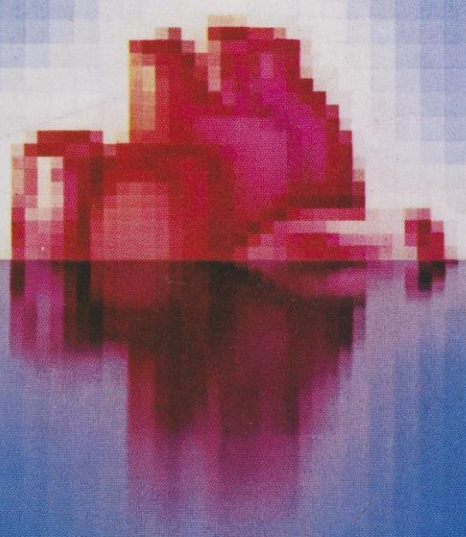
Tenormin advertisement.

[s.l.]: [s.n.], 1982

NEW PRODUCT

Stuart Pharmaceuticals announces a unique new beta blocker for hypertension...

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CALIBRATED
MILLIMETERS
B1

New...

The only beta blocker with both

one-tablet-a-day dosage and...

cardioselectivity*

ONE TABLET A DAY TENORMIN® (atenolol)

Tablets 50 mg

*Cardioselectivity denotes a relative preference for β_1 receptors, located chiefly in cardiac tissue. This preference is not absolute.

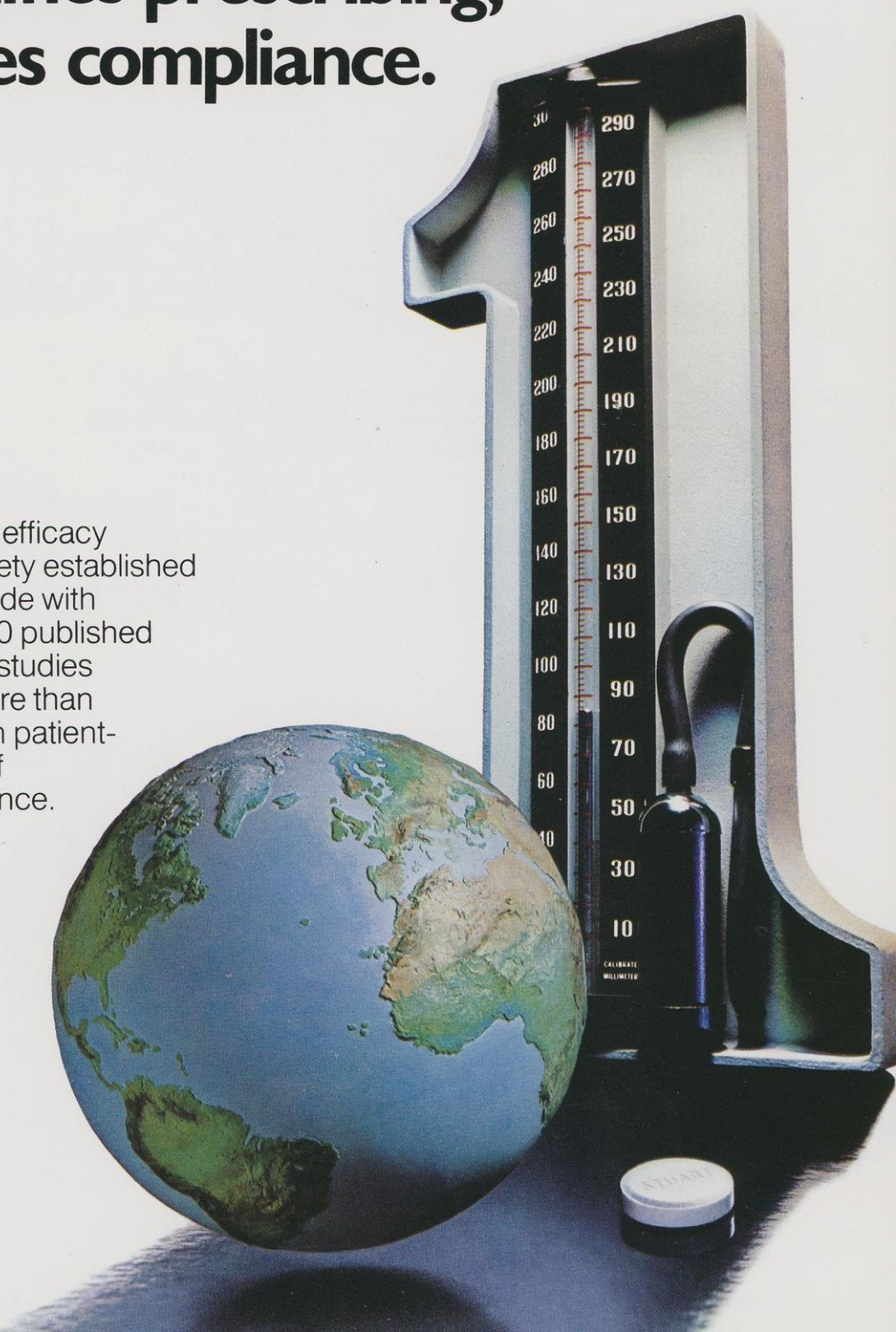
See next to last page of this advertisement for summary of prescribing information.

