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diabetes

A JOURNAL OF THE AMERICAN DIABETES ASSOCIATION®

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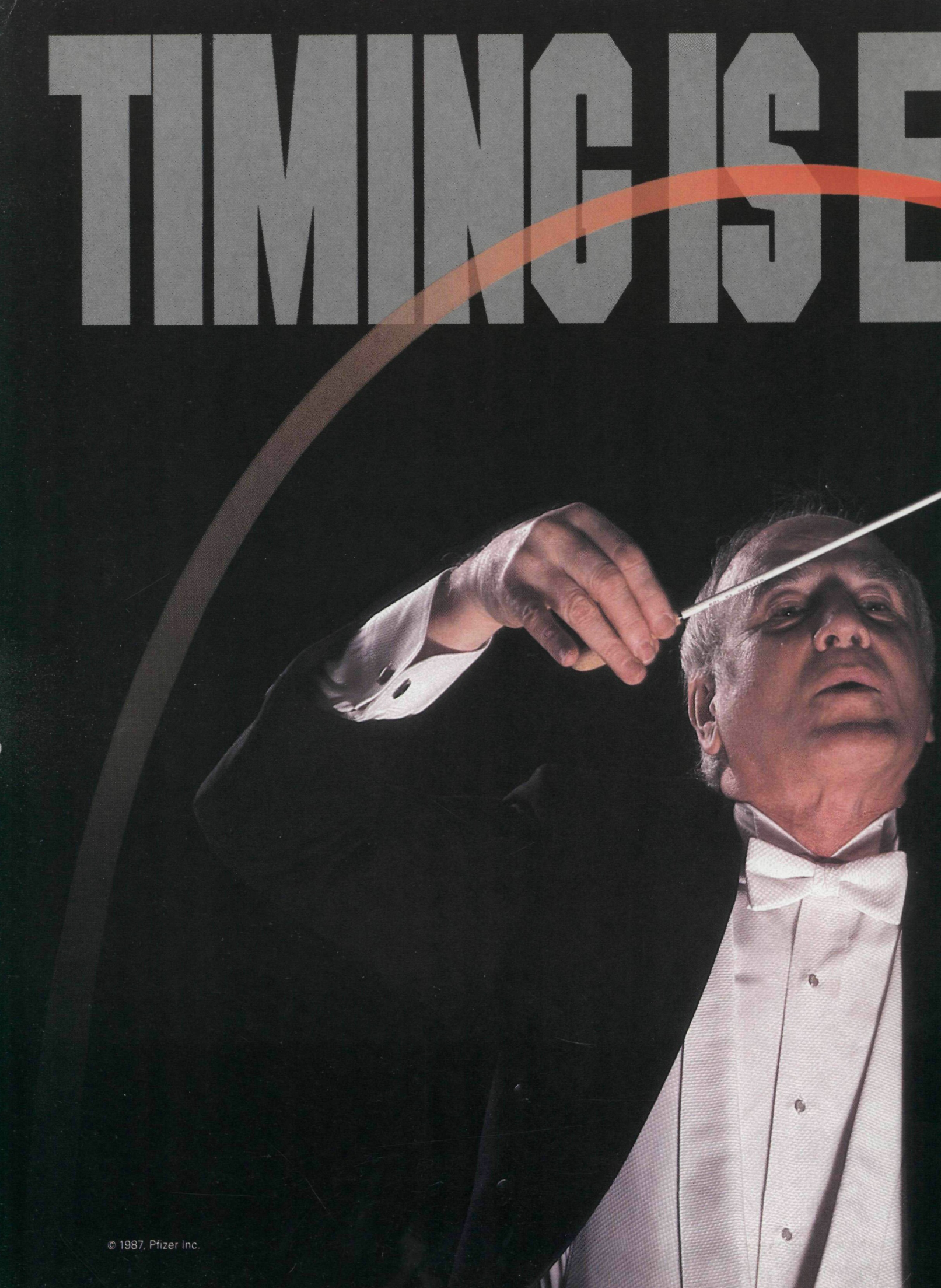


VERYTHING

Effective control time and time again[1]

Effective control of fasting and postprandial glucose—patient after patient, meal after meal, year after year.

Insulin when it's needed

Insulin levels are rapidly elevated in response to a meal, then return promptly to basal levels after the meal challenge subsides.

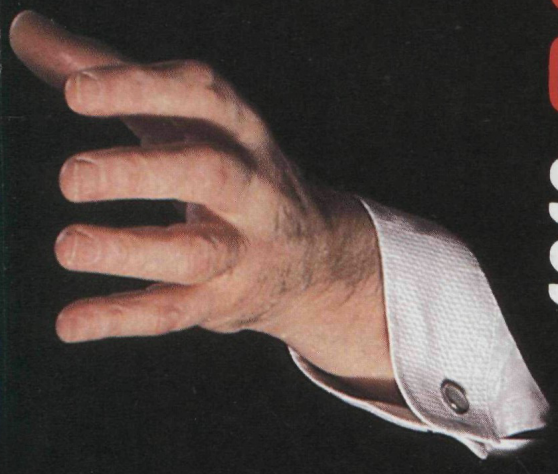
Timed to minimize risks

Rapidly metabolized and excreted, with an excellent safety profile.[1] As with all sulfonylureas, hypoglycemia may occur.

