

Sanorex® (mazindol)

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given a pressor amine agent (e.g., levarterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: An increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses.

Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia.

Cardiovascular: Palpitation, tachycardia. **Central Nervous System:** Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. **Gastrointestinal:** Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. **Skin:** Rash, excessive sweating, clamminess. **Endocrine:** Impotence, changes in libido have rarely been observed. **Eye:** Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: Usual dosage is 1 mg, three times daily, one hour before meals, or 2 mg, once daily, one hour before lunch. Use lowest effective dose, which can be determined by starting therapy at 1 mg, once a day and adjusting to the need and response of the patient. Should GI discomfort occur, mazindol may be taken with meals.

Overdosage: There are no data as yet on acute overdosage with mazindol in humans. Manifestations of acute overdosage with amphetamines and related substances include restlessness, tremor, rapid respiration, dizziness. Fatigue and depression may follow the stimulatory phase of overdosage. Cardiovascular effects include tachycardia, hypertension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting and abdominal cramps. While similar manifestations of overdosage may be seen with mazindol, their exact nature have yet to be determined. The management of acute intoxication is largely symptomatic. Data are not available on the treatment of acute intoxication with mazindol by hemodialysis or peritoneal dialysis, but the substance is poorly soluble except at very acid pH.

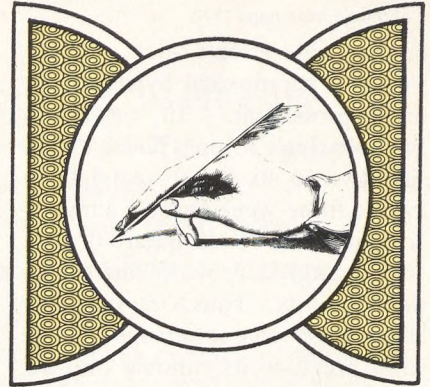
How Supplied: Tablets, 1 mg. and 2 mg., in packages of 100.

Before prescribing or administering, see package circular for Prescribing Information

SANDOZ PHARMACEUTICALS, EAST HANOVER, N.J. 07936



Letters to the Editor



The Journal welcomes Letters to the Editor; if found suitable, they will be published as space allows. Letters should be typed double-spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with journal style.

Nursing Practice and Medical Practice

To the Editor:

I read with interest the editorial in your December issue, "Is There a Difference Between Nursing Practice and Medical Practice?" (Geyman JP. *J Fam Pract* 5:935, 1977). Physician assistants and other mid-level practitioners have been addressing this issue on a local and national level for some time.

In striving toward the concept of independent practice, the nurse practitioner movement has diverged from the main body of physician extenders. We join our colleagues in condemning such an action as a dangerous trend which will ultimately benefit no one, least of all the patient (who is, after all, being confronted by an already confusing array of health-care providers).

In this time of rapidly expanding medical knowledge our efforts should be directed toward a unification of medical and psychosocial skills. A suitably trained physician extender is often an integral part of such an organized health-care team. However, the fragmentation of the team caused by the spin-off of independent practitioners is certainly a step backwards in terms of

the quality of care provided. To rationalize such lower-quality care as being more "accessible" still does nothing to improve the quality.

Les E. Landry, PA-C
Harold W. Muecke, PA-C
Family Practice Residency
Program
Medical Center of Central Georgia
Macon, Georgia

Phenobarbital for Febrile Convulsions

To the Editor:

Dr. Shrand, in his recent review, "Rational Drug Therapy of Common Illnesses in Children" (*J Fam Pract* 4:645, 1977), advocated the use of prophylactic oral phenobarbital at the onset of fever in the child with a history of febrile convulsions. Although there is significant controversy concerning the use of phenobarbital acutely and intermittently,¹⁻³ oral administration is hardly rational.⁴

Phenobarbital's oral absorption is 70 to 90 percent complete, but slow,⁵ so that even with high doses (10 mg/kg), a period of 12 hours is required for the drug to reach therapeutic levels of 10 to 20 mcg/ml.⁶ At this dosage level, of

Continued on page 1174

Continued from page 1173

course, side effects such as sedation and paradoxical hyperactivity are prominent. In addition, phenobarbital's long plasma half-life (two to six days)⁵ mandates a two to three-week chronic administration period of a standard dose (1 to 3 mg/kg) to provide anticonvulsant activity. Thus, the biopharmaceutical characteristics of the drug preclude its rational oral administration in this situation.

