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# Cylert<sup>®</sup>

PEMOLINE

## Central Nervous System Stimulant

**ACTION:** CYLERT (pemoline) is a central nervous system stimulant, which, although structurally different from the amphetamines and methylphenidate, possesses pharmacological activity similar to that of other known stimulants.

Peak serum levels after single doses are reached within 2 to 4 hours and the serum half-life is approximately 12 hours. Multiple dose studies in adults at several dose levels indicate that steady state is reached in approximately 2 to 3 days.

**INDICATIONS AND CLINICAL USES:** CYLERT (pemoline) is indicated as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be warranted.

Attention Deficit Disorder and Hyperkinetic Syndrome are among the terms being used to describe the above signs and symptoms. In the past, a variety of terms has been associated with these signs and symptoms including: Minimal Brain Dysfunction, Hyperkinetic Reaction of Childhood, Hyperkinetic Syndrome, Hyperactive Child Syndrome, Minimal Brain Damage, Minimal Cerebral Dysfunction, and Minor Cerebral Dysfunction.

**CONTRAINDICATIONS:** CYLERT (pemoline) is contraindicated in patients with known hypersensitivity or idiosyncrasy to the drug. (See ADVERSE REACTIONS).

**WARNINGS:** CYLERT (pemoline) is not recommended for children less than 6 years of age since its safety and efficacy in this age group have not been established.

Clinical experience suggests that in psychotic children, administration of pemoline may exacerbate symptoms of behavior disturbance and thought disorder.

Data are inadequate to determine whether chronic administration of pemoline may be associated with growth inhibition; therefore, growth should be monitored during treatment.

**PRECAUTIONS:** Drug treatment is not indicated in all cases of the behavioral syndrome characterized by moderate to severe distractibility, short attention span, hyperactivity, emotional lability and impulsivity. It should be considered only in light of the complete history and evaluation of the child. The decision to prescribe CYLERT (pemoline) should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his/her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with pemoline is usually not indicated.

Long-term effects of pemoline in children have not been well established.

Liver function tests should be performed prior to and periodically during therapy with pemoline. The drug should be discontinued if abnormalities are revealed and confirmed by follow-up tests. (See ADVERSE REACTIONS regarding reports of abnormal liver function tests and jaundice).

Pemoline should be administered with caution to patients with significantly impaired hepatic or renal function.

The interaction of pemoline with other drugs has not been studied in humans. Patients who are receiving pemoline concurrently with other drugs, especially drugs with CNS activity, should be monitored carefully.

Pemoline failed to demonstrate a potential for self-administration in primates. However, the pharmacologic similarity of pemoline to other psychostimulants with

known dependence liability suggests that psychological and/or physical dependence might also occur with pemoline. There have been isolated reports of transient psychotic symptoms occurring in adults following the long-term misuse of excessive oral doses of pemoline. Pemoline should be given with caution to emotionally unstable patients who may increase the dosage on their own initiative.

**Usage during Pregnancy and Lactation:** The safety of pemoline for use during pregnancy and lactation has not been established. (See REPRODUCTION AND TERATOLOGY). Although central nervous system stimulants are seldom indicated after puberty, it should be borne in mind that pemoline should not be used during pregnancy or in women who may become pregnant.

**ADVERSE REACTIONS:** Insomnia is the most frequently reported side effect of CYLERT (pemoline); it usually occurs early in therapy, prior to an optimum therapeutic response. In the majority of cases it is transient in nature or responds to a reduction in dosage.

Anorexia with weight loss may occur during the first weeks of therapy. In the majority of cases it is transient in nature; weight gain usually resumes within three to six months.

Stomach ache, skin rashes, increased irritability, mild depression, nausea, dizziness, headache, drowsiness, and hallucinations have been reported.

Elevations of SGOT, SGPT, and serum LDH have occurred in patients taking pemoline, usually after several months of therapy. These effects appear to be reversible upon withdrawal of the drug, and are thought to be manifestations of a delayed hypersensitivity reaction. There have also been a few reports of jaundice occurring in patients taking pemoline; a causal relationship between the drug and this clinical finding has not been established.

The following CNS effects have been reported with the use of pemoline: dyskinetic movements of the tongue, lips, face and extremities, nystagmus and nystagmoid eye movements, and convulsive seizures. Central nervous system stimulants have been reported to precipitate attacks of Gilles de la Tourette syndrome.