In concert with diet in non-insulin-dependent diabetes mellitus

Glucotrol®

(glipizide) 5-mg and 10-mg Scored Tablets



SYNCHRONIZED SULFONYLUREA THERAPY

Please see brief summary of Glucotrol® (glipizide) prescribing information on next page.

ROERIG Pfizer
A division of Pfizer Pharmaceuticals
New York, New York 10017

Reference:
1. Sachs R, Frank M, Fishman SK: Overview of clinical experience with glipizide. In *Glipizide: A Worldwide Review* Princeton, NJ, Excerpta Medica, 1984, pp 163-172.

NOVEMBER AUTHOR INDEX

(Volume 37, Number 11)

diabetes

A JOURNAL OF THE AMERICAN DIABETES ASSOCIATION®

Diabetes and *Diabetes Care* are scientific research journals published by the American Diabetes Association. Both publish original high-quality reports on biomedical research related to the broad field of diabetes mellitus.

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For studies involving experimental animals, state the species, strain, number used, and other pertinent descriptive characteristics. For human subjects or patients, describe their characteristics. When describing surgical procedures on animals, identify the preanesthetic and anesthetic agents used, and state the amount or concentration and the route and frequency of administration for each. The use of paralytic agents, such as curare or succinylcholine, is not an acceptable substitute for anesthetics. For other invasive procedures on animals, report the analgesic or tranquilizing drugs used; if none was used, provide justification for such exclusion. When reporting studies on unanesthetized animals or on humans, indicate that the procedures followed were in accordance with institutional guidelines.

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Rapid Publications: Observations considered to be of unusual importance may be submitted as a Rapid Publication. Editorial decision will be made within 10 days after receipt of the manuscript. No written review or explanation of the decision will be provided. Rejected papers may be resubmitted as a regular manuscript and reviewed accordingly. Rapid Publications may not exceed 10 double-spaced typewritten pages (including figures, tables, and references). Accepted papers will be published in the earliest possible issue of the Journal.

Manuscripts should be typewritten (not photocopied), with double-spacing; submit original and 2 photocopies with 2 prints of figures and photomicrographs. Manuscripts prepared in accord with the requirements specified in the document "Uniform Requirements for Manuscripts Submitted to Biomedical Journals," *Annals of Internal Medicine* 96:766–71, 1982, will be considered for publication.

References should be presented in the style of the following examples and numbered in order of appearance in the text: For Periodicals—Banting FG, Best CH: The internal secretion of the pancreas. *J Lab Clin Med* 7:251–66, 1922. For Books—Allen M: *Studies Concerning Glycosuria and Diabetes*. Cambridge, MA, Harvard Univ. Press, 1913, p. 461.

A summary of the content of the paper of not more than 250 words should be provided. This should be self-contained and understandable without reference to the text.

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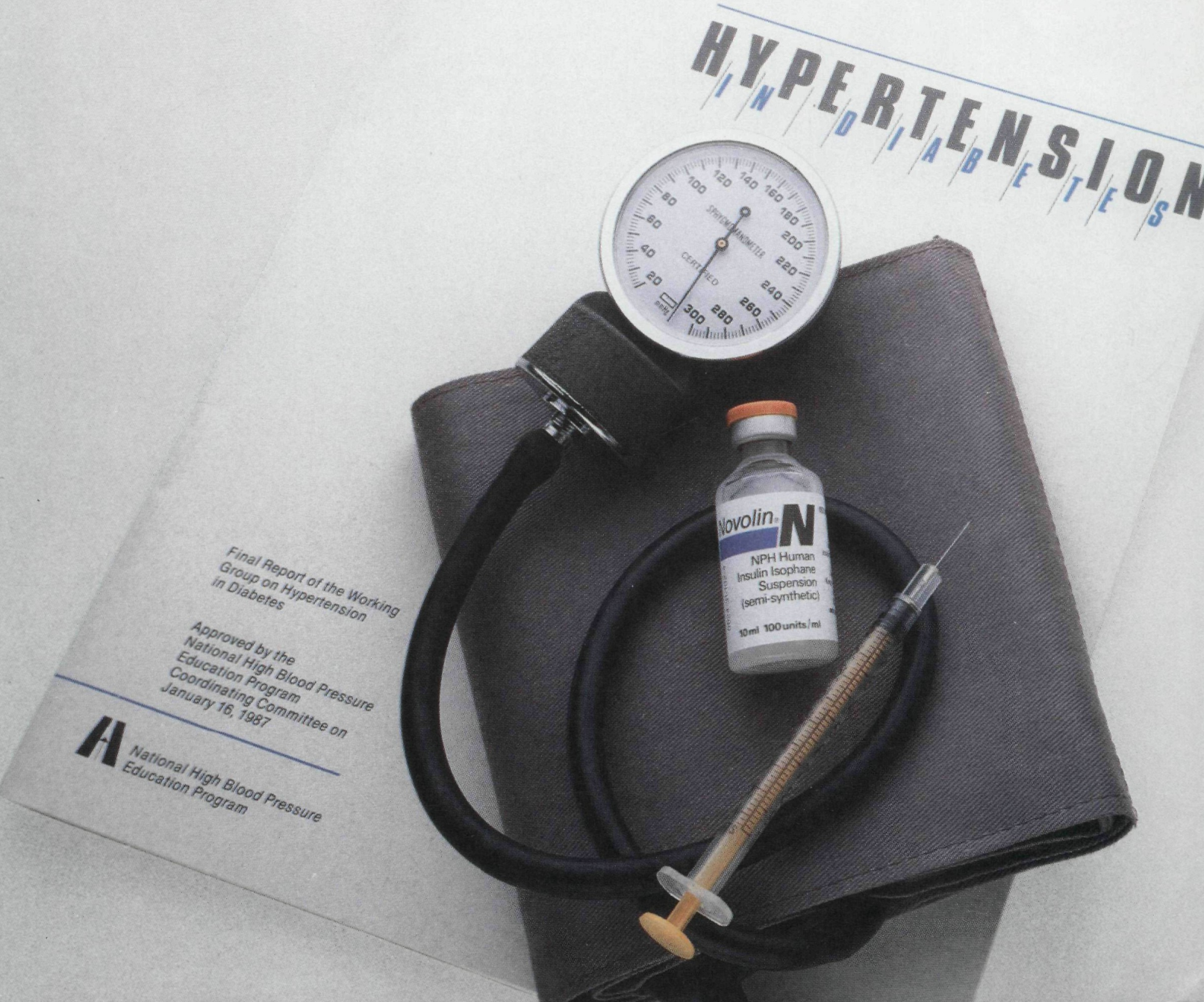
FINAL REPORT *The Working Group on Hypertension in Diabetes:*

