IN ESSENTIAL HYPERTENSION **TAKE CONTROL WITH...**

PROTECTS.....

REDUCES.....

NEGLIGIBLE.....

DOSED.....

Constipation, which can easily be managed in most patients, is the most frequently reported side effect of verapamil.

Please see brief summary of Prescribing Information including CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS on last page.

ONCE-A-DAY VERELAN®

Verapamil HCl 120 mg 180 mg 240 mg

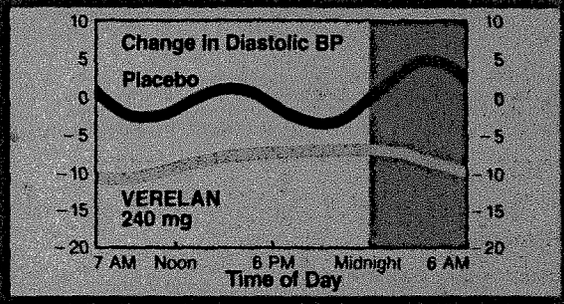
PELLET-FILLED CAPSULES

ENGINEERED FOR THE CONTROL YOU WANT, THE PROTECTION THEY NEED.

your hypertensive patients for 24 hours

The patented SODAS® delivery system is engineered to control hypertension at the 24th hour, protecting against breakthrough hypertension—diminished control at the end of the dosing cycle.[1]

Results of 24-hour ambulatory BP monitoring. VERELAN dosed 240 mg/day (n = 15); placebo (n = 10).[1]



wide variations in BP control

Ambulatory BP monitoring documents that VERELAN minimizes undesirable fluctuations of antihypertensive effect over 24 hours, providing excellent control throughout the dosing interval.[2]

discontinuation due to side effects

Only 2.8% of patients discontinued therapy due to side effects in a double-blind, placebo-controlled study; no patients discontinued therapy due to constipation, headache, or edema (n = 107).[1]

once daily at all doses

The SODAS® delivery system provides for *true* qd dosing—up to 480 mg daily—with no food requirement, unlike some calcium channel blockers.[3] VERELAN therapy is convenient and enhances compliance.

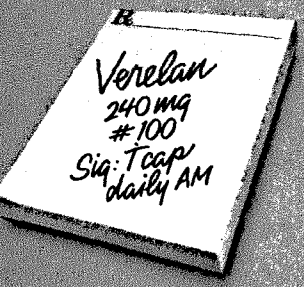
NOW AVAILABLE! 180 mg CAPSULES

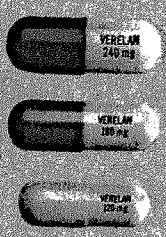
IN HYPERTENSION
SHIFT TO ONCE-A-DAY

VERELAN®

Verapamil HCl 120 mg 180 mg 240 mg

PELLET-FILLED CAPSULES





ENGINEERED FOR THE CONTROL YOU WANT, THE PROTECTION THEY NEED.

The usual dose is 240 mg once daily. If adequate response is not obtained, the dose may be titrated up to 360 mg or 480 mg once daily. VERELAN 120 mg is available for patients requiring lower-dose verapamil therapy.

And now...

THE VERELAN PLEDGE

Following appropriate dose titration, VERELAN will control blood pressure at the 24th hour after dosing, or your patients will be reimbursed 100% of their out-of-pocket costs for their most recent VERELAN prescription. See your VERELAN representative for more details.

References: 1. Carr AA, Bottini PB, Prisant LM, et al. Once-daily verapamil in the treatment of mild-to-moderate hypertension: a double-blind placebo-controlled dose-ranging study. *J Clin Pharmacol*. 1991;31:144-150. 2. Data on file for VERELAN 240 mg, Lederle Laboratories, Pearl River, NY. 3. *Physicians' Desk Reference* (PDR®), ed 46, Montvale, NJ: Medical Economics Co. Inc.; 1992:1181-1183 (Isoptin® SR), 2157-2159 (Calan® SR).

Brief Summary

VERELAN®
Verapamil HCl
Sustained-Release Pellet-Filled Capsules

For complete Prescribing Information, consult package insert.

CLINICAL PHARMACOLOGY

Food does not affect the extent or rate of the absorption of verapamil from the controlled release VERELAN capsule.

