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Fecal occult blood testing devices

Intense stable blue reactions in the Hemocult® Sensa™ test allow for enhanced readability and detection of fecal occult blood. Single slide testing for hospital use or Dispensapak™ Plus kits for home application are available. The latter features an easier collection method, and moisture-odor proof, postal approved mailing pouches for return to laboratory or office for processing.

Another test, the HemeSelect™ kit also permits patient home sampling. Because there are no special diet restrictions needed before use, the test has a low false-negative rate.

For more information on any of these kits, contact SmithKline Diagnostics, Inc, 225 Baypointe Pkwy, San Jose, CA 95134-1622, (408) 435-2660.

Added Doppler features

The pen-sized Mascot vascular Doppler can be connected to a standard electrocardiographic system for permanent diagnostic documentation of deep vein thrombosis and vascular-related impotence, among other such conditions.

Furthermore, an oversized clip on the back of the Pocket-Dop II handheld Doppler attaches to belt or pocket for easier access. Interchangeable vascular and obstetrical probes are standard equipment with this Doppler.

For more information on these products, contact Imex Medical Systems, Inc, 6355 Joyce Dr, Golden, CO 80403 (800) 525-2519 or (303) 431-9400.

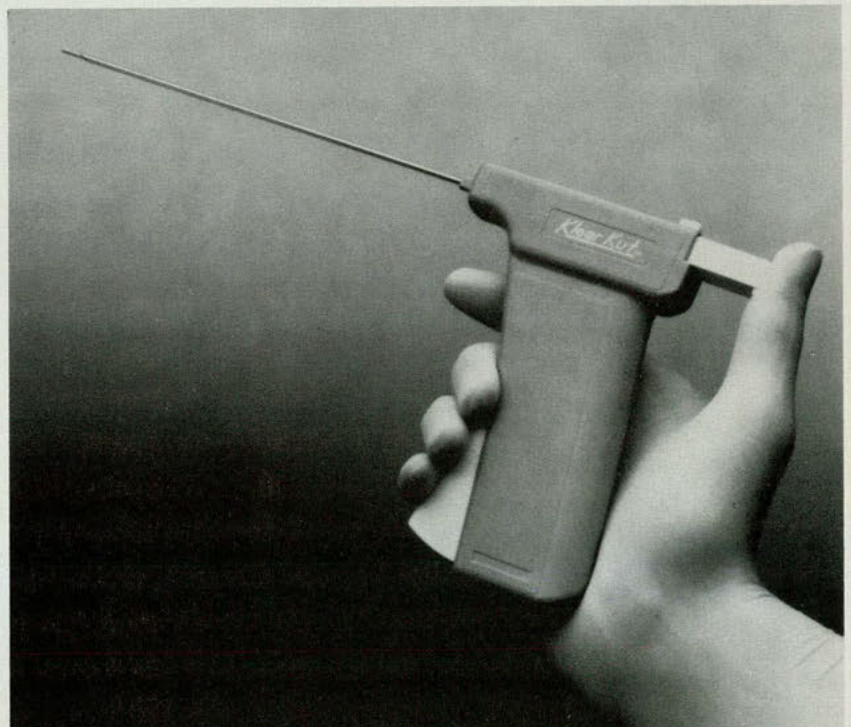
Biopsy cutting device

One-handed operation and a built-in contoured handle are the main features of the Klear Kut™ disposable soft tissue cutting device. The sharp, beveled stylet point permits penetration with minimum trauma to organs or tissue. A needle guard for stylet and cannula protect them from

damage and prevent user injury. The 14 gauge needles are available in 4 1/2- and 6-inch sizes. For more information, contact Perry Group, Ltd, 148-D Chesterfield Industrial Blvd, St Louis 63005, (314) 532-2055.

Cough medicine for seniors

Intended for the older adult, Naldecon Senior DX™ and Naldecon Senior EX™ cough preparations contain no decongestants, antihistamines, sugar, or alcohol. The former features the expectorant guaifenesin (200 mg/5 mL). In addition to the same level of guaifenesin, the latter cough syrup contains dextromethorphan (15 mg/5 mL) a non-narcotic antitussive comparable to codeine in efficacy but without its associated side effects. Both nonprescription products come packaged in easy-



TIMING IS



EVERYTHING



Effective control time and time again¹

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

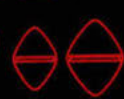
Insulin when it's needed

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

Timed to minimize risks

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

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

Glucotrol[®]
(glipizide) 5-mg and 10-mg
Scored Tablets 

**SYNCHRONIZED
SULFONYLUREA THERAPY**



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

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

Reference:

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

GLUCOTROL® (glipizide) Tablets

Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

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 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 GLUCOTROL 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: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur.

Hypoglycemia: All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of 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 or people 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: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

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

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering 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.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including non-steroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hyperglycemia and may lead to loss of control, including 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. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly fetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This fetotoxicity has been similarly noted with other sulfonylureas, such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well-controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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 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. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Cholestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL. If skin reactions persist, the drug should be discontinued. Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

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

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have each been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemia 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 that 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. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL (glipizide), dialysis is unlikely to be of benefit.

DOSE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL; in general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100; 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-66) Bottles of 100.

