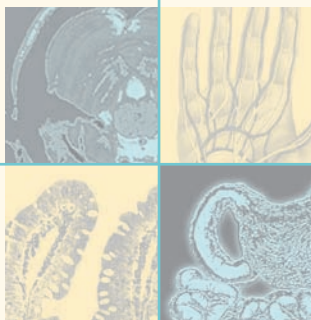


Octreotide
Pharmacodynamics...

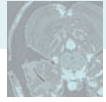


Critical Control

In All the Areas You
Want It Most.

 **Sandostatin LAR[®] Depot**
(octreotide acetate for injectable suspension)

The Power of Control. Made Easy.



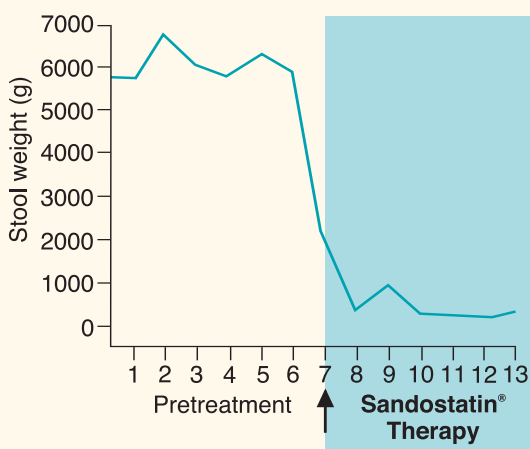
OCTREOTIDE.

Controls the Activity of Many of the Same Regulatory Hormones as Native Somatostatin – With Once-A-Month Convenience¹

- Inhibits growth hormone, glucagon, and insulin
- Suppresses LH response to GnRH
- Decreases splanchnic blood flow
- Inhibits release of gastroenteropancreatic secretions, including:
 - serotonin
 - gastrin
 - secretin
 - motilin
 - vasoactive intestinal peptide (VIP)
 - pancreatic polypeptide (PP)

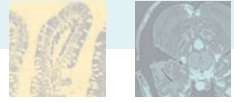
OCTREOTIDE.

Controls Diarrhea with the First Dose²



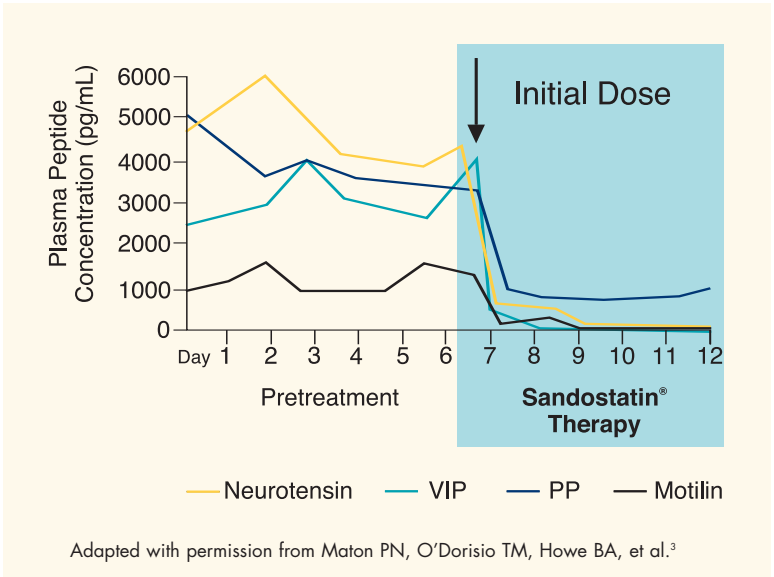
Mean stool output reduced from 4.0 stools/day
to 2.1 stools/day at 20-mg dose*

*All patients were first treated with and responded to subcutaneous (SC) Sandostatin[®] (octreotide acetate) Injection. Then, they underwent a 3- to 5-day drug-free washout period and had a return of their symptoms prior to their first dose of Sandostatin LAR[®] Depot. Those patients randomized to Sandostatin LAR[®] Depot received SC Sandostatin[®] Injection concomitantly for 11 days. Trial design was a prospective, multicenter, randomized study using double-blind dosing for Sandostatin LAR[®] Depot and open-label dosing for SC Sandostatin[®] Injection. N=92; patient numbers for the 4 arms ranged from 20 to 26 at baseline and endpoint.



