VOLUME 10/NUMBER 5/PAGES 545–669 SEPTEMBER/OCTOBER 1987

DIABETES CARE®

A PUBLICATION OF THE AMERICAN DIABETES ASSOCIATION®, INC.

ISSN 0149-5992

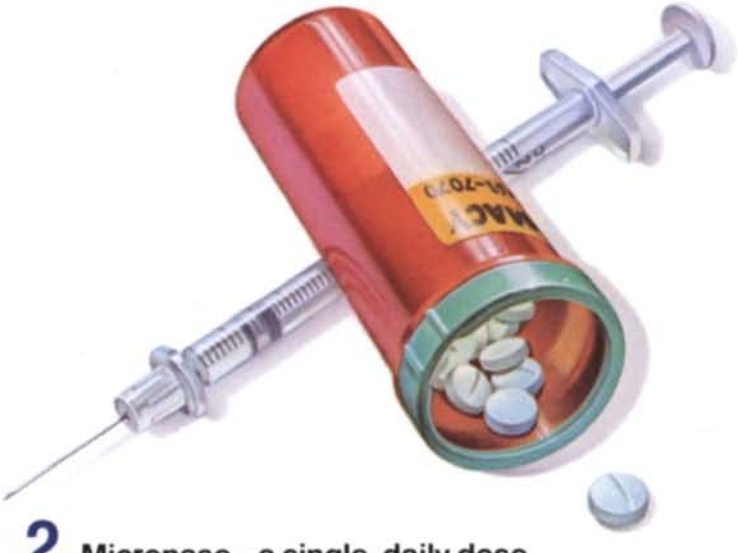
When a type II diabetic patient needs more than diet, unique MICRONASE® Tablets (glyburide) are a logical first choice.

Choosing antidiabetic

1. Micronase—a rational choice in type II diabetes

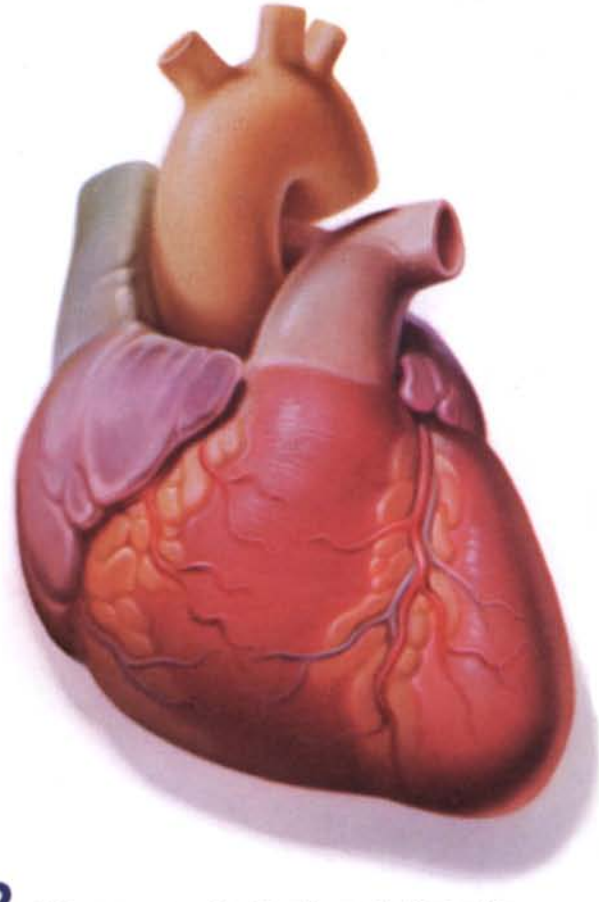
Insulin levels are normal or elevated in most patients with type II diabetes, although insulin action is markedly impaired. MICRONASE helps normalize the tissue response to endogenous insulin.

Initially, MICRONASE helps lower serum glucose in responsive patients by stimulating the release of additional insulin. As therapy continues, MICRONASE is believed to promote peripheral glucose metabolism by helping to correct defects at the cellular receptor and postreceptor levels.



2. Micronase—a single, daily dose provides 24-hour glycemic control

MICRONASE provides 24-hour control of blood glucose with a single, daily, low-milligram dose. MICRONASE may be taken with food, since food intake does not appear to affect its bioavailability.



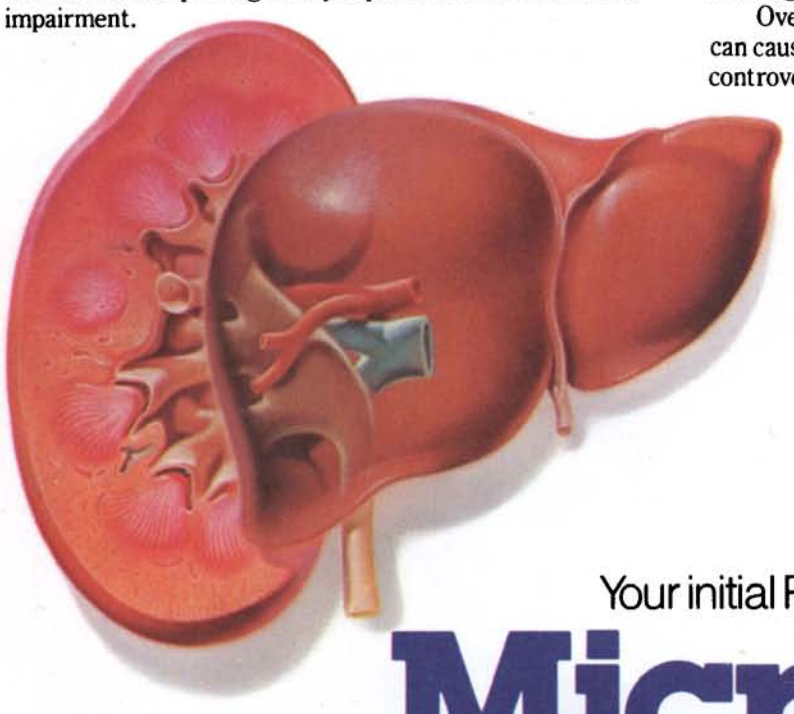
3. Micronase—for the type II diabetic patient who is also hypertensive: Control without risk of water retention

This may also be significant for the type II diabetic patient with congestive heart failure. MICRONASE actually causes a mild diuresis.

therapy today

4. Micronase—an important consideration in the type II diabetic patient with renal impairment: Control plus unique dual excretion... 50% urine, 50% bile

Elimination of MICRONASE equally in bile and urine reduces the risk of drug accumulation, which may result in hypoglycemia. MICRONASE should be used with caution in patients with renal impairment; however, in a single-dose study, plasma clearance of MICRONASE was prolonged only in patients with severe renal impairment.



5. Micronase—for the patient who fails on other diabetic therapy: Potency and dosage flexibility

MICRONASE may prove effective when other drugs fail. Five mg of MICRONASE is approximately equivalent to 250 mg of chlorpropamide or 500 mg of acetohexamide in its ability to lower blood glucose. The dosage range of MICRONASE allows for greater dosage flexibility than other agents.

Overdosage of sulfonylureas, including MICRONASE, can cause hypoglycemia. Although the interpretations are controversial, the UGDP study reported in 1970 that the use of tolbutamide, an oral hypoglycemic drug, was associated with increased cardiovascular mortality.

Upjohn The Upjohn Company
Kalamazoo, MI 49001

Your initial Rx in type II diabetes

Micronase®

glyburide, 5 mg Tablets

For brief summary of prescribing information, please turn page.

Micronase® Tablets (glyburide)

Dosage Guide:* Although relatively rare, hypoglycemia may occur during the conversion to MICRONASE from other therapy.

Prior therapy or condition	Considerations before starting therapy	Initial MICRONASE dose (mg/day)
Dietary therapy ineffective	No priming necessary	1.25 to 5 mg
Oral therapy	Discontinue oral hypoglycemic†	2.5 to 5 mg
Insulin therapy (<40 units/day)	Completely discontinue insulin injections under medical supervision	2.5 to 5 mg
Insulin therapy (>40 units/day)	Gradually discontinue insulin injections under close medical observation or hospitalization	5 mg

*See complete prescribing information.
†See package insert for special precautions when transferring patients from chlorpropamide.

Micronase Tablets (brand of glyburide tablets)

CONTRAINDICATIONS: MICRONASE Tablets are contraindicated in patients with: 1. Known hypersensitivity or allergy to the drug. 2. Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin. 3. Type I diabetes mellitus, as sole therapy.