CAUTION: Federal law prohibits dispensing without prescription.

More detailed professional information available on request.

to-open bottles with instructions printed in large type for easier reading. For more information, contact Bristol-Myers, 2400 Lloyd Expressway, Evansville, IN 47721, (812) 429-5000.

Medical records software

Centralized, continuous records for patients as well as performed procedures can be maintained using CaseLog™ medical software. Admissions through discharge and follow up procedures are summarized by major classification. The menu-driven program has no limit on the number of patients, procedures, or locations. It employs user-defined codes in addition to standard CPT and ICD-9 codes and automatic selection features. The software is compatible with any IBM XT/AT or 384K RAM and hard disk drive. For more information, contact PATH Systems™, 5600-B Scotts Valley Dr, Scotts Valley, CA 95066, (408) 438-PATH.

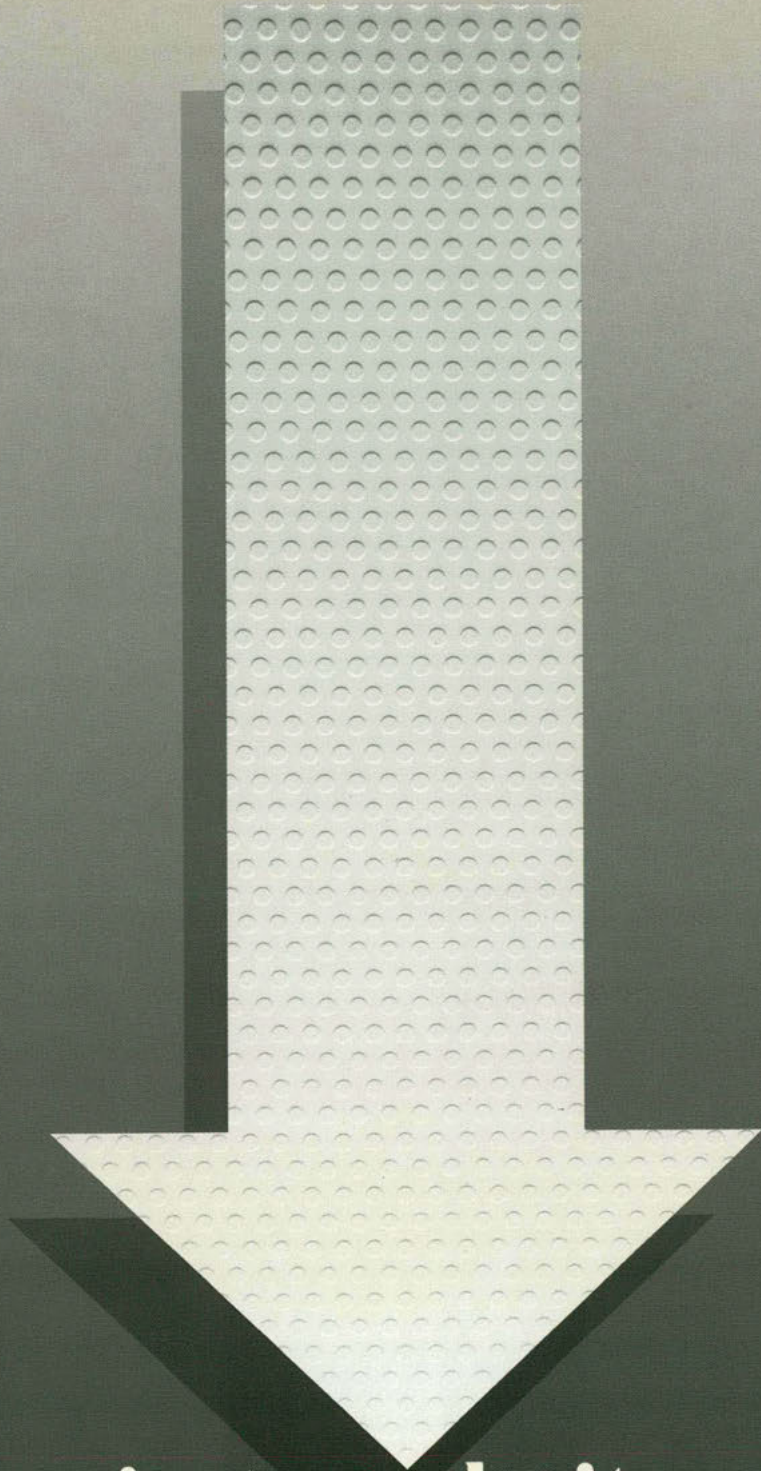
Intrasound pain reliever

The Pulsor Intrasound device uses sound waves of approximately 120 Hz to relax muscle tissues and improve blood circulation. This handheld unit features interchangeable pointed and mushroom-shaped nose tips and an adjustable head and collar. For more information, contact GMG Enterprises, Inc, PO Box 5274, Lake Wylie, SC 29710, (803) 831-2680.