Mild adverse reactions appearing early during the course of treatment with pemoline often remit with continuing therapy. If adverse reactions are of a significant or protracted nature, dosage should be reduced or the drug discontinued.

**SYMPTOMS AND TREATMENT OF OVERDOSAGE:** Signs and symptoms of acute CYLERT (pemoline) overdose may include agitation, restlessness, hallucinations, dyskinetic movements and tachycardia. The treatment for an acute overdose of pemoline is essentially the same as that for an overdose of any CNS stimulant. Management is primarily symptomatic and may include induction of emesis or gastric lavage, sedation, and other appropriate supportive measures.

Results of studies in dogs indicate that extracorporeal hemodialysis may be useful in the management of pemoline overdose; forced diuresis and peritoneal dialysis appear to be of little value.

**DOSE AND ADMINISTRATION:** CYLERT (pemoline) is administered as a single oral dose each morning. The recommended starting dose is 37.5 mg/day. This daily dose should be gradually increased by 18.75 mg at one week intervals until the desired clinical response is obtained. The effective daily dose for most patients will range from 56.25 to 75 mg. The maximum recommended daily dose of pemoline is 112.5 mg.

Clinical improvement with pemoline is gradual. Using the recommended schedule of dosage titration, significant benefit may not be evident until the third or fourth week of drug administration.

Where possible, drug administration should be interrupted occasionally to determine if there is a recurrence of behavioral symptoms sufficient to require continued therapy. Hyperactivity diminishes with age to the point where it remains a serious problem in only a minority, although other major handicaps may be present. Usually, by puberty the need for medication has diminished or is no longer required.

**AVAILABILITY:** CYLERT (pemoline) is supplied as monogrammed, grooved tablets in two dosage strengths:

37.5 mg tablets (orange-colored)  
in bottles of 100 (List 6057); and  
75 mg tablets (tan-colored); in bottles of 100 (List 6073).

**CHEMISTRY AND PHARMACOLOGY:** CYLERT (pemoline) is an oxazolone compound and is chemically identified as 2-amino-5-phenyl-2-oxazolin-4-one.

Pemoline is a white, tasteless, odorless powder, relatively insoluble (less than 1 mg/mL) in water, chloroform, ether, acetone, and benzene; its solubility in 95% ethyl alcohol is 2.2 mg/mL.

Pemoline has a pharmacological activity similar to that of other known central nervous system stimulants; however, it has minimal sympathomimetic effects. Although studies indicate that pemoline may act in animals through dopaminergic mechanisms, the exact mechanism and site of action of the drug in man is not known.

There is neither specific evidence which clearly establishes the mechanism whereby pemoline produces its mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

Metabolites of pemoline include pemoline conjugate, pemoline dione, mandelic acid, and unidentified polar compounds. Pemoline is excreted primarily by the kidneys; approximately 75% of an oral dose is recovered in the urine within 24 hours. Approximately 43% of pemoline is excreted unchanged.

## TOXICOLOGY

### Acute Toxicity:

The LD<sub>50</sub> of magnesium pemoline in mice was 500 mg/kg (= 375 mg/kg pemoline) orally and 487 mg/kg (= 365 mg/kg pemoline) intraperitoneally. In rats, the oral LD<sub>50</sub> was 581 mg/kg (= 436 mg/kg pemoline) and the intraperitoneal LD<sub>50</sub> was 497 mg/kg (= 373 mg/kg pemoline). The oral LD<sub>50</sub> in monkeys was 450 mg/kg (= 338 mg/kg pemoline). Principal signs observed were hyperactivity, increased muscle tone, biting, gnawing, squealing, mydriasis and piloerection. Death was often preceded by ataxia, labored breathing and respiratory paralysis.

### Long-Term Toxicity:

A six-month oral toxicity study was conducted in 16 dogs at doses of 0, 2, 5 and 10 mg/kg/day of magnesium pemoline (0, 1.5, 3.8, and 7.5 mg/kg/day of pemoline). Signs observed were those of central nervous system stimulation, characterized by moderate hyperactivity, hyperirritability and increased sensitivity to normal background noises or distractions. The severity of these signs was dose-related and diminished or disappeared with the passage of time, indicating the development of tolerance to the stimulant effects.