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 noninsulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (Diabetes, 19 [Suppl 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 2-1/2 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 MICRONASE 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 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 sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection and dosage and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may 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. *Loss of Control of Blood Glucose:* In diabetic patients exposed to stress such as fever, trauma, infection or surgery, a loss of control may occur. It may then be necessary to discontinue MICRONASE and administer insulin. Adequate adjustment of dose and adherence to diet should be assessed before classifying a patient as a secondary failure. *Information for Patients:* Patients should be informed of the potential risks and advantages of MICRONASE and of alternative modes of therapy. They also should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Laboratory Tests: Response to MICRONASE Tablets should be monitored by frequent urine glucose tests and periodic blood glucose tests. Measurement of glycosylated hemoglobin levels may be helpful in some patients. **Drug Interactions:** The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. Certain drugs tend to produce hyperglycemia and may lead to loss of control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. **Carcinogenesis, Mutagenesis, and Impairment of Fertility:** Studies in rats at doses up to 300 mg/kg/day for 18 months showed no carcinogenic effects. Glyburide is nonmutagenic when studied in the Salmonella microsome test (Ames test) and in the DNA damage/alkaline elution assay. **Pregnancy:** *Teratogenic Effects:* Pregnancy Category B. Reproduction studies in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to glyburide. There are no adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed. Insulin should be used during pregnancy to maintain blood glucose as close to normal as possible. *Nonteratogenic Effects:* Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. MICRONASE should be discontinued at least two weeks before the expected delivery date. **Nursing Mothers:** Some sulfonylurea drugs are known to be excreted in human milk. Insulin therapy should be considered. **Pediatric Use:** Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Hypoglycemia: See Precautions and Overdosage sections. **Gastrointestinal Reactions:** Cholestatic jaundice may occur rarely; MICRONASE Tablets should be discontinued if this occurs. Gastrointestinal disturbances, e.g., nausea, epigastric fullness, and heartburn, are the most common reactions, having occurred in 1.8% of treated patients during clinical trials. They tend to be dose-related and may disappear when dosage is reduced. Liver function abnormalities, including isolated transaminase elevations, have been reported. **Dermatologic Reactions:** Allergic skin reactions, e.g., pruritis, erythema, urticaria, and morbilliform or maculopapular eruptions, occurred in 1.5% of treated patients during clinical trials. These may be transient and may disappear despite continued use of MICRONASE; if skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas. **Hematologic Reactions:** Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas. **Metabolic Reactions:** Hepatic porphyria and disulfiram-like reactions have been reported with sulfonylureas; however, hepatic porphyria has not been reported with MICRONASE and disulfiram-like reactions have been reported very rarely.

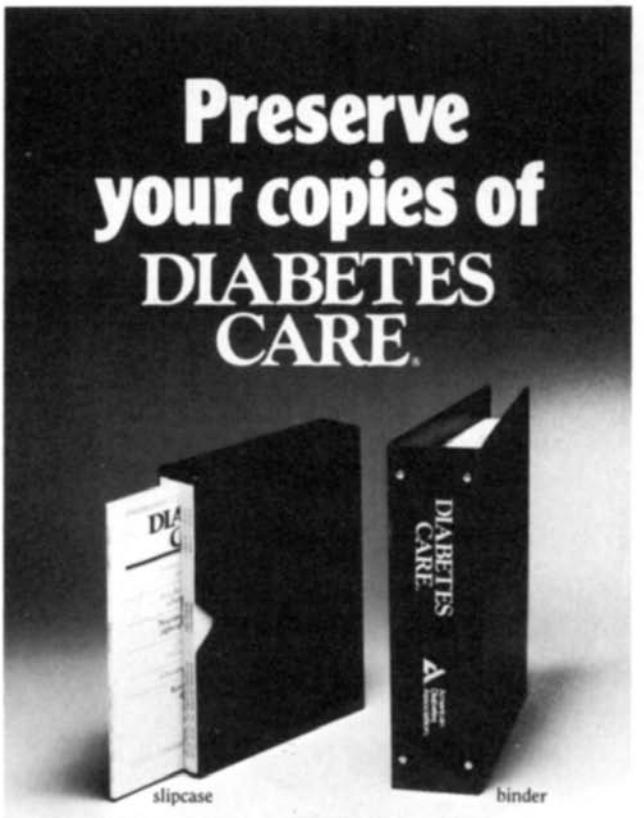
OVERDOSAGE: Overdosage of sulfonylureas, including MICRONASE Tablets, can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate which will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours, since hypoglycemia may recur after apparent clinical recovery.

Caution: Federal law prohibits dispensing without prescription. Store at controlled room temperature 15°-30°C (59°-86°F). Dispensed in well closed containers with safety closures. Keep container tightly closed.

For additional product information see your Upjohn representative. B-3-S

Upjohn THE UPJOHN COMPANY
Kalamazoo, MI 49001, USA

J-7349
January 1987



Custom-made for DIABETES CARE, these journal slipcases and binders turn back issues into a permanent reference source. Bound in attractive blue leatherette, and embossed with gold lettering, each slipcase and binder holds 1 year of DIABETES CARE (6 issues plus supplement). And each comes with gold transfers, allowing you to personalize your volume further. These durable, space saving cases make affordable gifts as well.

SLIPCASES: $7.95 each, three for $21.95, six for $39.95 (measures: 11½ × 8½ × 2⅛")
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Attn: Circulation Dept.

American Diabetes Association

DIABETES CARE®

SEPTEMBER-OCTOBER 1987/VOLUME 10/NUMBER 5

Contents

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Address manuscripts to F. John Service, M.D., Editor, DIABETES CARE, 4-407 Alfred Building, Mayo Foundation, Rochester, Minnesota 55905. Subscription correspondence should be addressed to Diabetes Care, Subscription Department, P.O. Box 2055, Harlan, Iowa 51593–0238.

First hundreds...

Then thousands...

Soon more than a million.

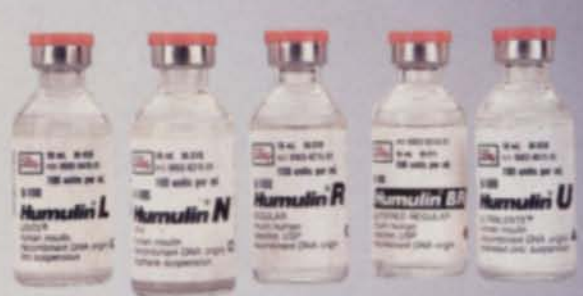
Soon more than a million insulin users will be taking Humulin.

And no wonder. Humulin is identical to the insulin produced by the human pancreas—except that it is made by rDNA technology.

Humulin is not derived from animal pancreases. So it contains none of the animal-source pancreatic impurities that may contribute to insulin allergies or immunogenicity.

The clinical significance of insulin antibodies in the complications of diabetes is uncertain at this time. However, high antibody titers have been shown to decrease the small amounts of endogenous insulin secretion some insulin users still have. The lower immunogenicity of Humulin has been shown to result in lower insulin antibody titers; thus, Humulin may help to prolong endogenous insulin production in some patients.

Any change of insulin should be made cautiously and only under medical supervision. Changes in refinement, purity, strength, brand (manufacturer), type (regular, NPH, Lente®, etc), species/source (beef, pork, beef-pork, or human), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.



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human insulin
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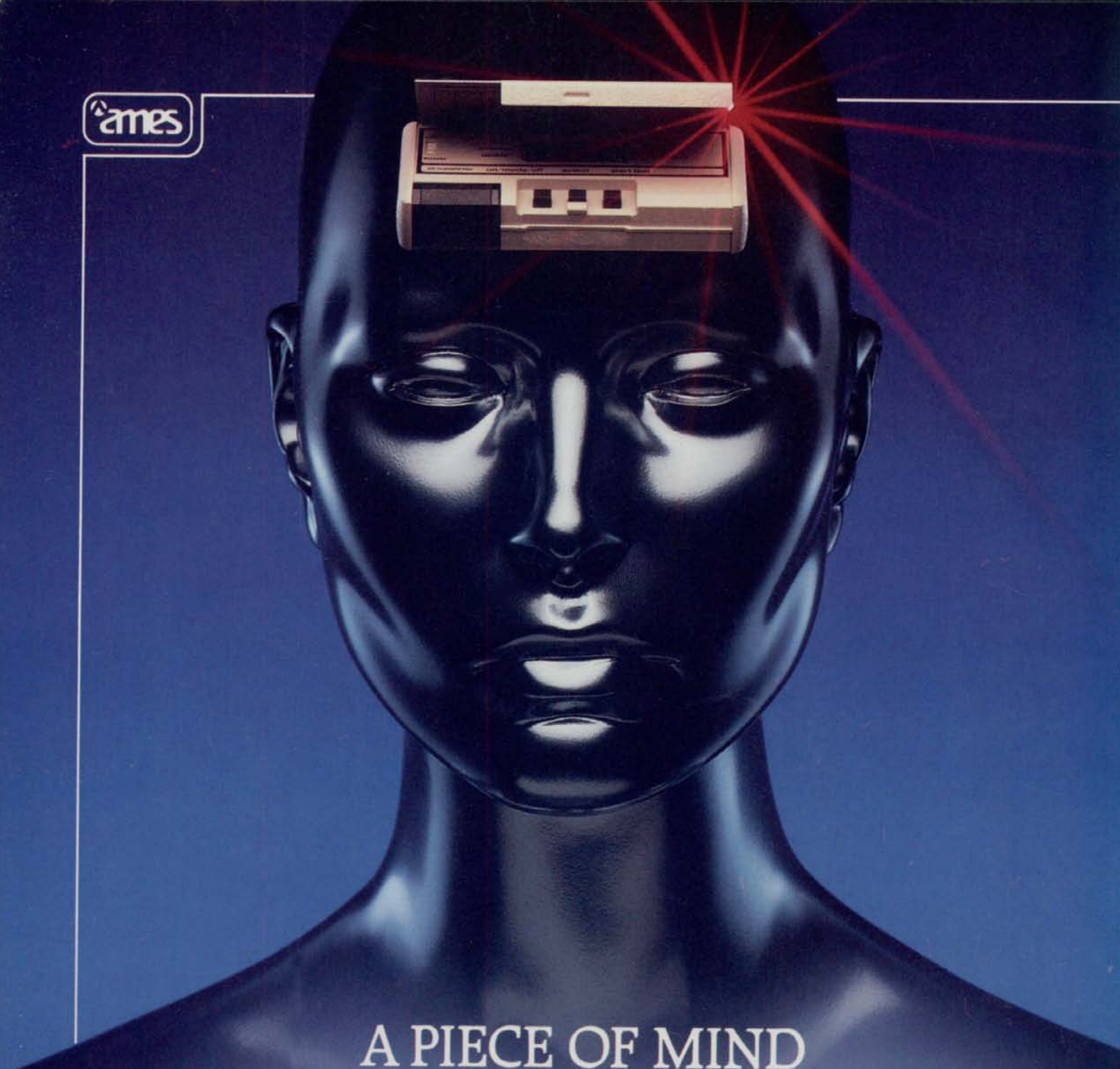
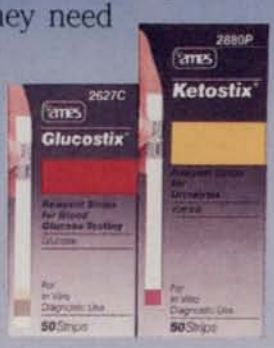


