

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 over-dosage or individual hypersensitivity, reactions similar to those after meperidine or morphine over-dosage 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 lincomycin (Lincocin[®]).

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.

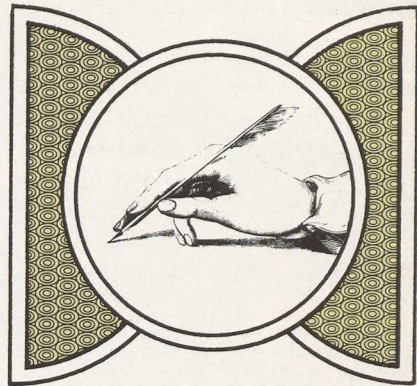
Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, 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, nystagmus, 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 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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.

Use of Cervical Cytology

To the Editor:

Dr. Hurt, in "Cervical Cytology: Use and Follow-Up," presents an excellent discussion of cervical cytology (*J Fam Pract* 7:579, 1978). However, I believe the endocervical aspiration technique of cytologic sampling, in spite of its proven efficacy, is just not going to be used by practicing physicians. Most will continue to use a "pancervical" Pap smear. Several studies¹⁻³ have evaluated the results of taking two "pancervical" Pap smears as a means of increasing the sensitivity of the procedure. Shulman et al¹ screened 2,823 patients and Sedlis et al² screened 17,737 patients by taking two "pancervical" smears *at the same sitting*. After removing excess mucus from the cervix with a cotton sponge, the pointed end of a spatula was inserted and rotated a full turn. The cellular material was then transferred to a slide and the same spatula was used to take the second specimen. Shulman's group increased the detection of abnormal cytology by 86 percent and Sedlis' by as much as 50 percent.

Further, a case can be made for using a cotton applicator for endocervical sampling in addition to the two pancervical smears. Garrite and Feldman⁴ found a significantly increased yield of abnormal cytology by adding a cotton applicator swab of the endocervix to an ectocervical sampling taken with a spatula. Interestingly, a third group was allowed to evaluate the cervix and select an "appropriate" method. If the cervix was everted (implying a visible squamocolumnar junction), only a spatula was used. If the cervix was not everted or the examiner was unsure, spatula and applicator were used. There was no significant improvement of this selective sampling group over those using the ectocervical technique alone. Thus, relying on the visualization of the squamocolumnar junction as an indication *not* to obtain an endocervical swab is probably not valid.

Thus, another reasonable cytologic sampling technique would be two "pancervical" smears, an endocervical swab as well as a vag-

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inal pool system—all at the same sitting.

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References

1. Shulman JJ, Hontz A, Sedlis A, et al: The pap smear: Take two. *Am J Obstet Gynecol* 121:1024, 1975
2. Sedlis A, Watters AT, Balin H, et al: Evaluation of two simultaneously obtained cervical cytological smears. *Acta Cytol* 18:291, 1974
3. Luthy DA, Briggs RM, Buyco A: Cervical cytology: Increased sensitivity with a second cervical smear. *Obstet Gynecol* 51:713, 1978
4. Garite TJ, Feldman MJ: An evaluation of cytologic sampling techniques. *Acta Cytol* 22:83, 1978

To the Editor:

I would like to take issue with one major point in Dr. Hurt's otherwise excellent review of "Cervical Cytology: Use and Follow-Up" (*J Fam Pract* 7:579, 1978). He suggests annual routine screening Pap smears on most women and routine biannual screening Pap smears on women after hysterectomy for benign disease.

