

# Catapres-TTS<sup>®</sup>

(clonidine) / TRANSDERMAL THERAPEUTIC SYSTEM

Programmed delivery in vivo of 0.1, 0.2 or 0.3 mg clonidine per day, for 1 week

## Brief Summary of Prescribing Information

**CONTRAINDICATIONS** Catapres-TTS<sup>®</sup> (clonidine) should not be used in patients with known hypersensitivity to clonidine or to any other component of the adhesive layer of the therapeutic system.

**PRECAUTIONS General** In patients who have developed localized contact sensitization to Catapres-TTS<sup>®</sup> (clonidine), substitution of oral clonidine hydrochloride therapy may be associated with development of a generalized skin rash.

In patients who develop an allergic reaction to Catapres-TTS<sup>®</sup> that extends beyond the local patch site (such as generalized skin rash, urticaria, or angioedema), oral clonidine hydrochloride substitution may elicit a similar reaction.

As with all antihypertensive therapy, Catapres-TTS<sup>®</sup> should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease, or chronic renal failure.

Transdermal clonidine systems should be removed before attempting defibrillation or cardioversion because of the potential for altered electrical conductivity which may enhance the possibility of arcing, a phenomenon associated with the use of defibrillators.

**Withdrawal** Patients should be instructed not to discontinue therapy without consulting their physician. Sudden cessation of clonidine treatment has resulted in subjective symptoms such as nervousness, agitation and headache, accompanied or followed by a rapid rise in blood pressure and elevated catecholamine concentrations in the plasma, but such occurrences have usually been associated with previous administration of high oral doses (exceeding 1.2 mg/day) and/or with continuation of concomitant beta blocker therapy. Rare instances of hypertensive encephalopathy and death have been reported.

An excessive rise in blood pressure following Catapres-TTS<sup>®</sup> discontinuance can be reversed by administration of oral clonidine or by intravenous phentolamine. If therapy is to be discontinued in patients receiving beta blockers and clonidine concurrently, beta blockers should be discontinued several days before cessation of Catapres-TTS<sup>®</sup> administration.

**Perioperative Use** As with oral clonidine therapy, Catapres-TTS<sup>®</sup> therapy should not be interrupted during the surgical period. Blood pressure should be carefully monitored during surgery and additional measures to control blood pressure should be available if required. Physicians considering starting Catapres-TTS<sup>®</sup> therapy during the perioperative period must be aware that therapeutic plasma clonidine levels are not achieved until 2 to 3 days after initial application of Catapres-TTS<sup>®</sup>.

**Information for Patients** Patients who engage in potentially hazardous activities, such as operating machinery or driving, should be advised of a potential sedative effect of clonidine. Patients should be cautioned against interruption of Catapres-TTS<sup>®</sup> therapy without a physician's advice. Patients should be advised that if the system begins to loosen from the skin after application, the adhesive overlay should be applied directly over the system to ensure good adhesion over its 7-day lifetime. Instructions for using the system are provided. Patients who develop moderate or severe erythema and/or localized vesicle formation at the site of application, or a generalized skin rash, should consult their physician promptly about the possible need to remove the patch.

**Drug Interactions** If a patient receiving clonidine is also taking tricyclic antidepressants, the effect of clonidine may be reduced, thus necessitating an increase in dosage. Clonidine may enhance the CNS-depressive effects of alcohol, barbiturates, or other sedatives. Amitriptyline in combination with clonidine enhances the manifestation of corneal lesions in rats.

**Carcinogenesis/Mutagenesis/Impairment of Fertility** In a 132-week (fixed concentration) dietary administration study in rats, Catapres<sup>®</sup> (clonidine HCl) administered at 32 to 46 times the oral maximum recommended daily human dose (MRDHD) was unassociated with evidence of carcinogenic potential. Results from the Ames test with clonidine hydrochloride revealed no evidence of mutagenesis. Fertility of male or female rats was unaffected by clonidine doses as high as 150 mcg/kg or about 3 times the oral MRDHD. Fertility of female rats did, however, appear to be affected (in another experiment) at the dose levels of 500 to 2000 mcg/kg or 10 to 40 times the oral MRDHD.

**Pregnancy/Teratogenic Effects** *Pregnancy Category C* Reproduction studies performed in rabbits at doses up to approximately 3 times the oral maximum recommended daily human dose (MRDHD) of Catapres have revealed no evidence of teratogenic or embryotoxic potential in rabbits. In rats, however, doses as low as 1/3 the oral MRDHD of clonidine were associated with increased resorptions in a study in which dams were treated continuously from 2 months prior to mating. Increased resorptions were not associated with treatment at the same or at higher dose levels (up to 3 times the oral MRDHD) when dams were treated days 6-15 of gestation. Increased resorptions were observed at much higher levels (40 times the oral MRDHD) in rats and mice treated days 1-14 of gestation (lowest dose employed in the study was 500 mcg/kg). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers** As clonidine is excreted in human milk, caution should be exercised when Catapres-TTS<sup>®</sup> is administered to a nursing woman.