A PIECE OF MIND FOR YOUR DIABETES PATIENTS.

We gave our popular blood glucose meter a mind of its own. So your patients can have the convenience, security and privacy they need to comply with your blood glucose monitoring recommendations.

The Glucometer® II Blood Glucose Meter with Memory is more convenient because it stores 26 readings and allows your patients to record them in their diary when they have time. It's more secure because patients don't have to worry about forgetting the readings the meter remembers. It's more private because patients can silence the audible signal when reading blood glucose levels in public.

Help take the worry out of blood glucose monitoring. A piece of mind from the Glucometer II with Memory can mean peace of mind for your patients. And for you.



Part of a complete system for blood glucose monitoring and urine ketone testing.

Ames Division MILES

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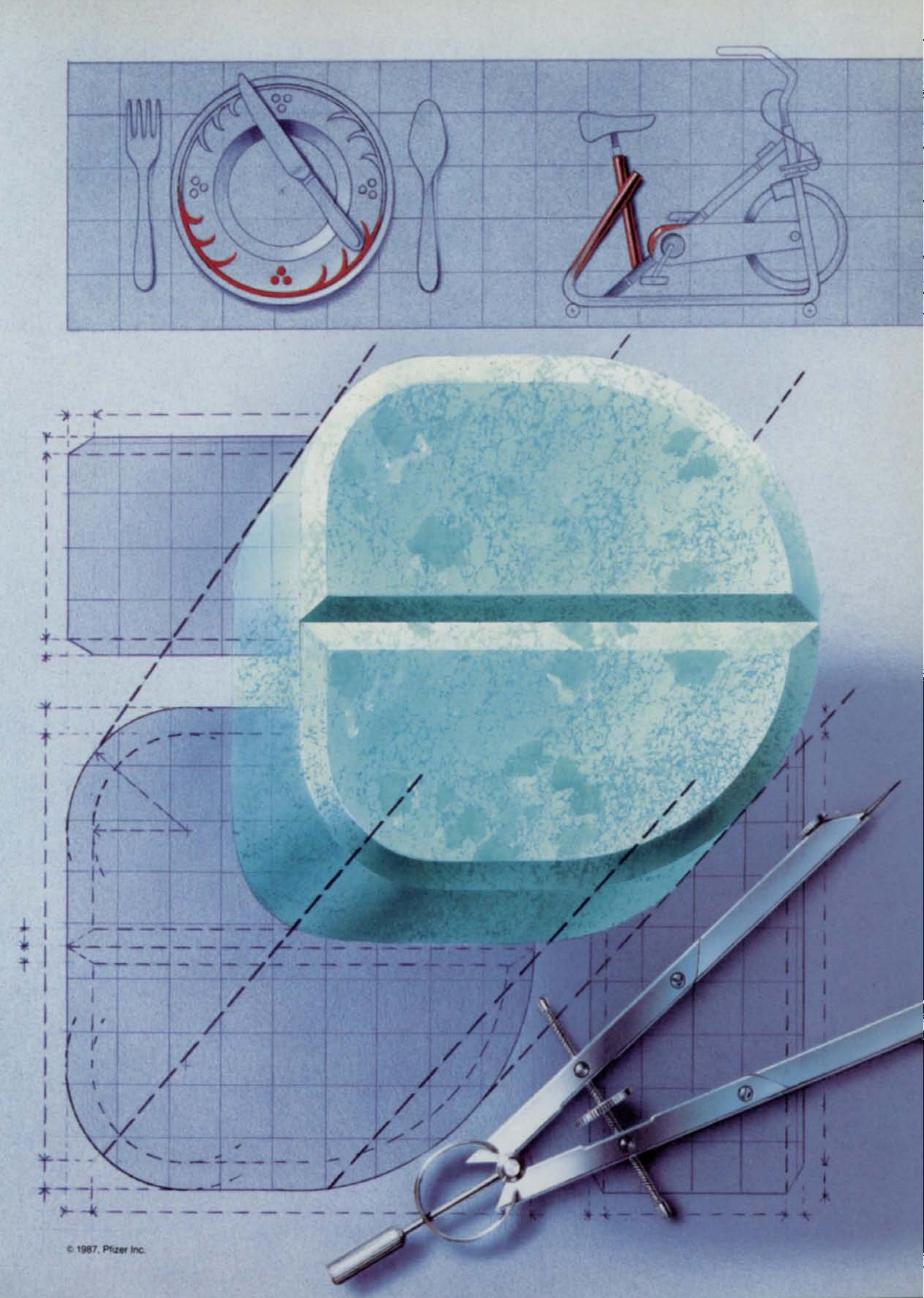
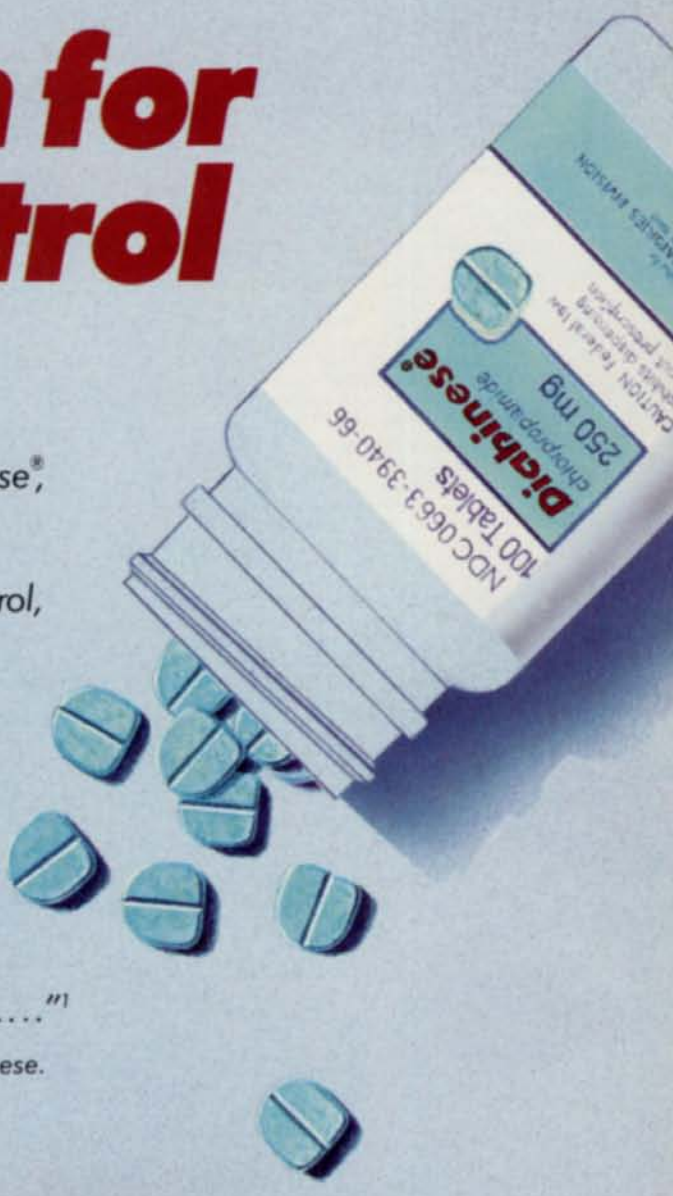
DIABETES CARE®

SEPTEMBER-OCTOBER 1987/VOLUME 10/NUMBER 5

Diabetes Care and *Diabetes* 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. *Diabetes Care* provides a forum for applied research primarily directed toward improving the welfare of people with diabetes mellitus and enhancing understanding of the diseases for health professionals. *Diabetes* provides a forum for animal and human research primarily directed toward expanding knowledge of physiology and pathophysiology of diabetes mellitus.



