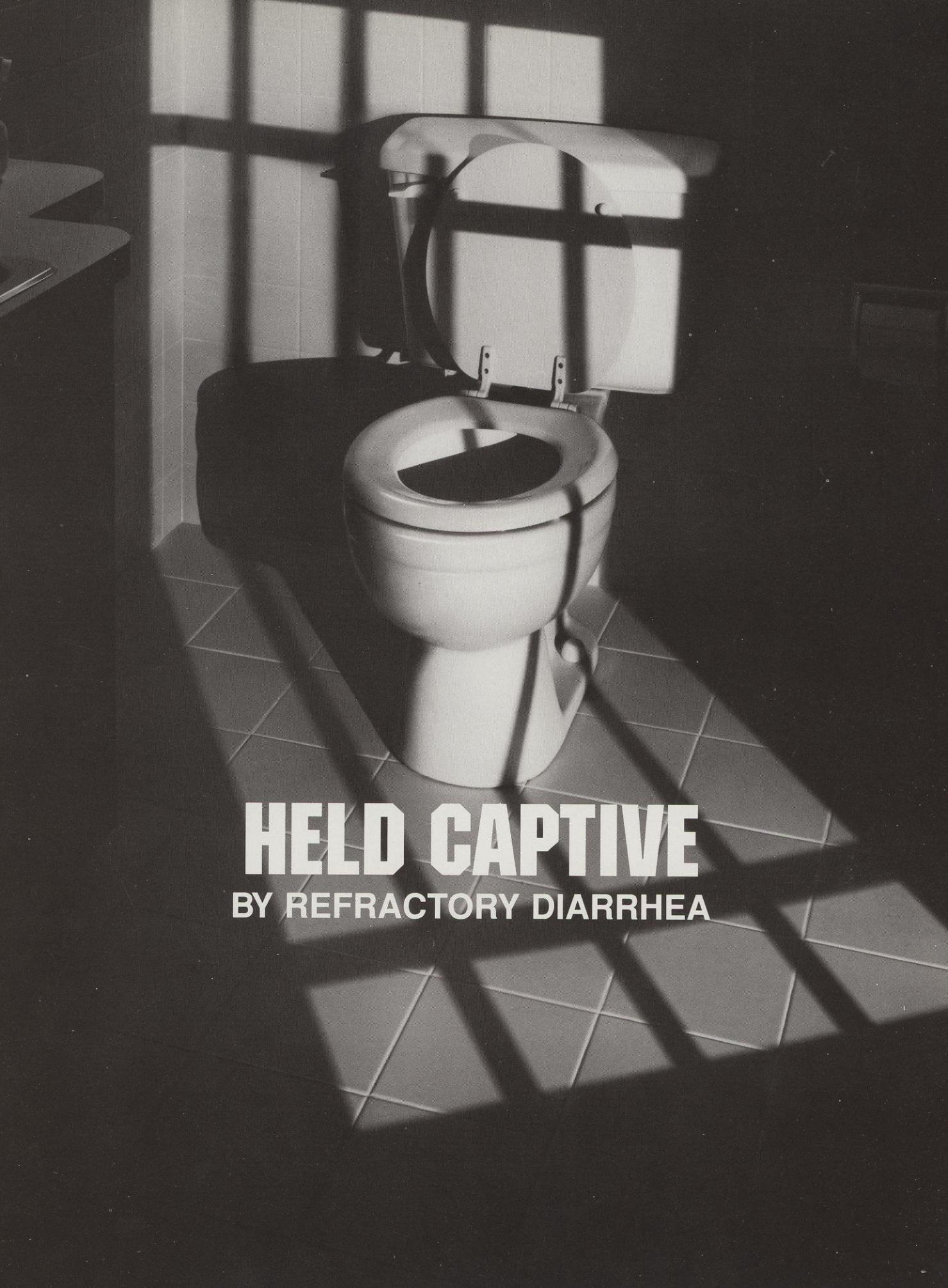
