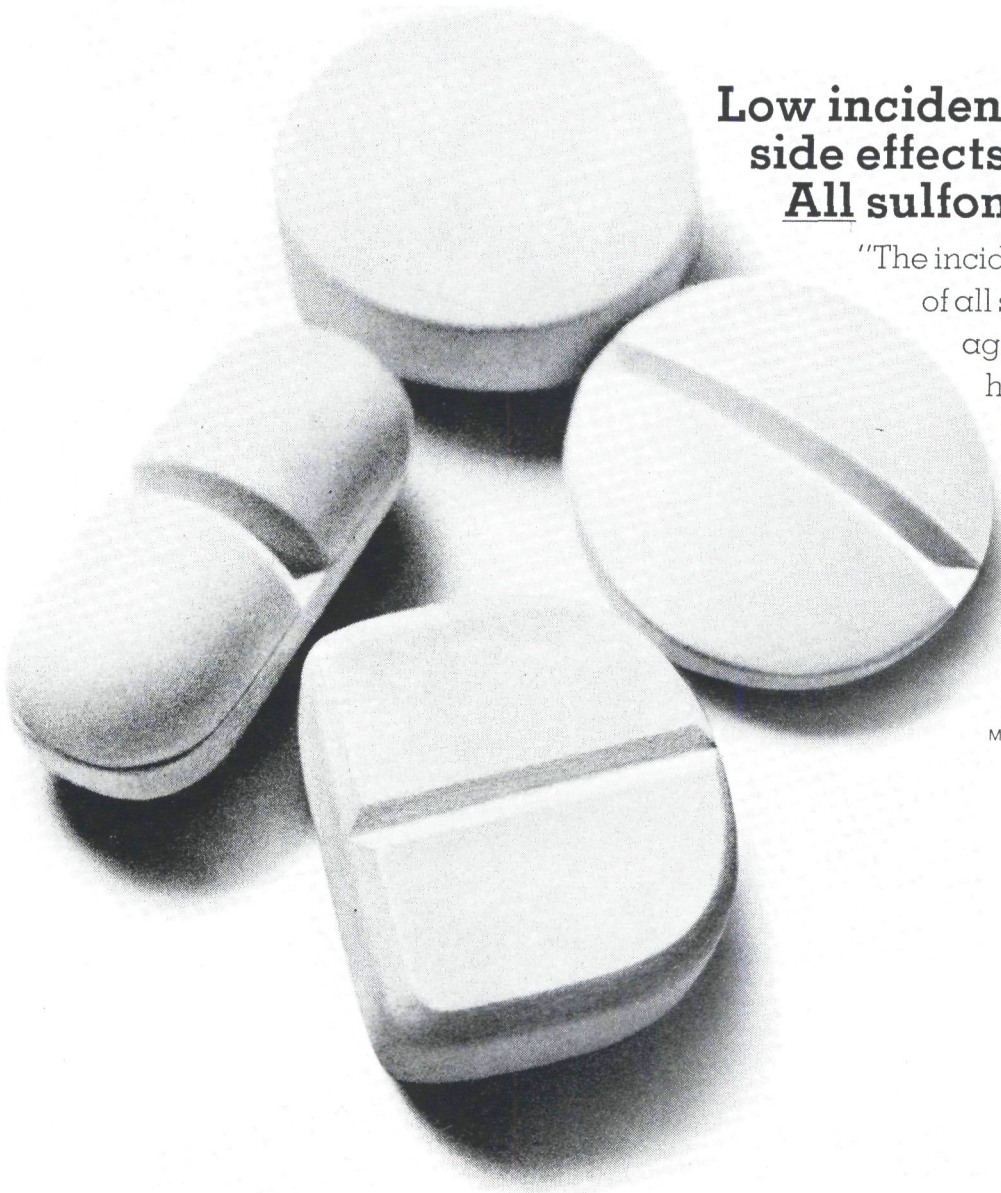
The Journal of the American Diabetes Association

