24-hour glycemic control can begin at the breakfast table.

When diet and exercise aren't enough, once-a-day MICRONASE provides 24-hour control of both postprandial and fasting blood glucose levels. The usual starting dosage, 2.5 mg to 5 mg once a day, should be taken with breakfast or the first main meal of the day. Some patients, particularly those receiving more than 10 mg daily, may have a more satisfactory response with twice-a-day dosage.

All sulfonylureas, including MICRONASE, can cause severe hypoglycemia. Proper patient selection, dosage, and instructions are important.

Please see adjacent page for brief summary of prescribing information.
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 1 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 diet alone or diet plus insulin. This warning is based on an interim analysis 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 Suppl 2): 747-836, 1976).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) showed an increase in cardiovascular mortality approximately 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 because of the increase in cardiovascular mortality, thus limiting the opportunity for the study to show any overall difference 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 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, 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 reviewed 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. 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.

ADVERSE REACTIONS:

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Studies in rats at doses up to 330 mg/kg/day for 18 months showed no carcinogenic effects. Glyburide is nonmutagenic when studied in the Salmonella mutagenesis assay and in the Drosophila melanogaster 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. The 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 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 has not been established.

ABRUPT REACTIONS: Hypoglycemia: See Precautions and Overdosage sections. Gastrointestinal Reactions: Cholestatic jaundice and hepatitis may occur rarely. MICRONASE Tablets should be discontinued if this occurs. Gastrointestinal disturbances (nausea, epigastric fullness, and heartburn) occurred in 1.8% of patients during clinical trials. They were the most commonly reported adverse reactions. They tend to be dose related and may disappear when dose is reduced. Liver abnormalities have been reported.

Drug Interactions: Allergic skin reactions, e.g., pruritus, erythema, urticaria, and morbilliform or maculopapular eruptions occurred in 1.5% of patients during trials. These may be transient and may disappear during 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. Cases of hyponatremia have been reported with glyburide and all other sulfonylureas, most often in patients who are on other medications or have medical conditions known to cause hyponatremia or increase release of antidiuretic hormone. (SIADH) secretion has been reported with certain other sulfonylureas, and it has been suggested that these sulfonylureas may augment the peripheral (antidiuretic) action of ADH and/or increase release of ADH.

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 level 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.

Maximum Dose: Daily doses of more than 20 mg are not recommended.

Dosage Interval: Once-a-day therapy is usually satisfactory. Some patients, particularly those receiving more than 10 mg/day, may have a more satisfactory response with twice-a-day dosage.

Specific Patient Populations: MICRONASE is not recommended for use in pregnancy or for use in children. In elderly patients, debilitated or malnourished patients, and patients with impaired renal or hepatic function, the initial and maintenance dosing should be conservative to avoid hypoglycemic reactions. (See Precautions Section)

For additional product information see your Upjohn representative.
Whether you’re treating, going to treat, or just thinking about treating HIV disease,
call: 1-800-HIV-INFO
to receive information on treatment programs for HIV disease.
Because safety cannot be taken for granted in H₂-antagonist therapy

**AXID**

nizatidine capsules

**Minimal potential for drug interactions**

Unlike cimetidine and ranitidine, AXID does not inhibit the cytochrome P-450 metabolizing enzyme system.

**Swift and effective H₂-antagonist therapy**

- Most patients experience pain relief with the first dose.
- Heals duodenal ulcer rapidly and effectively.
- Dosage for adults with active duodenal ulcer is 300 mg once nightly (150 mg b.i.d. is also available).

Hepatic — Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In most cases, there was marked elevation (≥ 500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was ≥ 2,000 IU/L. The incidence of elevated liver enzyme values overall and elevations of 3- to 10-fold the upper limit of normal, however, did not significantly differ from that in placebo patients. All abnormalities were reversible upon discontinuation of AXID.

Cardiovascular — In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in two individuals administered AXID and in three untreated subjects.

CNS — Rare cases of reversible mental confusion have been reported. AXID — Clinical pharmacology studies and controlled clinical trials showed no evidence of anticholinergic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. All abnormalities were reversible upon discontinuation of AXID.