Enzyme immunoassay kits

Precise serum values without automated instrumentation can be determined with the EZ-Bead Theophylline enzyme immunoassay kit. With an antibody coated 1/4-inch bead, the kit needs no reagent reconstitution or centrifugation and has a 45-minute incubation at room temperature. It requires one single point calibration that uses a stored standard curve. The kit has a correlation coefficient to radioimmunoassay of 0.96, negligible cross-reactivity to caffeine

**After 11 years of helping people
lower their cholesterol,**



we've just made it easier...

Introducing

LORELCO[®]

PROBUCOL 500[™]

500 mg tablets

New convenient dosage strength

- excellent patient compliance
- dependable efficacy
- well-established side effects profile*

**Reduces elevated cholesterol levels
by up to 27%**

one tablet b.i.d. with meals

Lorelco is indicated for the reduction of elevated serum cholesterol in patients with primary hypercholesterolemia, as an adjunct to diet.

 **a.m. meal**
p.m. meal

*Lorelco is not an innocuous drug and strict attention should be paid to the INDICATIONS, CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS.

Merrell Dow

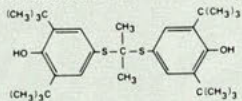
(Prescribing Information appears on next page.)



Lorelco® Tablets (probuco)

CAUTION: Federal law prohibits dispensing without prescription.

DESCRIPTION: Lorelco (probuco) film-coated tablets for oral administration contain 250 mg or 500 mg of probuconol per tablet. Each tablet also contains as inactive ingredients: corn starch, ethylcellulose, glycerin, hydroxypropyl cellulose, hydroxypropyl methylcellulose 2910, iron oxide, lactose, magnesium stearate, microcrystalline cellulose, polysorbate 80, talc, and titanium dioxide. Lorelco is an agent for the reduction of elevated serum cholesterol. The chemical name is 4,4'-[(1-methyl-ethylidene)bis(thio)]bis[2,6-bis(1,1-dimethyl-ethylphenyl)]]. Its chemical structure does not resemble that of any other available cholesterol-lowering agent. It is lipophilic.



CLINICAL PHARMACOLOGY: Lorelco lowers total serum cholesterol and has relatively little effect on serum triglycerides. Patients responding to probuconol exhibit a decrease in low-density lipoprotein (LDL) cholesterol. Cholesterol is reduced not only in the LDL fraction, but also in the high-density lipoprotein (HDL) fraction with proportionately greater effect on the high-density portion. Epidemiologic studies have shown that both low HDL-cholesterol and high LDL-cholesterol are independent risk factors for coronary heart disease. The risk of lowering HDL-cholesterol while lowering LDL-cholesterol remains unknown. There is little or no effect reported on very low-density lipoprotein (VLDL).

Studies on the mode of action of Lorelco indicate that it increases the fractional rate of LDL catabolism. This effect may be linked to the observed increased excretion of fecal bile acids, a final metabolic pathway for the elimination of cholesterol from the body. Lorelco also exhibits inhibition of early stages of cholesterol biosynthesis and slight inhibition of absorption of dietary cholesterol. There is no increase in the cyclic precursors of cholesterol, namely desmosterol and 7-dehydrocholesterol. On this basis, it is concluded that Lorelco does not affect the later stages of cholesterol biosynthesis.

Absorption of Lorelco from the gastrointestinal tract is limited and variable. When it is administered with food, peak blood levels are higher and less variable. With continuous administration in a dosage of 500 mg b.i.d., the blood levels of an individual gradually increase over the first three to four months and thereafter remain fairly constant. In 116 patients treated with Lorelco, levels observed after seven years of treatment in 40 patients yielded an average value of 21.5 ± 16.5 mcg/mL ($\pm$ S.D.) ranging to 62.0 mcg/mL. In a separate study in eight patients, blood levels averaged 19.0 mcg/mL at the end of 12 months of treatment. Six weeks after cessation of therapy, the average had fallen by 60%. After six months, the average had fallen by 80%.

In December 1984, a National Institutes of Health Consensus Development Conference Panel concluded that lowering definitely elevated blood cholesterol levels (specifically blood levels of LDL-cholesterol) will reduce the risk of heart attacks due to coronary heart disease. The effect of probuconol-induced reduction of serum cholesterol or triglyceride levels, or reduction of HDL-cholesterol levels on morbidity or mortality due to coronary heart disease has not been established.

INDICATIONS AND USAGE: Serious animal toxicity has been encountered with probuconol. See WARNINGS and ANIMAL PHARMACOLOGY AND TOXICOLOGY sections. Probuconol is not an innocuous drug and strict attention should be paid to the INDICATIONS, CONTRAINDICATIONS, and WARNINGS.

Drug therapy should not be used for the routine treatment of elevated blood lipids for the prevention of coronary heart disease. Dietary therapy specific for the type of hyperlipidemia is the initial treatment of choice. Excess body weight may be an important factor and should be addressed prior to any drug therapy. Physical exercise can be an important ancillary measure. Contributory disease such as hypothyroidism or diabetes mellitus should be looked for and adequately treated. The use of drugs should be considered only when reasonable attempts have been made to obtain satisfactory results with nondrug methods. If the decision ultimately is to use drugs, the patient should be instructed that this does not reduce the importance of adhering to diet.

