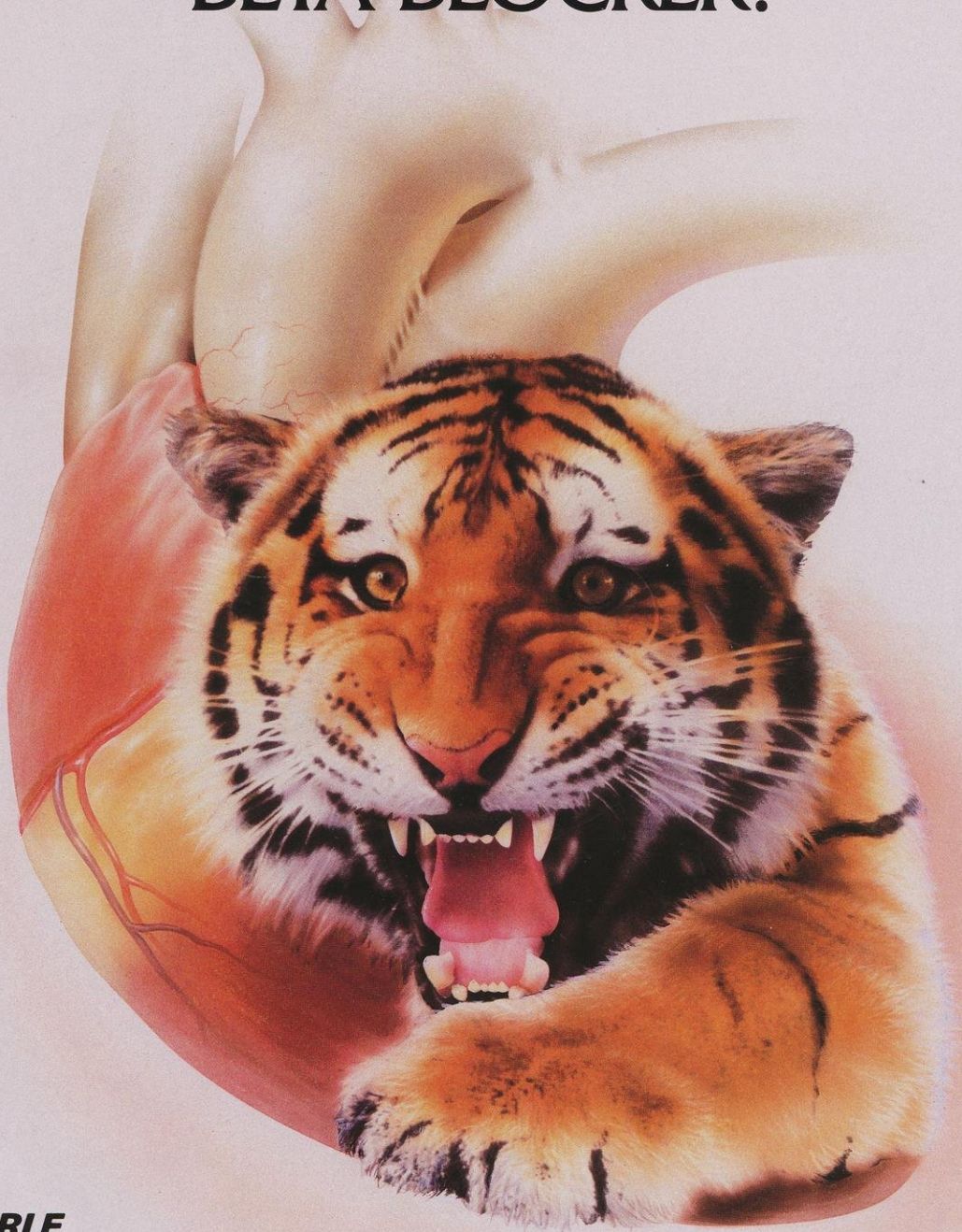
Kerlone advertisement.

[s.l.]: [s.n.], 1988

Catecholamines surge in the AM

IS TODAY'S WAKING HEART STILL PROTECTED BY YESTERDAY'S BETA-BLOCKER?