Gastrointestinal — AXID and other H₂-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Because cross-sensitivity among this class has been observed, H₂-receptor antagonists should not be administered to those with a history of hyposensitivity to these agents. Rare episodes of hyperuricemia (rarely, gout) have been reported.

**References**

1. USP DI Update. September/October 1988, p 120.
1525 Endoprosthetic insertion for malignant obstructive jaundice: A retrospective review
KENNETH P. TARR, DO; JOSEPH C. ANDREWS, DO; LOUIS G. PUTZ, DO; PETER J. MOORTON, DO; DAVID F. KARIBO, DO; JONATHAN L. GOLDSMITH, DO
This article illustrates the role of interventional radiology in the nonsurgical, palliative therapy of malignant obstructive jaundice.

1543 Electrocardiographic criteria of left atrial enlargement: Do they correlate with atrial size?
BRIAN PAHLOW, DO; FRANK CORBALLY, DO; ALAN GEISLER, DO; JACQUELINE CATER, PhD;
This retrospective study compares the New York Heart Association criteria for left atrial enlargement with actual dimensions obtained by echocardiography. No significant correlation could be established between the two.

1547 Acquired immunodeficiency syndrome-associated malignancies
RICHARD L. THERIAULT, DO
As the number of patients with AIDS increases, recognition of signs and symptoms of disease becomes important. One manifestation of AIDS is the clinical presentation with malignant disease. This article reviews the types of malignancy associated with immune deficiency due to HIV and the clinical manifestations.

1553 Use of platelets in transfusion medicine
DANIEL B. BRUBAKER, DO
Platelet transfusions currently are overused in the United States. This article discusses platelet products and the indications, complications, and methods of monitoring platelet transfusions.

continued on page 1495
...on the consumer promotion of infant formula.

There is a development that undermines your control over the infant's diet and health, and that undermines breastfeeding—the advertisement of formulas directly to the mother through TV, magazines and mail.

On June 1, the President of the American Academy of Pediatrics sent a letter to all Fellows of the Academy reaffirming its stance against consumer advertising, and expressing concern that other formula companies might follow Nestlé/Carnation.

This concern was justified. On June 15, it was announced at a press conference that Mead Johnson/Bristol-Myers will be producing an infant formula to be sold and marketed under the Gerber label. Part of the program is a multimillion-dollar budget for advertising the formula directly to mothers via TV and print.

Speaking at the press conference, Gerber Products Division President Robert L. Johnston, Jr., said that Gerber was entering the market because it had, "identified significant changes in usage that convinced us the timing was right...."

"First," he said, "there is a rapid decline in breast-feeding after mothers leave the hospital." And, "...parent decision regarding baby formula brand selection has grown...."

The irony is inescapable and appalling. In other words, because breastfeeding is declining, more infant formulas should be promoted to the mother. In other words, because some mothers are making feeding decisions on their own, even more mothers should follow suit.

When Nestlé/Carnation entered the marketplace and, again, when Mead Johnson/Bristol-Myers joined with Gerber, we reexamined the Ross philosophy of promoting SIMILAC® Infant Formulas. The result of our deliberations was an even deeper resolve to support the doctor/patient relationship.

Our philosophy remains unchanged. Ross Laboratories has no plans to resort to direct consumer advertising for SIMILAC and our other infant formula products.

We will continue as an ally of health care professionals by supporting your prerogative to prescribe and recommend products as training and experience dictate.

We stand behind you.

Richard W. Gast
Hyperthyroidism with an FSH- and TSH-secreting pituitary adenoma

JOHN BERMINGHAM, DO; LOUIS C. HAENEL, DO

Secondary hyperthyroidism may not be as rare as one was once led to believe. Making the correct diagnosis of secondary hyperthyroidism is imperative because treatment and prognosis are totally different from those of primary hyperthyroidism. This report documents the rare occurrence of a combined follicle-stimulating hormone- and thyroid-stimulating hormone-secreting pituitary adenoma.