The selection of patients for cholesterol-lowering drug therapy should take into account other important coronary risk factors such as smoking, hypertension, and diabetes mellitus. Consideration should be given to the efficacy, safety, and compliance factors for each of the cholesterol-lowering drugs prior to selecting the one most appropriate for an individual patient.

Lorelco may be indicated for the reduction of elevated serum cholesterol in patients with primary hypercholesterolemia (Types IIa and IIb hyperlipoproteinemia),² whose elevated LDL-cholesterol has not responded adequately to diet, weight reduction, and control of diabetes mellitus. Lorelco may be useful to lower elevated LDL-cholesterol that occurs in those patients with combined hypercholesterolemia and hypertriglyceridemia (Type IIb) due to elevation of both LDL and VLDL, but it is not indicated where hypertriglyceridemia is the abnormality of most concern. After establishing that the elevation in serum total cholesterol represents a primary lipid disorder, it should be determined that patients being considered for treatment with Lorelco have an elevated LDL-cholesterol as the cause for an elevated total serum cholesterol. This may be particularly relevant for patients with elevated triglycerides or with markedly elevated HDL-cholesterol values, where non-LDL fractions may contribute significantly to total cholesterol levels without apparent increase in cardiovascular risk. In most patients, LDL-cholesterol may be estimated according to the following equation:

$$\text{LDL-cholesterol} = \text{Total cholesterol} - [(0.16 \times \text{triglycerides}) + \text{HDL-cholesterol}]$$

When total triglycerides are greater than 400 mg/dL, this equation is less accurate. In such patients, LDL-cholesterol may be obtained by ultracentrifugation.

It is not always possible to predict from the lipoprotein type or other factors which patients will exhibit favorable results. Lipid levels, including HDL-cholesterol, should be periodically assessed.

The effect of probuconol-induced reduction of serum cholesterol or triglyceride levels, or reduction of HDL-cholesterol levels on morbidity or mortality due to coronary heart disease has not been established.

CONTRAINDICATIONS: (See also WARNINGS and PRECAUTIONS.) Lorelco is contraindicated in patients who are known to have a hypersensitivity to it. Lorelco is contraindicated in patients with evidence of recent or progressive myocardial damage or findings suggestive of serious ventricular arrhythmias or with unexplained syncope or syncope of cardiovascular origin.

Lorelco is contraindicated in patients with an abnormally long QT interval.

WARNINGS: SERIOUS ANIMAL TOXICITY HAS BEEN ENCOUNTERED WITH PROBUCONOL IN RHESUS MONKEYS FED AN ATHEROGENIC DIET AND IN BEAGLE DOGS. (See ANIMAL PHARMACOLOGY AND TOXICOLOGY SECTION.)

Prolongation of the QT interval can occur in patients on Lorelco. Serious arrhythmias have been seen in association with an abnormally long QT interval in patients on Lorelco alone and in patients on Lorelco and a concomitant antiarrhythmic drug. The following precautions are deemed prudent:

1. Patients should be advised to adhere to a low cholesterol, low fat diet at the start of treatment with Lorelco and throughout the treatment period.
2. An ECG should be done prior to starting treatment and repeated at appropriate intervals during treatment. If an abnormally long QT interval is observed, the possible benefits and risks should be carefully considered before making a decision to continue Lorelco.
- Lorelco therapy should be discontinued or not started if the QT interval at an observed heart rate on a resting ECG is persistently more than one of the values listed below:

Observed Heart Rate (beats/min)	QT Interval in sec (15% above the upper limit of normal)*	
	Males	Females
40	0.56	0.58
50	0.52	0.53
60	0.49	0.50
70	0.46	0.47
80	0.43	0.44
86	0.42	0.43
92	0.40	0.41
100	0.39	0.40
109	0.37	0.38
120	0.36	0.36
133	0.34	0.35

*Values calculated from Burch GE, Winsor T. A primer of electrocardiography. Philadelphia, PA: Lea and Febiger; 1958; p. 272 (Table 6).

3. Patients developing unexplained syncope or syncope of cardiovascular origin should have Lorelco therapy discontinued and should have ECG surveillance.
4. Drugs that prolong the QT interval are more likely to be associated with ventricular tachycardia after:
 - a. An increase in the dose of the drug.
 - b. Addition of a second drug that prolongs the QT interval (including tricyclic antidepressants, class I and III antiarrhythmics, and phenothiazines).
 - c. Hypokalemia or hypomagnesemia.
 - d. Severe bradycardia due to intrinsic heart disease or drug effects on the atrial rate (beta-blockers) or AV block (digoxin).
 - e. Development of recent or acute myocardial infarction, ischemia, or inflammation.

The use of Lorelco in patients receiving any of these drugs should be based on the conclusion that alternate methods of hypercholesterolemia therapy are either ineffective or not tolerated, and the potential benefits of cholesterol lowering outweigh the risk of serious arrhythmia.

The following conditions should be resolved or corrected prior to initiation of therapy with Lorelco:

- a. Hypokalemia
- b. Hypomagnesemia
- c. Severe bradycardia due to intrinsic heart disease or drug effects on the atrial rate (beta-blockers) or AV block (digoxin).
- d. Recent or acute myocardial infarction, ischemia, or inflammation.

