounds, lactation, first trimester of pregnancy.

Usage in Pregnancy
As safety has not been established, TEGRETOL should not be given to women of childbearing potential unless, in the opinion of the physician, the expected benefits to the patient outweigh the possible risk to the foetus.

Precautions
Monitoring of Haematological 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 and frequent clinical and laboratory supervision should be maintained throughout treatment. If any signs or symptoms or abnormal laboratory findings suggestive of blood dyscrasia or liver disorder occur, TEGRETOL should be immediately discontinued.
Urinary Retention and Increased Intraocular Pressure:
Caution is advised in patients with increased intraocular pressure or urinary retention due to the drug's anticholinergic action.
Occurrence of Behavioural Disorders:
TEGRETOL may activate a latent psychosis, or, in elderly patients, produce agitation or confusion. Caution is advised in alcoholics.
Use in Patients with Cardiovascular Disorders:
Caution is advised in patients with a history of coronary artery disease, organic heart disease, or congestive failure. An E.K.G. should be performed if a defective conductive system is suspected before administering TEGRETOL, in order to exclude patients with atrioventricular block.
Use in Patients taking Oral Contraceptives:
Women under treatment with TEGRETOL and oral contraceptives, should be advised to use some alternative, non-hormonal method of contraception as the reliability of oral contraceptives may be adversely affected.
Driving and Operating Hazardous Machinery:
Warn patients about the possible hazards of operating machinery or driving automobiles as dizziness and drowsiness are possible side effects of TEGRETOL.

Adverse Reactions
Haematological reactions: Transitory leucopenia, eosinophilia, leucocytosis, thrombocytopenic purpura, agranulocytosis, macrocytic anemia and aplastic anemia. In a few instances, deaths have occurred.
Hepatic Disturbances: Abnormalities in liver function tests, cholestatic or hepatocellular jaundice.
Dermatological Reactions: Skin sensitivity reactions and rashes, erythematous rashes, pruritic eruptions, urticaria, photosensitivity, pigmentary changes, neurodermatitis and in rare cases Stevens-Johnson syndrome, exfoliative dermatitis, alopecia, diaphoresis, erythema multiforme, erythema nodosum, and aggravation of disseminated lupus erythematosus.
Neurological Reactions: Vertigo, dizziness, somnolence, disturbances of coordination, confusion, headache, fatigue, blurred vision, transient diplopia and oculomotor disturbances, speech disturbances, abnormal involuntary movements, increase in motor seizures, peripheral neuritis, paresthesia, depression with agitation, talkativeness, nystagmus, tinnitus, paralysis and other symptoms of cerebral arterial insufficiency.
Cardiovascular Systems: Recurrence of 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 Reactions: Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, impotence, elevation of BUN, albuminuria, and glycosuria.
Digestive Tract: Nausea, vomiting, gastric or abdominal discomfort, diarrhoea, anorexia, dryness of the mouth and throat, glossitis and stomatitis.
Eyes: 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 slitlamp fundoscopy and tonometry, are recommended.
Other Reactions: Fever and chills, lymphadenopathy, aching joints and muscles, leg cramps and conjunctivitis.

Symptoms and Treatment of Overdosage
Symptoms: Dizziness, ataxia, drowsiness, stupor, nausea, vomiting, restlessness, agitation, disorientation; tremor, involuntary movements, opisthotonos, abnormal reflexes (slowed or hyperactive); mydriasis, nystagmus; flushing, cyanosis, urinary retention, hypotension, hypertension, coma. The EEG may show dysrhythmias. The laboratory findings have included leukocytosis, reduced leukocyte count, glycosuria and acetonuria.
Treatment: No known specific antidote. Induce emesis. Perform gastric lavage. Watch vital signs and administer symptomatic treatment as required. Hyperirritability may be controlled by the administration of parenteral barbiturates. Barbiturates should not be used if monoamine oxidase inhibitors have also been taken by the patient, either in overdosage or in recent therapy (within two weeks). Barbiturates may induce respiratory depression, particularly in children, therefore, have equipment available for artificial ventilation and resuscitation. Paraldehyde may be used to counteract muscular hypertonus without producing respiratory depression. Treat shock (circulatory collapse) with supportive measures, including intravenous fluids, oxygen, and corticosteroids. Electrocardiogram should 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 with a gradual increase in dosage is advised. Dosage should be adjusted to the needs of the individual patient.
Adults and Children over 12 years of age: Initially: 100 to 200 mg once or twice a day. The initial dosage is progressively increased, until the best response is obtained, up to 600 mg daily. Usual Daily Dosage: 600 mg, however up to 800 to 1000 mg have been used for short periods. 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: Initial daily dosage: 100 mg twice daily may be increased by 200 mg per day until relief of pain is obtained. Usual dosage: 200 to 800 mg daily. Up to 1200 mg daily may be necessary. As soon as relief of pain has been obtained and maintained, progressive reduction in dosage should be attempted until a minimum 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 in trigeminal neuralgia is not recommended.
Administer in two or three divided doses daily, with meals whenever possible.

Dosage Forms
TEGRETOL® *tablets 200 mg:* Each white, round, flat, bevelled-edge double-scored tablet engraved GEIGY on one side contains 200 mg carbamazepine.
TEGRETOL® *Chewtabs™ 100 mg:* Pale pink, round, flat, bevel-edged 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.
TEGRETOL® *Chewtabs™ 200 mg:* Pale pink, oval biconvex tablets with distinct red spots. GEIGY engraved on one side and PU on the other. Fully bisected between the P and U. Each chewable tablet contains 200 mg carbamazepine.

Availability
TEGRETOL® *tablets 200 mg:* Bottles of 100 and 500 tablets. Protect from heat and humidity. TEGRETOL® *Chewtabs™ 100 mg:* Bottles of 100. Protect from heat and humidity.
★ TEGRETOL® *Chewtabs™ 200 mg:* Bottles of 100. Protect from heat and humidity. (Available September 1985.)

Full information available on request.

Geigy
Mississauga, Ontario
L5N 2W5

G-5088

See OBC

https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press

ADVERTISERS' INDEX

https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press

https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press

Which generation will beat Huntington's Disease... forever?

Veronica Tennant

Right now we're so close.

We've identified a "marker" that will lead us to the defective gene that sits in the body like a time bomb waiting for middle age before it goes off.

We know that the progressive memory loss and involuntary muscle spasms of Huntington's are brought on by this defective gene causing the premature death of brain cells.

What we don't know is why this gene is present in 1 out of every 10,000 people in our population. Or why it is inherited by only 50% of the children of a Huntington parent. Or why it waits until middle age to strike, often after another generation has been born to live every day with the fear that they too may have inherited the Huntington gene from their parent.

For those with Huntington's today, the struggle is not only for survival. Their fight is for their children and their children's children. They want so desperately to be the last generation that must suffer through the horror of Huntington's.

Medical research paid for by your generous donations has brought us to the brink of victory. Now we need your dollars more than ever to bring the final discovery.

This is a fight we can win. This is suffering we can end... together. Please take the time to fill out the coupon and send in your cheque today. It will make a difference. And it could make ours the generation that beats Huntington's Disease... forever.

Here's my cheque to help you beat Huntington's Disease forever.

Name _____

Address _____

_____

Amount of cheque $ _____

A receipt for tax purposes will be sent by return mail.

Huntington Society of Canada
Box 333,
Cambridge, Ontario N1R 5T8

https://doi.org/10.1017/S031716710003626X Published online by Cambridge University Press