CAPOTEN® (*captopril tablets*) FIRST-LINE THERAPY FOR HYPERTENSIVE DIABETIC PATIENTS*



SQUIBB

Controls hypertension today

CAPOTEN controls blood pressure without altering insulin secretion or complicating diabetes management.[1,2]

Offers potential long-term benefits

CAPOTEN does not deplete potassium or alter lipid levels.

THE CAPOTEN® (captopril tablets) DIFFERENCE

*CAPOTEN may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. See INDICATIONS AND USAGE, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary on the adjacent page.

References:
1. The Working Group on Hypertension in Diabetes: Statement on Hypertension in Diabetes Mellitus: Final Report. Arch Intern Med 147:830-842, 1987.
2. D'Angelo A, Sartori L, Gambaro G, et al: Captopril in the treatment of hypertension in type I and type II diabetic patients. Postgrad Med J 62(suppl 1):69-72, 1986.

THE CAPOTEN® (captopril tablets) DIFFERENCE

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension—CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

CONTRAINDICATIONS: CAPOTEN is contraindicated in patients who are hypersensitive to this product.

WARNINGS: Neutropenia/Agranulocytosis—Neutropenia (<1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine less than 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during the subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors. **Evaluation of the hypertensive or heart failure patient should always include assessment of renal function.** If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever). If infection is suspected, perform white cell counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm³) withdraw captopril and closely follow the patient's course.

Proteinuria: Total urinary proteins >1 g per day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy with captopril, patients with prior renal disease or those receiving captopril at doses >150 mg per day, should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter.

Hypotension: Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]). In heart failure, where the blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function*—Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis*—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction. *Surgery/Anesthesia*—If hypotension occurs during surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension—Patients on Diuretic Therapy*—Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial of captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity—In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release—Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis—Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C: There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. CAPOTEN (captopril) should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal—About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic—Neutropenia/agranulocytosis has occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic—Rash, (usually maculopapular, rarely urticarial), often with pruritus, and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity, have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients—reversible on discontinuance of captopril therapy. One case of laryngeal edema has been reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular—Hypotension may occur; see WARNINGS and PRECAUTIONS [Drug Interactions] for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia—Approximately 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice, and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertension patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