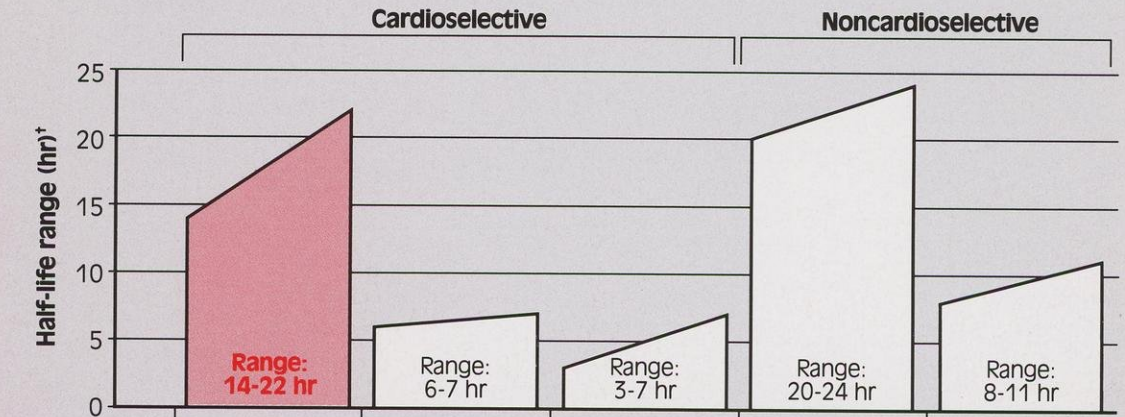


SEARLE

For hypertension

Artist's interpretation of
the dangers associated with
morning catecholamine surges.

24-HOUR BETA$_1$-BLOCKADE THAT'S STILL GOING STRONG WHEN THE "BIG CATS"* SURGE



	Kerlone® (betaxolol HCl)[1]	Tenormin® (atenolol)‡	Lopressor® (metoprolol)‡	Corgard® (nadolol)‡	Inderal® LA (propranolol HCl)§
Bioavailability†	89%	50%	50%	30%	9%-18%
Interpatient variations in plasma levels (n-fold)[2]†	2	4	10	7	NA

NA=not available in references cited.
† Numbers shown are not directly comparable since these data have been compiled from different study populations.
‡ Adapted from product information in *Physicians' Desk Reference®*, ed 44. Oradell, NJ, Medical Economics Co Inc, 1990.
§ *Drug Facts & Comparisons*. St Louis, Mo, JS Lippincott Co, 1990.

*Refers to catecholamines, norepinephrine and epinephrine, serum concentrations of which may increase two- to threefold in the morning compared with trough levels (Reference: Tofler GH, Brezinski D, Schafer AI, et al: Concurrent morning increase in platelet aggregability and the risk of myocardial infarction and sudden death. *N Engl J Med* 1987;316:1514-1518.)

Please see last page of this advertisement for references and a brief summary of prescribing information.

Kerlone is contraindicated in patients with known hypersensitivity to betaxolol hydrochloride. As are other beta-blockers, Kerlone is contraindicated in patients with sinus bradycardia, heart block greater than first degree, cardiogenic shock, and overt cardiac failure.

Tenormin® is a registered trademark of ICI Pharma. Lopressor® is a registered trademark of Geigy Pharmaceuticals. Corgard® is a registered trademark of Princeton Pharmaceutical Company. Inderal® is a registered trademark of Wyeth-Ayerst Laboratories.

β_1 Once-a-day

KERLONE®

(betaxolol HCl)

24 hours and still going strong

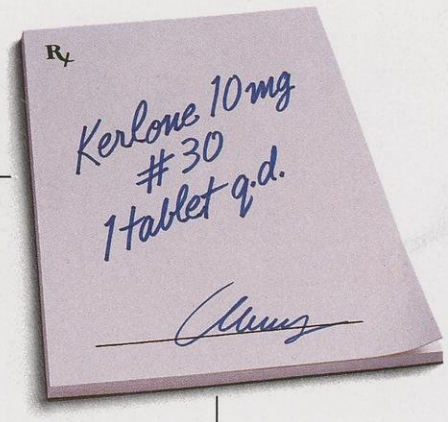
SEARLE

β_1 Once-a-day

KERLONE®

(betaxolol HCl)

24 hours and still going strong



10 mg

Usual initial dosage of Kerlone is 10 mg once a day. — In some patients, a 5-mg starting dose should be considered. Please see complete prescribing information.

If desired response is not achieved, dose may be doubled after 7 to 14 days.

- Available in 10-mg (scored) and 20-mg tablets
- Costs significantly less than any other cardioselective beta-blocker [2,3]

References:
1. Kerlone complete prescribing Information. **2.** Data on file, G.D. Searle & Co.
3. *Drug Topics® Red Book,* ed 94. Oradell, NJ, Medical Economics Co Inc, April 1990.