PRECAUTIONS

General: Before instituting therapy with Lorelco, adequate baseline studies should be performed to determine that the patient has no preexisting elevated total and LDL-cholesterol levels representing a primary lipid disorder, and that the increased cholesterol is not due to secondary conditions such as hypothyroidism, poorly controlled diabetes mellitus, obstructive liver disease, nephrotic syndrome, or dysproteinemias. Serum lipid levels, including HDL-cholesterol, should be determined after an overnight fast before treatment, during an adequate trial of diet and weight reduction therapy prior to addition of drug therapy, and periodically during combined diet and drug therapy, including assessment during the first several months of drug treatment. A favorable trend in levels should be evident during the first three to four months of administration of Lorelco, and if satisfactory lipid alteration is not achieved, the drug should be discontinued. Lorelco lowers serum total and LDL-cholesterol, and also lowers HDL-cholesterol in most patients with elevated LDL-cholesterol. Epidemiologic studies within hypercholesterolemic populations have shown that serum HDL-cholesterol is an independent, inversely correlated, risk factor for coronary heart disease (see CLINICAL PHARMACOLOGY). Human studies which will attempt to confirm or deny the hypothesis that Lorelco-induced alteration in HDL-cholesterol affects cardiovascular risk are currently under evaluation. It is not known whether drug-induced reduction of serum HDL-cholesterol will affect cardiovascular risk since no long-term, controlled clinical trials of Lorelco for the prevention of coronary heart disease, similar to the LRC-CPPT (see CLINICAL STUDIES), have been performed. The probable benefits obtained from LDL-cholesterol reduction must be weighed against the possible risk of a reduction in HDL-cholesterol when assessing the response of each patient receiving Lorelco treatment. If satisfactory lipid alteration is not achieved, the drug should be discontinued.

Information for Patients: The patient should be instructed to adhere to a prudent diet. Females should be cautioned against becoming pregnant for at least six months after discontinuing Lorelco and should not breast-feed their infants during therapy with Lorelco.

Laboratory Tests: The physician should schedule periodic blood lipid determinations and periodic ECGs. (See WARNINGS.)

Elevations of the serum transaminases (SGOT, SGPT), bilirubin, alkaline phosphatase, creatine phosphokinase, uric acid, blood urea nitrogen, and blood glucose above the normal range were observed on one or more occasions in various patients treated with Lorelco. Most often these were transient and/or could have been related to the patient's clinical state or other modes of therapy. Although the basis for the relationship between Lorelco and these abnormalities is not firm, the possibility that some of these are drug related cannot be excluded. In controlled trials, the incidence of abnormal laboratory values was no higher in the patients treated with Lorelco than in the patients who received placebo. If abnormal laboratory tests persist or worsen, if clinical signs consistent with the abnormal laboratory tests develop, or if systemic manifestations occur, Lorelco should be discontinued.

Drug Interactions: The addition of clofibrate to Lorelco is not recommended, since the lowering effect on mean serum levels of either LDL or total cholesterol is generally not significantly additive and, in some patients, there may be a pronounced lowering of HDL-cholesterol.

Neither oral hypoglycemic agents nor oral anticoagulants affect the effect of Lorelco on serum cholesterol. The dosage of these agents is not usually modified when given with Lorelco.

Monkeys fed a high fat, high cholesterol diet admixed with probuconol exhibited serious toxicity. (See WARNINGS and ANIMAL PHARMACOLOGY AND TOXICOLOGY sections.) Prolongation of the QT interval can occur in patients on Lorelco and serious arrhythmias have been seen in association with an abnormally long QT interval in patients on Lorelco. The addition of a second drug that prolongs the QT interval (including tricyclic antidepressants, class I and III antiarrhythmics, and phenothiazines) may increase the risk of serious arrhythmia. (See CONTRAINDICATIONS AND WARNINGS.)

Carcinogenesis, Mutagenesis, Impairment of Fertility

In chronic studies of two years' duration in rats, no toxicity or carcinogenicity was observed. These results are consistent with the lack of any adverse effect on fertility and the negative findings in tests for mutagenic activity in rats.

Pregnancy

Teratogenic Effects

Pregnancy—Category B: Reproduction studies have been performed in rats and rabbits at doses up to 50 times the human dose, and have revealed no evidence of impaired fertility or harm to the fetus due to probuconol. There are, however, no adequate animal or 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. Furthermore, if a patient wishes to become pregnant, it is recommended that the drug be withdrawn and birth control procedures be used for at least six months because of persistence of the drug in the body for prolonged periods. (See CLINICAL PHARMACOLOGY.)

Labor And Delivery: The effect of Lorelco on human labor and delivery is unknown.

