

## HALOG® (Halcinonide)

### Cream/Ointment/Solution

Halog Cream 0.025% (Halcinonide Cream 0.025%) and Halog Cream 0.1% (Halcinonide Cream 0.1%) contain 0.25 mg. and 1 mg. halcinonide per gram, respectively, in a specially formulated cream base. Halog Ointment (Halcinonide Ointment 0.1%) contains 1 mg. halcinonide (0.1%) per gram in Plastibase® (Plasticized Hydrocarbon Gel), a polyethylene and mineral oil gel base. Halog Solution (Halcinonide Solution 0.1%) contains 1 mg. halcinonide (0.1%) per ml.

**CONTRAINDICATIONS:** Topical steroids are contraindicated in vaccinia, varicella, and in those patients with a history of hypersensitivity to any of the components of the preparations. These preparations are not for ophthalmic use.

**PRECAUTIONS: General**—If local infection exists, suitable concomitant antimicrobial or antifungal therapy should be administered. If a favorable response does not occur promptly, application of the corticosteroid should be discontinued until the infection is adequately controlled. If extensive areas are treated or if the occlusive technique is used, the possibility exists of increased systemic absorption of the corticosteroid and suitable precautions should be taken. If irritation or sensitization develops, the preparation should be discontinued and appropriate therapy instituted. Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use during pregnancy has not been absolutely established; therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

**Occlusive Dressing Technique**—The use of occlusive dressing increases the percutaneous absorption of corticosteroids; their extensive use increases the possibility of systemic effects. For patients with extensive lesions it may be preferable to use a sequential approach, occluding one portion of the body at a time. The patient should be kept under close observation if treated with the occlusive technique over large areas and over a considerable period of time. Occasionally, a patient who has been on prolonged therapy, especially occlusive therapy, may develop symptoms of steroid withdrawal when the medication is stopped. Thermal homeostasis may be impaired if large areas of the body are covered. Use of the occlusive dressing should be discontinued if elevation of the body temperature occurs. Occasionally, a patient may develop a sensitivity reaction to a particular occlusive dressing material or adhesive and a substitute material may be necessary. If infection develops, discontinue the use of the occlusive dressing and institute appropriate antimicrobial therapy.

**ADVERSE REACTIONS:** The following local adverse reactions have been reported with topical corticosteroids: burning, itching, irritation, striae, skin atrophy, secondary infection, dryness, folliculitis, hypertrichosis, acneiform eruptions, and hypopigmentation. The following may occur more frequently with occlusive dressings: maceration of the skin, secondary infection, skin atrophy, striae, and miliaria. Contact sensitivity to a particular dressing material or adhesive may occur occasionally (see PRECAUTIONS).

For full prescribing information, consult package insert.

**HOW SUPPLIED:** The 0.025% and 0.1% Cream and the 0.1% Ointment are supplied in tubes of 15 g. and 60 g., and in jars of 240 g. (8 oz.). The 0.1% Solution is supplied in plastic squeeze bottles of 20 ml. and 60 ml.

**SQUIBB®**

# 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.



## Early Exposure to Medical Practice

To the Editor:

A relatively new medical program has come into existence at the Ventura County General Hospital in Ventura, California.

Dr. Harvey M. Harris, originator and director, developed a five-week Health Professions Student Scholarship Program (HPSSP) for high school seniors and college freshmen showing interest in medical or paramedical occupations.

The HPSSP enabled 15 students to be chosen from both public and private schools with the County of Ventura. I was fortunate in being selected as one of the 15 student scholars. For the duration of five summer weeks, we entered into the world of medicine and were encouraged to explore, observe, and inquire into all phases of medical activity. We encountered life and death and all the dimensions connecting the two. Throughout the Program, each student was assigned to alternate departments to observe surgery, obstetrics, emergency cases, autopsies and, of course, the less dramatic events, although of equal importance, that occur daily throughout the hospital. Through participation in this

Program, we have a far greater understanding of what medicine is really like and whether or not the field of medicine is what we truly desire. It is the most valuable and informative five-week investment a student could make.

Each physician may well recall the time when he stood on the threshold of college and therefore can evaluate instantly the enormous asset this type of program could have provided him. A brief example: probably all medical sources will stress the importance of upcoming physicians being expected to maintain good physical condition. A student of books only cannot possibly realize the full meaning of such a statement, for he has not had the opportunity to accompany a physician during a typical work day. He has no real way of knowing the extremely long hours and arduous work required of the physician until he has stood beside him hour after hour.

As in most professions a medical student must, out of necessity, choose his career blindly. The student who says, "I want to be a doctor," usually has only booklets and counselors to accommodate his inquiries. While such sources are indeed helpful, only fragments of

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knowledge can be obtained from them. The ultimate opportunity is to work at his chosen field: to be there, to see, to experience for oneself the reality of medicine.

At 17 years of age, I was privileged to witness that which is otherwise unavailable to students until the third year of medical school. There is no way to measure the knowledge received from having participated in this Program. I have gained such insight pertaining to the field of medicine that I feel absolutely confident in making a decision. And for me, that decision is to become a physician.

It is my sincere hope that physicians throughout the United States will recognize this Program for the valuable concept it is, and perhaps apply a similar one to other areas. Future physicians will be indebted to you for years to come, as I am indebted to Dr. Harris and the staff at General Hospital, Ventura, California.