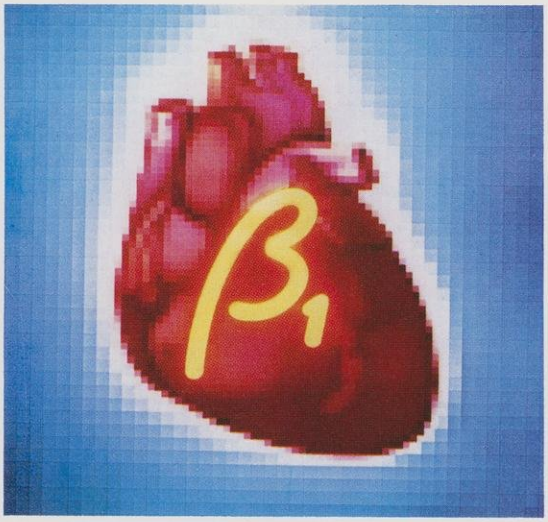
STUART PHARMACEUTICALS

New

One tablet a day controls blood pressure for 24 hours... simplifies prescribing, enhances compliance.

Clinical efficacy and safety established worldwide with over 100 published clinical studies and more than 2 million patient-years of experience.





Cardioselectivity extends the benefits of beta blockade to patients with bronchospastic disease.

May be tried with caution in these patients.*

*Although beta blockers in general should not be used in patients with bronchospastic disease, the cardioselectivity of TENORMIN allows it to be tried, with caution, in such patients. Cardioselectivity is not absolute. See WARNINGS section in prescribing information.

ONE TABLET A DAY

TENORMIN®

(atenolol)

See next to last page of this advertisement for summary of prescribing information.