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.

HOW SUPPLIED

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.

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

Scientific research has demonstrated there are three steps needed to enhance chronic wound healing

Open

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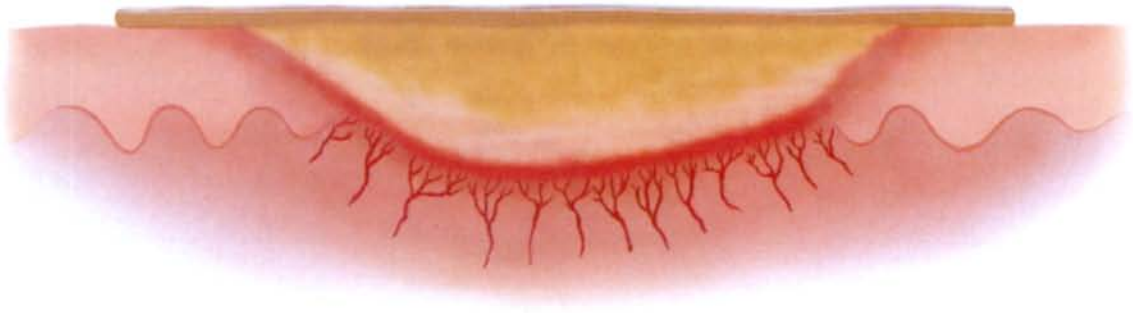
Apply

DuoDERM® Hydroactive® Dressing
The only dressing proven* to create the optimum healing environment



Many dressings can maintain an appropriate moisture balance, but only DuoDERM Hydroactive Dressing is proven to stimulate new capillary growth[1]—a fundamental property of a healing wound.

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...putting science into healing*

ConvaTec
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*Preclinical data, Bibliography upon request.

1. Cherry GW, Ryan TJ: Enhanced wound angiogenesis with a new hydrocolloid dressing, in Ryan TJ (ed): An Environment for Healing: The Role of Occlusion. London: The Royal Society of Medicine, pp 61–68, 1985.

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THE DIASCAN* BLOOD GLUCOSE SELF-MONITORING SYSTEM

Featuring the *New* Diascan-S Meter

It's simple: Easy to learn . . . easier to use. Everything about it is easy . . . from applying the sample to the test strip (no need for hanging drop) to removing the sample from the pad . . . from touch calibration to adjustable prompts. Even the door has been eliminated . . . just insert the strip and read.

It's smart: So smart that it remembers the last ten tests, compensates for variations in temperature, and tells you if the strip is not seated correctly. The DIASCAN-S offers the broadest available range (10-600 mg/dl), plus unsurpassed accuracy and reliability that has made DIASCAN the fastest growing blood glucose self-monitoring system in America.

DIASCAN-S: The sensible choice. Simplicity of use plus superior technology add up to the ideal blood glucose self-monitoring system. For more information contact your local Diabetes Training Center or call Home Diagnostics, Inc. 1-800-DIASCAN (in New Jersey and outside the USA, please call 201-542-7788).

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ATTENTION ADA MEMBERS:

HELP US CHART THE FUTURE

The American Diabetes Association has embarked on one of the most important projects it has ever undertaken: the development of the Long-Range Plan that will set the Association's direction through the 1990s. As a member of the Association, you are both a provider and a recipient of ADA services. You are a provider in your role as an ADA volunteer, working with ADA Affiliates and Chapters around the country to help us achieve our mission. You are also a recipient of the benefits of membership in the Association through your professional journals and the other benefits of professional membership, including program activities of the ADA Affiliate Associations. Therefore, you are critical to the success of our work. That is why we are inviting you to provide input into the development of ADA's Long-Range Plan.

A Consensus Development Conference will be held in December of this year to formulate the core principles upon which the Long-Range Plan will be based. We would like you to provide input to the conference by answering the two questions listed below. Your answers will be tabulated and a summary presented to the participants in the Conference. This is your opportunity to have an impact on the direction your Association takes for the rest of this century. Please answer the questions and know that your voice will be heard and your opinions considered. Thank you for your help.

S. Douglas Dodd
Chairman of the Board

John A. Colwell, M.D., Ph.D.
President

Question 1

On a national basis, how should ADA allocate its resources among the following program areas? Please rank the following in order of importance to you. (1 = most important; 5 = least important)

____ Patient education (includes education classes, support groups, etc., for people with diabetes and their families).

____ Professional education (includes training programs to enable health professionals to provide up-to-date care).

____ Public awareness (includes materials and activities designed to make the general public aware of the seriousness of diabetes and its risk factors and symptoms).

____ Research (includes support of researchers).

____ Youth Activities (includes camps and other special programs for children with diabetes).

Question 2

In your community, what are the three most pressing needs ADA should address?

Please give your city _____ state _____ and Zip Code _____

1. _____

2. _____

3. _____

Additional Comments:

_____

_____

_____

Return to: Long-Range Plan, ADA, 1660 Duke Street, Alexandria, VA 22314, *before October 31, 1987.* Thank you.

NEW Medi-Jector® *EZ*

Advanced needle-free insulin injection system

New size
□ easy to hold

New slimline design
□ easy to use at all sites

New simplified operation
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New digital dosage display
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New light weight, only eight ounces
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New Medi-Jector *EZ*. It's smaller, lighter weight, and much easier to use. And it's the most affordable Medi-Jector ever.

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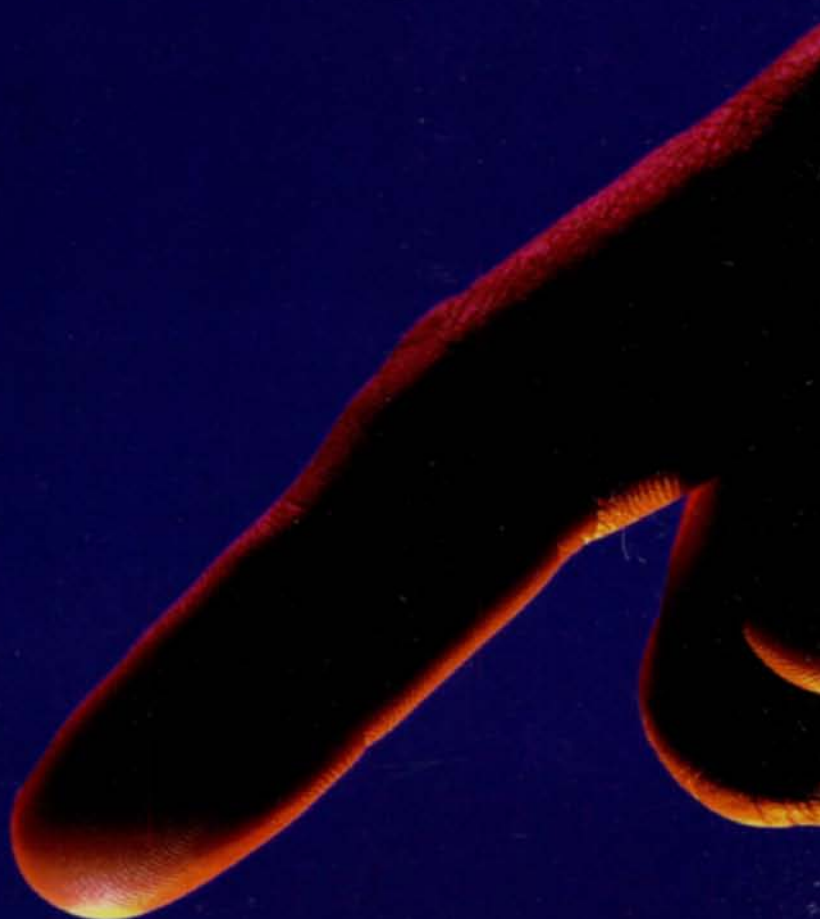


I N T R O D U C I N G

ONE TOUCH™ SYSTEM

A revolutionary blood glucose monitoring system from LifeScan.

One Touch— the first truly simple system.