Nursing Mothers: It is not known whether this drug is excreted in human milk, but it is likely, since such excretion has been shown in animals. It is recommended that nursing not be undertaken while a patient is on Lorelco.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Gastrointestinal

diarrhea or loose stools, flatulence, abdominal pain, nausea, vomiting, indigestion, gastrointestinal bleeding

Cardiovascular

prolongation of the QT interval on ECG, syncope, ventricular arrhythmias (ventricular tachycardia, torsades de pointes, ventricular fibrillation), sudden death

Neurologic

headache, dizziness, paresthesia, insomnia, tinnitus, peripheral neuritis

Hematologic

eosinophilia, low hemoglobin and/or hematocrit, thrombocytopenia

Dermatologic

rash, pruritus, ecchymosis, petechiae, hyperhidrosis, itchy sweat

Genitourinary

impotency, nocturia

Ophthalmic

conjunctivitis, tearing, blurred vision

Endocrine

enlargement of multinodular goiter

Idiosyncrasies

observed with initiation of therapy and characterized by dizziness, palpitations, syncope, nausea, vomiting and chest pain

Other

diminished sense of taste and smell, anorexia, angioneurotic edema

DRUG ABUSE AND DEPENDENCE: No evidence of abuse potential has been associated with Lorelco, nor is there evidence of psychological or physical dependence in humans.

OVERDOSAGE: There is a single report of a 15-kg, three-year-old, male child who ingested 5 g of probuconol. Emesis was induced by ipecac. The child remained well, apart from a brief episode of loose stools and flatulence. No specific information is available on the treatment of overdosage with Lorelco and no specific antidote is available. Probuconol is not known to be dialyzable. Symptoms of overdosage have been shown in non-identifiable acute toxicity in mice and rats. In these animals the LD₅₀ (oral) is in excess of 5 g/kg of body weight.

DOSEAGE AND ADMINISTRATION: For adult use only. The recommended and maximal dose is 1000 mg daily given in two divided doses of 500 mg each (two 250 mg tablets or one 500 mg tablet) with the morning and evening meals.

HOW SUPPLIED: 250 mg round, white, film-coated tablets imprinted with either the DOW diamond trademark over the code number 51 or LORELCO 250. Bottles of 120 (NDC 0068-0051-52)

500 mg capsule-shaped, white, film-coated tablets, marked LORELCO 500. Bottles of 100 (NDC 0068-0053-61)

Keep well closed. Store in a dry place. Avoid excessive heat. Dispense in well-closed light-resistant containers with child-resistant closure.

ANIMAL PHARMACOLOGY AND TOXICOLOGY: In rhesus monkeys, administration of probuconol in diets containing unusually high amounts of cholesterol and saturated fat resulted in the death of four of eight animals after several weeks. Premortem syncope was frequently observed and was associated with a pronounced prolongation of the QT intervals (30 to 50% longer than that observed in untreated monkeys). Serum levels of probuconol greater than 20 mcg/mL were generally associated with some prolongation in the QT interval in the cholesterol-fed monkey. A 75 mcg or greater increase in QT interval from control values was usually seen at 4 mcg/mL and above. Blood levels in humans receiving Lorelco average approximately 20 mcg/mL and not uncommonly reach levels of 40 mcg/mL and higher. Rhesus monkeys fed normal (low fat) chow and receiving probuconol three to thirty times the human dose equivalent achieved blood levels only one-third those of many human subjects. No adverse effects were detected in these monkeys over an eight-year period of continuous drug administration. In another study in rhesus monkeys, an atherogenic diet was fed for two years and daily treatment with probuconol, separated in time from the atherogenic diet, was carried out during the second year. Serum probuconol levels ranged from 20 to 50 mcg/mL, in five of ten monkeys, and less in the remaining animals. Marked prolongation of the QT interval in the ECG or syncopeal behavior was never observed over the entire one-year treatment period. Regression of gross aortic lesions comparable to that observed in a parallel group of monkeys receiving cholestyramine was seen in animals receiving probuconol. It should be emphasized that both HDL-cholesterol and LDL-cholesterol were markedly reduced in this regression study. During the performance of a two-year chronic study involving 32 probuconol-treated dogs (beagles), there were 12 fatalities.

Subsequent experiments have indicated that probuconol sensitizes the canine myocardium to epinephrine, resulting in ventricular fibrillation in many dogs. Among the animal species in which probuconol has been studied, the dog is peculiar with respect to the phenomenon of sudden death due to the sensitization of the myocardium to epinephrine. In contrast to findings in the dog, injections of epinephrine to probuconol-treated monkeys did not induce ventricular fibrillation.

In other studies, monkeys were given probuconol either before and/or after myocardial infarction was induced by coronary artery ligation. In these studies, there was no difference between probuconol- and placebo-treated groups with respect to either survival or detailed blind quantitation of myocardial changes (gross and histopathologic).

Probuconol has shown no identifiable toxicity in mice and rats. In these animals, the LD₅₀ (oral) is in excess of 5 g/kg of body weight. In chronic studies of two years' duration in rats, no toxicity or carcinogenicity was observed.

From studies in rats, dogs, and monkeys, it is known that probuconol accumulates slowly in adipose tissue. Approximately 90% of probuconol administered orally is unabsorbed. For that which is absorbed, the biliary tract is the major pathway for clearance from the body and very little is excreted by way of the kidneys.

Myocardial injury was produced in various groups of rats by one of the following procedures: aortic coarctation, coronary ligation, or cobalt or isoproterenol injection. After probuconol administration, no deleterious effects related to treatment occurred as measured by survival and microscopic examination of myocardial damage.

Probuconol was administered to minipigs beginning ten days before ligation of coronary artery and continued for 60 days after surgery. Challenge with epinephrine at the end of 80 days failed to induce ventricular fibrillation in any of the coronary-ligated, probuconol-treated minipigs.