diabetes

CONTENTS

DECEMBER 1967
Volume 16 • Number 12

Time to get down about the



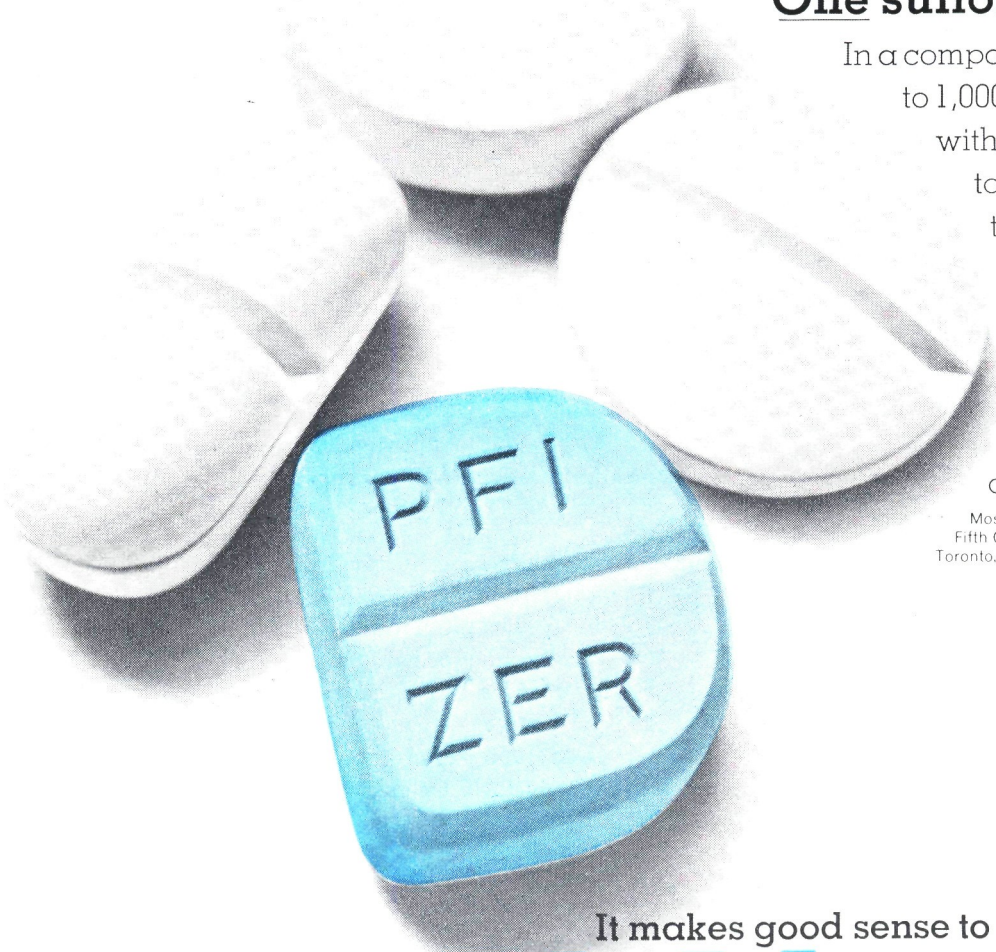
Low incidence of side effects? All sulfonylureas.*

"The incidence of side effects of all sorts [with all oral agents], including hypoglycemia, is very low—perhaps 3%. It may be less than that of insulin therapy and no greater than many drugs in current us

Beaser, S. B.: Oral therapy and diabetes mellitus, presented at Ann.M Minnesota Acad. Gen. Pract.. Minneapo Minn., Sept. 29-30, 1965.

*While the incidence of side effects with all sulfonylureas is low, they can be severe, with variations in severity in specific instances depending on the physiologic status of the patient and on the pharmacologic properties of the drug used. See brief summary for side effects with Diabinese.

to brass tacks sulfonylureas



Outstanding record of effectiveness? One sulfonylurea.

In a comparative study of close to 1,000 patients treated with chlorpropamide, tolbutamide and the nonsulfonylurea phenformin, "Chlorpropamide had the highest overall success rate and is the most effective drug tested."

Moss, J. M. et al.: Scientific Exhibit, Fifth Cong. Int. Diabetes Fed., Toronto, Canada, July 20-24, 1964.

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chlorpropamide

Pfizer

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The Journal of the American Diabetes Association

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Contributions are invited from practicing physicians, clinical and laboratory investigators, and others who have data of importance to offer in these fields. Manuscripts, if suitable, will be accepted providing that the text has not been printed elsewhere.

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The Editors will be pleased to consider for publication papers presented at the Annual Meeting of the American Diabetes Association.