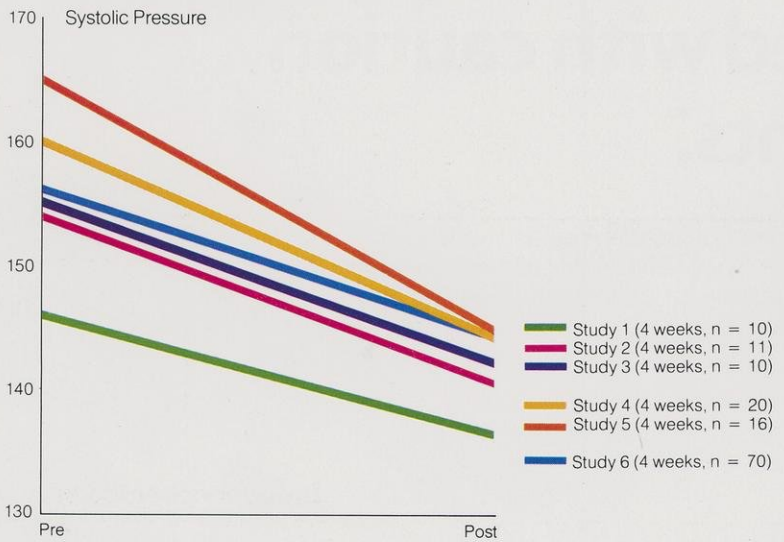
STUART PHARMACEUTICALS

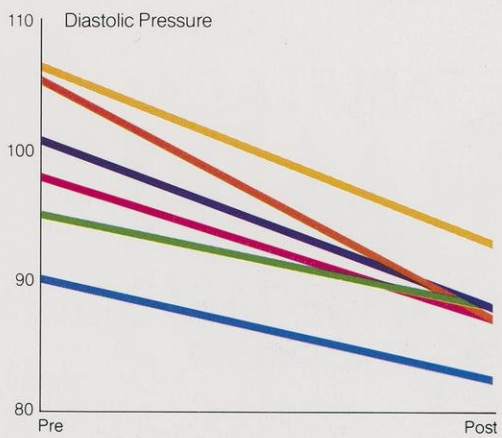
New

One tablet a day provides predictable, smooth reduction of blood pressure.[1]

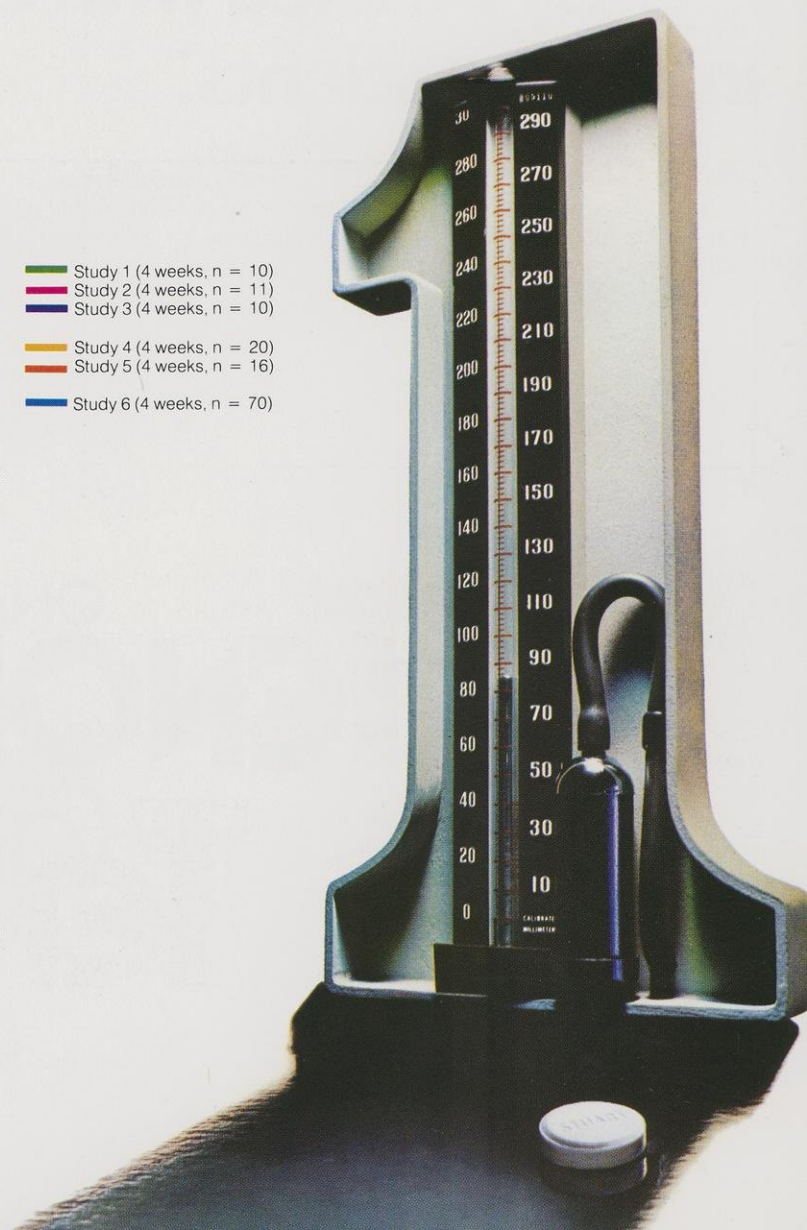
Tolerance not reported.