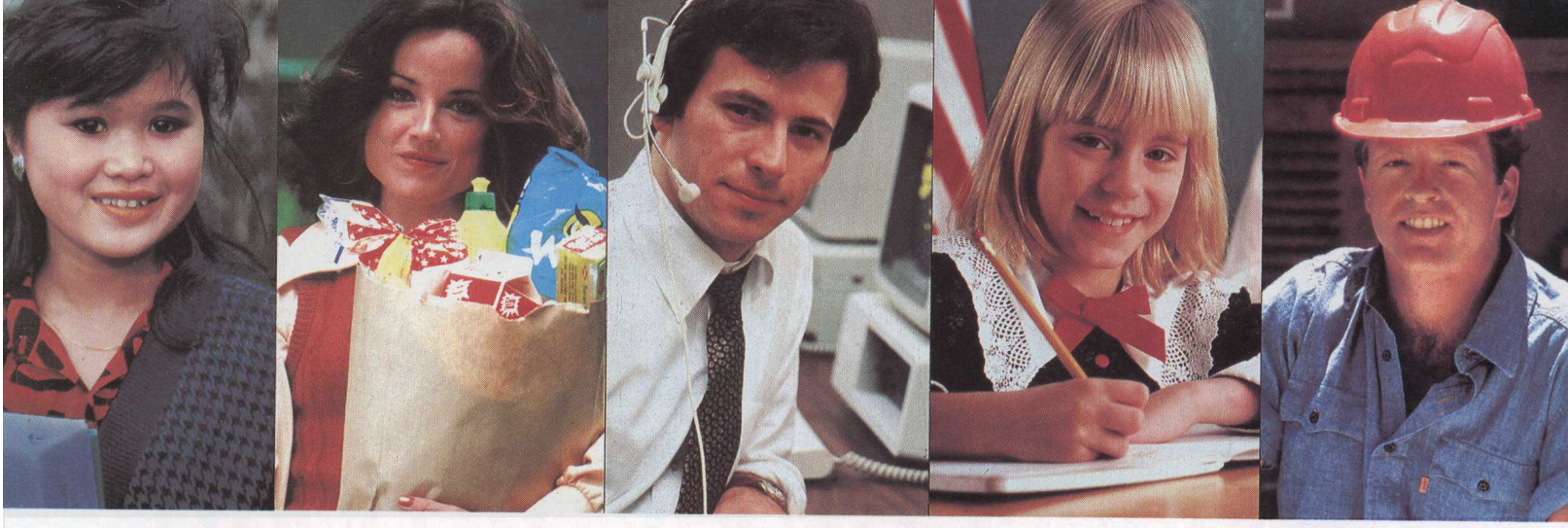
DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, and 50 mg in bottles of 100 and 1000; 100 mg in bottles of 100; and in UNIMATIC® unit-dose packs of 100 tablets.
(J3-658K)

SQUIBB®

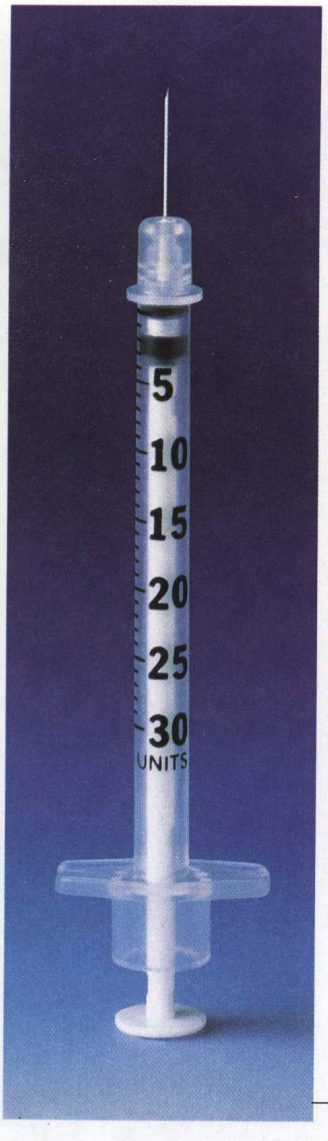
 528-521 Issued: June 1988



For your patients who inject 30 units or less.

The innovative B-D 3/10 cc syringe

- Easier-to-read scale
- More precise measurement
- More accurate dosage



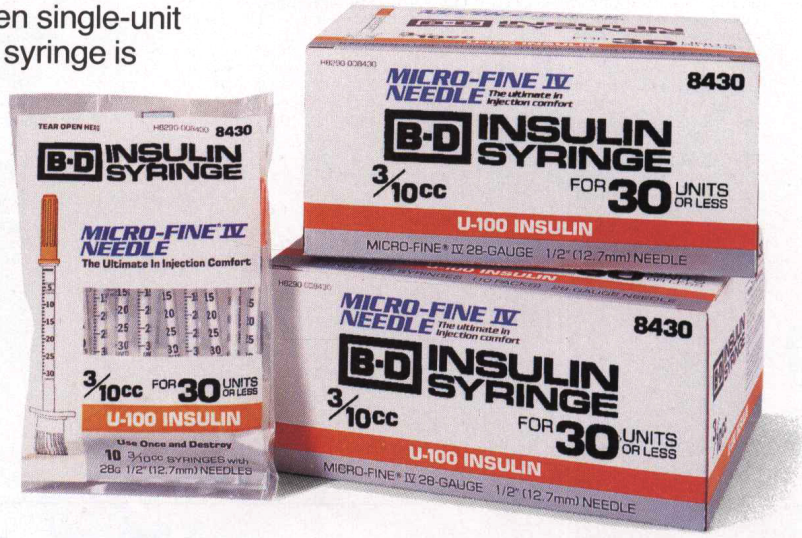
Almost half of all diabetes patients being treated with insulin are prescribed smaller, more frequent injections—30 units or less.

Which makes the B-D 3/10 cc syringe ideal for many of your patients.

The spacing between single-unit markings on the 3/10 cc syringe is extra wide so your patients can read the scale more easily. This, in turn, provides greater dosage accuracy—a significant improvement.

The unique B-D 3/10 cc syringe comes with the famous Micro-Fine® IV Needle for the *ultimate* in injection comfort.

One more reason doctors, nurses and hospitals use B-D syringes more than all other brands combined.