Manuscript Specifications: The length of manuscripts (not including special articles or lectures) should be limited to 5,000 words, exclusive of illustrations, etc. Exceptions to this limitation may be made at the discretion of the Editors.

Communications for the "Brief Notes and Comments" department should not exceed 1,000 words except in unusual circumstances. Figures and tables in these brief communications should be limited to one of each, and references should not exceed twenty in number.

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References should be presented in the style illustrated by the following examples:

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For Books—Allen, Frederick M.: Studies Concerning Glycosuria and Diabetes. Cambridge, Harvard University Press, 1913, p. 461.

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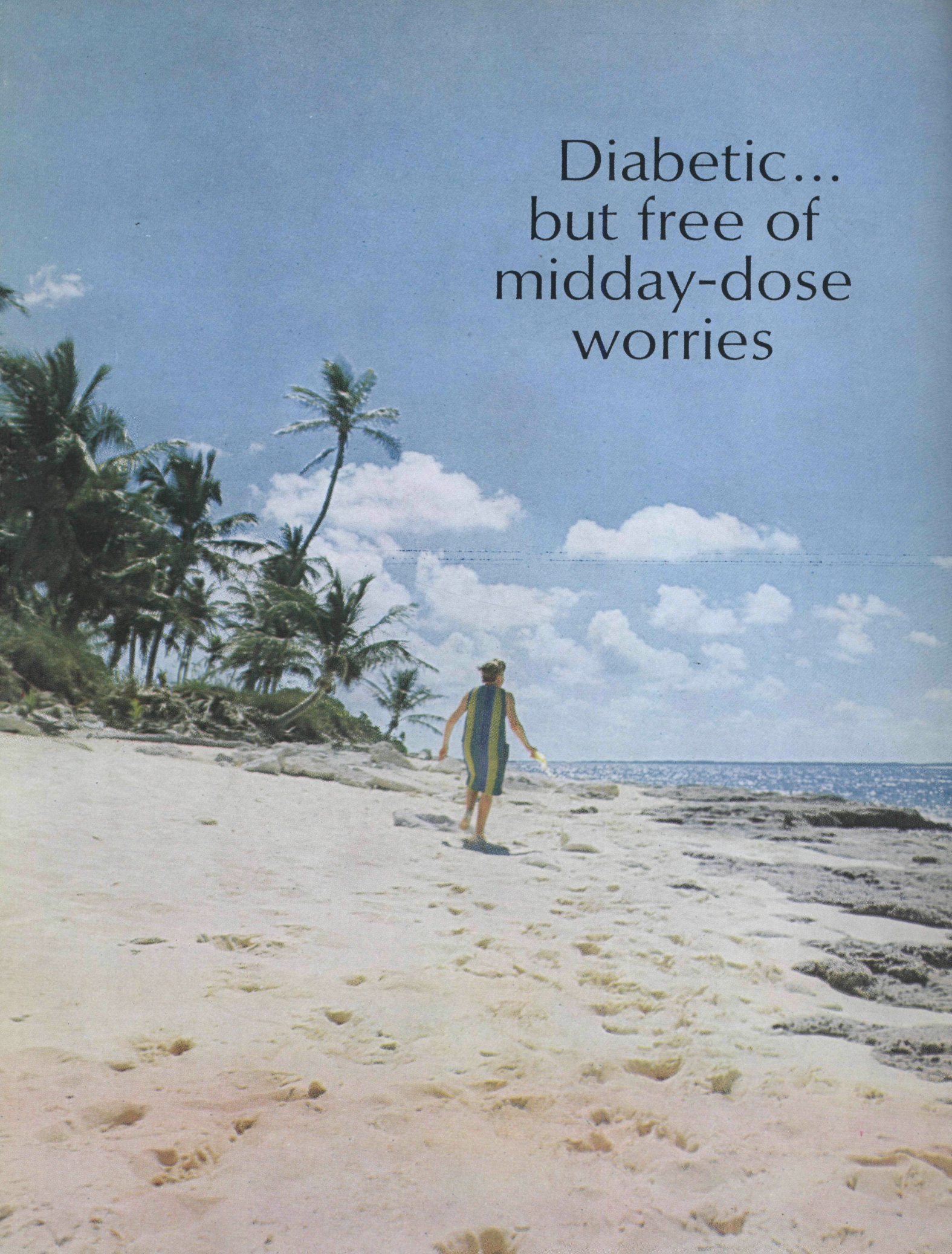

Diabetic...
but free of
midday-dose
worries

No matter where she is or what she's doing, she's free of the burden of taking tablets two or three times daily.