CLINICAL STUDIES: In a multicenter, randomized, double-blind study, the LRC-CPPT,³ hypercholesterolemic patients treated with an oral bile acid sequestrant (cholestyramine) and a cholesterol-lowering diet experienced average total and LDL-cholesterol reductions greater than those obtained in the placebo group treated with diet alone. The cumulative seven-year incidence of the primary end point—combined incidence of definite CHD death and/or definite nonfatal myocardial infarction—was 7% in the cholestyramine group and 8.6% in the placebo group. This was a 19% reduction in risk (P less than 0.05, single-tail test) of the primary end point reflecting a 24% reduction in definite CHD death and a 19% reduction in nonfatal myocardial infarction.

The subjects included in the study were middle-aged men (35-59 years old) with serum cholesterol levels at least 265 mg/dL and no previous history of heart disease. It is not clear to what extent these findings can be extrapolated to other segments of the hypercholesterolemic population not studied.

The bile acid sequestrant, cholestyramine, was used in the above trial. Caution should be exercised in extrapolating these results to Lorelco since it differs from cholestyramine with regard to its mode of action, spectrum of cholesterol-lowering potency, effect on HDL-cholesterol, and possible toxicity. The effect of probuconol-induced reduction of serum cholesterol levels on morbidity or mortality due to coronary heart disease has not been established.

REFERENCES

1. Consensus Development Panel. Lowering blood cholesterol to prevent heart disease. *JAMA*. 1985; 253:2080-2086.
2. Fredrickson DS, Levy RI, Lees RS. Fat transport in lipoproteins—an integrated approach to mechanisms and disorders. *N Engl J Med*. 1967; 276:344.
3. The Lipid Research Clinics Program. The Lipid Research Clinics coronary primary prevention trial results: 1. Reduction in incidence of coronary heart disease. *JAMA*. 1984; 251:351-364.

Product Information as of June, 1988

MERRELL DOW PHARMACEUTICALS INC.
Subsidiary of The Dow Chemical Company
Cincinnati, Ohio 45215, U.S.A.

Merrell Dow

8-1220 (LO055) MDA 051

June, 1988

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OBESITY. RESULTS OF SURVEY MAY



According to responses from over 6,800 physicians, obesity has become a serious health threat.

A problem so significant... 77% of responding physicians view it as the single most prevalent chronic condition in the US.¹

A problem so widespread... 88% of physicians realize it afflicts at least 1 out of 3 American adults.^{1,2}

A "disease" so serious... 81% of physicians acknowledge it is related, either directly or indirectly, to 20% or more of the nation's mortality.^{1,3}

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FASTIN®[®] (phentermine HCl) 30 mg capsules

FASTIN® (phentermine HCl) can help. It effectively curbs hunger—the critical first step. In fact, 46% of responding physicians prefer FASTIN over two other well-known anorectics.

As an adjunct to prescribed diet, exercise, and counseling, FASTIN can help provide the early motivation many patients need to overcome obesity...and its serious health risks.

*Preferred by physicians over
other well-known anorectics.¹*

Please see summary of prescribing information on next page.

References:

1. Results based on 6,831 physician responses to a recent survey (note: Not all responding physicians answered all questions). Data on file, Beecham Laboratories.
2. Weiss ST: Obesity: Pathogenesis, consequences, and approaches to treatment. *Psychiatr Clin North Am* 1984;7:307-319.
3. Eastman P: Call obesity "a killer", costing the US \$30.6 billion a year. *Medical Tribune* 1985;(March 20):26.

FASTIN®^{IV}

(phentermine HCl)
30 mg capsules

*Preferred by physicians over
other well-known anorectics.¹*

Brief Summary
Indicated only for use as a short-term adjunct in the management of exogenous obesity.

INDICATION: FASTIN is indicated in the management of exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class (see ACTIONS) should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

FASTIN may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

DRUG DEPENDENCE: FASTIN is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of FASTIN should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

Use in Pregnancy: Safe use in pregnancy has not been established. Use of FASTIN by women who are or who may become pregnant, and those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Use in Children: FASTIN is not recommended for use in children under 12 years of age.

Use with Alcohol: Concomitant use of alcohol with FASTIN may result in an adverse drug interaction.

PRECAUTIONS: Caution is to be exercised in prescribing FASTIN for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of FASTIN and the concomitant dietary regimen.

FASTIN may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose.

ADVERSE REACTIONS: Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.

Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses.

Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances.

Allergic: Urticaria.

Endocrine: Impotence, changes in libido.

DOSAGE AND ADMINISTRATION: Exogenous Obesity: One capsule at approximately 2 hours after breakfast for appetite control. Late evening medication should be avoided because of the possibility of resulting insomnia.

Administration of one capsule (30 mg) daily has been found to be adequate in depression of the appetite for twelve to fourteen hours.

FASTIN is not recommended for use in children under 12 years of age.