Atrioventricular block can occur in patients without preexisting condition defects (see **WARNINGS**).

Acceleration of ventricular rate and/or ventricular fibrillation has been reported in patients with atrial flutter or atrial fibrillation and a coexisting accessory AV pathway following administration of verapamil (see **WARNINGS**).

In patients with hepatic insufficiency, metabolism is delayed and elimination half-life prolonged up to 14 to 16 hours (see **PRECAUTIONS**), the volume of distribution is increased, and plasma clearance reduced to about 30% of normal.

CONTRAINDICATIONS

Severe LV dysfunction (see **WARNINGS**), hypotension (systolic pressure <90 mmHg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), second- or third-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), (see **WARNINGS**), hypersensitivity to verapamil.

WARNINGS

Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction <30%) or moderate-to-severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta blocker. Control milder heart failure with optimum digitalization and/or diuretics before VERELAN is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported.

Several cases of hepatocellular injury have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving IV verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (second- or third-degree, 0.8%). Development of marked first-degree block or progression to second- or third-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, second-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

PRECAUTIONS

Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digitoxin. The digoxin dose should be reduced when verapamil is given and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Verapamil has been given concomitantly with short- and long-acting nitrates without any undesirable drug interactions. Interaction between cimetidine and chronically administered verapamil has not been studied. In healthy volunteers, clearance of verapamil was reduced or unchanged. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully.

Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporine. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. Adequate animal carcinogenicity studies have not been performed. One study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. **Pregnancy Category C:** There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use. Safety and efficacy of verapamil in children below the age of 18 years have not been established.

ADVERSE REACTIONS

Reversible (upon discontinuation of verapamil) nonobstructive, paralytic ileus has been infrequently reported in association with the use of verapamil.

In clinical trials with 285 hypertensive patients on VERELAN for more than 1 week, the following adverse reactions were reported: constipation (7.4%); headache (5.3%); dizziness (4.2%); lethargy (3.2%); dyspepsia (2.5%); rash (1.4%); ankle edema (1.4%); sleep disturbance (1.4%); myalgia (1.1%). In clinical trials of other formulations of verapamil HCl (N = 4,954), the following reactions have occurred at rates greater than 1.0%: constipation (7.3%); dizziness (3.3%); nausea (2.7%); hypotension (2.5%); edema (1.9%); headache (2.2%); rash (1.2%); CHF/pulmonary edema (1.8%); fatigue (1.7%); bradycardia (HR<50/min) (1.4%); AV block-total 1°, 2°, 3° (1.2%); 2° and 3° (0.8%); flushing (0.6%); elevated liver enzymes (see **WARNINGS**).

The following reactions, reported in 1.0% or less of patients, occurred under conditions (open trials, marketing experience) where a causal relationship is uncertain. **Cardiovascular:** angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope. **Digestive System:** diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia. **Hemic and Lymphatic:** ecchymosis or bruising. **Nervous System:** cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence. **Respiratory:** dyspnea. **Skin:** arthralgia and rash, exanthema, hair loss, hyperkeratosis, maculae, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme. **Special Senses:** blurred vision. **Urogenital:** gynecomastia, impotence, increased urination, spotty menstruation.

VERELAN® Verapamil HCl

Rev. 1/92
20801-92

Lederle

Manufactured for
LEDERLE LABORATORIES DIVISION
American Cyanamid Company
Pearl River, NY 10965

by ELAN PHARMACEUTICAL RESEARCH CORP.
Gainesville, GA 30501

WYETH-AYERST LABORATORIES

Advantus™ Pharmaceuticals

April 1992 Printed in USA 5049-2R

INFORMATION FOR AUTHORS

The *Journal of the American Board of Family Practice* welcomes for editorial review manuscripts that contribute to family practice as a clinical scientific discipline. High priority is given to reports of clinically relevant studies that have practical implications for improved patient care. Manuscripts are considered in relation to the extent to which they represent original work, their significance to the advancement of family medicine, and their interest to the practicing family physician. Some papers that are accepted by the *Journal* will be selected for an accompanying guest editorial or concurrent commentary by other invited authors addressing issues raised by the papers. The *Journal* publishes the following features:

Original Articles. Reports of original research, usually dealing with a clinical, health services, or other clinically relevant study.