You can simplify the dosage regimen for many of your maturity-onset diabetics with Dymelor®.

One tablet a day usually provides daylong activity—not too short, not too long...

(and with little risk of hypoglycemia).

DYMELOR®
ACETOHEXAMIDE

Lilly

701477

(See next page for prescribing information.)

Once-daily dosage frees many maturity-onset diabetics from midday-dose worries

Description: Dymelor is an oral hypoglycemic sulfonylurea effective in stable diabetes mellitus. It is not an oral Insulin. Sulfonylurea drugs, as a group, lower blood sugar primarily by stimulating the release of endogenous insulin and secondarily by inhibiting release of glucose from liver glycogen.

Indications: Dymelor is indicated in stable, maturity-onset, nonketotic diabetes not controlled solely by diet. Given alone or with phenformin, it may result in resumption of response to oral therapy in certain patients who fail to be controlled initially or secondarily by other oral agents.

There is no contraindication to trial of Dymelor and Insulin in patients whose response to Insulin alone is unsatisfactory. However, since better control is rarely accomplished, the addition of a sulfonylurea should not be a substitute for increased attention to diet and other factors in control of diabetes.

Therapeutic trial is the only reliable method of patient selection. During trial of perhaps one week, absence of glycosuria and ketonuria, together with satisfactory control of hyperglycemia or maintenance of previously satisfactory control, indicates response. Appearance of glycosuria and ketonuria after withdrawal of Insulin and initiation of Dymelor suggests a need for dosage adjustment or possibly a poor response to Dymelor. In the absence of clinical improvement after dosage adjustment, therapy with Insulin is usually indicated.

Insulin is standard therapy during stress, complications, infections, and surgery. Dymelor can be continued, if tolerated, and Insulin given as supportive treatment.

Contraindications: Juvenile, brittle, unstable, or severe diabetes (on occasion, Dymelor may be given jointly with Insulin); diabetes complicated by acidosis, ketosis, coma, major surgery, infections, gangrene, or severe trauma; pregnancy; renal glycosuria; hyperglycemia associated with uremia; nondiabetic conditions.

Precautions: Inappropriate dosage may result in severe and prolonged hypoglycemia. Treat immediately with intravenous hypertonic glucose solution (10 to 50 percent), and continue until hypoglycemia subsides.

New diabetics starting on Dymelor must receive full instructions in the management of diabetes, prevention of complications, diet, personal hygiene, methods of testing for glycosuria and ketonuria, and the causes, signs, and prevention of hypoglycemia. A regular follow-up regimen with the physician is imperative.

Use Dymelor with care in patients with hepatic or renal impairment, acute alcoholism, adrenal or pituitary insufficiency, or porphyria; in those who are elderly, debilitated, malnourished, or semistarved; and in patients on antimicrobial sulfas, phenylbutazone, or probenecid. Administer thiazide diuretics with caution to patients on sulfonylurea therapy.

Very rarely, patients receiving sulfonylureas have experienced "disulfiram reactions" following ingestion of alcohol. Sulfonylureas may have an antithyroid effect.

Adverse Reactions: In the changeover from Insulin to Dymelor, hypoglycemia can occur while both drugs are given simultaneously. Follow dosage recommendations in package literature.

Occasional side-effects are G.-I. disturbances, including nausea and gastritis; cutaneous manifestations of hypersensitivity, characterized by maculopapular skin eruption or other dermatoses; headache, nervousness, and tingling, all possibly related to hypoglycemia; and elevations in alkaline phosphatase. Rarely, photosensitivity reactions, bleeding from the upper G.-I. tract, jaundice, thrombocytopenia, pancytopenia, agranulocytosis, leukopenia, hemolytic anemia, or aplastic anemia may occur.

Administration and Dosage: There can be no fixed dosage of Dymelor or Insulin. Daily dosage of Dymelor may range between 250 mg. and 1.5 Gm. No loading dose is required. Doses in excess of 1.5 Gm. daily are not recommended.

Patients on 1 Gm. or less daily can be controlled with once-daily dosage. Patients receiving 1.5 Gm. daily usually benefit from twice-daily dosage, given before the morning and evening meals. Dymelor may be used with phenformin as well as with Insulin.