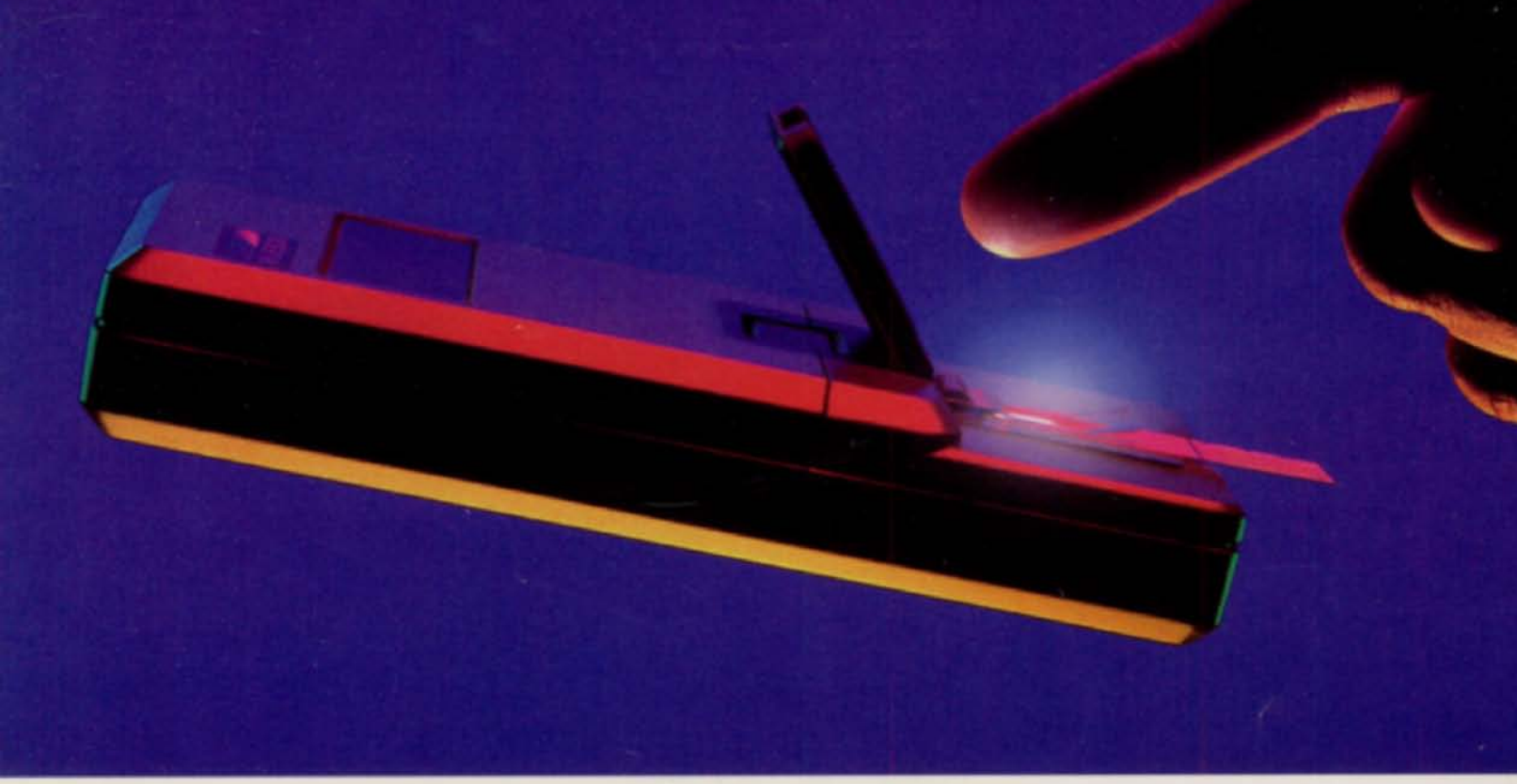
The new One Touch System makes reliable blood glucose monitoring easier than ever. With One Touch, results can be achieved by touching the reagent pad just once—to apply blood—because no wiping or blotting is required.

One Touch—no timing, no wiping, no blotting, no user demands.

The One Touch System eliminates three major demands on your patients: starting the test, timing the test and removing the blood. With the test strip in the meter, the patient presses Power, then applies the blood sample to the reagent pad at any time. At this

1. Insert test strip.

2. Press POWER.



point the meter takes over, starting the test automatically when it detects blood on the reagent pad. No blood removal is required, and results appear in just 45 seconds. *The opportunity for procedural error is virtually eliminated.*

One Touch—easier to use, easier to handle.

The One Touch Meter provides a stable platform for the test strip while the blood sample is applied. The reagent pad is smaller, so less blood is required for each test. The test strip is wider, so it's easier to handle.

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One Touch is the first blood glucose meter to provide interactive messages in plain English on a large, easy-to-read display.

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One Touch—designed for technique-independent testing.

When blood glucose monitoring is kept simple, results are more reliable. The One Touch testing procedure accomplishes this goal.

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Result appears in just 45 seconds—with no timing, wiping, or blotting.

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The Complete One Touch™ System Includes:
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Technology that tests the glucose, not the patient.

Specifications:

Fast test time
Results appear in just 45 seconds.

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0 to 600 mg/dL (0 to 33.3 mmol/L).

Unsurpassed accuracy
When compared to a clinical laboratory instrument (YSI Model 23A Glucose Analyzer) at three different clinical locations, results from patients using the One Touch System demonstrated excellent correlation with the reference method.
slope 1.02
y intercept 4.7 mg/dL
correlation coefficient (r) 0.979

Automatic memory
Stores most recent 250 readings. Data port for transferring memory contents to Data Manager™ unit for printed test histories with time and date.

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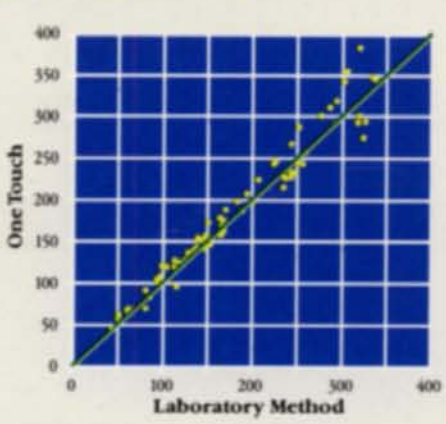
Comparison of One Touch used by patients vs. laboratory reference method*



Customer satisfaction guarantee
No risk money-back guarantee on One Touch System within 30 days of purchase. Full three-year warranty on One Touch Meter.

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*Data on file, LifeScan, Inc.

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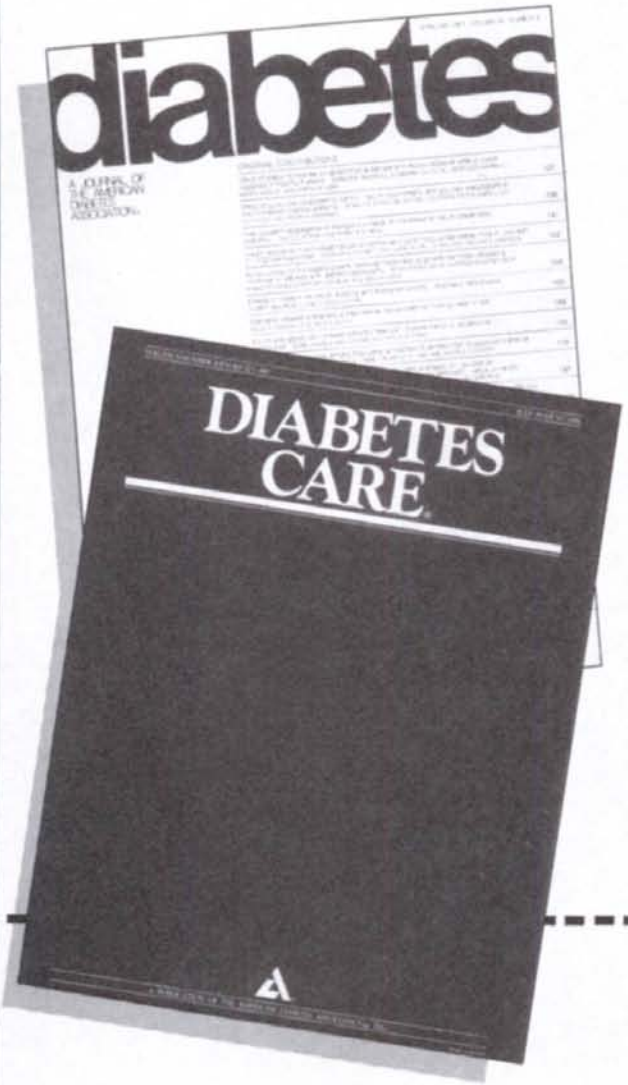
Essential diabetes reading.



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American Diabetes Association® Inc.

B74801

1 **Diaβeta**®: Controls blood glucose with 24-hour duration of action. This once-a-day dosage for most patients helps avoid drug overlap and its associated problems.

2 **Diaβeta**®: Increases free water clearance, an important consideration for patients with coexisting hypertension or CHF.

3 **Diaβeta**®: Very rare incidence of embarrassing disulfiram-like reactions.

4 **Diaβeta**®: Excreted equally in urine and bile which reduces the risk of accumulation in patients with nephropathy.*

Compare these benefits with what you know about other agents. We believe you would take DiaBeta®.