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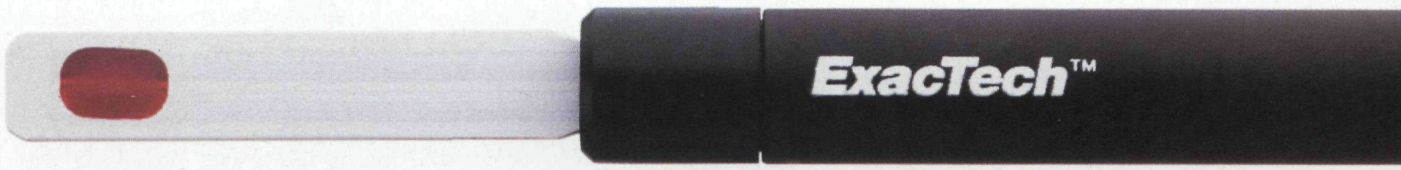
Amazingly Enough, This Blood Glucose Meter's Biggest Breakthrough Isn't Size.



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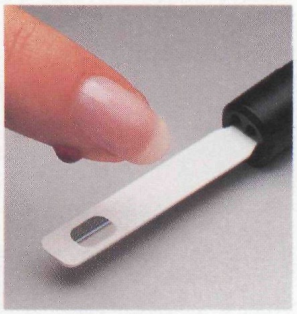
It's Accuracy.

Presenting the ExacTech™ Blood Glucose Meter. It's accurate because it's less dependent on user technique.

Technique-dependent steps like wiping, blotting, timing and cleaning have been eliminated. In fact, because this meter is so easy to use, patients are inclined to test themselves regularly.