**Pediatric Use** Safety and effectiveness in children below the age of 12 have not been established.

**ADVERSE REACTIONS** Most systemic adverse effects during therapy with Catapres-TTS<sup>®</sup> (clonidine) have been mild and have tended to diminish with continued therapy. In a 3-month, multiclinic trial of Catapres-TTS<sup>®</sup> in 101 hypertensive patients, the most frequent systemic reactions were dry mouth (25 patients) and drowsiness (12 patients).

Transient localized skin reactions, primarily localized pruritus, occurred in 51 patients. Twenty-six patients experienced localized erythema. This erythema and pruritus were more common in patients utilizing an adhesive overlay for the entire 7-day treatment period. Allergic contact sensitization to Catapres-TTS<sup>®</sup> was observed in 5 patients.

In additional clinical experience contact dermatitis resulting in treatment discontinuation was observed in 128 of 673 patients (about 19 in 100) after a mean duration of treatment of 37 weeks. The incidence in white females was about 34 in 100; in white males about 18 in 100; in black females about 14 in 100; and in black males about 8 in 100.

The following less frequent adverse experiences were also reported in patients involved in the multiclinic trial with Catapres-TTS<sup>®</sup>.

**Gastrointestinal** Constipation (1 patient); nausea (1); and change in taste (1).

**Central Nervous System** Fatigue (6 patients); headache (5); lethargy (3); sedation (3); insomnia (2); dizziness (2); and nervousness (1).

**Genitourinary** Impotence/sexual dysfunction (2 patients).

**Dermatological** Localized vesiculation (7 patients); hyperpigmentation (5); edema (3); excoriation (3); burning (3); papules (1); throbbing (1); blanching (1); and generalized macular rash (1).

In additional clinical experience involving 3539 patients, less common dermatologic reactions have occurred, where a causal relationship to Catapres-TTS<sup>®</sup> was not established: maculopapular skin rash (10 cases); urticaria (2 cases); angioedema involving the face (2 cases), one of which also involved the tongue.

**Oro-otolaryngeal** Dry throat (2 patients).

In long experience with oral Catapres (clonidine HCl), the most common adverse reactions have been dry mouth (about 40%), drowsiness (about 35%) and sedation (about 8%). In addition, the following adverse reactions have been reported less frequently:

**Gastrointestinal** Nausea and vomiting, about 5 in 100 patients; anorexia and malaise, each about 1 in 100; mild transient abnormalities in liver function tests, about 1 in 100; rare reports of hepatitis; parotitis, rarely.

**Metabolic** Weight gain, about 1 in 100 patients; gynecomastia, about 1 in 1000; transient elevation of blood glucose or serum creatine phosphokinase, rarely.

**Central Nervous System** Nervousness and agitation, about 3 in 100 patients; mental depression, about 1 in 100; and insomnia, about 5 in 1000. Vivid dreams or nightmares, other behavioral changes, restlessness, anxiety, visual and auditory hallucinations and delirium have been reported.

**Cardiovascular** Orthostatic symptoms, about 3 in 100 patients; palpitations and tachycardia, and bradycardia, each about 5 in 1000. Raynaud's phenomenon, congestive heart failure, and electrocardiographic abnormalities (i.e., conduction disturbances and arrhythmias) have been reported rarely. Rare cases of sinus bradycardia and atrioventricular block have been reported, both with and without the use of concomitant digitalis.

**Dermatological** Rash, about 1 in 100 patients; pruritus, about 7 in 1000; hives, angioneurotic edema and urticaria, about 5 in 1000; alopecia, about 2 in 1000.

**Genitourinary** Decreased sexual activity, impotence and loss of libido, about 3 in 100 patients; nocturia, about 1 in 100; difficulty in micturition, about 2 in 1000; urinary retention, about 1 in 1000.

**Other** Weakness, about 10 in 100 patients; fatigue, about 4 in 100; headache, and discontinuation syndrome, each about 1 in 100; muscle or joint pain, about 6 in 1000; and cramps of the lower limbs, about 3 in 1000. Dryness, burning of the eyes, blurred vision, dryness of the nasal mucosa, pallor, weakly positive Coombs' test, increased sensitivity to alcohol, and fever have been reported.

**HOW SUPPLIED** Catapres-TTS<sup>®</sup>-1 (clonidine) and Catapres-TTS<sup>®</sup>-2 are supplied as 4 pouched systems and 4 adhesive overlays per carton, 3 cartons per shipper. Catapres-TTS<sup>®</sup>-3 is supplied as 4 pouched systems and 4 adhesive overlays per carton. See chart below.