Reduction of Blood Pressure with TENORMIN® (atenolol) 50 mg*





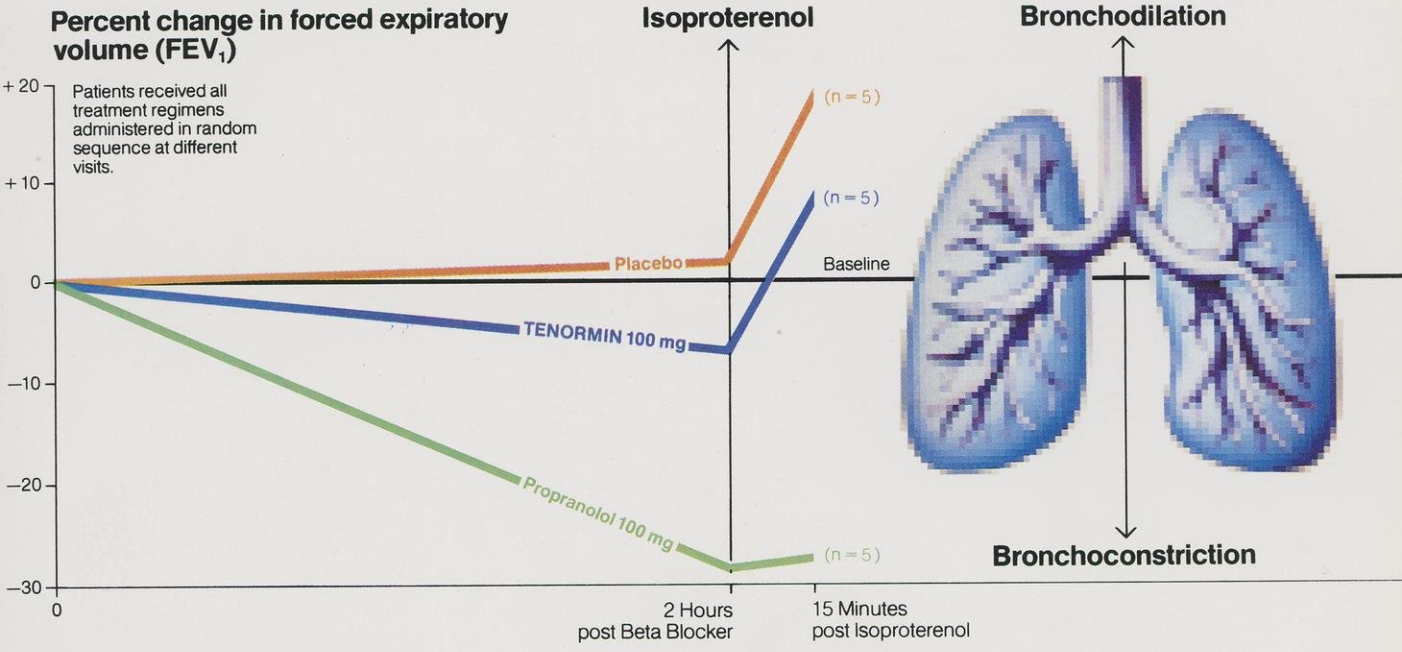
*All reductions in blood pressure were statistically significant ($P < .05$).



Cardioselectivity lessens risk of bronchospasm.*

In a study of patients with asthma[2], TENORMIN produced a smaller decrease in forced expiratory volume (FEV_1) when compared to propranolol.

After administration of isoproterenol, TENORMIN permitted significantly greater bronchodilation than propranolol and allowed bronchodilation to exceed baseline values.



*Although beta blockers in general should not be used in patients with bronchospastic disease, the cardioselectivity of TENORMIN allows it to be tried, with caution, in such patients. Cardioselectivity is not absolute. See WARNINGS section in prescribing information.

See next to last page of this advertisement for summary of prescribing information.