DIET &

Diaβeta® TABLETS 1.25, 2.5 and 5mg

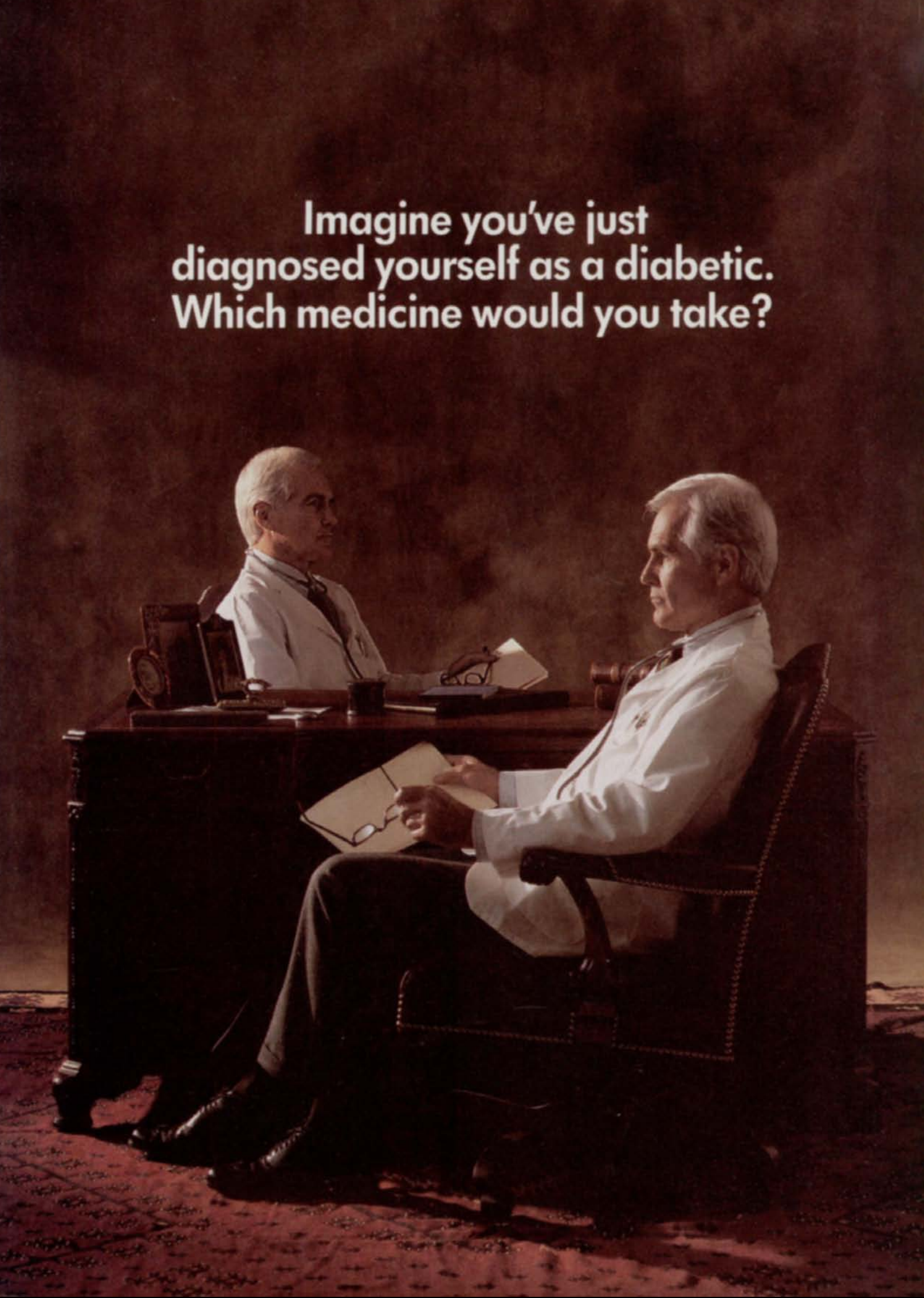
(GLYBURIDE)

The differences are important.

*Dosage should be monitored in patients with hepatic or renal insufficiency to avoid hypoglycemia. Please refer to Warnings and Precautions section of prescribing information.

Although the findings are controversial, the UGDP study reported in 1970 that the use of tolbutamide, an oral sulfonylurea, was associated with increased cardiovascular risk.

Please see last page of this ad for brief summary of prescribing information.


Imagine you've just
diagnosed yourself as a diabetic.
Which medicine would you take?

DiaBeta®(glyburide)
For effective control of Type II Diabetes.

DiaBeta®(glyburide) Tablets 1.25, 2.5 and 5mg

BRIEF SUMMARY

INDICATIONS AND USAGE

Diaβeta® (glyburide) is indicated as an adjunct to diet to lower the blood glucose in patients with non-insulin-dependent diabetes mellitus (Type II) whose hyperglycemia cannot be controlled by diet alone.

In initiating treatment for non-insulin-dependent diabetes, diet should be emphasized as the primary form of treatment. Caloric restriction and weight loss are essential in the obese diabetic patient. Proper dietary management alone may be effective in controlling the blood glucose and symptoms of hyperglycemia. The importance of regular physical activity should also be stressed, and cardiovascular risk factors should be identified and corrective measures taken where possible.

If this treatment program fails to reduce symptoms and/or blood glucose, the use of an oral sulfonylurea or insulin should be considered. Use of Diaβeta® (glyburide) must be viewed by both the physician and patient as a treatment in addition to diet, and not as a substitute for diet or as a convenient mechanism for avoiding dietary restraint. Furthermore, loss of blood glucose control on diet alone may be transient, thus requiring only short-term administration of Diaβeta® (glyburide).

During maintenance programs, Diaβeta® (glyburide) should be discontinued if satisfactory lowering of blood glucose is no longer achieved. Judgments should be based on regular clinical and laboratory evaluations.

In considering the use of Diaβeta® (glyburide) in asymptomatic patients, it should be recognized that controlling the blood glucose in non-insulin dependent diabetes has not been definitely established to be effective in preventing the long-term cardiovascular or neural complications of diabetes.

CONTRAINDICATIONS

Diaβeta® (glyburide) 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 Diaβeta® (glyburide) 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 Diaβeta® (glyburide) 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.

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 Diaβeta® (glyburide) and administer insulin.

The effectiveness of any oral hypoglycemic drug, including Diaβeta® (glyburide), 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.

Information for Patients

Patients should be informed of the potential risks, advantages, alternative modes of therapy, importance of adherence to dietary instructions, to a regular exercise program, and regular testing of urine and/or blood glucose. Also explain to the patient and responsible family members, the risks of hypoglycemia, its symptoms, treatment, conditions that predispose to its development, and primary and secondary failure.

Laboratory Tests

Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Drug Interactions

The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. When such drugs are administered to a patient receiving Diaβeta® (glyburide), the patient should be observed closely for hypoglycemia. When such drugs are withdrawn from a patient receiving Diaβeta® (glyburide), the patient should be observed closely for loss of control.

Certain drugs tend to produce hyperglycemia and may lead to loss of control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. When such drugs are administered to a patient receiving Diaβeta® (glyburide), the patient should be closely observed for loss of control. When such drugs are withdrawn from a patient receiving Diaβeta® (glyburide), the patient should be observed closely for hypoglycemia.

A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Diaβeta® (glyburide) is non-mutagenic when studied in the Salmonella microsome test (Ames test) and in the DNA damage/alkaline elution assay. Studies in rats at doses up to 300 mg/kg/day for 18 months showed no carcinogenic effects.

Pregnancy

Teratogenic Effects: Pregnancy Category B

Reproduction studies have been performed in rats and rabbits at doses up to 500 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Diaβeta® (glyburide). There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects

Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. If Diaβeta® (glyburide) is used during pregnancy, it should be discontinued at least two weeks before the expected delivery date.

Nursing Mothers

Although it is not known whether Diaβeta® (glyburide) is excreted in human milk, some sulfonylureas are known to be excreted in human milk. Because the potential for hypoglycemia in nursing infants may exist, a decision should be made whether to discontinue nursing or to discontinue administering the drug, taking into account the importance of the drug to the mother. If Diaβeta® (glyburide) is discontinued and if diet alone is inadequate for controlling blood glucose, insulin therapy should be considered.

PEDIATRIC USE

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Hypoglycemia: See **PRECAUTIONS** and **OVERDOSAGE** Sections.

Gastrointestinal Reactions: Cholestatic jaundice may occur rarely; Diaβeta® (glyburide) should be discontinued if this occurs. Gastrointestinal disturbances, e.g., nausea, epigastric fullness, and heartburn, are the most common reactions and occur in 1.8% of treated patients. They tend to be dose-related and may disappear when dosage is reduced.

Dermatologic Reactions: Allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions, occur in 1.5% of treated patients. These may be transient and may disappear despite continued use of Diaβeta® (glyburide); if skin reactions persist, the drug should be discontinued.

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

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

Metabolic Reactions: Hepatic porphyria reactions have been reported with sulfonylureas; however, these have not been reported with Diaβeta® (glyburide). Disulfiram-like reactions have been reported very rarely with Diaβeta® (glyburide).

OVERDOSAGE

Overdosage can produce hypoglycemia. Aggressively treat the mild symptoms (without loss of consciousness or neurologic findings) with oral glucose and adjustments in drug dosage and/or meal patterns. Continue close monitoring until patient is out of danger. Severe hypoglycemic reactions with coma, seizure, or other neurological impairment, are medical emergencies requiring immediate hospitalization. With hypoglycemic coma (diagnosed or suspected), administer rapid intravenous injection of concentrated (50%) glucose solution, followed by continuous infusion of a more dilute (10%) glucose solution at a rate to maintain a blood glucose level above 100 mg/dL. Monitor closely for a minimum of 24-48 hours; hypoglycemia may recur after apparent clinical recovery.

