Maxzide advertisement.

[s.l.]: [s.n.], 1993

Specify "Dispense As Written"

In Mild Hypertension[1]

Dependable Control Is Shaped Like This

Effective in mild hypertension[1*†]

Excellent safety profile[1]

Potassium and magnesium conservation[1,2]

Prescribe the Shape to Remember

Once-a-day **MAXZIDE®-25 MG**

Triamterene **37.5 mg** / Hydrochlorothiazide **25 mg**

* Normalization of diastolic BP (<90 mmHG) in 79% of mildly hypertensive patients within 4 weeks.

† **MAXZIDE-25 MG** is indicated for the treatment of hypertension or edema in patients who develop hypokalemia on hydrochlorothiazide alone or in whom the development of hypokalemia cannot be risked.

®Unique tablet shape is a registered trademark of American Cyanamid Company.

Please see adjacent page for Brief Summary, including **WARNINGS**, **CONTRAINDICATIONS**, and **ADVERSE REACTIONS**.

Specify

"Dispense As Written"

Prescribe the Shape to Remember

Once-a-day

MAXZIDE®-25 MG

Triamterene **37.5 mg** / Hydrochlorothiazide **25 mg**

MAXZIDE® and MAXZIDE®-25 MG Tablets
Triamterene and Hydrochlorothiazide

Brief Summary

Please see package insert for full prescribing information.

INDICATIONS AND USAGE

This fixed combination drug is not indicated for the initial therapy of edema or hypertension except in individuals in whom the development of hypokalemia cannot be risked.

CONTRAINDICATIONS

Elevated serum potassium levels (≥5.5 mEq/L). Discontinue if hyperkalemia develops. Concomitant use with other potassium-sparing agents. Concomitant potassium supplementation. Anuria, acute and chronic renal insufficiency, significant renal impairment. Hypersensitivity to either component or to other sulfonamide-derived drugs.

WARNINGS

Hyperkalemia: Abnormal elevation of serum potassium levels (≥5.5 mEq/L) can occur with all potassium-conserving agents including MAXZIDE. Hyperkalemia is more likely to occur in patients with renal impairment, diabetes (even without evidence of renal impairment), or elderly or severely ill patients. Since uncorrected hyperkalemia may be fatal, serum potassium levels must be monitored at frequent intervals, especially in patients first receiving MAXZIDE, when dosages are changed, or with any illness that may influence renal function.

Obtain ECG if signs and symptoms of hyperkalemia occur. Discontinue MAXZIDE immediately if hyperkalemia is present. If the serum potassium level exceeds 6.5 mEq/L, more vigorous therapy is required. Avoid MAXZIDE in diabetic patients. If used, monitor serum electrolytes. Avoid in severely ill patients in whom respiratory or metabolic acidosis may occur. If MAXZIDE is used, frequently evaluate acid/base and serum electrolytes.

Use cautiously, if at all, with angiotensin-converting enzyme (ACE) inhibitors. (See **PRECAUTIONS, Drug Interactions**.)

PRECAUTIONS

Monitor for fluid or electrolyte imbalances at appropriate intervals. Do frequent serum and urine electrolyte determinations (especially when the patient is vomiting or receiving parenteral fluids). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy usually is water restriction. In actual salt depletion, appropriate replacement is the therapy of choice.

Hypokalemia may develop with thiazide therapy, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids, ACTH, amphotericin B or after prolonged thiazide therapy.

Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia can sensitize or exaggerate the response of the heart to the toxic effects of digitalis (eg, increased ventricular irritability).

MAXZIDE may produce an elevated blood urea nitrogen level (BUN), creatinine level, or both. Elevations in BUN and creatinine levels may be more frequent in patients receiving divided dose diuretic therapy. Discontinue if azotemia increases.

Thiazide diuretics have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Use with caution in patients with impaired hepatic function or progressive liver disease and in patients with histories of renal lithiasis. Triamterene is a weak folic acid antagonist. Periodic blood evaluations are recommended. Hyperuricemia may occur or acute gout may be precipitated in certain patients receiving thiazide therapy. The thiazides may decrease serum PBI level without signs of thyroid disturbance.

Calcium excretion is decreased by thiazides. Pathological changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in a few patients on prolonged thiazide therapy. Discontinue thiazides before conducting tests for parathyroid function.

Insulin requirements in diabetic patients may be changed. Thiazides may cause manifestation of latent diabetes mellitus. Sensitivity reactions to thiazides may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus by thiazides has been reported.

Thiazides may add to or potentiate the action of other antihypertensive drugs. Thiazides may decrease arterial responsiveness to norepinephrine. Thiazides have also been shown to increase responsiveness to tubocurarine. Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Acute renal failure has been reported in a few patients receiving indomethacin and other formulations containing triamterene and hydrochlorothiazide. Caution is therefore advised when administering nonsteroidal anti-inflammatory agents with MAXZIDE.

Use potassium-sparing agents very cautiously, if at all, in conjunction with angiotensin-converting enzyme (ACE) inhibitors due to a greatly increased risk of hyperkalemia. Monitor serum potassium frequently.