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Clinical Review. In-depth reviews of specific clinical problems, disease entities, or treatment modalities; comprehensive and critical analysis of the literature is required (usual maximum length 5000 words).

Clinical Guidelines and Primary Care. Summaries of major clinical guidelines proposed by various specialty, governmental, or health care organizations, with critical commentary from a primary care perspective.

Special Articles. Articles in other areas that may relate to the role of the family physician, education for family practice, or other subjects important to family practice as a clinical specialty.

Brief Reports. Short reports of pilot studies or case reports with a teaching point of clinical relevance (usual length 1000–1500 words).

Family Practice — World Perspective. Papers reporting developments related to the practice or education of family physicians in various countries around the world (usual length 1200–1800 words).

Reflections in Family Practice. Papers in narrative or essay format that illuminate qualitative aspects of family practice, including such areas as ethical issues, the physician-patient relationship, or the diverse roles of the family physician.

Editorial. Focused opinion or commentary that bears on an issue relevant to the field. May or may not accompany an original article in the same issue (usual length 1000–1500 words).

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The following guidelines are in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals." The current (fourth) edition was published in the February 7, 1991, issue of the *New England Journal of Medicine*.

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Submit an original and 3 copies of the complete manuscript, including text pages, legends, tables, references, and glossy prints of figures. Only typed copy, on standard-sized typewriter paper and double-spaced throughout, with margins of at least 2.5 cm, is acceptable. Address all submissions to John P. Geyman, M.D., Editor, the *Journal of the American Board of Family Practice*, Department of Family Medicine (HQ-30), School of Medicine, University of Washington, Seattle, WA 98195. A covering letter should identify the person (with the address and telephone number) responsible for negotiations concerning the manuscript; the letter should make it clear that the final manuscript has been seen and approved by all authors. If authors acknowledge by name persons who provided important technical, advisory, or reviewer contributions, the corresponding author should sign the following statement: "I have obtained written permission from all persons named in the acknowledgment."

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With the manuscript, provide a page giving the title of the paper; a running foot of fewer than 40 letter spaces; the name(s) of the author(s), including first name(s) and academic degree(s); the name of the department and institution in which the work was done; and the name and address of the author to whom reprint requests should be addressed. All funding sources supporting the work should be routinely acknowledged on the title page, as should all institutional or corporate affiliations of the authors. Two to four key words should be submitted with the manuscripts to be used for purposes of classification by subject. Use terms from the Medical Subject Headings from *Index Medicus* when possible.

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Drug Names

Generic names should, in general, be used. If an author so desires, brand names may be inserted in parentheses.

Inclusive Language

Sex bias should be avoided and gender-inclusive language used whenever possible.

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References must by typed in double spacing and numbered consecutively as they are cited. References first cited in tables or figure legends must be numbered so that they will be in sequence with references cited in the text. The style of references is that of the *Index Medicus*. List all authors when there are 6 or fewer; when there are 7 or more, list the first 6, then "et al." Sample references are as follows:

Standard Journal Article

(List all authors, but if the number exceeds 6, give 6 followed by et al. Note that month and issue number are omitted when a journal has continuous pagination throughout a volume.)

Morrow JD, Margolies GR, Rowland J, Roberts LJ 2nd. Evidence that histamine is the causative toxin of scombroid-fish poisoning. N Engl J Med 1991; 324:716-20.

Organization as Author

Clinical Experience Network (CEN). A large-scale, office-based study evaluates the use of a new class of nonsedating antihistamines. A report from CEN. J Am Board Fam Pract 1990; 3:241-58.

Book

Rakel RE. Textbook of family practice. 4th ed. Philadelphia: WB Saunders, 1990.

Chapter in Book

Haynes RC Jr. Agents affecting calcification: calcium, parathyroid hormone, calcitonin, vitamin D, and other compounds. In: Gilman AG, Rall TW, Nies AS, Taylor P, editors. Goodman and Gilman's the pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press, 1990.

Government Agency

Schwartz JL. Review and evaluation of smoking cessation methods: the United States and Canada, 1978-1985. Bethesda, MD: Department of Health and Human Services, 1987. (NIH publication no. 87-2940.)

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