DIABETES RESEARCH & EDUCATION FOUNDATION

Hoechst-Roussel Pharmaceuticals Inc. is proud to support the efforts of the Diabetes Research & Education Foundation. The Foundation is an independent, non-profit organization which provides funding to individuals for work in diabetes research or education.

If you are interested, grant applications can be obtained by writing to:
Diabetes Research & Education Foundation, Inc., P.O. Box 6168, Bridgewater, NJ 08807-9998.

Support for the foundation is provided by Hoechst-Roussel via a donation derived from a percentage of sales of their diabetes products.

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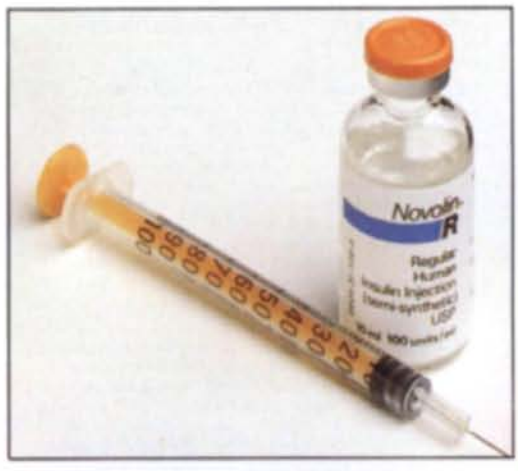
WHEN HYPERTENSION COEXISTS WITH DIABETES...



Consider the CAPOTEN difference...

Effective control*

- 50 mg to 100 mg daily effectively controls most patients with mild hypertension[1]

Fewer complications

- Studies of hypertensive patients with concurrent Type I or Type II diabetes show that CAPOTEN does not affect glucose metabolism[2,3]
- Unlike some beta-blockers,[4] CAPOTEN is not associated with hyperglycemic or hypoglycemic changes and does not mask the symptoms of hypoglycemia
- Unlike diuretics,[4] CAPOTEN is not associated with impairment of glucose tolerance in diabetics

CAPOTEN® *LOW DOSE*
captopril tablets

SQUIBB

*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. Overall, the most frequently occurring adverse reactions associated with CAPOTEN are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on adjacent page.

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.

WARNINGS: Neutropenia/Agranulocytosis – Neutropenia ($<1000/mm^3$) 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 <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 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 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 $<1000/mm^3$) withdraw captopril and closely follow the patient's course.

Proteinuria – Total urinary proteins >1 g/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, patients with prior renal disease or those receiving captopril at doses >150 mg/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 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 major 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 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. 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 have 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 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 – About 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, and 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 hypertensive 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, 50, and 100 mg in bottles of 100 (25 mg also available in bottles of 1000), and in UNIMATIC® single dose packs of 100 tablets. (J3-658D)

References: 1. Drayer JM, Weber MA: Monotherapy of essential hypertension with a converting-enzyme inhibitor. Hypertension 5(5-Suppl III):108-113, 1983.
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 I):69-72, 1986.
3. Matthews DM, Wathen CG, Bell D, et al: The effect of captopril on blood pressure and glucose tolerance in hypertensive non-insulin dependent diabetics. Postgrad Med J 62(Suppl I):73-75, 1986.
4. Christlieb AR: Management of hypertension in the patient with diabetes mellitus. Practical Cardiol 8:94-103, 1982.

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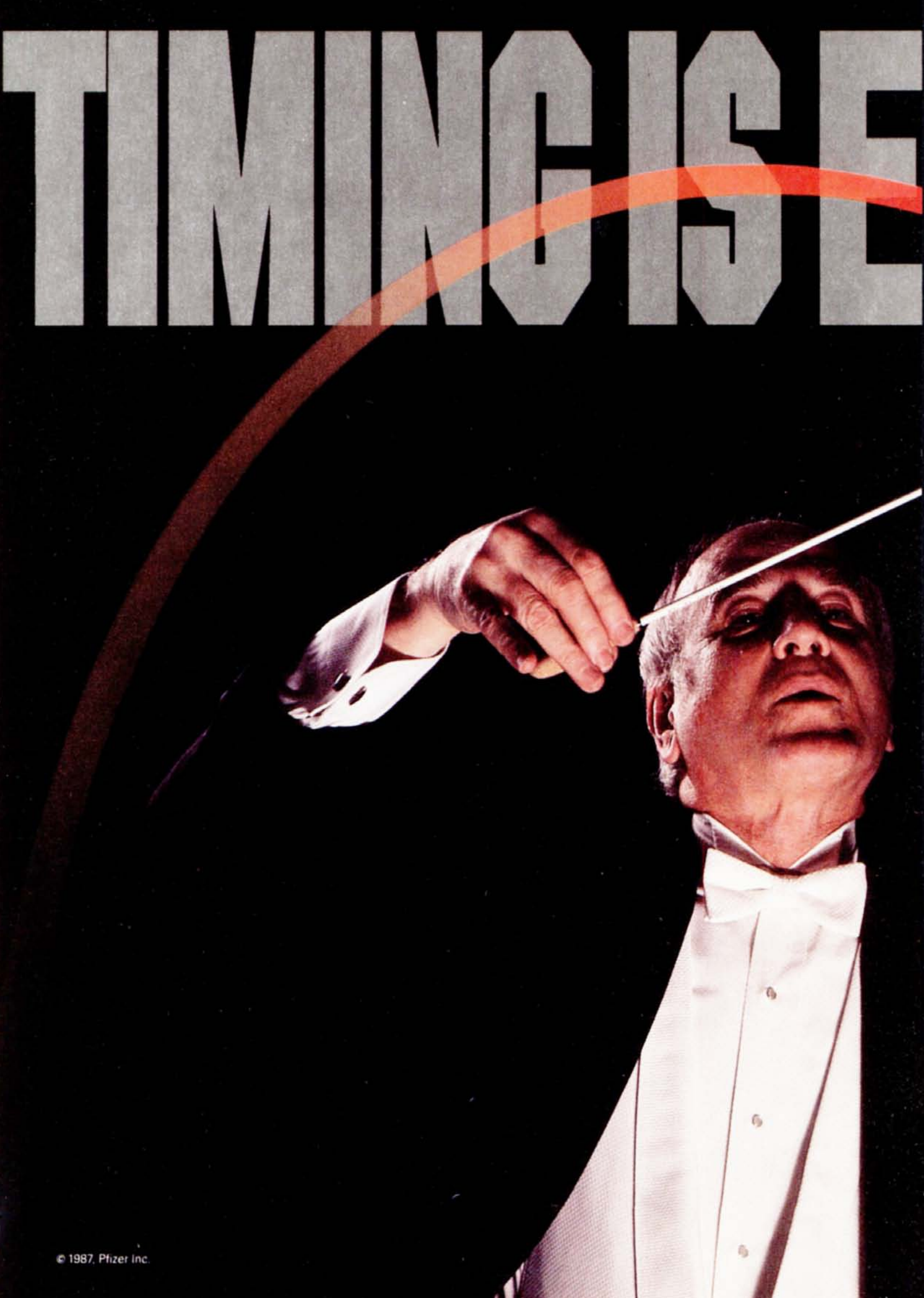

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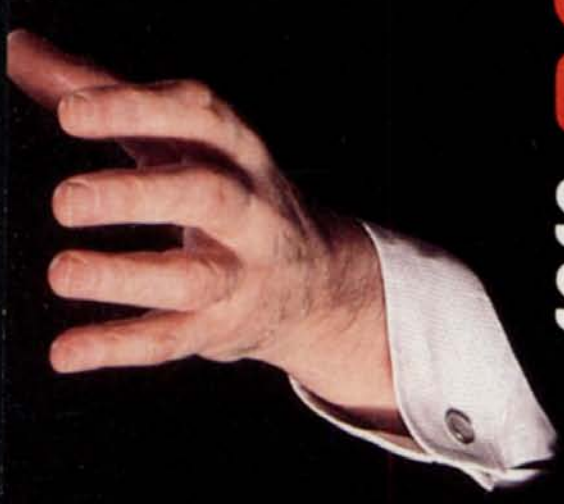

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ERRATUM

In the article titled "Interaction Between Plastic Catheter Tubings and Regular Insulin Preparations Used for Continuous Subcutaneous Insulin-Infusion Therapy" by E. Chantelau and associates (*Diabetes Care* 10:348–51, 1987), all values in Table 2 should be expressed as mg/ml and percentages. In addition, the last line of text should read: "It might be concluded, however, that polyethylene catheters may have advantages for CSII treatment, because this material was shown to interact less than others (e.g., PVC) with commercial insulin preparations.

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A. Bistrian, B. R., Blackburn, G. L., et al: ***NITROGEN METABOLISM AND INSULIN REQUIREMENTS IN OBESE DIABETIC ADULTS ON A PROTEIN SPARING MODIFIED FAST.*** Diabetes, Vol. 25, No. 6: 494-504, June 1976.

B. Vertes, V., Genuth, S. M., Hazelton, I.M.: ***SUPPLEMENTED FASTING AS A LARGE SCALE OUTPATIENT PROGRAM.*** JAMA, 238: 2151-2153, Nov. 14, 1977.