For full prescribing information for new cases of diabetes, elderly diabetics, patients on Insulin, and those transferring from other oral agents, see package literature.

How Supplied: Tablets (scored), 250 and 500 mg., in bottles of 50, 200, and 500. [022167]

DYMELOR®
ACETOHEXAMIDE

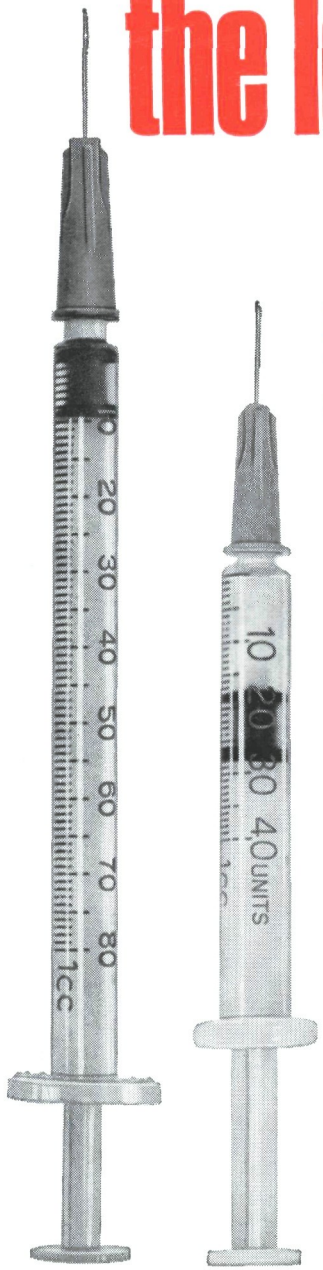
Lilly

701477

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.

the long....

and short....



of the matter is this:

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(whether long or short)
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Now available from B-D is a choice of sterile disposable insulin syringes: The standard diabetic preferred short-type or the new "long-type" for easier reading. Both types are available in either U-40 or U-80 single scales, and both are color-coded (red for U-40 and green for U-80) to aid in instant identification. With either the "long" or short type single scale syringe, your patients can now have comfort, safety and convenience for only pennies a day.

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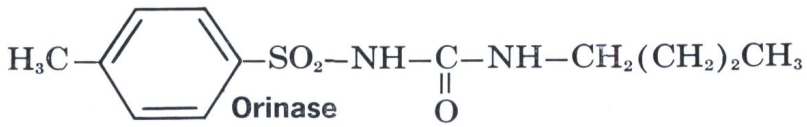
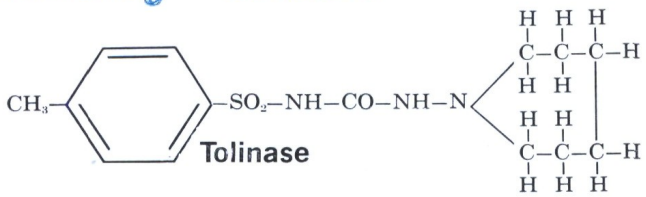
competitive or complementary?