A 46-week oral toxicity study was conducted in rats at doses of 0, 2.5, 35 and 100 mg/kg/day of magnesium pemoline (0, 1.9, 26.3 and 75 mg/kg/day of pemoline). Early in the test, the animals in all drug groups displayed dose-related hyperactivity and increased sensitivity to external stimuli. These effects gradually subsided and disappeared after 2 to 3 weeks, indicating development of tolerance. At 6 and 9 months, a significant increase was observed in the incidence of mortality in the high-dose group compared to the control group. Similar but less marked trends were found in the middle-dose group at these time intervals. A 66-week study in female rats resulted in a cumulative maximal consumption of 0.3 g and 58 g/rat of pemoline after oral doses of 0, 5 and 100 mg/kg/day of magnesium pemoline (0, 3.8 and 75 mg/kg/day of pemoline). The growth rate in the low dosage group approximated that of the controls, while the high dosage group exhibited some retardation of growth during the first 46 weeks, showing average growth during the final 20 weeks of the study, when magnesium pemoline was not present in the diet.

**REPRODUCTION AND TERATOLOGY:** Standard studies of fertility, teratology and reproduction were conducted in rats and rabbits. Daily oral doses of magnesium pemoline of 25 and 50 mg/kg (18.75 and 37.5 mg/kg of pemoline) beginning at conception produced no abnormalities in the fetuses and did not affect viability at birth, although postnatal survival of pups was impaired. Further studies using similar dose levels with drug administration beginning 14 days before conception demonstrated an increased incidence of stillbirths and cannibalization. A significantly lower postnatal survival of pups occurred at the 50 mg/kg dose level, with similar but less marked effects noted at the 25 mg/kg level. There is some indication that the impaired survival of pups was drug related.

## REFERENCES

1. Connors CK, Taylor E. Pemoline, Methylphenidate, and Placebo in Children with Minimal Brain Dysfunction. *Arch Gen Psych* 1980; 37:922-930.
2. Weinberg F. Symposium on Clinical Applications of Pemoline in Attention Deficit Disorder. February 1987, Toronto.
3. Dulcan MK. Attention Deficit Disorder: Evaluation and Treatment. *Pediatric Annals* 1985; 14(5):383-400.
4. Langer DH, Sweeney KP, Bartenbach DE, Davis PM, Menander KB. Evidence of Lack of Abuse or Dependence Following Pemoline Treatment: Results of a Retrospective Survey. *Drug and Alcohol Dependence* 1986; 17:213-227.

\* T M

PHARMACEUTICAL PRODUCTS DIVISION  
ABBOTT LABORATORIES LIMITED  
MONTREAL, CANADA



# Prolopa® (levodopa/benserazide)

Rx Summary  
Antiparkinsonian Agent

## Indications

Treatment of Parkinson's syndrome when not drug induced.

## Contraindications

Known hypersensitivity to levodopa or benserazide; in patients in whom sympathomimetic amines are contraindicated; concomitantly with, or within 2 weeks of, MAOI administration; uncompensated cardiovascular, endocrine, renal, hepatic, hematologic or pulmonary disease; narrow-angle glaucoma.

## Warnings

Discontinue levodopa at least 12 hours before initiating

'Prolopa'. See Dosage section for substitution recommendations.

Not indicated in intention tremor, Huntington's chorea or drug-induced Parkinsonism.

Increase dosage gradually to avoid CNS side effects (involuntary movements). Observe patients for signs of depression with suicidal tendencies or other serious behavioural changes. Caution in patients with history of psychotic disorders or receiving psychotherapeutic agents.

In patients with atrial, nodal or ventricular arrhythmias or history of myocardial infarction initiate treatment cautiously in hospital. Caution in patients with history of melanoma or suspicious undiagnosed skin lesions. Safety in patients under 18 years has not been established. In women who are or may become pregnant, weigh benefits against possible hazards to mother and fetus. Not recommended for nursing mothers.

## Precautions

Monitor cardiovascular, hepatic, hematopoietic and renal function during extended therapy. Caution in patients with history of convulsive disorders. Upper gastrointestinal hemorrhage possible in patients with a history of peptic ulcer.

Normal activity should be resumed gradually to avoid risk of injury.