Frame, Rosser, and Gray, who have reviewed screening procedures, recommend less frequent Pap smears.¹⁻³ This recommendation is based on the prolonged course from dysplasia to invasive carcinoma of the cervix. Dr. Hurt states the mean age of presentation of carcinoma in situ and invasive carcinoma is 34 and 48 years, respectively. The Walton Study, to which he refers, also presents

newer data based upon age specific incident peaks. These peaks are at age 25 to 29 for carcinoma in situ and age 60 to 64 for clinical invasive carcinoma.⁴

The Walton study does not address dysplasia, which is most prevalent in the 20 to 29-year age group.⁵ Riehart found that the average progression time from dysplasia to carcinoma in situ was 44 months.⁶

Mathematical models using this information have recommended screening at set ages which vary from three to five years apart.^{7,8}

Regarding females after hysterectomy, I see no reason to do Pap smears on them if the pathology report of the cervix was benign. Carcinoma of the cervix arises from the squamocolumnar junction and the transition zone, which is absent in these women.

It would appear that our energies are better directed to women who have had very infrequent or no Pap smears rather than simply repeating Pap smears on women who have had many consecutive years of negative results.

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References

1. Frame PS, Carlson SJ: A critical review of periodic health screening using specific screening criteria: Part 3. *J Fam Pract* 2:189, 1975
2. Rosser WW: Screening in family medicine: The current situation. *J Fam Pract* 6:503, 1978
3. Gray LA: The frequency of taking cervical smears. *Obstet Gynecol Surv* 24:909, 1969
4. Cervical cancer screening programs: Part 1: Epidemiology and natural history of carcinoma of the cervix. *Can Med Assoc J* 114:1003, 1976

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Brief Summary

Indication: Hypertension. (See box warning.)
Contraindications: Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

Warnings:

These fixed combination drugs are not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton or Demi-Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adrenergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. If use of the drug is essential, the patient should stop nursing. **Precautions:** Antihypertensive therapy with these drugs should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with these agents two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** These drugs are generally well tolerated. The most frequent adverse reactions are anorexia, nausea, vomiting, gastric irritation, diarrhea, constipation, headache, dizziness, weakness, muscle cramps, nasal congestion, drowsiness and mental depression. Other potential side effects include skin rash, urticaria, ecchymosis; hyperglycemia and glycosuria (diabetics should be checked regularly); hyperuricemia and acute gout, and impotence. With chlorthalidone: restlessness, transient myopia; with reserpine: orthostatic hypotension (may be potentiated by alcohol, barbiturates or narcotics), rare idiosyncratic reactions such as aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, purpura, necrotizing angitis and Lyell's syndrome (toxic epidermal necrolysis); pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged

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5. Stern E: Epidemiology of dysplasia. *Obstet Gynecol Surv* 24:711, 1969

6. Riehart RM, Barron BA: A follow-up study of patients with cervical dysplasia. *Am J Obstet Gynecol* 105:386, 1969

7. Knox EG: Ages and frequencies for cervical cancer screening. *Br J Cancer* 34:444, 1977

8. Coppleson LW, Brown B: Observations on a model of the biology of carcinoma of the cervix. *Am J Obstet Gynecol* 122:127, 1975

The preceding letters were referred to Dr. Hurt who responds as follows:

The suggestions for cytologic screening included in the article "Cervical Cytology: Use and Follow-Up" (*Hurt WG: J Fam Pract* 7:579, 1978) are those of the American College of Obstetricians and Gynecologists. They were formulated for the screening of all women on an unselected basis and to satisfy the objectives of early detection and accuracy while compensating for errors inherent in sampling and interpretation. Now that consumerism has become an issue of top priority, I would concede that less frequent screening of selected groups of women at low risk is perhaps acceptable. I do not believe that any woman with a cervix should have routine screening any less frequently than every three years. Those considered to be at high risk for developing cervical neoplasia and carcinoma should continue to have annual cervical cytology. The decision to do less frequent smears must be made by a knowledgeable and responsible person on an individual basis. It is

true that when taken as a whole cervical intraepithelial neoplasia runs a somewhat prolonged and orderly course prior to becoming invasive carcinoma. The rate of progression or arrest of any particular lesion, however, is less predictable. Time must be allowed for detection, documentation, eradication, follow-up, and possibly a repeat cycle of the same.