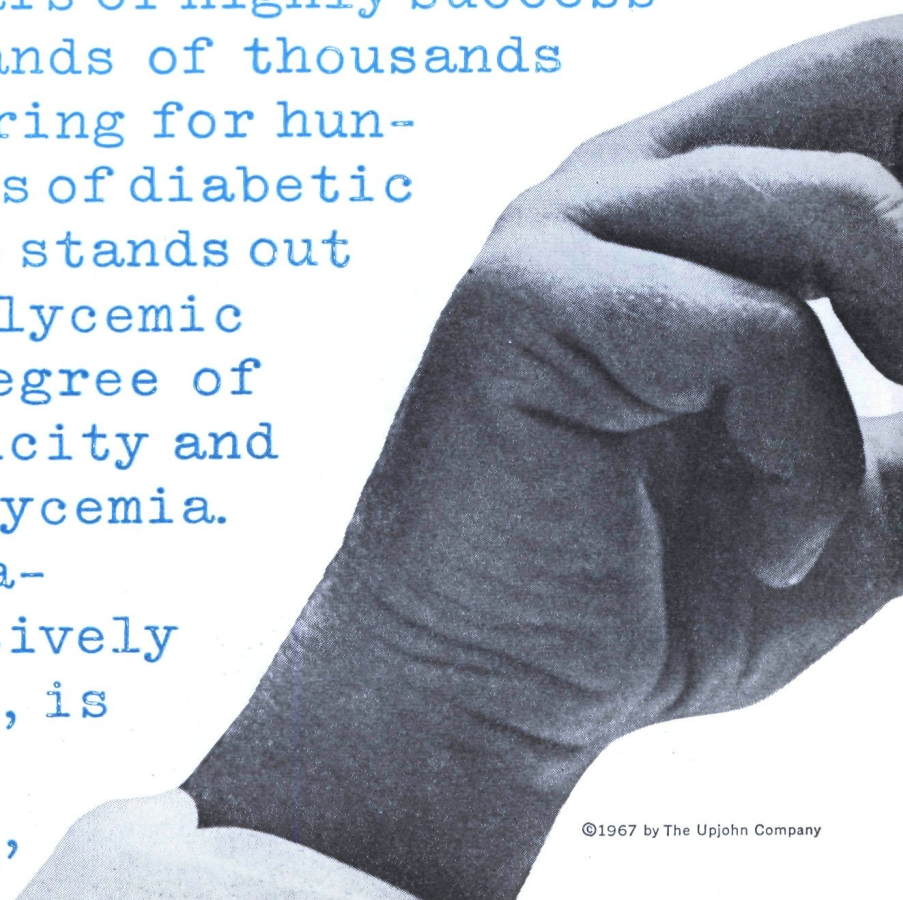


Upjohn makes two oral hypoglycemic agents—in fact, two sulfonylureas. They form a "therapeutic team." Between them, these drugs can cover the treatment needs for a majority of stable, maturity-onset diabetics.

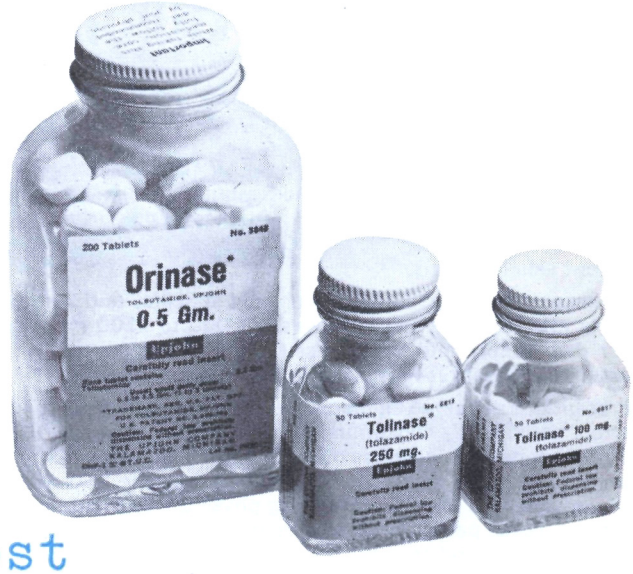


Orinase®(tolbutamide) is the "senior" sulfonylurea, widely used as an oral drug of choice in the newly diagnosed, adult patient. A standard of comparison for effectiveness and safety, Orinase has had more than nine years of highly successful use in the hands of thousands of physicians caring for hundreds of thousands of diabetic patients. Orinase stands out among oral hypoglycemic agents for its degree of freedom from toxicity and excessive hypoglycemia.