	Programmed Delivery Clonidine in vivo Per Day Over 1 Week	Clonidine Content	Size	Code
Catapres-TTS <sup>®</sup> -1 (clonidine)	0.1 mg	2.5 mg	3.5 cm <sup>2</sup>	BI-31
Catapres-TTS <sup>®</sup> -2 (clonidine)	0.2 mg	5.0 mg	7.0 cm <sup>2</sup>	BI-32
Catapres-TTS <sup>®</sup> -3 (clonidine)	0.3 mg	7.5 mg	10.5 cm <sup>2</sup>	BI-33

Consult package insert before prescribing. CT-BS-788

**References:**  
1. Haynes RB, Taylor DW, Sackett DL, eds. *Compliance in Health Care*. Baltimore, Md: The Johns Hopkins University Press; 1981:14, 18, 22, 135, 140-141.  
2. Burns JF, Mikoczki WJ. Transdermal administration of clonidine: a new approach to antihypertensive therapy. *Pharmacotherapy*. 1986;6(1):30-34.

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## LETTERS TO THE EDITOR

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azole, and either pentan or trimethoprim sulfamethoxazole for pneumocystis (PCP) prophylaxis.

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## Partial Breast Irradiation for Early Breast Cancer

*To the Editor:*

An icon of modern radiation oncology is the notion that patients with breast cancer treated by partial mastectomy require ipsilateral whole breast irradiation. One reason for this stems from the easy adaptability of the original McWhirter technique of tangential radiation to the chest wall for this purpose. Another reason is the need to obtain wide radiotherapeutic margins around the primary tumor. In addition, there is the belief that the rest of the ipsilateral breast outside the immediate tumor bed is "at risk."

A critical look at this practice in light of a recent negative personal experience with whole breast irradiation showed the following:

1. In patients treated with partial mastectomy and radiation, the recurrence rate in the ipsilateral breast at 20 years is 20%.<sup>1-4</sup>
2. Of these recurrences, 50% to 90% occur in the immediate vicinity of the original primary tumor.<sup>2,3,5</sup>
3. These same patients followed for 10 years would be expected to have a 5% rate of new cancers in the opposite breast.
4. Early ipsilateral recurrences (< 2 years) tend to be at the site of the primary tumor, whereas later recurrences tend to be remote from the primary.<sup>3,5</sup>

My interpretation of the above

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# Micronase<sup>®</sup>

Tablets (glyburide) Usual starting dosage  
2.5 mg-5 mg once a day

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

**SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY:** The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with noninsulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (Diabetes, 19 [Suppl 2]: 747-830, 1970).

UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2½ times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of MICRONASE and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

**PRECAUTIONS: General—Hypoglycemia:** All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection and dosage and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may increase the risk of serious hypoglycemic reactions. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency, are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly and in people who are taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

**Loss of Control of Blood Glucose:** In diabetic patients exposed to stress such as fever, trauma, infection or surgery, a loss of control may occur. It may then be necessary to discontinue MICRONASE and administer insulin. Adequate adjustment of dose and adherence to diet should be assessed before classifying a patient as a secondary failure. **Information for Patients:** Patients should be informed of the potential risks and advantages of MICRONASE and of alternative modes of therapy. They also should be informed about the importance of adherence to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

**Laboratory Tests:** Response to MICRONASE Tablets should be monitored by frequent urine glucose tests and periodic blood glucose tests. Measurement of glycosylated hemoglobin levels may be helpful in some patients.

**Drug Interactions:** The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta adrenergic blocking agents.

Certain drugs tend to produce hyperglycemia and may lead to loss of control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid.

A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported.

**Carcinogenesis, Mutagenesis, and Impairment of Fertility:** Studies in rats at doses up to 300 mg/kg/day for 18 months showed no carcinogenic effects. Glyburide is nonmutagenic when studied in the Salmonella microsome test (Ames test) and in the DNA damage/alkaline elution assay.

**Pregnancy: Teratogenic effects:** Pregnancy Category B. Reproduction studies in rats and rabbits have revealed no evidence of impaired fertility or harm to the fetus due to glyburide. There are no adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed. Insulin should be used during pregnancy to maintain blood glucose as close to normal as possible. **Nonteratogenic Effects:** Prolonged severe hypoglycemia (4 to 10 days) has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. MICRONASE should be discontinued at least two weeks before the expected delivery date.

**Nursing Mothers:** Some sulfonylurea drugs are known to be excreted in human milk. Insulin therapy should be considered.

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

**ADVERSE REACTIONS:** 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 dosage is reduced. Liver function abnormalities have been reported.

**Dermatologic Reactions:** 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 despite continued use of MICRONASE; if skin reactions persist, the drug should be discontinued. **Porphyria cutanea tarda** and photosensitivity reactions have been reported with sulfonylureas. **Hematologic Reactions:** Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas. **Metabolic Reactions:** Hepatic porphyria and disulfiram-like reactions have been reported with sulfonylureas; however, hepatic porphyria has not been reported with MICRONASE and disulfiram-like reactions have been reported very rarely. 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 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 daily, 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.