C. Kirschner, M. A., Schneider, G. et al: ***SUPPLEMENTAL STARVATION: A SUCCESSFUL METHOD FOR CONTROL OF MAJOR OBESITY.*** Journal Med. Soc. New Jersey, Vol. 76, No. 3: 175-179, March 1979.

D. Genuth, S., ***SUPPLEMENTED FASTING IN THE TREATMENT OF OBESITY AND DIABETES.*** The American Journal of Clinical Nutrition, Vol. 32, No. 12: 2579-2586, Dec. 1979.

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Servings Per Box — 18
Calories Per Packet — 60

	Per Serving (One Packet)	Per Five Servings*	Percent Of U S RDA** (Five Servings)
Protein	9 Gm	45 Gm	100
Carbohydrate	6 Gm	30 Gm	***
Fat	0 Gm	0 Gm	***
Calories	60	300	***
Vitamin A	1.000 IU	5.000 IU	100
Vitamin D	80 IU	400 IU	100
Vitamin E	6 IU	30 IU	100
Vitamin C	12 Mg	60 Mg	100
Thiamin	30 Mg	1 5 Mg	100
Riboflavin	34 Mg	1 7 Mg	100
Vitamin B_6	40 Mg	2 Mg	100
Vitamin B_{12}	1 20 Mcg	6 Mcg	100
Niacin	4 Mg	20 Mg	100
Folic Acid	80 Mcg	4 Mg	100
Biotin	60 Mcg	3 Mg	100
Pantothenic Acid	2 Mg	10 Mg	100
Calcium	120 Mg	60 Gm	60
Phosphorus	70 Mg	35 Gm	35
Iron	3 6 Mg	18 Mg	100
Iodine	30 Mcg	15 Mg	100
Magnesium	30 Mg	150 Mg	35
Zinc	3 Mg	15 Mg	100
Copper	4 Mg	2 Mg	100
Manganese	8 Mg	4 Mg	***
Sodium	180 Mg	92 Gm	***
Potassium	170 Mg	86 Gm	***
Selenium	–	–	–
Chromium	–	–	–
Molybdenum	–	–	–

Approximate Analysis by Weight: Nutrimed (Vanilla Flavor)
Protein – 50%, Carbohydrate – 33%, Fat – 3%

*Typical Daily Serving
**For Adults and Children Four Or More Years Of Age
***U S RDA Has Not Been Established

INGREDIENTS: (Vanilla Flavor) Pasteurized egg white solids, sucrose, nonfat dry milk, calcium phosphate, natural and artificial flavors, magnesium oxide, sodium ascorbate, alpha tocopheryl acetate, niacin, ferrous sulfate, vitamin A palmitate, manganese sulfate, D-calcium pantothenate, pyridoxine hydrochloride, copper gluconate, vitamin D_2, thiamin, folic acid, biotin, riboflavin, potassium iodide, cyanocobalamin

NUTRIMED 420

Serving Size — One Packet (26 94 Grams, 93 Ounces)
Servings Per Box — 12
Calories Per Packet — 84

	Per Serving (One Packet)	Per Five Servings*	Percent Of U S RDA** (Five Servings)
Protein	14 Gm	70 Gm	150
Carbohydrate	6 Gm	32 Gm	***
Fat	2 Gm	1 Gm	***
Calories	84	420	***
Vitamin A	1.000 IU	5.000 IU	100
Vitamin D	80 IU	400 IU	100
Vitamin E	6 IU	30 IU	100
Vitamin C	18 Mg	90 Mg	150
Thiamin	45 Mg	2 25 Mg	150
Riboflavin	52 Mg	2 6 Mg	150
Vitamin B_6	60 Mg	3 0 Mg	150
Vitamin B_{12}	1 2 Mcg	6 0 Mcg	100
Niacin	4 Mg	20 Mg	100
Folic Acid	08 Mg	4 Mg	100
Biotin	90 Mcg	450 Mcg	150
Pantothenic Acid	2 Mg	10 Mg	100
Calcium	200 Mg	1 Gm	100
Phosphorus	124 Mg	62 Gm	60
Iron	3 6 Mg	18 Mg	100
Iodine	30 Mcg	150 Mcg	100
Magnesium	80 Mg	400 Mg	100
Zinc	3 Mg	15 Mg	100
Copper	4 Mg	2 Mg	100
Manganese	8 Mg	4 Mg	***
Sodium	190 Mg	95 Gm	***
Potassium	200 Mg	1 Gm	***
Selenium	30 Mcg	150 Mcg	***
Chromium	30 Mcg	150 Mcg	***
Molybdenum	60 Mcg	300 Mcg	***

Approximate Analysis by Weight: Nutrimed 420 (Chocolate Flavor)
Protein – 52%; Carbohydrate – 24% Fat – 1%

*Typical Daily Serving
**For Adults and Children Four Or More Years Of Age
***U.S. RDA Has Not Been Established

INGREDIENTS: (Chocolate Flavor) Pasteurized egg white solids, sucrose, calcium sodium caseinate, dutch cocoa (processed with alkali), nonfat milk, fructose, vegetable gums, calcium phosphate, artificial flavor, magnesium oxide, sodium ascorbate, aspartame,* ferrous sulfate, zinc sulfate, alpha tocopheryl acetate, vitamin A palmitate, niacin, copper gluconate, manganese sulfate, vitamin D_2, pyridoxine hydrochloride, thiamin, riboflavin, chromic acetate, sodium molybdate, biotin, folic acid, sodium selenite, potassium iodide, cyanocobalamin
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NATIONAL ACHIEVEMENT AWARDS

Each year during the Annual Meeting, the ADA presents awards to honor individuals who have made significant contributions to the ADA through their work in the area of diabetes research, education, and service. These awards are designed to recognize excellence in these fields and to stimulate continuing achievement in these areas. Winners will be selected in the following categories:

- Outstanding Scientific Achievement by an Investigator (sponsored by Eli Lilly and Co.)
- Outstanding Physician Educator in Diabetes (sponsored by the Upjohn Co.)
- Outstanding Clinician in Diabetes (sponsored by Pfizer/Roerig)
- Outstanding Contribution to Camping and Diabetes (sponsored by Becton Dickinson Consumer Products)
- Outstanding Contribution to Diabetes in Youth (sponsored by Boehringer Mannheim Diagnostics)
- Outstanding Health Professional Educator in Diabetes (sponsored by Ames Division, Miles Laboratories)
- Outstanding Affiliate Service (sponsored by Squibb-Novo)
- Youth Leadership Award (sponsored by the NutraSweet Co.)

By December 15, 1986, each affiliate is invited to nominate *one* person in each of the award categories. The following criteria apply to all nominations:

- Current committee members are not eligible for the particular awards that their committees are presenting.
- There should be no more than *one* nominee per affiliate for each award.
- Nominees *may not* be current ADA officers or have held office within the past five years.
- If a nominee is not selected for the award, his/her nomination will remain on file and receive consideration for an additional 2 years. To ensure that these candidates receive consideration each year, it is necessary to reconfirm their nomination by submitting updated supporting material annually.

The awards process provides an opportunity to acknowledge those individuals who play a major part in the accomplishment of our goals, and represents one of the highlights of the Annual Meeting. We look forward to each affiliate's participation in this endeavor.

Please submit all nominations to the ADA's National Service Center, 1660 Duke Street, Alexandria, VA 22314, to the attention of Elaine Wells.

Due to an inadvertent printing error the date in the National Achievement Awards ad in this issue is incorrect. The corrected version is printed below.

NATIONAL ACHIEVEMENT AWARDS

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- Outstanding Affiliate Service (sponsored by Squibb-Novo)
- Youth Leadership Award (sponsored by the NutraSweet Co.)

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4. A processing fee of $15.00 (U.S. dollars) must accompany each abstract submitted to the American Diabetes Association.

5. The processing fee payment must be in the form of a check or money order made payable to the American Diabetes Association, Inc. Purchase orders are unacceptable. Foreign payments must be prepaid in U.S. funds and drawn on a U.S. bank.

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8. Authors must adhere to the rule that scientific material presented at the Annual Meeting will not have been published or presented before at a major national or international meeting prior to the Annual Meeting of the American Diabetes Association.

9. Abstracts are limited to the space provided. Those exceeding the limit will not be accepted.

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12. Use of standard abbreviations is desirable (RBC, for example). This journal uses kg, g, mg, ml, L (liter), meq, m (meter), mosm (milliosmols), / (per), and % (percent). Place special or unusual abbreviations in parentheses after the full word, the first time it appears. Use numerals to indicate numbers, except to begin sentences.

13. Nonproprietary (generic) names should be used the first time a drug is mentioned, and typed in lower case letters. The first letter of proprietary names is always capitalized, e.g., aspirin (Bufferin).

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It was observed previously that glucosamine (20 mM) combined with theophylline (10 mM) causes

Cytochemical Localization of Adrenyl Cyclase and Cyclic AMP Phosphodiesterase in Rat Islets of Langerhans, S. L. HOWELL, S. A. KENNEDY, and MARGARET WHITFIELD, Sussex, England (Introduced by PAUL E. LACY,* St. Louis, Mo.)
Rates of insulin secretion may be altered by agents which affect the enzymes responsible for

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