ONE TABLET A DAY

TENORMIN®

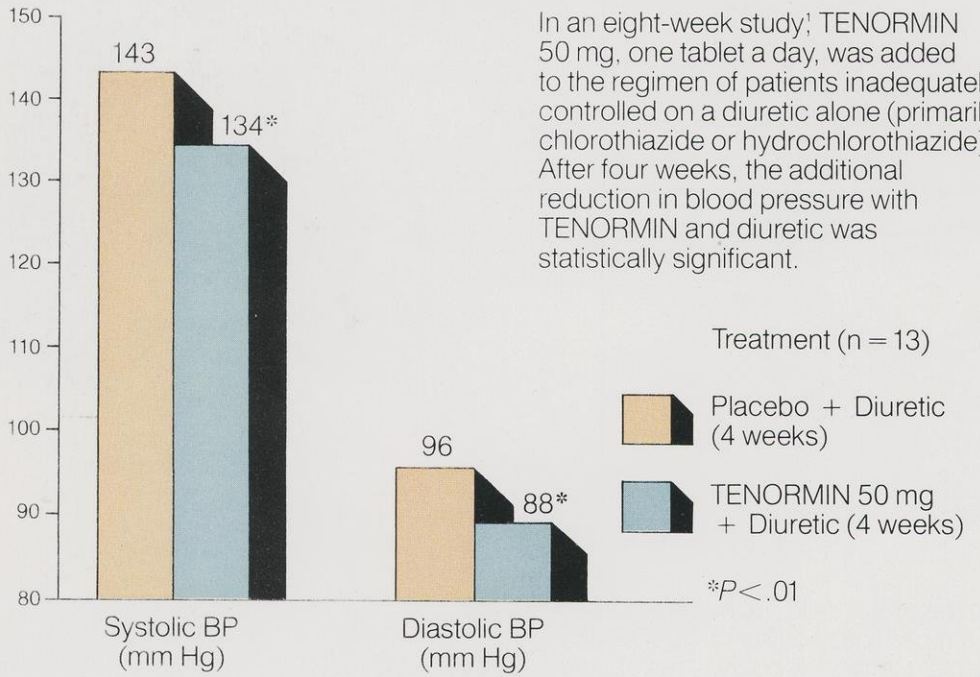
(atenolol)

STUART PHARMACEUTICALS

New

One tablet a day further reduces blood pressure when added to diuretic therapy.[1]

Reduction of Blood Pressure with Diuretic and TENORMIN 50 mg



In an eight-week study[1] TENORMIN 50 mg, one tablet a day, was added to the regimen of patients inadequately controlled on a diuretic alone (primarily chlorothiazide or hydrochlorothiazide). After four weeks, the additional reduction in blood pressure with TENORMIN and diuretic was statistically significant.

ONE TABLET A DAY

TENORMIN®

(atenolol)

Side effects are mild and transient...

little or no postural hypotension or impotence reported. Few CNS-related effects.[1]

In 11 well-controlled studies,[1] the incidence of side effects attributable to TENORMIN® (atenolol) was often similar to the incidence seen with placebo. TENORMIN therapy was discontinued because of side effects in less than 3% of patients studied.

Incidence of Side Effects:* Placebo Comparison		TENORMIN® (all dosages studied) % of Patients (n = 235)	Placebo % of Patients (n = 298)
Cardio-vascular	Bradycardia	3	0
	Cold extremities	4	2
	Edema	3	2
	Postural hypotension	3	3
CNS	Depression	3	5
	Dizziness	4	3
	Insomnia	4	4
GI	Diarrhea	3	2
	Indigestion	3	2
	Nausea	3	2
Respiratory	Dyspnea	3	3
Miscella-neous	Fatigue	3	4
	Headache	9	16
	Tiredness	6	4
	Impotence	0	1

*No other side effects were reported in more than 2% of patients on TENORMIN, nor was the incidence significantly different than with placebo.

In certain other studies, when side effects were elicited, dizziness was also noted.

See next to last page of this advertisement for summary of prescribing information.

STUART PHARMACEUTICALS

New

One tablet a day simplifies prescribing, enhances compliance... 28-day calendar pak offers even greater convenience.

Available as 50 mg and 100 mg tablets.