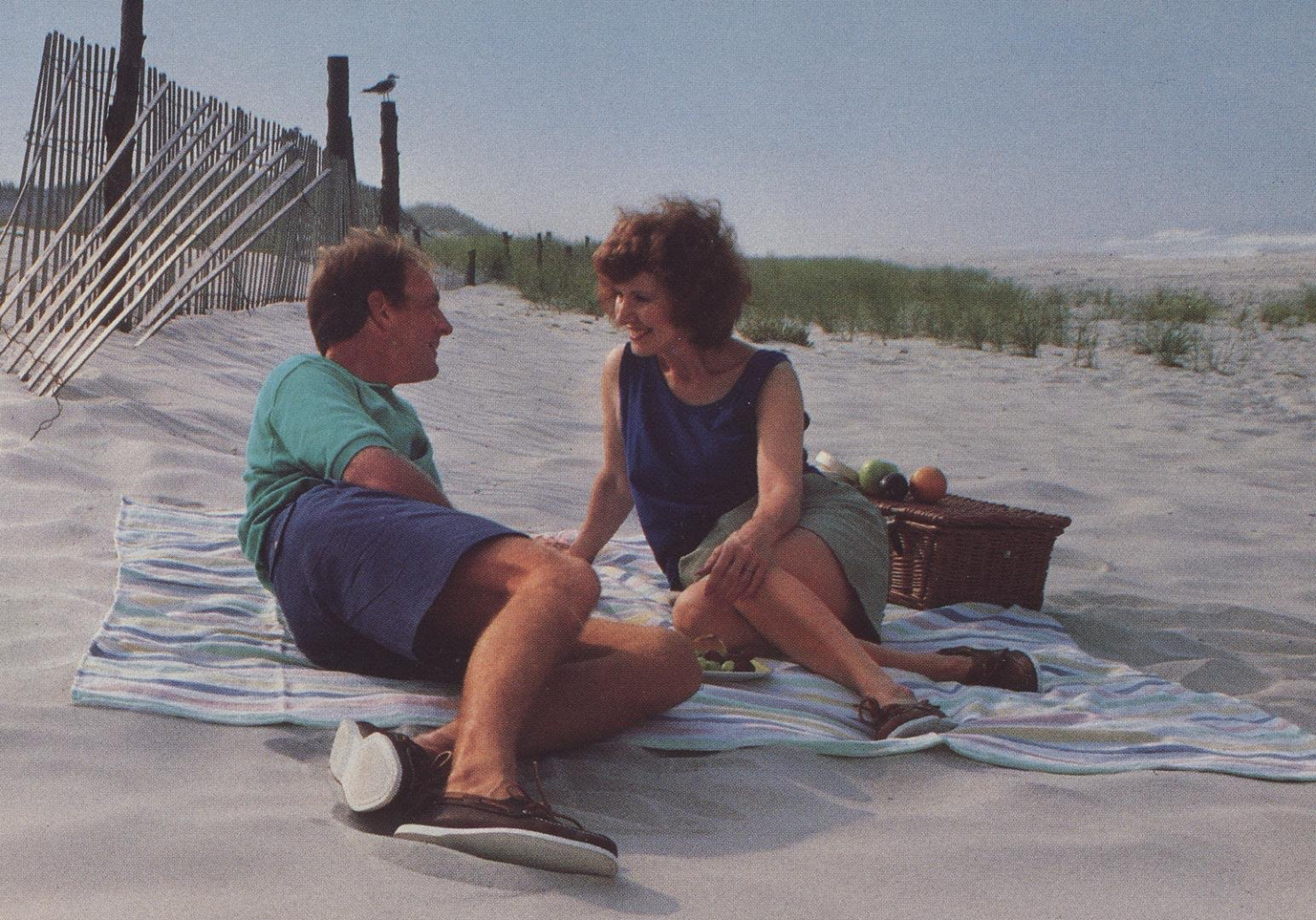
Sandostatin advertisement.