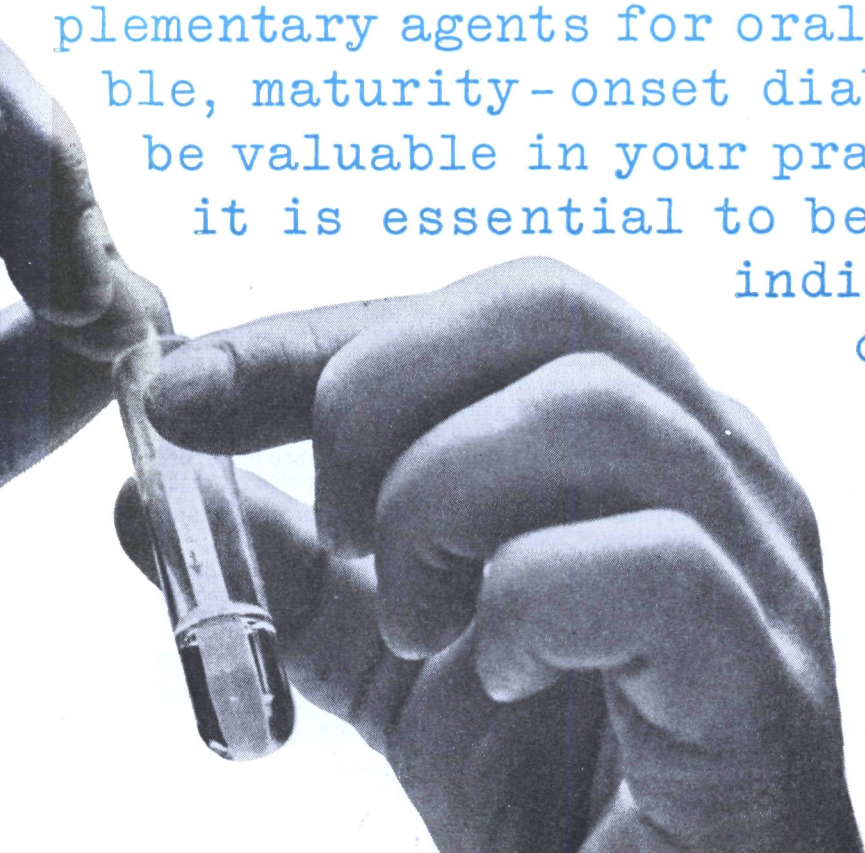
Tolinase® (tolazamide), a comparatively new sulfonylurea, is recommended for use in the stable,



maturity-onset diabetic who shows signs of unsatisfactory control or untoward reactions on a previously used oral agent. Of such difficult-to-control patients, about one-third can be expected to respond favorably to Tolinase, but this "salvage" rate may not be sustained and some patients will eventually fail. And, once-a-day dosage is effective dosage in most Tolinase-responsive patients—often a desirable attribute in switching (or starting) oral therapy.



In summary, Orinase and Tolinase are complementary agents for oral therapy in stable, maturity-onset diabetes. Both can be valuable in your practice. However, it is essential to be familiar with indications, limits of application, and criteria for selection of patients.



Please turn the page for more product information.

Orinase®
(tolbutamide, Upjohn)
0.5 Gm. tablets

Contraindications: As sole therapy in juvenile diabetes and unstable or brittle diabetes which require insulin; tolbutamide may be used adjunctively. Diabetes complicated by acidosis, ketosis or coma; severe renal insufficiency or persistent skin reactions.

Pregnancy Warning: Tolbutamide has feticidal and teratogenic effects in animals at doses of 1000 to 2500 mg./kg. per day. Safety and usefulness during pregnancy not yet established; not recommended in obstetrical patients.

Precautions: Observe all measures indicated with insulin. Instruct patient fully concerning his disease and consequences of dietary neglect, careless attitude, failure to follow instructions concerning weight control, exercise, hygiene, avoidance of infection and need for informing physician of any unusual feeling. Teach patient to recognize and counteract impending hypoglycemia and test for glycosuria and ketonuria. Acute complications such as fever, severe trauma, major surgery, severe diarrhea, nausea or vomiting may require supplemental insulin.
During insulin withdrawal, take care to avoid ketosis, acidosis and coma. Thiazide diuretics may aggravate diabetes resulting in increased tolbutamide requirement or loss of control; administer with caution to patients on tolbutamide. Careful observation and dosage adjustment essential in patients with impaired hepatic and/or renal function and debilitated, malnourished or semi-starved patients because of increased danger of severe hypoglycemia, which may require several days to correct.