OCTREOTIDE.

Well-Established Control of Peptide Secretions³

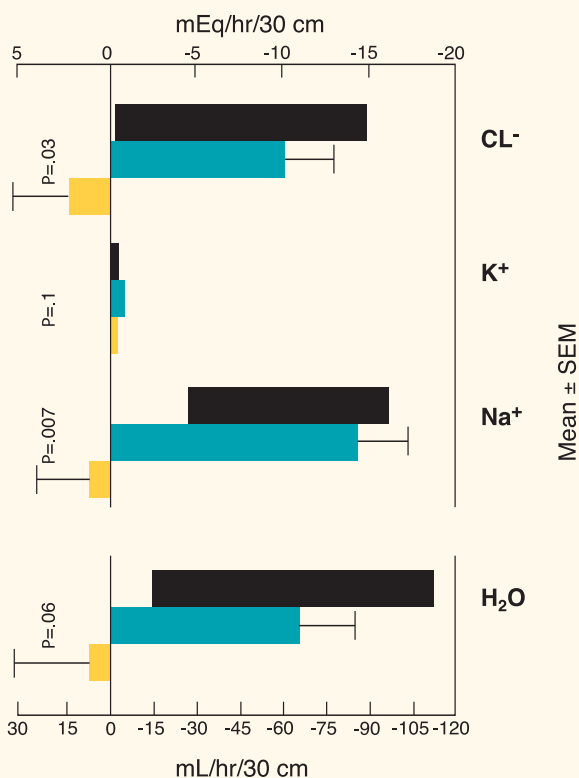


Peptide concentrations rapidly reduced after initiation of therapy in a patient with VIPoma[†]

[†]Therapy with Sandostatin® Injection, 100 µg SC bid.

OCTREOTIDE.

Increases Your Control of Patients' Water/Electrolyte Absorption⁴



Adapted with permission from Vinik A, Moattari AR.4

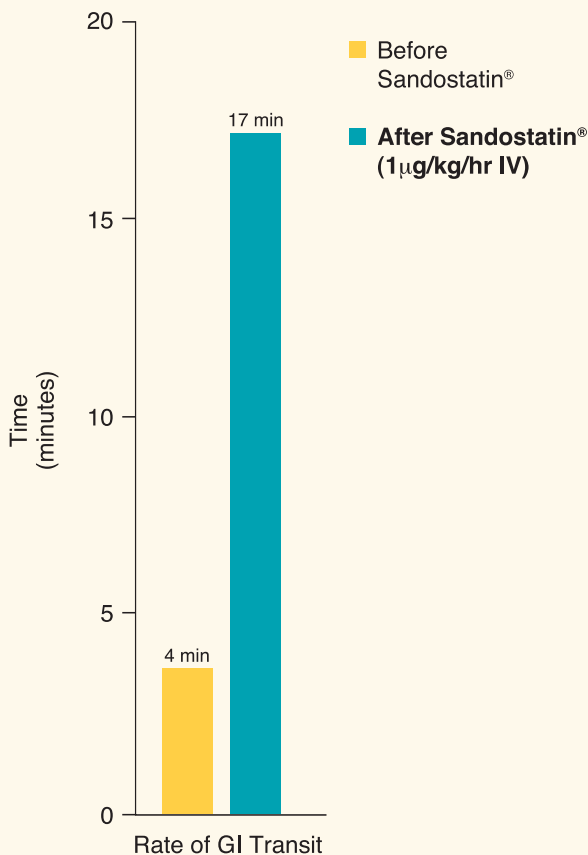
Overall "secretory state" changed to an "absorptive state" after treatment with octreotide*

*Therapy with Sandostatin[®] Injection, 100 µg SC bid. N=6.



OCTREOTIDE.

Slows Gastrointestinal Transit Time^{†5}



Adapted with permission from Dueno MI, Bai JC, Santangelo WC, et al.⁵

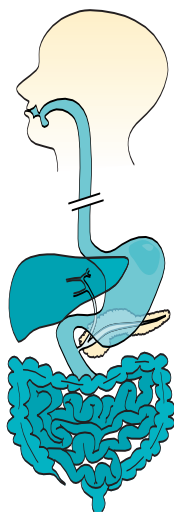
GI transit time prolonged in 30-cm
jejunal segments in 6 healthy patients.^{††}

[†]When given at appropriate doses.