Monitor intraocular pressure in patients with chronic wide-angle glaucoma. Pupillary dilation and activation of Horner's syndrome have been reported rarely. Exercise caution and monitor blood pressure in patients on anti-hypertensive medication. 'Prolopa' can be discontinued 12 hours prior to anesthesia. Observe patients on concomitant psychoactive drugs for unusual reactions.

## Adverse Reactions

Most common are abnormal involuntary movements, usually dose dependent, which necessitate dosage reduction. Other serious reactions are periodic oscillations in performance (end of dose akinesia, on-off phenomena and akinesia paradoxa) after prolonged therapy, psychiatric disturbances (including paranoia, psychosis, depression, dementia, increased libido, euphoria, sedation and stimulation), and cardiovascular effects (including arrhythmias, orthostatic hypotension, hypertension, ECG changes and angina pectoris).

Neurologic, intellectual, gastrointestinal, dermatologic, hematologic, musculoskeletal, respiratory, genitourinary and ophthalmologic reactions have also been reported. Consult Product Monograph for complete list.

## Dosage

Individualize therapy and titrate in small steps to maximize benefit without dyskinesias. Do not exceed the recommended dosage range.

Initially, one capsule 'Prolopa' 100-25 once or twice daily, increased carefully by one capsule every third or fourth day (slower in post-encephalitic Parkinsonism) until optimum therapeutic effect obtained without dyskinesias. At upper limits of dosage, increment slowly at 2-4 week intervals. Administer with food.

Optimal dosage is usually 4-8 'Prolopa' 100-25 capsules daily, in 4-6 divided doses.

'Prolopa' 200-50 capsules are intended for maintenance therapy once optimal dosage has been determined using 'Prolopa' 100-25 capsules. No patient should receive more than 1000-1200mg levodopa daily during the first year of treatment. 'Prolopa' 50-12.5 capsules should be used when frequent dosing is required to minimize adverse effects.

For patients previously treated with levodopa, allow at least 12 hours to elapse and initiate 'Prolopa' at 15% of previous levodopa dosage.

During maintenance, reduce dosage slowly, if possible, to a maximum of 600 mg levodopa daily.

## Supply

'Prolopa' 50-12.5 capsules containing 50 mg levodopa and 12.5 mg benserazide. Contains mannitol.

'Prolopa' 100-25 capsules containing 100 mg levodopa and 25 mg benserazide.

'Prolopa' 200-50 capsules containing 200 mg levodopa and 50 mg benserazide.

Bottles of 100.

Product Monograph available on request.

## References:

1. Rondot P. Advantages of a low dosage of the levodopa/benserazide combination in the treatment of Parkinson's disease. Med et Hyg 1981; 39:3832-5.

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Etobicoke, Ontario M9C 5J4

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See page xxii

Original Research in Medicine and Chemistry



# 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.

## DOSE 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. Carlidge, 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).

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J.H. Noseworthy,  
University Hospital,  
London, Ontario N6A 5A5

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The Behavioural Neurology of Aging and Dementia Research Program invites applications for two RESEARCH SCIENTIST positions within the new multidisciplinary Research Institute at Baycrest Centre for Geriatric Care in Toronto. The successful candidate will be a Ph.D. or M.D. (or equivalent) with expertise in neuro-behavioural research as applied to aging and dementia.

Please send CV to:

Dr. Morris Freedman  
Director, Behavioural Neurology Program  
Baycrest Hospital, Rm. 4W36  
3560 Bathurst Street  
Toronto, Ontario  
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## Clinical Neuropharmacology Research Fellow

The Clinical Institute, a teaching hospital affiliated with the University of Toronto and a major division of the Addiction Research Foundation, is seeking a Clinical Neuropharmacology Research Fellow to contribute to studies on the treatment and pathogenesis of drug-induced encephalopathies. This position is part of a training program based at the Clinical Institute, and the Toronto Western Hospital. Preference will be given to candidates with neurological training. The position is available from July 1, 1988.

Applicants must be eligible for educational licensure by the Ontario College of Physicians and Surgeons.

Please forward a curriculum vitae to:

Dr. Peter L. Carlen,  
Head, Neurology Program, Clinical Institute,  
Addiction Research Foundation,  
33 Russell Street, Toronto, Ontario M5S 2S1

Addiction  
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## Brief Prescribing Information

ANALGESIC  
**Mersyndol**<sup>®</sup>  
WITH CODEINE TABLETS

**Indications:** For relief of headaches, muscular aches and pains, and neuralgia. Also indicated for relief of cold symptoms.