MAXZIDE may interfere with quinidine measurement.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies have not been performed to evaluate the mutagenic or carcinogenic potential of MAXZIDE.

Hydrochlorothiazide: Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic

MAXZIDE® and MAXZIDE®-25 MG Tablets
Triamterene and Hydrochlorothiazide

potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic in *in vitro* assays using strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 of *Salmonella typhimurium* (Ames assay) and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or in *in vivo* assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the *Drosophila* sex-linked recessive lethal trait gene. Positive test results were obtained only in the *in vitro* CHO Sister Chromatid Exchange (clastogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 μg/mL, and in the *Aspergillus nidulans* nondisjunction assay at an unspecified concentration.

In rat and mice studies, hydrochlorothiazide, given in the diet in doses up to 100 mg/kg and 4 mg/kg prior to conception and during gestation, had no adverse effects on the fertility of either sex.

Triamterene: Studies have not been performed to determine the carcinogenic or mutagenic potential of triamterene. Reproductive studies have been performed in rats at doses up to 30 times the human dose and have revealed no evidence of impaired fertility.

Pregnancy Category C: Teratogenic Effects–Animal reproduction studies have not been conducted with MAXZIDE. It is also not known if MAXZIDE can cause fetal harm when administered to a pregnant woman.

Hydrochlorothiazide: Studies in which hydrochlorothiazide was orally administered to pregnant mice and rats during their respective periods of major organogenesis at doses up to 3000 mg and 1000 mg hydrochlorothiazide/kg, respectively, provided no evidence of harm to the fetus. There are, however, no adequate and well-controlled studies in pregnant women.

Triamterene: Reproduction studies performed in rats at doses up to 30 times the human dose have revealed no evidence of harm to the fetus due to triamterene. There are no adequate and well-controlled studies in pregnant women.

Because animal reproduction studies are not always predictive of human response, MAXZIDE should be used during pregnancy only if clearly needed.

Nonteratogenic Effects: Thiazides and triamterene cross the placental barrier and appear in cord blood of animals. Anticipated benefit of the use of MAXZIDE should be weighed against possible hazards to the fetus, including fetal or neonatal jaundice, thrombocytopenia following thiazides, and possible other adverse reactions that have occurred in the adults.

Nursing Mothers: Thiazides appear and triamterene may appear in breast milk. If use is essential, the patient should stop nursing.

Pediatric Use: The safety and effectiveness of MAXZIDE in children have not been established.

ADVERSE REACTIONS

Side effects observed in association with the use of MAXZIDE, other combination products containing triamterene/hydrochlorothiazide, and products containing triamterene or hydrochlorothiazide include the following:

Gastrointestinal: jaundice (intrahepatic cholestatic jaundice), pancreatitis, nausea, appetite disturbance, taste alteration, vomiting, diarrhea, constipation, anorexia, gastric irritation, cramping. **Central Nervous System:** drowsiness and fatigue, insomnia, headache, dizziness, dry mouth, depression, anxiety, vertigo, restlessness, paresthesias. **Cardiovascular:** tachycardia, shortness of breath and chest pain, orthostatic hypotension (may be aggravated by alcohol, barbiturates or narcotics). **Renal:** acute renal failure, acute interstitial nephritis, renal stones composed of triamterene in association with other calculus materials, urine discoloration. **Hematologic:** leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, hemolytic anemia and megaloblastosis. **Ophthalmic:** xanthopsia, transient blurred vision. **Hypersensitivity:** anaphylaxis, photosensitivity, rash, urticaria, purpura, necrotizing angiitis (vasculitis, cutaneous vasculitis), fever, respiratory distress including pneumonitis. **Other:** muscle cramps and weakness, decreased sexual performance and sialadenitis. Whenever adverse reactions are moderate to severe, therapy should be reduced or withdrawn.

Altered Laboratory Findings: Serum Electrolytes: hyperkalemia, hypokalemia, hyponatremia, hypomagnesemia, hypochloremia (see **WARNINGS, PRECAUTIONS**). **Creatinine, Blood Urea Nitrogen:** Reversible elevations in BUN and serum creatinine have been observed in hypertensive patients treated with MAXZIDE. **Glucose:** hyperglycemia, glycosuria and diabetes mellitus (see **PRECAUTIONS**). **Serum Uric Acid, PBI and Calcium:** (see **PRECAUTIONS**). **Other:** Elevated liver enzymes have been reported in patients receiving MAXZIDE.

Rev. 7/92
22119-92

References

1. Schnaper HW, Maxwell MH: Efficacy and safety of triamterene/hydrochlorothiazide combinations in mild systemic hypertension. *Am J Cardiol.* 1989;63:32B-36B.
2. Data on file, Lederle Laboratories, Pearl River, NY.

Lederle
LEDERLE LABORATORIES
A Division of American Cyanamid Company
Wayne, New Jersey 07470

Advantus™ Pharmaceuticals

December 1992 8511-21