How to initiate therapy with TENORMIN® (atenolol)

In patients beginning drug therapy	Simply begin treatment with TENORMIN 50 mg, one tablet a day.
In patients receiving a diuretic	Add TENORMIN 50 mg, one tablet a day, to the regimen.
in patients receiving methyldopa	Switch to TENORMIN 50 mg, one tablet a day.
In patients receiving another beta blocker	Switch to TENORMIN 50 mg, one tablet a day. In patients receiving high doses of another beta blocker (eg, 320 mg or more of propranolol), switch to TENORMIN 100 mg, one tablet a day.

TENORMIN® (atenolol)

A beta$_1$-selective blocking agent for hypertension.

INDICATIONS AND USAGE: TENORMIN (atenolol) is indicated in the management of hypertension. It may be used alone or concomitantly with other antihypertensive agents, particularly with a thiazide-type diuretic.

CONTRAINDICATIONS: TENORMIN is contraindicated in sinus bradycardia, heart block greater than first degree, cardiogenic shock, and overt cardiac failure (see WARNINGS).

WARNINGS: Cardiac Failure: Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure. In hypertensive patients who have congestive heart failure controlled by digitalis and diuretics, TENORMIN should be administered cautiously. Both digitalis and atenolol slow AV conduction.

In Patients Without a History of Cardiac Failure: Continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or be given a diuretic and the response observed closely. If cardiac failure continues, despite adequate digitalization and diuretic, TENORMIN therapy should be withdrawn.

Ischemic Heart Disease: Following abrupt cessation of therapy with certain beta-blocking agents in patients with coronary artery disease, exacerbations of angina pectoris and, in some cases, myocardial infarction have been reported. Therefore, such patients should be cautioned against interruption of therapy without the physician's advice. Even in the absence of overt angina pectoris, when discontinuation of TENORMIN is planned, the patient should be carefully observed and should be advised to limit physical activity to a minimum. TENORMIN should be reinstated if withdrawal symptoms occur.

Bronchospastic Diseases: PATIENTS WITH BRONCHOSPASTIC DISEASE SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. Because of its relative beta, selectivity, however, TENORMIN may be used with caution in patients with bronchospastic disease who do not respond to, or cannot tolerate, other antihypertensive treatment. Since beta, selectivity is not absolute the lowest possible dose of TENORMIN should be used, with therapy initiated at 50 mg and a beta$_2$-stimulating agent (bronchodilator) made available. If dosage must be increased, dividing the dose should be considered in order to achieve lower peak blood levels.

Anesthesia and Major Surgery: As with all beta-receptor blocking drugs it may be decided to withdraw TENORMIN before surgery. In this case, 48 hours should be allowed to elapse between the last dose and anesthesia. If treatment is continued, care should be taken when using anesthetic agents which depress the myocardium, such as ether, cyclopropane, and trichloroethylene.

TENORMIN, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects on the heart can be reversed by administration of such agents (eg, dobutamine or isoproterenol with caution—see OVERDOSAGE). Manifestations of excessive vagal tone (eg, profound bradycardia, hypotension) may be corrected with atropine (1-2 mg I.V.).

Diabetes and Hypoglycemia: TENORMIN should be used with caution in diabetic patients if a beta-blocking agent is required. Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected. TENORMIN does not potentiate insulin-induced hypoglycemia and, unlike nonselective beta blockers, does not delay recovery of blood glucose to normal levels.

Thyrotoxicosis: Beta-adrenergic blockade may mask certain clinical signs (eg, tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm; therefore, patients suspected of developing thyrotoxicosis from whom TENORMIN therapy is to be withdrawn should be monitored closely.

PRECAUTIONS: Impaired Renal Function: The drug should be used with caution in patients with impaired renal function (see DOSAGE AND ADMINISTRATION).

Drug Interactions: Catecholamine-depleting drugs (eg, reserpine) may have an additive effect when given with beta-blocking agents. Patients treated with TENORMIN plus a catecholamine depletor should therefore be closely observed for evidence of hypotension and/or marked bradycardia which may produce vertigo, syncope, or postural hypotension.

Should it be decided to discontinue therapy in patients receiving beta blockers and clonidine concurrently, the beta blocker should be discontinued several days before the gradual withdrawal of clonidine.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Two long-term (maximum dosing duration of 18 or 24 months) rat studies and one long-term (maximum dosing duration of 18 months) mouse study, each employing dose levels as high as 300 mg/kg/day or 150 times the maximum recommended human dose, did not indicate a carcinogenic potential in rodents. Results of various mutagenicity studies support this finding.