[s.l.]: [s.n.], 1987


HELD CAPTIVE
BY REFRACTORY DIARRHEA



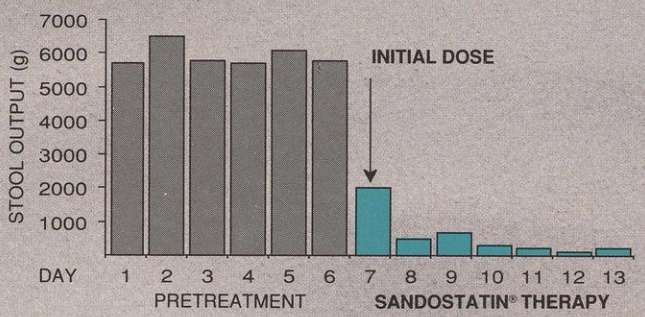
SET FREE

BY SANDOSTATIN STOPPING POWER

The power to stop severe refractory diarrhea is the power to free your patient to resume a normal lifestyle. SANDOSTATIN® (octreotide acetate), the first long-acting synthetic peptide to mimic the actions of somatostatin, has the power to rapidly relieve diarrhea associated with metastatic carcinoid syndrome or VIPoma in 63-83% of patients.[1] It works in the GI tract by slowing transit, increasing water and electrolyte absorption, and inhibiting endocrine gland secretion.[1-4]

The most common adverse reactions associated with SANDOSTATIN® therapy, burning at injection site (8%) and nausea (10%), are usually mild and transient.* The usual starting dose, 50 mcg administered by subcutaneous injection once or twice a day, should be titrated according to patient response.

Dramatic reduction of stool output in VIPoma patient treated with SANDOSTATIN® (octreotide acetate) 100 mcg bid sc
(Adapted from Maton.[5])



Sandostatin®
octreotide acetate | SANDOZ

Stopping Symptoms through the ***Power*** of Inhibition

*Patients undergoing chronic SANDOSTATIN® therapy should be periodically monitored for gallbladder disease, thyroid function and fecal fat.

See brief summary of prescribing information on adjacent page.

Brief Summary

SANDOSTATIN® (octreotide acetate) **INJECTION**

CONTRAINDICATIONS

Sensitivity to this drug or any of its components.

WARNINGS

Sandostatin® (octreotide acetate) therapy, like the natural hormone, somatostatin, may be associated with cholelithiasis, presumably by altering fat absorption and possibly by decreasing the motility of the gallbladder. Because patients with somatostatinomas have been reported to be at risk for these dysfunctions, patients being treated with Sandostatin® (octreotide acetate) should be monitored periodically for gallbladder disease. Surgical intervention has been required in a few patients who developed severe abdominal pain associated with cholelithiasis while on Sandostatin® (octreotide acetate) therapy. It is recommended that patients on extended therapy be evaluated periodically using ultrasound evaluations of the gallbladder and bile ducts.

PRECAUTIONS

General: In the treatment of patients with carcinoid syndrome or VIPomas, dosage adjustment may be required to maintain symptomatic control. Sandostatin® (octreotide acetate) therapy is occasionally associated with mild transient hypo- or hyperglycemia due to alterations in the balance between the counterregulatory hormones; insulin, glucagon, and growth hormone. Patients should be closely observed on introduction of Sandostatin® (octreotide acetate) therapy and at each change of dosage for symptomatic evidence of hyper- or hypoglycemia. Data on the effect of chronic therapy with Sandostatin® (octreotide acetate) on hypothalamic/pituitary function has not been obtained. A progressive drop in T_3 levels has been reported, culminating in clinical and biochemical hypothyroidism after 19 months of therapy in one clinical trial patient (carcinoid) receiving 1500 mcg of Sandostatin® (octreotide acetate) daily. Therefore, baseline and periodic thyroid function tests using total and free T_4 are advised to monitor patients. In insulin-dependent diabetics, reduction of insulin requirements may result following initiation of Sandostatin® (octreotide acetate) therapy.

There is evidence that Sandostatin® (octreotide acetate) therapy may alter absorption of dietary fats in some patients. It is suggested that periodic quantitative 72-hour fecal fat and serum carotene determinations be performed to aid in the assessment of possible drug-induced aggravation of fat malabsorption. In patients with severe renal failure requiring dialysis, the half-life of the drug may be increased, necessitating adjustment of the maintenance dosage. Because decreased gallbladder contractility and bile stasis may result from treatment with Sandostatin® (octreotide acetate), baseline and periodic ultrasonography may be useful to assess the presence of gallstones *(See WARNINGS)*.

Information for Patients: Careful instruction in sterile subcutaneous injection technique should be given to the patients and to other persons who may administer Sandostatin® (octreotide acetate) Injection.