**Contraindications:** Hypersensitivity to acetaminophen, codeine, or doxylamine. Pre-existing respiratory depression or embarrassment.

**Precautions:** Patients should be cautioned not to operate vehicles or hazardous machinery until their response to the drug has been determined. Since the depressant effects of antihistamines are additive to those of other drugs affecting the CNS, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, psychotherapeutic agents or other drugs with CNS depressant effects during antihistaminic therapy.

Use with caution in patients with asthma or pulmonary emphysema, in sedated or debilitated patients and those who have undergone thoracotomies or laparotomies. Use in pregnancy is not recommended since codeine phosphate crosses the placental barrier. Prolonged use may have a constipating effect.

### Adverse Reactions:

**Acetaminophen:** The incidence of gastrointestinal upset is less than after salicylate administration. Abnormal liver function has been associated with therapeutic doses ranging from 3 to 8 g per day. In patients with compromised liver function, acetaminophen could exacerbate liver insufficiency. Renal papillary necrosis has been reported following prolonged acetaminophen administration of up to 19 g per day. Rarely, asthmatic attacks have been precipitated. Skin rashes and fixed dermatitis with pruritus have been rarely reported.

**Codeine phosphate:** Drowsiness, nausea, vomiting and constipation may occur. Infrequent reports of palpitation, pruritus and, rarely, hyperhidrosis and agitation have occurred. Respiratory depression is seen in the higher dosage and habituation or true addiction should be guarded against.

**Doxylamine succinate:** Drowsiness, vertigo, nervousness, epigastric pain, headache, palpitation, diarrhea, disorientation, irritability, convulsions, urinary retention, or insomnia have been reported.

**Dosage:** Adults and children over 12 years: 1 to 2 tablets every 4 hours as required. Do not exceed 12 tablets in a 24-hour period.

**Availability:** Each round, flat, white tablet carries a stylized S and contains: 325 mg acetaminophen; 8 mg codeine phosphate; 5 mg doxylamine succinate. Available in amber glass bottles of 30 and 100 tablets.

Prescribing information available on request.

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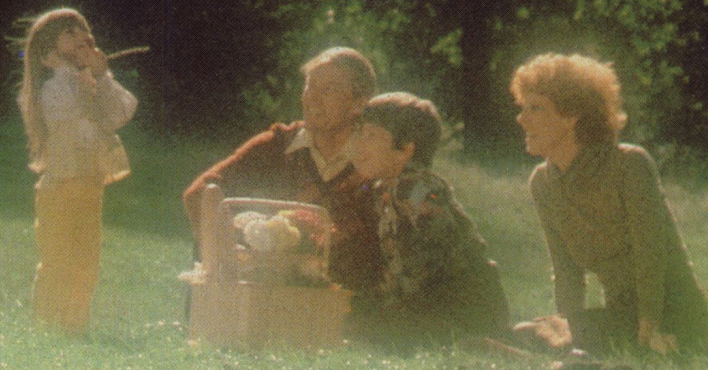
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## DILANTIN

(phenytoin)

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No other antiepileptic is more widely prescribed<sup>1</sup>.

No other antiepileptic has been the subject of more extensive clinical studies<sup>2</sup>.

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The slow absorption of Dilantin Capsules allows a single daily dose for maintenance therapy in many adults, once the divided dose of three 100 mg capsules has adequately controlled seizures.

References: 1. CDTI 2. Goodman and Gilman, Sixth Edition.