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LETTERS TO THE EDITOR

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data is that the risk of recurrence in the ipsilateral breast resides almost entirely in the immediate vicinity of the primary tumor (eg, tumor bed + a 2-cm margin). The risk of recurrence in the rest of the ipsilateral breast is of the same order of magnitude as the risk of recurrence/new primary in the opposite breast. Radiation has no influence on remote recurrences/new primaries but only on true recurrences in the tumor bed.

In other words, there may be just as much point in radiating the whole of the ipsilateral breast as there is in radiating the contralateral non-cancerous breast.<sup>6</sup> For these reasons, partial breast irradiation, eg, of the tumor bed + a 2-cm margin, should be considered, particularly:

- for very early lesions (smaller than 1 cm),
- when the tumor is well-defined clinically or with clips placed at lumpectomy, and
- for patients with large breasts in whom whole breast radiation may produce severe acute reactions and in whom improved cosmetic appearance would be expected from partial breast treatment.

Certainly, a prospective randomized study of partial breast treatment versus whole breast treatment would be an interesting one.

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**Zantac® 150 Tablets**  
(ranitidine hydrochloride)  
**Zantac® 300 Tablets**  
(ranitidine hydrochloride)  
**Zantac® Syrup**  
(ranitidine hydrochloride)

**CONDENSED BRIEF SUMMARY**

The following is a brief summary only. Before prescribing, see complete prescribing information in Zantac® product labeling.

**INDICATIONS AND USAGE:** Zantac® is indicated in:

1. Short-term treatment of **active duodenal ulcer.** Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg. Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD).** Symptomatic relief commonly occurs within one or two weeks after starting therapy and is maintained throughout a six-week course of therapy.

In active duodenal ulcer, active, benign gastric ulcer, hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

**CONTRAINDICATIONS:** Zantac® is contraindicated for patients known to have hypersensitivity to the drug. **PRECAUTIONS:** General: 1. Symptomatic response to Zantac® therapy does not preclude the presence of gastric malignancy. 2. Since Zantac is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since Zantac is metabolized in the liver.

**Laboratory Tests:** False-positive tests for urine protein with Multistix® may occur during Zantac therapy, and therefore testing with sulfosalicylic acid is recommended.

**Drug Interactions:** Although recommended doses of Zantac do not inhibit the action of cytochrome P-450 enzymes in the liver, there have been isolated reports of drug interactions that suggest that Zantac may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

**Pregnancy: Teratogenic Effects: Pregnancy Category B:** Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Zantac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers:** Zantac is secreted in human milk. Caution should be exercised when Zantac is administered to a nursing mother.

**Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS:** Headache, sometimes severe, seems to be related to Zantac® administration. Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and, rarely, pancreatitis have been reported. There have been rare reports of malaise, dizziness, somnolence, insomnia, vertigo, tachycardia, bradycardia, atrioventricular block, premature ventricular beats, and arthralgias. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid intravenously for seven days, and in 4 of 24 subjects receiving 50 mg qid intravenously for five days. There have been occasional reports of hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice. In such circumstances, ranitidine should be immediately discontinued. These events are usually reversible, but in exceedingly rare circumstances death has occurred.

Blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. These were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia have been reported.

Although controlled studies have shown no antiandrogenic activity, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving Zantac, but the incidence did not differ from that in the general population.

Incidents of rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia, have been reported, as well as rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema, and small increases in serum creatinine.

**OVERDOSAGE:** Information concerning possible overdosage and its treatment appears in the full prescribing information.

**DOSAGE AND ADMINISTRATION:** (See complete prescribing information in Zantac® product labeling.) **Dosage Adjustment for Patients with Impaired Renal Function:** On the basis of experience with a group of subjects with severely impaired renal function treated with Zantac, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

**HOW SUPPLIED:** Zantac® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) tablets and unit dose packs of 100 (NDC 0173-0393-47) tablets.

Zantac® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 (NDC 0173-0344-42) and 100 (NDC 0173-0344-09) tablets and unit dose packs of 100 (NDC 0173-0344-47) tablets.

Store between 15° and 30° C (59° and 86° F) in a dry place. Protect from light. Replace cap securely after each opening.

Zantac® Syrup, a clear, peppermint-flavored liquid, contains 16.8 mg of ranitidine hydrochloride equivalent to 15 mg of ranitidine per 1 ml in bottles of 16 fluid ounces (one pint) (NDC 0173-0383-54).

Store between 4° and 25° C (39° and 77° F). Dispense in tight, light-resistant containers as defined in the USP/NF.

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LETTERS TO THE EDITOR

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