Adverse Reactions: Severe hypoglycemia, which may mimic acute neurologic disorders such as cerebral thrombosis, is uncommon, but hepatic and/or renal disease, malnutrition, debility, advanced age, alcoholism, adrenal and pituitary insufficiency may predispose to it. The following may prolong or enhance the action of tolbutamide and increase the risk of hypoglycemia: insulin, phenformin, sulfonamides, oxyphenbutazone, phenylbutazone, bishydroxycoumarin, phenyramidol, salicylates, probenecid and monoamine oxidase inhibitors.
Tolbutamide, in high doses, is mildly goitrogenic in animals. In humans, reduction of RAI uptake after long use, without evidence of hypothyroidism or thyroid enlargement, has been reported. Photosensitivity reactions and disulfiram-like reactions have occurred after ingestion of alcohol. Crystalluria or other renal effects have not been observed. Jaundice rare; has cleared after drug withdrawal. In persistent jaundice, rule out carcinoma of pancreas or other obstructive lesions of the bile duct. Leukopenia, agranulocytosis, thrombocytopenia and hemolytic anemia have been reported. Other reactions usually mild—headache, nausea, epigastric fullness, heartburn—frequently disappear when dosage reduced or given in divided doses with meals. Allergic skin reactions (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) frequently disappear with continued administration; if persistent, discontinue Orinase. No effect on body weight.

Supplied: 0.5 Gm. scored tolbutamide tablets in bottles of 50, 200 and 500. JA67-6964-2

Tolinase®
(tolazamide, Upjohn)
250 mg. tablets

Contraindications: Do not use in juvenile or labile (brittle) diabetes or in diabetics undergoing surgery or those with infections, severe trauma, ketosis, acidosis or coma, or a history of repeated ketoacidosis. Do not use in patients with renal, hepatic or endocrine disease or uremia.
Safety and usefulness during pregnancy not established; not recommended in obstetrical patients.

Precautions: Observe all measures indicated with insulin or other sulfonylureas. Instruct patient fully concerning his disease, how to prevent and detect complications, and consequences of dietary neglect, careless attitude, importance of weight control, exercise, hygiene, avoidance of infection and need for informing physician of any unusual feeling. Teach patient to recognize and counteract impending hypoglycemia and how and when to test for glycosuria and ketonuria.
During insulin withdrawal, take care to avoid ketosis, acidosis and coma. Patients previously treated with phenformin plus sulfonylureas, being transferred to tolazamide, should be carefully observed during the transitional period. Thiazide diuretics may aggravate diabetes increasing sulfonylurea requirements, administer with caution to patients on tolazamide. Careful observation and dosage adjustment is essential in debilitated, malnourished or semi-starved patients, or patients not eating properly, because of the increased possibility of severe hypoglycemia, which may require corrective therapy. Advanced age, alcoholism, hepatic and renal disease, adrenal and pituitary insufficiency may also predispose to severe hypoglycemia which may mimic acute neurologic disorders such as cerebral thrombosis. The following may enhance or prolong the action of tolazamide and increase the risk of hypoglycemia: insulin, phenformin, sulfonamides, oxyphenbutazone, phenylbutazone, salicylates, probenecid and monoamine oxidase inhibitors.

Adverse Reactions: Hypoglycemia observed in 2.2% of cases. When mild to moderately severe, alleviated by reducing dose (see under Precautions for factors increasing danger of hypoglycemia). Less frequently, gastrointestinal—nausea, vomiting, gas; dermal reactions—rash, and pruritus. Others possibly not drug related—weakness, fatigue, dizziness, vertigo, malaise and headache.
Although not demonstrated to be drug related, leukopenia occurred in a few patients, but the count returned to normal with continued administration of drug.
Transient elevations in alkaline phosphatase values may be associated occasionally with sulfonylurea therapy, but may not be drug related.
Although disulfiram-like alcoholic flushes have not been reported with Tolinase, the possibility should be kept in mind.

Supplied: 100 mg. and 250 mg. compressed, scored tablets in bottles of 50.

For more detailed information on these products, see the package circular or consult your Upjohn representative.

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

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$500 Prize — for the best paper reporting original work, whether laboratory investigation or clinical observation.

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Medical students and physicians within five years after completion of medical school and bioscientists who are predoctoral or not more than two years postdoctoral are eligible to participate in the contests. (*Note:* A doctoral thesis should not be submitted.)

Prize winners, as well as those receiving honorable mention, will also be given a one year subscription to DIABETES, *The Journal of the American Diabetes Association.*

The papers will be judged on the basis of value of the material and manner of presentation. Any subject relating to diabetes and basic metabolic problems may be selected.

Manuscripts must not have been previously published. Appropriate papers will be considered for publication in DIABETES.

The deadline for *receipt* of entries is April 1, 1968. Manuscripts (and accompanying illustrations) should be submitted in triplicate (original and two copies), typewritten and double spaced. A letter of transmittal should accompany the manuscript specifying the contest being entered, and addressed to:

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