Fertility of male or female rats (evaluated at dose levels as high as 200 mg/kg/day or 100 times the maximum recommended human dose) was unaffected by atenolol administration.

Animal Toxicology: Chronic studies performed in animals have revealed the occurrence of vacuolation of epithelial cells of Brunner's glands in the duodenum of both male and female dogs at all tested dose levels of atenolol (starting at 15 mg/kg/day or 7.5 times the maximum recommended human dose) and increased incidence of atrial degeneration of hearts of male rats at 300 mg but not 150 mg atenolol/kg/day (150 and 75 times the maximum recommended human dose, respectively).

USAGE IN PREGNANCY: Pregnancy Category C. Atenolol has been shown to produce a dose-related increase in embryo/fetal resorptions in rats at doses equal to or greater than 50 mg/kg or 25 or more times the maximum recommended human dose. Although similar effects were not seen in rabbits, the compound was not evaluated in rabbits at doses above 25 mg/kg or 12.5 times the maximum recommended human dose. There are no adequate and well-controlled studies in pregnant women. TENORMIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not established to what extent this drug is excreted in human milk. Since most drugs are excreted in human milk, nursing should not be undertaken by mothers receiving atenolol.

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

ADVERSE REACTIONS: Most adverse effects have been mild and transient. Frequency estimates were derived from controlled studies in which adverse reactions were either volunteered by the patient (U.S. studies) or elicited (eg, by checklist—foreign studies). The reported frequency of elicited adverse effects was higher for both TENORMIN and placebo-treated patients than when these reactions were volunteered. Where frequency of adverse effects for TENORMIN and placebo is similar, causal relationship is uncertain.

The following adverse-reaction data present frequency estimates in terms of percentages: first from the U.S. studies (volunteered side effects) and then from both U.S. and foreign studies (volunteered and elicited side effects):

U.S. STUDIES (% ATENOLOL-% PLACEBO):

CARDIOVASCULAR: bradycardia (3%-0%), cold extremities (0%-0.5%), postural hypotension (2%-1%), leg pain (0%-0.5%)

CENTRAL NERVOUS SYSTEM/NEUROMUSCULAR: dizziness (4%-1%), vertigo (2%-0.5%), light-headedness (1%-0%), tiredness (0.6%-0.5%), fatigue (3%-1%), lethargy (1%-0%), drowsiness (0.6%-0%), depression (0.6%-0.5%), dreaming (0%-0%)

GASTROINTESTINAL: diarrhea (2%-0%), nausea (4%-1%)

RESPIRATORY (See WARNINGS): wheeziness (0%-0%), dyspnea (0.6%-1%)

TOTALS U.S. AND FOREIGN STUDIES:

CARDIOVASCULAR: bradycardia (3%-0%), cold extremities (12%-5%), postural hypotension (4%-5%), leg pain (3%-1%)

CENTRAL NERVOUS SYSTEM/NEUROMUSCULAR: dizziness (13%-6%), vertigo (2%-0.2%), light-headedness (3%-0.7%), tiredness (26%-13%), fatigue (6%-5%), lethargy (3%-0.7%), drowsiness (2%-0.5%), depression (12%-9%), dreaming (3%-1%)

GASTROINTESTINAL: diarrhea (3%-2%), nausea (3%-1%)

RESPIRATORY (see WARNINGS): wheeziness (3%-3%), dyspnea (6%-4%)

MISCELLANEOUS: There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is small and, in most cases, the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable. Patients should be closely monitored following cessation of therapy.

POTENTIAL ADVERSE EFFECTS: In addition, a variety of adverse effects have been reported with other beta-adrenergic blocking agents, and may be considered potential adverse effects of TENORMIN (atenolol).

Hematologic: Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Allergic: Fever, combined with aching and sore throat, laryngospasm and respiratory distress.

Central Nervous System: Reversible mental depression progressing to catatonia, visual disturbances, hallucinations, an acute reversible syndrome characterized by disorientation of time and place, short-term memory loss, emotional lability with slightly clouded sensorium, decreased performance on neuropsychometrics.