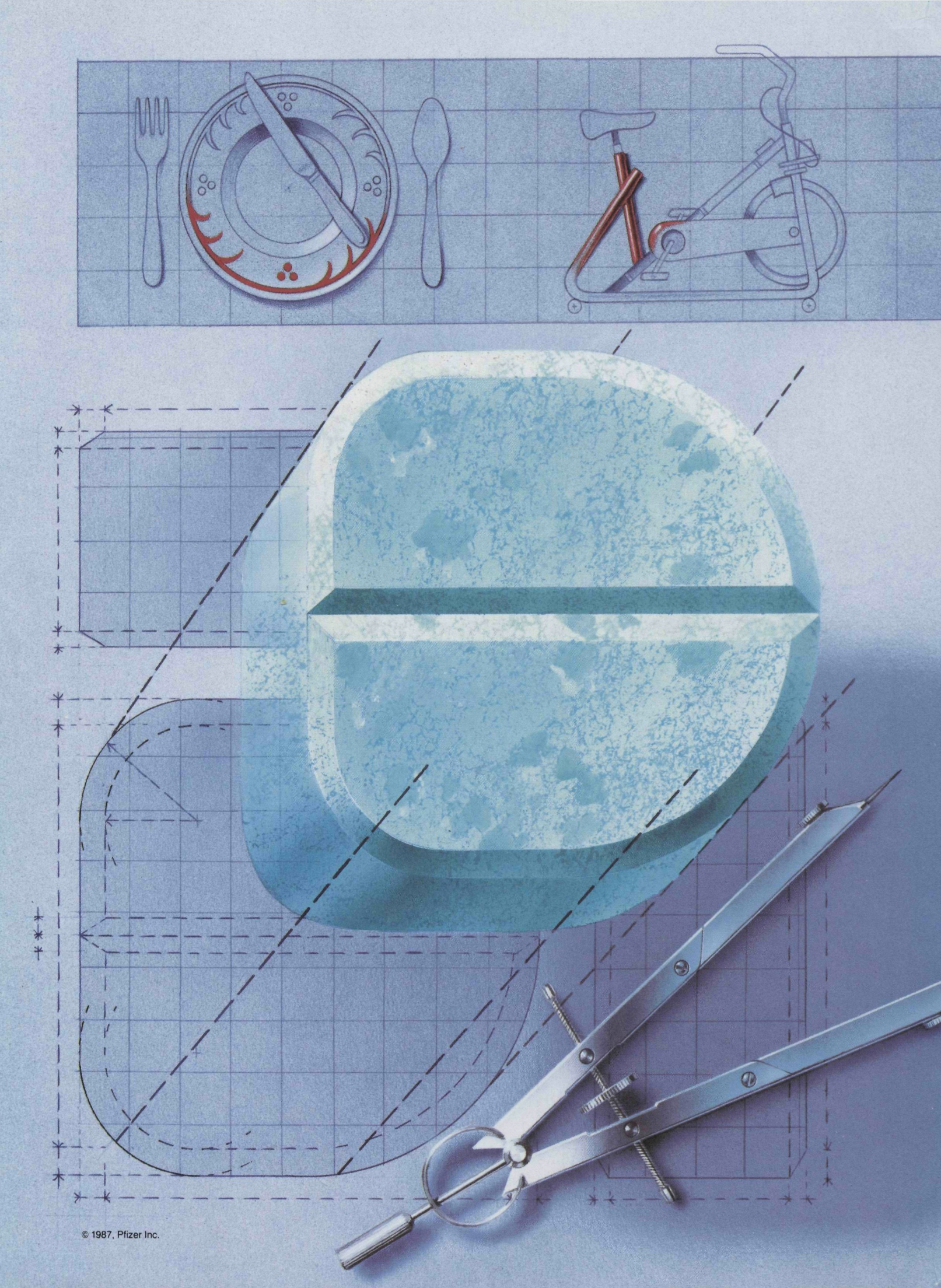


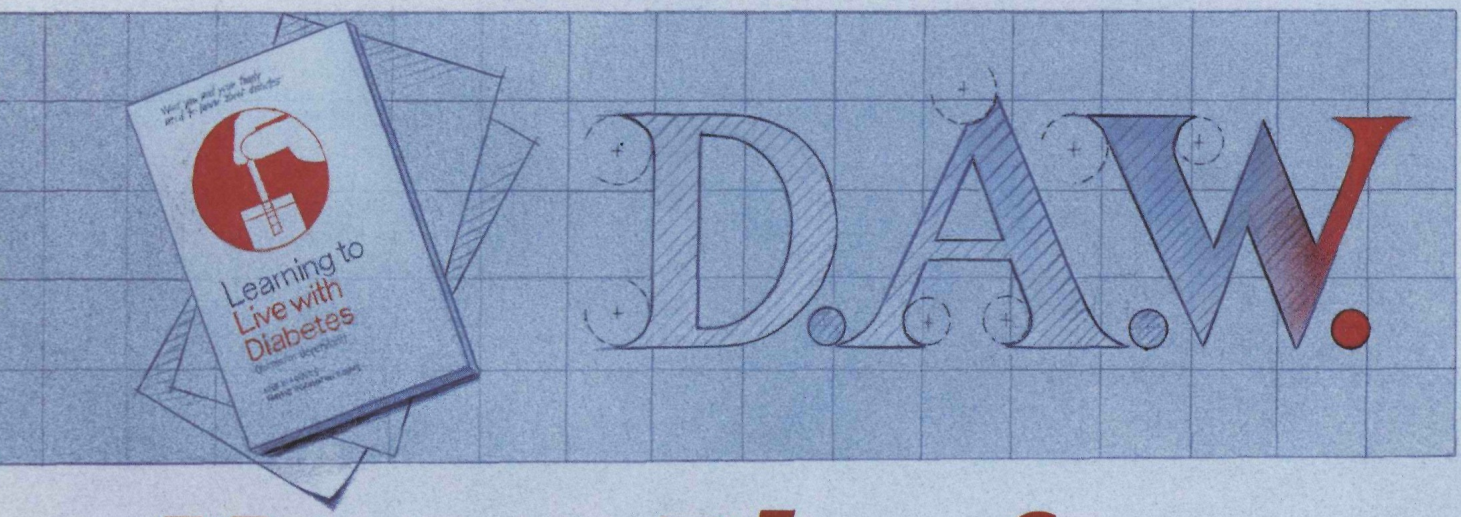
They simply insert a test strip into the meter, put a small drop of blood on the target area and press the button. Results appear on the display in just 30 seconds.

It's all due to our exclusive system. One part is the ExacTech Meter, which determines blood glucose levels through a unique electronic measuring method. The other is the ExacTech Test Strip, which has a small, hydrophilic target area that attracts blood.

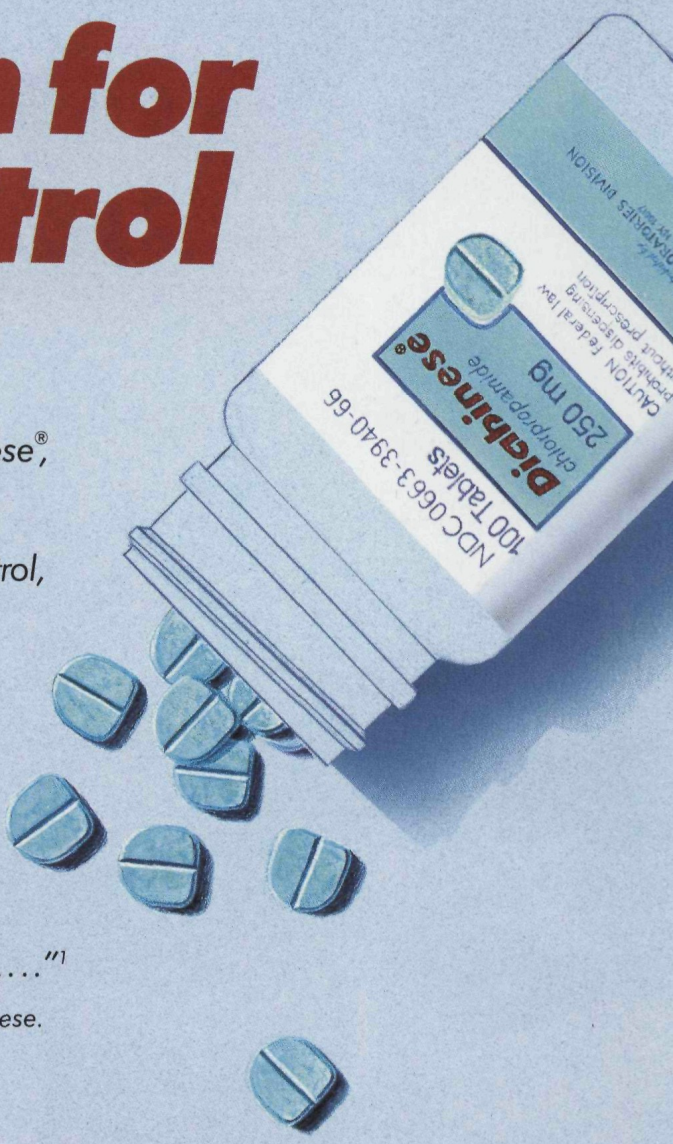
At last, there's been a breakthrough in meter technology. Recommend it to your patients. Call 1-800-527-3339, ext. 700, for more information, or write Baxter Healthcare Corporation, Physician Diagnostics Division, Attn: ExacTech, 1415 Lake Cook Road, P.O. Box 852, Deerfield, Illinois 60015-0852.