BRIEF SUMMARY

Contraindications: Known hypersensitivity to the drug, sinus bradycardia, heart block greater than first degree, cardiogenic shock, and overt cardiac failure (see *Warnings*).

Warnings: In hypertensive patients who have congestive heart failure controlled by digitalis and diuretics, beta-blockers should be administered cautiously. At the first sign or symptom of cardiac failure, discontinuation of Kerlone should be considered. In some cases Kerlone can be continued while cardiac failure is treated with cardiac glycosides, diuretics, and other agents, as appropriate. Abrupt cessation of therapy with certain beta-blocking agents in patients with coronary artery disease has been followed by exacerbations of angina pectoris and, in some cases, myocardial infarction has been reported; patients should be warned against interruption of therapy without the physician's advice. When discontinuation of Kerlone is planned, the patient should be carefully observed and therapy should be reinstituted, at least temporarily, if withdrawal symptoms occur. **PATIENTS WITH BRONCHOSPASTIC DISEASE SHOULD NOT IN GENERAL RECEIVE BETA-BLOCKERS. Because of its relative β_1 selectivity, low doses of Kerlone may be used with caution in patients with bronchospastic disease who do not respond to or cannot tolerate alternative treatment. Since β_1 selectivity is not absolute and is inversely related to dose, the lowest possible dose of Kerlone should be used (5 to 10 mg once daily) and a bronchodilator should be made available. If dosage must be increased, divided dosage should be considered to avoid the higher peak blood levels associated with once-daily dosing.** The risk of excessive myocardial depression during general anesthesia may be increased and difficulty in restarting and maintaining the heart beat has been reported with beta-blockers. If treatment is continued, particular care should be taken when using anesthetic agents which depress the myocardium, and it is prudent to use the lowest possible dose of Kerlone. Beta-blockers should be used with caution in diabetic patients as they may mask tachycardia occurring with hypoglycemia (patients should be warned of this), although other manifestations such as dizziness and sweating may not be significantly affected. Beta-adrenergic blockade may mask certain clinical signs of hyperthyroidism. Abrupt withdrawal might precipitate a thyroid storm; therefore, patients known or suspected of being thyrotoxic from whom Kerlone is to be withdrawn should be monitored closely.

Precautions: Beta-adrenoceptor blockade can cause reduction of intraocular pressure. Since betaxolol hydrochloride is marketed as an ophthalmic solution for treatment of glaucoma, patients should be told that Kerlone may interfere with the glaucoma-screening test. Withdrawal may lead to a return of increased intraocular pressure. Patients receiving beta-adrenergic blocking agents orally and beta-blocking ophthalmic solutions should be observed for potential additive effects. Kerlone clearance is somewhat reduced in patients with renal failure but little changed in patients with hepatic disease. Dosage reductions have not routinely been necessary when hepatic and/or renal insufficiency is present but patients should be observed. Patients on dialysis require a reduced dose. Patients should be warned against interruption or discontinuation of Kerlone therapy without the physician's advice. Patients being treated with beta-adrenergic blocking agents should be advised to consult a physician at the first sign or symptom of cardiac failure. Patients should know how they react to this medicine before they operate automobiles and machinery or engage in other tasks requiring alertness; contact their physician if any difficulty in breathing occurs, and before surgery of any type; and inform their physicians or dentists that they are taking Kerlone. Patients with diabetes should be warned that beta-blockers may mask tachycardia occurring with hypoglycemia. Patients treated with a beta-adrenergic receptor blocking agent plus a catecholamine depletor should be closely observed for evidence of hypotension or marked bradycardia, which may produce vertigo, syncope, or postural hypotension. When discontinuing therapy in patients receiving beta-blockers and clonidine concurrently, the beta-blocker should be discontinued slowly over several days before the gradual withdrawal of clonidine. Literature reports suggest that oral calcium antagonists may be used in combination with beta-adrenergic blocking agents when heart function is normal, but should be avoided in patients with impaired cardiac function. Hypotension, AV conduction disturbances, and left ventricular failure have been reported in some patients receiving beta-adrenergic blocking agents when an oral calcium antagonist was added to the treatment regimen. Hypotension was more likely to occur if the calcium antagonist were a dihydropyridine derivative, eg, nifedipine, while left ventricular failure and AV conduction disturbances, including complete heart block, were more likely to occur with either verapamil or diltiazem. Severe allergic reactions including anaphylaxis have been reported in patients exposed to a variety of allergens either by repeated challenge, or accidental contact, and with diagnostic or therapeutic agents while receiving beta-blockers. Such patients may be unresponsive to the usual doses of epinephrine used to treat allergic reaction. Pregnancy Category C. In a study in which pregnant rats received betaxolol, the highest dose (600 X MRHD) was associated with increased postimplantation loss, reduced litter size and weight, and an increased incidence of skeletal and visceral abnormalities, which may have been a consequence of drug-related maternal toxicity. Other than a possible increased incidence of incomplete descent of testes and sternebral reductions, betaxolol (6 X MRHD and 60 X MRHD) caused no fetal abnormalities. In a second study with a different strain of rat, betaxolol (300 X MRHD) was associated with maternal toxicity and an increase in resorptions, but no teratogenicity. In a study in which pregnant rabbits received betaxolol (54 X MRHD), a marked increase in postimplantation loss occurred at the highest dose. In a peri- and postnatal study in rats, betaxolol (380 X MRHD) was associated with a marked increase in total litter loss within 4 days postpartum. In surviving offspring, growth and development were also affected. There are no adequate and well-controlled studies in pregnant women. Kerlone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Since Kerlone is excreted in human milk caution should be exercised when Kerlone is administered to a nursing mother. Safety and efficacy in children have not been established. Kerlone may produce bradycardia more frequently in elderly patients.