Laboratory Tests: Laboratory tests that may be helpful as biochemical markers in determining and following patient response depend on the specific tumor. Based on diagnosis, measurement of the following substances may be useful in monitoring the progress of therapy:

Carcinoid: 5-HIAA (urinary 5-hydroxyindole acetic acid), plasma serotonin, plasma Substance P

VIPoma: VIP (plasma vasoactive intestinal peptide)

Baseline and periodic total and/or free T_4 measurements should be performed during chronic therapy *(See PRECAUTIONS—General)*.

Drug Interactions: Many patients with carcinoid syndrome or VIPomas being treated with Sandostatin® (octreotide acetate) have also been, or are being, treated with many other drugs to control the symptomatology or progression of the disease, generally without serious drug interaction. Included are chemotherapeutic agents, H_2 antagonists, antimotility agents, drugs affecting glycemic states, solutions for electrolyte and fluid support or hyperalimentation, antihypertensive diuretics, and anti-diarrheal agents. Where symptoms are severe and Sandostatin® (octreotide acetate) therapy is added to other therapies used to control glycemic states such as sulfonylureas, insulin, diazoxide, and to beta blockers or agents for the control of fluid and electrolyte balance, patients must be monitored closely and adjustment made in the other therapies as the symptoms of the disease are controlled. Evidence currently available suggests these imbalances in fluid and electrolytes or glycemic states are secondary to correction of pre-existing abnormalities and not to a direct metabolic action of Sandostatin® (octreotide acetate). Adjustment of the dosage of drugs, such as insulin, affecting glucose metabolism may be required following initiation of Sandostatin® (octreotide acetate) therapy in patients with diabetes. Since Sandostatin® (octreotide acetate) has been associated with alterations in nutrient absorption, its effect on absorption of any orally administered drugs should be carefully considered. A single case of transplant rejection episode (renal/whole pancreas) in a patient immunosuppressed with cyclosporine has been reported. Sandostatin® (octreotide acetate) treatment to reduce exocrine secretion and close a fistula in this patient resulted in decreases in blood levels of cyclosporine and may have contributed to the rejection episode.

Drug/Laboratory Test Interactions: No known interference exists with clinical laboratory tests, including amine or peptide determinations.

Carcinogenesis/Mutagenesis/Impairment of Fertility: Studies in laboratory animals have demonstrated no mutagenic potential of Sandostatin® (octreotide acetate). No long-term studies in animals to assess carcinogenicity have been completed. Sandostatin® (octreotide acetate) did not impair fertility in rats at doses up to 1 mg/kg/day.

Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 30 times the highest human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Sandostatin® (octreotide acetate). 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: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in milk, caution should be exercised when Sandostatin® (octreotide acetate) is administered to a nursing woman.

Pediatric Use: Experience with Sandostatin® (octreotide acetate) in the pediatric population is limited. The youngest patient to receive the drug was 1 month old. Doses of 1-10 mcg/kg body weight were well tolerated in the young patients. A single case of an infant (nesidioblastosis) was complicated by a seizure thought to be independent of Sandostatin® (octreotide acetate) therapy.