We're committed to helping people with diabetes live better lives.





Master Plan for NIDDM Control



A Diabinese® (chlorpropamide) prescription completes the design

Diet, exercise, education and once-daily Diabinese®, dispensed as written, comprise the Master Plan for successful non-insulin-dependent diabetes mellitus (NIDDM) control. For overall NIDDM control, specify Diabinese® by name.

Proven Efficacy and Safety

In a two-year study comparing Diabinese® to glyburide, "...chlorpropamide was clinically more effective with a smaller number of primary and secondary drug failures and a greater proportion of patients successfully controlled at the end of 2 years. Severe hypoglycemia was a greater hazard during treatment with glyburide...."[1]

As with all sulfonylureas, hypoglycemia may occur with Diabinese.

Once-a-day

Diabinese®

(chlorpropamide)

Tablets, USP, 100 mg, 250 mg and D-Pak

A GENERATION AHEAD IN NIDDM CONTROL

Reference: 1. Clarke BF: Comparative effectiveness of glyburide in the treatment of non-insulin-dependent diabetes, in *Diagnosis and Management of Diabetes Mellitus*. Postgraduate Medicine: Custom Communications, April 1982, pp 57-65.

Please see Diabinese® (chlorpropamide) brief summary on the following page.

Pfizer LABORATORIES DIVISION
PFIZER INC. NEW YORK, N.Y. 10017

BRIEF SUMMARY
DIABINESE* (chlorpropamide)
TABLETS, USP

CONTRAINDICATIONS
DIABINESE is contraindicated in patients with:
1. Known hypersensitivity to the drug.
2. Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.

WARNINGS
SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY

The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19 (supp. 2):747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2½ times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of DIABINESE (chlorpropamide) and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS
General

Hypoglycemia: All sulfonylurea drugs are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may cause elevated blood levels of DIABINESE and the latter may also diminish gluconeogenic capacity, both of which increase the risk of serious hypoglycemic reactions. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly, and in people who are taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Because of the long half-life of chlorpropamide, patients who become hypoglycemic during therapy require careful supervision of the dose and frequent feedings for at least 3 to 5 days. Hospitalization and intravenous glucose may be necessary.

Loss of control of blood glucose: When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a loss of control may occur. At such times, it may be necessary to discontinue DIABINESE (chlorpropamide) and administer insulin.

The effectiveness of any oral hypoglycemic drug, including DIABINESE, in lowering blood glucose to a desired level decreases in many patients over a period of time, which may be due to progression of the severity of the diabetes or to diminished responsiveness to the drug. This phenomenon is known as secondary failure, to distinguish it from primary failure in which the drug is ineffective in an individual patient when first given.

ADVERSE REACTIONS

Hypoglycemia: See PRECAUTIONS section.

Gastrointestinal Reactions: Cholestatic jaundice may occur rarely; DIABINESE should be discontinued if this occurs. Gastrointestinal disturbances are the most common reactions; nausea has been reported in less than 5% of patients, and diarrhea, vomiting, anorexia, and hunger in less than 2%. Other gastrointestinal disturbances have occurred in less than 1% of patients including proctocolitis. They tend to be dose related and may disappear when dosage is reduced.

Dermatologic Reactions: Pruritus has been reported in less than 3% of patients. Other allergic skin reactions, e.g., urticaria and maculopapular eruptions have been reported in approximately 1% or less of patients. These may be transient and may disappear despite continued use of DIABINESE (chlorpropamide); if skin reactions persist the drug should be discontinued.

Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis have also been reported.

Hematologic Reactions: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, pancytopenia, and eosinophilia have been reported with sulfonylureas.

Metabolic Reactions: Hepatic porphyria and disulfiram-like reactions have been reported with DIABINESE.

Endocrine Reactions: On rare occasions, chlorpropamide has caused a reaction identical to the syndrome of inappropriate antidiuretic hormone (ADH) secretion. The features of this syndrome result from excessive water retention and include hyponatremia, low serum osmolality, and high urine osmolality.

DOSAGE AND ADMINISTRATION

There is no fixed dosage regimen for the management of diabetes mellitus with DIABINESE or any other hypoglycemic agent. In addition to the usual monitoring of urinary glucose, the patient's blood glucose must also be monitored periodically to determine the minimum effective dose for the patient; to detect primary failure, and to detect secondary failure. Glycosylated hemoglobin levels may also be of value in monitoring the patient's response to therapy.

The total daily dosage is generally taken at a single time each morning with breakfast. Occasionally cases of gastrointestinal intolerance may be relieved by dividing the daily dosage. A LOADING OR PRIMING DOSE IS NOT NECESSARY AND SHOULD NOT BE USED.