The mean ages of presentation of cervical intraepithelial neoplasia and invasive carcinoma may be shifting. This depends somewhat upon one's interpretation of microinvasive carcinoma. In our patient population, it appears that both the cervical intraepithelial neoplasias and invasive carcinoma are moving into the younger years and not undergoing a separation as suggested by the Walton Study. Perhaps the findings in the Walton Study are the result of years of systematic screening on a more homogenous and less mobile population (ie, British Columbia) with cytologic interpretation by a few centralized high quality laboratories. More studies will be needed to more accurately establish the trend.

We continue to perform vaginal cytology every two or three years on patients who have had a hysterectomy for benign disease. Occasionally, a dysplasia or carcinoma in situ of the cuff will be diagnosed. In addition, vaginal smears are routinely evaluated for evidence of infection and for hormonal status, and we have found the information which they provide to be of value in patient care.

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NOVAFED® Capsules

pseudoephedrine hydrochloride
Controlled-Release Decongestant

DESCRIPTION: Each capsule contains 120 mg. of pseudoephedrine hydrochloride in specially formulated pellets designed to provide continuous therapeutic effect for 12 hours. About one half of the active ingredient is released soon after administration and the rest slowly over the remaining time period.

ACTIONS: Pseudoephedrine is an orally effective nasal decongestant with peripheral effects similar to epinephrine and central effects similar to, but less intense than, amphetamines. It has the potential for excitatory side effects. At the recommended oral dosage, it has little or no pressor effect in normotensive adults. Patients have not been reported to experience the rebound congestion sometimes experienced with frequent, repeated use of topical decongestants.

INDICATIONS: Relief of nasal congestion or eustachian tube congestion. May be given concomitantly with analgesics, antihistamines, expectorants and antibiotics.

CONTRAINDICATIONS: Patients with severe hypertension, severe coronary artery disease, and patients on MAO inhibitor therapy. Also contraindicated in patients with hypersensitivity or idiosyncrasy to sympathomimetic amines which may be manifested by insomnia, dizziness, weakness, tremor or arrhythmias.

Children under 12: Should not be used by children under 12 years.

Nursing Mothers: Contraindicated because of the higher than usual risk for infants from sympathomimetic amines.

WARNINGS: Use judiciously and sparingly in patients with hypertension, diabetes mellitus, ischemic heart disease, increased intraocular pressure, hyperthyroidism or prostatic hypertrophy. See, however, Contraindications. Sympathomimetics may produce central nervous stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

Do not exceed recommended dosage.

Use in Pregnancy: Safety in pregnancy has not been established.

Use in Elderly: The elderly (60 years and older) are more likely to have adverse reactions to sympathomimetics. Overdosage of sympathomimetics in this age group may cause hallucinations, convulsions, CNS depression, and death. Safe use of a short-acting sympathomimetic should be demonstrated in the individual elderly patient before considering the use of a sustained-action formulation.

PRECAUTIONS: Patients with diabetes, hypertension, cardiovascular disease and hyper-reactivity to ephedrine.

ADVERSE REACTIONS: Hyper-reactive individuals may display ephedrine-like reactions such as tachycardia, palpitations, headache, dizziness or nausea. Sympathomimetics have been associated with certain untoward reactions including fear, anxiety, tenseness, restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucinations, convulsions, CNS depression, arrhythmias, and cardiovascular collapse with hypotension.

DRUG INTERACTIONS: MAO inhibitors and beta adrenergic blockers increase the effects of pseudoephedrine. Sympathomimetics may reduce the antihypertensive effects of methyldopa, mecamylamine, reserpine and veratrum alkaloids.

DOSAGE AND ADMINISTRATION: One capsule every 12 hours. Do not give to children under 12 years of age.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: Brown and orange colored hard gelatin capsules, monogrammed with the Dow diamond followed by the number 104. Bottle of 100 capsules (NDC 0183-0104-02).



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