Gastrointestinal: Mesenteric arterial thrombosis, ischemic colitis.

Other: Reversible alopecia, Peyronie's disease, erythematous rash, Raynaud's phenomenon.

Miscellaneous: The oculomucocutaneous syndrome associated with the beta blocker practolol has not been reported with TENORMIN during investigational use and foreign marketing experience. Furthermore, a number of patients who had previously demonstrated established practolol reactions were transferred to TENORMIN therapy with subsequent resolution or quiescence of the reaction.

OVERDOSAGE: To date, there is no known case of acute overdosage, and no specific information on emergency treatment of overdosage is available. The most common effects expected with overdosage of a beta-adrenergic blocking agent are bradycardia, congestive heart failure, hypotension, bronchospasm, and hypoglycemia.

In the case of overdosage, treatment with TENORMIN should be stopped and the patient carefully observed. TENORMIN can be removed from the general circulation by hemodialysis. In addition to gastric lavage, the following therapeutic measures are suggested if warranted:

Bradycardia: Atropine or another anticholinergic drug.

Heart Block (Second or Third Degree): Isoproterenol or transvenous cardiac pacemaker.

Congestive Heart Failure: Conventional therapy.

Hypotension (Depending on Associated Factors): Epinephrine rather than isoproterenol or norepinephrine may be useful in addition to atropine and digitalis.

Bronchospasm: Aminophylline, isoproterenol, or atropine.

Hypoglycemia: Intravenous glucose.

DOSAGE AND ADMINISTRATION: The initial dose of TENORMIN is 50 mg given as one tablet a day either alone or added to diuretic therapy. The full effect of this dose will usually be seen within one to two weeks. If an optimal response is not achieved, the dosage should be increased to TENORMIN 100 mg given as one tablet a day. Increasing the dosage beyond 100 mg a day is unlikely to produce any further benefit.

TENORMIN may be used alone or concomitantly with other antihypertensive agents including thiazide-type diuretics, hydralazine, prazosin, and alpha-methyldopa.

Since TENORMIN is excreted via the kidneys, dosage should be adjusted in cases of severe impairment of renal function. No significant accumulation of TENORMIN occurs until creatinine clearance falls below 35 ml/min/1.73 m² (normal range is 100-150 ml/min/1.73 m²); therefore, the following maximum dosages are recommended for patients with renal impairment:

Creatinine Clearance (ml/min/1.73 m²)	Atenolol Elimination Half-life (hrs)	Maximum Dosage
15-35	16-27	50 mg daily
<15	>27	50 mg every other day

Patients on hemodialysis should be given 50 mg after each dialysis; this should be done under hospital supervision as marked falls in blood pressure can occur.

HOW SUPPLIED: Tablets of 50 mg TENORMIN (atenolol): round, flat, uncoated, white tablets with Stuart embossed on one side and NDC No. 105 embossed on the other side are supplied in monthly calendar packages of 28 tablets, bottles of 100 tablets, and unit-dose packages of 100 tablets. Tablets of 100 mg TENORMIN (atenolol): round, flat, uncoated, white tablets with Stuart embossed on one side and NDC No. 101 embossed on the other side are supplied in bottles of 100 tablets and unit-dose packages of 100 tablets.

Protect from heat, light, and moisture. Store unit-dose and calendar packages at controlled room temperature.

References: 1. Data on file, Stuart Pharmaceuticals. **2.** Benson MK, et al: Cardioselective and non-cardioselective beta blockers in reversible obstructive airways disease. *Postgrad Med J* 53(suppl 3):143-148, 1977.

ONE TABLET A DAY

TENORMIN®

(atenolol)

The only beta blocker with <u>both</u>

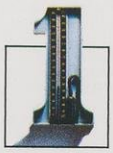
☐ one-tablet-a-day dosage and...

☐ cardioselectivity

STUART PHARMACEUTICALS

New...
for hypertension

The only beta blocker with <u>both</u>

 one-tablet-a-day dosage and...

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ONE TABLET A DAY

TENORMIN®

(atenolol)

See preceding page for summary of prescribing information

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