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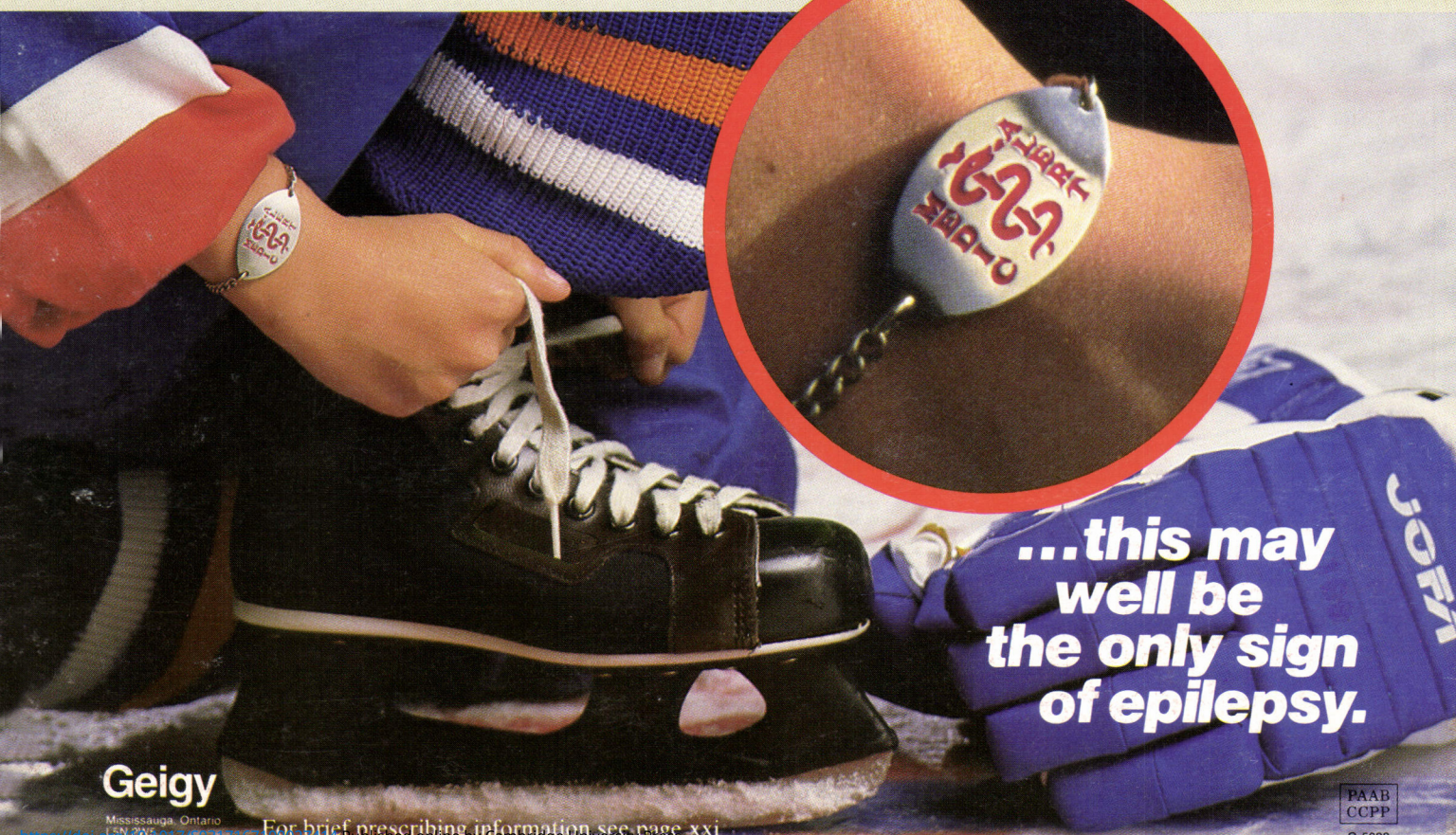
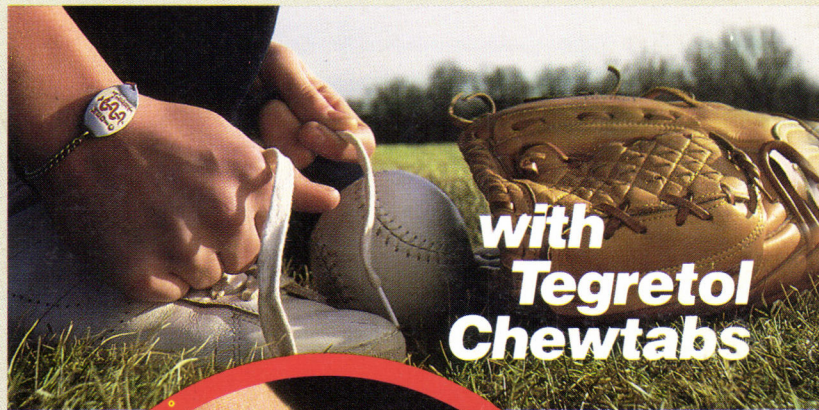


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