Initial Therapy: 1. The mild to moderately severe, middle-aged, stable, non-insulin-dependent diabetic patient should be started on 250 mg daily. Older patients should be started on smaller amounts of DIABINESE (chlorpropamide), in the range of 100 to 125 mg daily.

2. No transition period is necessary when transferring patients from other oral hypoglycemic agents to DIABINESE. The other agent may be discontinued abruptly and chlorpropamide started at once. In prescribing chlorpropamide, due consideration must be given to its greater potency.

Many mild to moderately severe, middle-aged, stable non-insulin-dependent diabetic patients receiving insulin can be placed directly on the oral drug and their insulin abruptly discontinued. For patients requiring more than 40 units of insulin daily, therapy with DIABINESE may be initiated with a 50 per cent reduction in insulin for the first few days, with subsequent further reductions dependent upon the response.

Five to seven days after the initial therapy, the blood level of chlorpropamide reaches a plateau. Dosage may subsequently be adjusted upward or downward by increments of not more than 50 to 125 mg at intervals of 3 to 5 days to obtain optimal control. More frequent adjustments are usually undesirable.

Maintenance Therapy: Most moderately severe, middle-aged, stable non-insulin-dependent diabetic patients are controlled by approximately 250 mg daily. Many investigators have found that some milder diabetics do well on daily doses of 100 mg or less. Many of the more severe diabetics may require 500 mg daily for adequate control. PATIENTS WHO DO NOT RESPOND COMPLETELY TO 500 MG DAILY WILL USUALLY NOT RESPOND TO HIGHER DOSES. MAINTENANCE DOSES ABOVE 750 MG DAILY SHOULD BE AVOIDED.

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Blue, 'D'-shaped, scored tablets in strengths of 100 mg, tablet code 393; (100's, NDC #0663-3930-66; 500's, NDC #0663-3930-73; and 100 unit dose of 10 X 10, NDC #0663-3930-41) and 250 mg, tablet code 394; (100's, NDC #0663-3940-66; 250's, NDC #0663-3940-71; 1000's, NDC #0663-3940-82; 100 unit dose of 10 X 10, NDC #0663-3940-41; and 30's D-Pak, NDC #0663-3940-30).

RECOMMENDED STORAGE: Store below 86°F (30°C).

CAUTION: Federal law prohibits dispensing without prescription.

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PS Form 3526, Dec. 1987 (See instructions on reverse)

ERRATA

The May issue of *Diabetes* contains an error in the article "Glomerular Na^+-K^+-ATPase Activity in Acute and Chronic Diabetes and With Aldose Reductase Inhibition," by Margo P. Cohen and Henry Klepser. The last sentence of the first paragraph of DISCUSSION (p. 560) should read "A report of increased Na^+-K^+-ATPase activity in renal cortex from STZ-D rats used animals with diabetes of 4–7 wk duration, and the increase was ascribed to the tubular Na^+ pump activity (17)."

In the August issue, in the last sentence of the figure legend on p. 1126, the words *top* and *bottom* were reversed. The editors at the publishing office apologize for the error.

INTERNATIONAL RESEARCH SYMPOSIUM: "DIABETES, LIPOPROTEINS, AND ATHEROSCLEROSIS"

The American Diabetes Association is sponsoring a symposium, "Diabetes, Lipoproteins, and Atherosclerosis", on March 6–8, 1989 at the Hyatt Regency Hotel in Hilton Head, South Carolina.

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Abstract deadline: November 18, 1988. For abstract and registration information, contact the
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1989 Research Symposium
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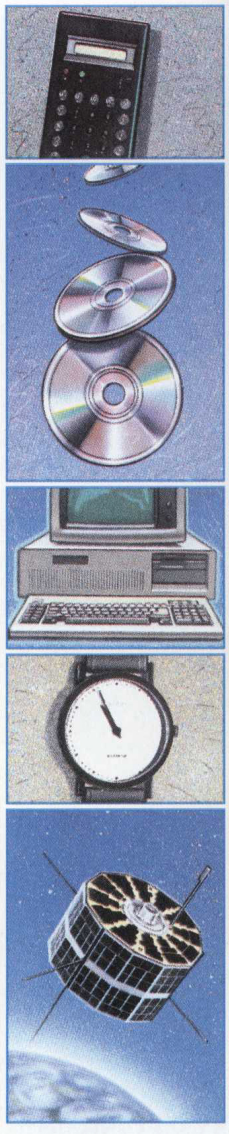

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References: 1. Data on file, Boehringer Mannheim Diagnostics. 2. Nielsen Audits (Jan.-Feb., 1988).

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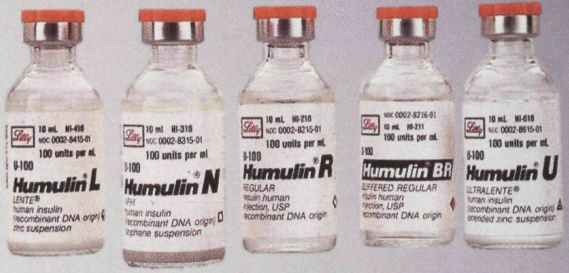

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