Adverse Reactions: Kerlone has been associated with the development of antinuclear antibodies (5.3%). Betaxolol adverse events reported in U.S. controlled studies: bradycardia (8.1), symptomatic bradycardia (0.8), edema (1.8), headache (6.5), dizziness (4.5), fatigue (2.9), lethargy (2.8), insomnia (1.2), nervousness (0.8), bizarre dreams (1.0), depression (0.8), impotence (1.2), dyspnea (2.4), pharyngitis (2.0), rhinitis (1.4), upper respiratory infection (2.6), dyspepsia (4.7), nausea (1.6), diarrhea (2.0), chest pain (2.4), arthralgia (3.1), rash (1.2). Betaxolol adverse events reported in European controlled clinical trials: bradycardia (5.8), symptomatic bradycardia (1.9), palpitation (1.9), edema (1.3), cold extremities (1.9), headache (14.8), dizziness (14.8), fatigue (9.7), asthenia (7.1), insomnia (5.0), paresthesia (1.9), nausea (5.8), dyspepsia (3.9), diarrhea (1.9), chest pain (7.1), joint pain (5.2), myalgia (3.2). The following adverse events reported in less than 2% of patients occurred under conditions where a causal relationship is uncertain: flushing, salivation, sweating, allergy, fever, malaise, pain, rigors, angina pectoris, arrhythmia, heart failure, hypertension, hypotension, myocardial infarction, thrombosis, syncope, neuropathy, numbness, speech disorder, stupor, tremor, twitching, anorexia, constipation, dry mouth, increased appetite, mouth ulceration, rectal disorders, vomiting, dysphagia, earache, labyrinth disorders, tinnitus, deafness, leucocytosis, lymphadenopathy, thrombocytopenia, increased AST, increased ALT, acidosis, diabetes, hypercholesterolemia, hyperglycemia, hyperkalemia, hyperlipemia, hyperuricemia, hypokalemia, weight gain, increased LDH, arthropathy, neck pain, muscle cramps, tendonitis, abnormal thinking, amnesia, confusion, emotional lability, hallucinations, decreased libido, breast pain, breast fibroadenosis, menstrual disorder, prostatitis, bronchitis, bronchospasm, cough, epistaxis, flu, pneumonia, sinusitis, pruritus, skin disorders, abnormal taste, taste loss, cystitis, dysuria, proteinuria, abnormal renal function, renal pain, cerebrovascular disorder, leg cramps, peripheral ischemia, thrombophlebitis, abnormal lacrimation, abnormal vision, conjunctivitis, dry eyes, iritis, cataract. Although not reported in clinical studies with betaxolol, a variety of adverse effects have been reported with other beta-adrenergic blocking agents and may be considered potential adverse effects of betaxolol: reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability with slightly clouded sensorium, and decreased performance on neuropsychometric tests, intensification of AV block and congestive heart failure (or cardiac failure), erythematous rash, fever combined with aching and sore throat, laryngospasm, respiratory distress, agranulocytosis, thrombocytopenic purpura, and nonthrombocytopenic purpura, mesenteric arterial thrombosis, ischemic colitis, reversible alopecia, Peyronie's disease, Raynaud's phenomena, skin rashes and/or dry eyes, and oculomucocutaneous syndrome.

7/5/90 • P90KE4912V

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