OVERDOSEAGE: Manifestations of acute overdose with phentermine include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension, and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management of acute phentermine intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard. Acidification of the urine increases phentermine excretion. Intravenous phenolamine (REGITINE) has been suggested for possible acute, severe hypertension, if this complicates phentermine overdose.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: Blue and clear capsules with blue and white beads containing 30 mg phentermine hydrochloride (equivalent to 24 mg phentermine).

NDC 0029-2205-30 bottles of 100

NDC 0029-2205-39 bottles of 450

NDC 0029-2205-31 pack of 30

Beecham
laboratories
Bristol, Tennessee 37620

and xanthenes, and run-to-run coefficient variants of 5.5%.

The EZ-Bead T4 enzyme immunoassay kit yields T4 serum values comparable to radioimmunoassay without the need for licensing, gamma counters, or waste disposal requirements. It features one-hour incubation at room temperature and can be applied to various chemical analyzer systems. It has a correlation coefficient to radioimmunoassay of 0.93, negligible cross-reactivity to other thyroid hormones, and run-to-run coefficient variants of 4.5%.

For more information on these solid phase kits, contact Immunotech Corp, PO Box 860, 90 Windom St, Boston, 02134, (800) 343-0555 or (617) 787-1010.

Prostate biopsy kits

The Transperineal Biopsy Kit features a reusable mounting adapter and 15 plastic disposable needle guides. Eight needle tracks offer access to all parts of the prostate from the anterior to posterior. The kit is compatible with 18-22 gauge needles.

A reusable stainless steel mounting adapter and 24 stainless steel, latex-tipped cannulas comprise the Transrectal Biopsy Kit. Latex covers the cannula tip until the biopsy needle passes through it, minimizing risk of infection and preventing feces from entering the guide. The device offers two locked positions for anterior and posterior sections of the prostate.

For more information on either kit, contact Philips Ultrasound International, 2722 S Fairview St, Santa Ana, CA 92704, (714) 556-7608.

Palpable lesion biopsy system

The DiacyteTM fine needle aspiration biopsy system for palpable lesions can be performed during patient visits. Specimen suspension is mounted to a fixative/preservative solution at room temperature and shipped overnight express for evaluation to a cen-

tral laboratory. For more information, contact Dianon Systems, Inc, 555 Lordship Blvd, Stratford, CT 06497-7124, (800) 328-2666 or (203) 381-4000.

Diabetic paraphernalia case

A blood glucose monitor, lancing device and several days' supply of syringes can be carried in the RoCo case. It has two pockets, three elastic loops, and two adjustable straps and measures 7 1/2 x 5 7/8 x 2 3/4 inches. For more information, contact RoCo Designs, 702 S Chapin St, PO Box 1762, South Bend, IN 46634-1762, (219) 233-8498.

In-office hematology analyzer

Using a single specimen, the CellstarTM hematology analyzer provides simultaneous results for either white blood count and hemoglobin or red blood count, hematocrit, and mean corpuscular volume as well as separate results for each. Premeasured reagent and automatic features—rinsing, blanking, cleaning, coincidence correction, operator alert system, liquid crystal display—complement this system, which has a throughput of 45 samples per hour for all five parameters. For more information, contact Electro-Nucleonics[®], 350 Passaic Ave, PO Box 2803, Fairfield, NJ 07007-2803, (201) 227-6700.

Sprained ankle treatment and patella stabilizer

The Edema II offers rigid ankle support and edema control for treatment of ankle sprains. The Fast-Wrap boot design with elastic straps provide adjustable, gradient compression. U-shaped foam pads feature open channels for fluid disbursement.

The Camp Patella Stabilizer features elastic traction straps that control patella positioning. A firm, crescent-shaped pad can be placed medially or laterally on the leg depending on the direction of instability. The open-back design eliminates pos-

For more information on these products, contact Camp International, PO Box 89, Jackson, MI 49204, (800) 492-1088.

The Platinum ultrasound system is designed with refined wide aperture linear arrays and variable focal windowing for clear image resolution. Up to four 2-dimensional images can be processed simultaneously. Interactive data packages simplify calculations, and provide for information recall on specific areas, as well as display expected normals for various examinations.

Sector arrays feature maximized aperture size and equal-pitch circular elements that provide for lower phase error. Dropdown menus can be accessed using an electronic mouse. Doppler and angiodynography options can be added. For more information, contact Philips Ultrasound International, 2722 S Fairview St, Santa Ana, CA 92704 (714) 556-7608.

The Jones Flow/Volume calibrator digitally displays forced vital capacity, peak flow, forced expiratory flow rate, and forced inspiratory flow. It can be used to calibrate all spirometry systems, including electronic flow devices. For more infor-

mation, contact Jones Medical Instrument Co, 200 Windsor Dr, Oak Brook, IL 60521 (800) 323-7336 or (312) 571-1980.

An alternative to the open-back hospital gown, the Raymond Keltner gowns are designed with VelcroTM closures on the shoulders or along the sides. Available in a variety of styles, the gowns come in different colors coded by size (small, medium, large, and extra large). For more information, contact Raymond Keltner, Inc., PO Box 6051, Shawnee Mission, KS 66206 (913) 649-7304.

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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.

Micronase[®]
Tablets (glyburide) **Usual starting dosage
2.5 mg-5 mg once a day**

Please see adjacent page for brief summary of prescribing information.