^{††}Sandostatin[®] Injection 1 µg/kg/hr IV.

OCTREOTIDE.

Exerts Control Throughout
the Gastrointestinal System^{1,6}



**Reduces liver
blood flow**

**Inhibits gastric acid and
pepsin secretion**

**Inhibits gallbladder
contractility and bile flow**

**Inhibits pancreatic
exocrine secretion**

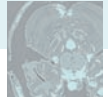
**Inhibits gastrointestinal
and pancreatic peptide
hormone secretion**

**Slows gastrointestinal transit
time and inhibits absorption
of glucose and amino acids**

**Reduces splanchnic
blood flow**

**Stimulates water and
electrolyte absorption**

**Inhibits tissue growth
and proliferation**



OCTREOTIDE.

Decreases Splanchnic Blood Flow^{1,7}

Splanchnic Effects:	Systemic Effects:
<ul style="list-style-type: none">▼ splanchnic blood flow 25%▼ total hepatic blood flow 25%▼ wedged hepatic vein pressure 10% to 15%▼ varix pressure 35%▼ transhepatic venous pressure gradient 20% to 30%◀▶ splanchnic oxygen uptake (no change)	<ul style="list-style-type: none">◀▶ pulse rate (no change)◀▶ arterial blood pressure (no change)◀▶ cardiac index (no change)

Adapted with permission from Cello, JP, Chan MF.⁷

OCTREOTIDE.

A Well-Established Safety Profile¹

Sandostatin LAR[®] Depot – Proven Safe in Carcinoid Syndrome

As with subcutaneous Sandostatin[®] (octreotide acetate) Injection, the most frequently reported drug-related adverse events were biliary disorders (62%), gastrointestinal disorders (14% to 38%), and injection site pain (20% to 50%). Hypoglycemia (4%), hyperglycemia (27%), sinus bradycardia (19%), conduction abnormalities (9%), and arrhythmias (3%) have been reported.

Sandostatin LAR[®] Depot – Proven Safe in Acromegaly

As with subcutaneous Sandostatin[®] (octreotide acetate) Injection, the most frequently reported drug-related adverse events were biliary disorders (52%), gastrointestinal disorders (7% to 36%), and injection site pain (2% to 11%). Hypoglycemia (2%), hyperglycemia (15%), and hypothyroidism (2%) have been reported. While not measured in acromegalic patients receiving Sandostatin LAR[®] Depot, ECG changes have been reported in patients receiving subcutaneous Sandostatin[®] Injection; the degree to which these abnormalities are related to octreotide acetate is not clear as many acromegalics have cardiovascular disease.



References

1. Sandostatin LAR[®] Depot (octreotide acetate for injectable suspension) prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 1998.
2. Data on file. Novartis Pharmaceuticals Corporation.
3. 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.* 1985;312:17-21.
4. Vinik A, Moattari AR. Use of somatostatin analog in management of carcinoid syndrome. *Dig Dis Sci.* 1989;34(March suppl):14S-27S.
5. Dueno MI, Bai JC, Santangelo WC, et al. Effect of somatostatin analog on water and electrolyte transport and transit time in human small bowel. *Dig Dis Sci.* 1987;32:1092-1096.
6. Lamberts SWJ, van Der Lely A-J, de Herder WW, et al. Octreotide. *N Eng J Med.* 1996;334:246-254.
7. Cello JP, Chan MF. Octreotide therapy for variceal hemorrhage. *Digestion.* 1993;54(suppl):20-26.

OCTREOTIDE.

Pharmacologically-Suited to Provide The Control You Require

- Rapidly controls diarrhea²
- Promotes water and electrolyte absorption⁴
- Prolongs gastrointestinal transit time at appropriate doses⁵
- Inhibits hormonal hypersecretion¹
- Rapidly reduces peptide secretions³
- Decreases splanchnic blood flow⁷
- Offers a well-established safety profile¹



The Power of Control. Made Easy.

Please see enclosed full prescribing information for Sandostatin LAR[®] Depot (octreotide acetate for injectable suspension).



NOVARTIS PHARMACEUTICALS CORPORATION
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