ADVERSE REACTIONS

The incidence of adverse reactions by patient group and in the total cohort (N=491) of patients follows. These adverse reactions were largely of mild to moderate severity and of short duration. Adverse reactions occurring in 3 to 10% of patients: Nausea, injection site pain, diarrhea, abdominal pain/discomfort, loose stools, vomiting. Adverse reactions occurring in 1 to 3% of patients: Headache, fat malabsorption, dizziness/light-headedness, hyperglycemia, fatigue, flushing, hypoglycemia, edema, asthenia/weakness, injection site wheal/erythema. In addition, the following infrequent reactions were reported (fewer than 1% of patients): **Gastrointestinal:** Constipation, flatulence, hepatitis, jaundice, slight increase in liver enzymes, rectal disorder (spasm), GI bleeding, stomach swollen, heartburn, fluttering sensation, abnormal stools, and cholelithiasis. **Integumentary:** Hair loss, thinning of skin, skin flaking, bruising, bleeding from a superficial wound, pruritus, and rash. **Musculoskeletal:** Backache pain, muscle pain, muscle cramping, joint pain, shoulder and leg pain, leg cramps, and chest pain. **Cardiovascular:** Shortness of breath, hypertensive reaction, thrombophlebitis, ischemia, congestive heart failure, hypertension, palpitations, orthostatic BP decrease, and chest pain. **CNS:** Anxiety, anorexia, convulsions, depression, drowsiness, vertigo, hyperesthesia, pounding in head, insomnia, irritability, libido decrease/frigidity, forgetfulness, malaise, nervousness, shakiness, syncope, tremor, and Bell's Palsy. **Respiratory:** Rhinorrhea. **Endocrine:** Galactorrhea. Clinical hypothyroidism requiring thyroid hormone replacement was observed after 19 months of therapy with 1500 mcg daily of Sandostatin® (octreotide acetate) in a clinical trial patient. A progressive fall to low total and free T_4 values was observed, without an elevated TSH, indicative of hypothalamic-pituitary dysfunction, probably related to Sandostatin® (octreotide acetate) therapy. **Urogenital:** Oliguria, pollakiuria, prostatitis, and urine hyperosmolarity. **Autonomic:** Burning sensation, dry mouth, numbness, hyperhidrosis, hyperdipsia, warm feeling, and visual disturbance. **Miscellaneous:** Chills, fever, throat discomfort, increased CPK, arm pain, and eyes burning. Evaluation of 20 patients treated for at least 6 months has failed to demonstrate titers of antibodies exceeding background levels.

DOSAGE AND ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. **Do not use if particulates and/or discoloration are observed.**

Subcutaneous injection is the recommended route of administration of Sandostatin® (octreotide acetate) for control of symptoms in most instances. Intravenous bolus injections have been used under emergency conditions. Multiple injections at the same site within short periods of time should be avoided. The initial dosage is 50 mcg, administered subcutaneously, once or twice daily. Thereafter, the number of injections and dosage may be increased gradually based on patient tolerability and response. Dosage information for patients with specific tumors follows. The drug is usually given in a b.i.d. or t.i.d. schedule.

Carcinoid Tumors: The suggested daily dosage of Sandostatin® (octreotide acetate) during the first two weeks of therapy ranges from 100 to 600 mcg per day in two to four divided doses (mean daily dosage is 300 mcg). In the clinical studies, the **median** daily maintenance dosage was approximately 450 mcg, but clinical and biochemical benefits were obtained in some patients with as little as 50 mcg, while others required doses up to 1500 mcg per day. However, experience with doses above 750 mcg per day is limited.

VIPomas: Daily dosages of 200 to 300 mcg in two to four divided doses are recommended during the initial 2 weeks of therapy (range 150 to 750 mcg) to control symptoms of the disease. On an individual basis, dosage may be adjusted to achieve a therapeutic response, but usually doses above 450 mcg per day are not required.

Manufactured by Sandoz, Ltd., Basle, Switzerland for Sandoz Pharmaceuticals Corporation, East Hanover, NJ 07936 [SEPTEMBER 1, 1989 SDS-Z3]

Available in a Convenient Outpatient Administration Kit

References 1. Dueno MI, Bai JC, Santangelo WC *et al*: Effect of somatostatin analog on water and electrolyte transport and transit time in the human small bowel. *Dig Dis Sci* 32:1092-1096, 1987. **2.** Vinik AI, Tsai S, Moattari AR *et al*: Somatostatin analogue (SMS 201-995) in the management of gastroenteropancreatic tumors and diarrhea syndromes. *Am J Med* 81(suppl 6B):23-39, 1986. **3.** Edwards CA, Cann PA, Read NW *et al*: The effect of somatostatin analogue SMS 201-995 on fluid and electrolyte transport in a patient with secretory diarrhoea. *Scand J Gastroenterol* 21(suppl 119):259-261, 1986. **4.** Santangelo WC, O'Dorisio TM, Kim JG *et al*: VIPoma syndrome. Effect of a synthetic somatostatin analogue. *Scand J Gastroenterol* 21(suppl 119):187-190, 1986. **5.** Maton PN, O'Dorisio TM, Howe BA *et al*: Effect of a long-acting somatostatin analogue (SMS 201-995) in a patient with pancreatic cholera. *N Engl J Med* 312:17-21, 1985.

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