Perry Santos  
Senior, Ventura High  
Ventura, California

### Teratogenic Effects of Drugs During Pregnancy

To the Editor:

I was surprised to find the statement that "teratogenic effects have not been reported with diazepam" in your recent article entitled "Drug Risks in Pregnancy Revisited" (*J Fam Pract* 4:1043, 1977). I believe it to be fairly common knowledge among clinicians that there have been numerous reports linking the use of Valium during the first trimester of pregnancy to increased incidents of cleft palate. Safra MJ and Oakley GP have

published an article entitled "Valium, An Oral Cleft Teratogen?" (*Cleft Palate Journal* 13:198, 1976) which reviews several of the reports of this association. These reports date back at least as far as the September 13, 1975 article in *Lancet* (2:478) entitled "Association Between Cleft Lip With or Without Cleft Palate and Prenatal Exposure to Diazepam" by Safra, Oakley, et al. While further tests may be required to conclusively prove that the use of diazepam during the first trimester of pregnancy does cause an increased incidence of cleft lip or cleft palate, it would not seem wise to ignore the possibility completely as was done in your article.

Phillip R. Canfield, MD  
Marshfield, Wisconsin

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

Dr. Canfield is correct. Several articles have associated diazepam (Valium) (and other benzodiazepine tranquilizers including chlordiazepoxide [Librium] and oxazepam) with oral cleft defects in the newborn. The incidence rate reported is so low, however, that at this time chance could explain it. A virtual doubling of Valium prescriptions between 1970 and 1974 was not accompanied by an apparent increase in the incidence in lip or palatal clefts.

Updating is needed for three other drugs. Hydroxyzine hydrochloride (Atarax, Vistaril) has been thought free of neonatal withdrawal and teratogenic effects. Prolonged jitteriness and hyperirritability in the newborn have been reported when 600 mg of hy-

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## 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 36 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 teaspoonsfuls (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 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

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# VALIUM® (diazepam)

Before prescribing, please consult complete product information, a summary of which follows:

**Contraindications:** Tablets in children under 6 months of age; known hypersensitivity; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** As with most CNS-acting drugs, caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of predisposition to habituation/dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations, as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**ORAL:** Advise patients against simultaneous ingestion of alcohol and other CNS depressants.

Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral form adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may be associated with temporary increase in frequency and/or severity of seizures.

**INJECTABLE:** To reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling, and, rarely, vascular impairment when used I.V.: inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute with other solutions or drugs, or add to I.V. fluids.

Administer with extreme care to elderly, very ill, those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; concomitant use of barbiturates, alcohol or other CNS depressants increases depression with increased risk of apnea; have resuscitative facilities available. When used with narcotic analgesic eliminate or reduce narcotic dosage at least 1/3, administer in small increments. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs.

Has precipitated tonic status epilepticus in patients treated for petit mal status or petit mal variant status.

Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals under careful surveillance because of predisposition to habituation/dependence. Not recommended for OB use.

Efficacy/safety not established in neonates (age 30 days or less); prolonged CNS depression observed. In children, give slowly (up to 0.25 mg/kg over 3 minutes) to avoid apnea or prolonged somnolence; can be repeated after 15 to 30 minutes. If no relief after third administration, appropriate adjunctive therapy is recommended.

**Precautions:** If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), i.e., phenothiazines, narcotics, barbiturates, MAO inhibitors and antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed or tolerated).

**INJECTABLE:** Although promptly controlled, seizures may return; readminister if necessary; not recommended for long-term maintenance therapy. Laryngospasm/increased cough reflex are possible during peroral endoscopic procedures; use topical anesthetic, have necessary countermeasures available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly/debilitated.

**Adverse Reactions:** Side effects most commonly reported were drowsiness, fatigue, ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, discontinue drug.

Because of isolated reports of neutropenia and jaundice, periodic blood counts, liver function tests advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium therapy and are of no known significance.

**INJECTABLE:** Venous thrombosis/phlebitis at injection site, hypoactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia.

In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm/pain in throat or chest have been reported.

**Management of Overdosage:** Manifestations include somnolence, confusion, coma, diminished reflexes. Monitor respiration, pulse, blood pressure; employ general supportive measures, I.V. fluids, adequate airway. Use levaterenol or metaraminol for hypotension, caffeine and sodium benzoate for CNS-depressive effects. Dialysis is of limited value.

**Supplied:** Tablets, 2 mg, 5 mg and 10 mg, bottles of 100 and 500; Tel-E-Dose® (unit dose) packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Ampuls, 2 ml, boxes of 10; Vials, 10 ml, boxes of 1; Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffers, and 1.5% benzyl alcohol as preservative.

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droxyzine was taken throughout pregnancy. Unfortunately, the mother had received 60 mg of phenobarbital daily long term, sufficient in itself to have evoked withdrawal symptoms in the neonate.

Male genital deformities as presenting signs of teratogenic effect have been associated recently with two drugs of known risk to the fetus. Diethylstilbestrol, notorious for its later association with vaginal adenocarcinoma, apparently affects the male urogenital tract as well. Genital defects, including hypospadias, have been described with the other and better known features of hydantoin embryopathy involving facies and digits.

Teratology dramatically bridges the clinical and research aspects of medicine; rapid interaction between practitioners and researchers serves the patient best in helping to eliminate or reduce this form of therapeutic risk.

Thank you for the opportunity of commenting on Dr. Canfield's thoughtful letter.

Noel Guillozet, MD  
King City, California

## References

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Prenner BM: Neonatal withdrawal syndrome associated with hydroxyzine hydrochloride. *Am J Dis Child* 131:529, 1977

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Pinto W Jr, Gardner LI, Rosenbaum P: Abnormal genitalia as a presenting sign in two male infants with hydantoin embryopathy syndrome. *Am J Dis Child* 131:452, 1977