Rapid (one hour) therapeutic levels can be obtained and maintained through the use of an intramuscular loading dose (10 mg/kg) followed by oral dosing until the fever defervesces,² if the intermittent method is chosen.

Allan Ellsworth, Pharm D
University of Iowa
College of Pharmacy
Pioneer Medical Center
Mechanicsville, Iowa

F. L. Thompson, MD
Cedar Rapids Medical
Education Program
Pioneer Medical Center
Mechanicsville, Iowa

References

1. Wolf SM, Carr A, Davis DC, et al: The value of phenobarbital in the child who has had a single febrile seizure: A controlled prospective study. *Pediatrics* 59:378, 1977
2. Wolf SM: Effectiveness of daily phenobarbital in the prevention of febrile seizure recurrences in "simple" febrile convulsions and "epilepsy triggered by fever." *Epilepsia* 18:95, 1977
3. Heckmatt JZ, Houston AB, Clow DJ, et al: Failure of phenobarbitone to prevent febrile convulsions. *Br Med J* 1:559, 1976
4. Wallace SJ: Febrile fits. *Br Med J* 1:333, 1976
5. Woodbury DM, Fingl F: Drugs effective in the therapy of the epilepsies. In Goodman LS, Gillman A (eds): *The Pharmacological Basis of Therapeutics* (ed 5). New York, Macmillan, 1975, pp 201-226
6. Svensmark O, Buchthal F: Accumulation of phenobarbital in man. *Epilepsia* 4:199, 1963

The preceding letter was referred to Dr. Shrand who responds as follows:

Regarding the use of oral phenobarbital given at the onset of the fever in the hope of preventing a febrile seizure, I must agree with the comments of Ellsworth and Thompson.

On the other hand, continuous oral phenobarbital (or other appropriate anticonvulsant) administration is recommended if the first febrile convulsion meet any of the following criteria:¹

1. The patient is less than 18 months of age.
2. The seizures lasted longer than 15 minutes, were focal, or occurred more than once in 24 hours.
3. EEG abnormalities are found seven to ten afebrile days after the seizures.
4. Signs of a neurological deficit are present.
5. There is a family history of seizures.

If the patient shows none of the above characteristics with the first seizure but has a second one, then phenobarbital on a long-term basis is also recommended.

If the patient is actually having a seizure, anticonvulsants should be given by the intramuscular or intravenous route for the reasons stated by Ellsworth and Thompson.

Hyman Shrand, MD
Chief of Division of Pediatrics and
Adolescent Medicine
Mount Auburn Hospital
Cambridge, Massachusetts

Reference

1. Rabe EF: Editorial comment on Nelson KB, Ellenberg JH: Predictors of epilepsy in children who have experienced febrile seizures (*N Engl J Med* 295:1029, 1976). In Gellis SS: *Year Book of Pediatrics* 1978. Chicago, Year Book Medical Publishers, 1978, pp 305-307

LOMOTIL®

brand of diphenoxylate hydrochloride with atropine sulfate

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdose or individual hypersensitivity, reactions similar to those after meperidine or morphine overdose may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine, and in diarrhea associated with pseudomembranous enterocolitis occurring during, or up to several weeks following, treatment with antibiotics such as clindamycin (Cleocin®) or lincosycin (Lincoicin®).

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml. 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, myasthenia, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

SEARLE Searle & Co.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Communications Department
Box 5110
Chicago, Illinois 60680