

ADVERSE REACTIONS

In two placebo-controlled clinical trials in which 205 patients were treated with Serostim® [somatropin (rDNA origin) for injection] the most common adverse reactions judged to be associated with Serostim® were musculoskeletal discomfort and increased tissue turgor (swelling, particularly of the hands or feet) (see PRECAUTIONS: GENERAL). These symptoms were generally rated by investigators as mild to moderate in severity and usually subsided with continued treatment. Discontinuities as a result of these events were rare.

Because of the diverse clinical manifestations of AIDS, and the frequent occurrence of adverse events associated with underlying disease process, it was often difficult to distinguish adverse events possibly associated with the administration of Serostim® from underlying signs or symptoms of AIDS or associated intercurrent illnesses.

Clinical adverse events which occurred during the first 12 weeks of study in at least 10% of those who received Serostim® during the two placebo-controlled trials are listed below by treatment group, without regard to causality assessment.

Table 2: Controlled Trials Adverse Events

Adverse Event	Serostim® (n=205) %	Placebo (n=150) %
Musculoskeletal discomfort	53.7	33.3
Fever	31.2	29.3
Increased tissue turgor	27.3	2.7
Diarrhea	25.9	20.0
Neuropathy	25.9	17.3
Nausea	25.9	16.0
Headache	19.0	20.7
Abdominal pain	17.1	18.7
Fatigue	17.1	16.0
Leukopenia	15.1	24.7
Albuminuria	15.1	9.3
Granulocytopenia	14.1	21.3
Lymphadenopathy	14.1	16.0
Increased sweating	14.1	8.7
Anorexia	12.2	9.3
Anemia	12.2	8.7
Vomiting	11.7	12.0
SGOT increased	11.7	6.0
Insomnia	11.2	9.3
Tachycardia	11.2	6.0
Hyperglycemia	10.2	6.0
SGPT increased	10.2	5.3

Adverse events that occurred in 1% to less than 10% of study participants receiving Serostim® in the two placebo-controlled clinical efficacy studies are listed below by body system. The list of adverse events has been compiled regardless of causal relationship to Serostim®.

Body as a Whole: rigors, flu-like symptoms, back pain, malaise, asthenia, carpal tunnel syndrome (see PRECAUTIONS: GENERAL), chest pain, hot flashes, allergic reaction.

Gastrointestinal System: oral leukoplakia, flatulence, dyspepsia, dry mouth, constipation, ulcerative stomatitis, increased amylase, dysphagia, esophagitis, colitis, pancreatitis, rectal disorder, gastritis, tongue ulceration, gingivitis

Musculoskeletal System: muscle weakness

Central and Peripheral Nervous System: dizziness, convulsions, hypertonia, neuralgia, tremor, encephalopathy, nystagmus, meningism
Respiratory System: dyspnea, coughing, sinusitis, upper respiratory tract infection, pharyngitis, rhinitis, pneumonia, bronchitis, increased sputum, respiratory disorder, bronchospasm, pneumonitis, pleurisy

White Blood Cell and Reticuloendothelial System Disorders: cervical lymphadenopathy, eosinophilia

Skin and Appendages: skin disorder, folliculitis, rash, alopecia, photosensitivity reaction, erythematous rash, pruritus, abnormal pigmentation, seborrhea, dermatitis, skin ulceration, acne, skin discoloration, verruca

Psychiatric: depression, anxiety, somnolence, nervousness, appetite increased, amnesia, abnormal thinking

Metabolic and Nutritional: hypertriglyceridemia, increased alkaline phosphatase, dehydration, increased creatine phosphokinase, increased LDH, glycosuria, hypokalemia, cachexia, thirst, acidosis

Immune System Dysfunction: moniliasis, bacterial infection, Pneumocystis carinii infection, viral infection, infection, Herpes simplex, sepsis, abscess, fungal infection, Herpes zoster

Urinary System: hematuria, urinary tract infection, nocturia

Liver and Biliary System: abnormal hepatic function, hepatomegaly, hepatitis

Vision: retinitis, abnormal vision, photophobia

Platelet, Bleeding and Clotting: thrombocytopenia, purpura

Cardiovascular, General: abnormal ECG, heart murmur, hypertension, hypotension

Application Site: injection site pain, injection site reaction

Neoplasms: Kaposi's sarcoma

Male Reproductive: Epididymitis, penis disorder, inguinal hernia

Hearing and Vestibular: earache, ear disorder, decreasing hearing

Endocrine: gynecomastia, male breast pain

The types and incidences of adverse events reported in an open-label, extension trial and in a single, foreign trial, for up to one year, were not different from, or greater in frequency, than those observed in the primary, placebo-controlled, clinical trials.

During post-marketing surveillance, cases of new onset glucose intolerance, diabetes mellitus and exacerbation of pre-existing diabetes mellitus have been reported in patients receiving Serostim®. Some patients developed diabetic ketoacidosis and diabetic coma. In some patients, these conditions improved when Serostim® was discontinued while in others the glucose intolerance persisted. Some patients necessitated initiation or adjustment of antidiabetic treatment while on Serostim®.

OVERDOSAGE

Glucose intolerance can occur with overdosage. Long-term overdosage with growth hormone could result in signs and symptoms of acromegaly.

DOSAGE AND ADMINISTRATION

Serostim® [somatropin (rDNA origin) for injection] should be administered subcutaneously daily at bedtime according to the following dosage recommendations:

Weight Range	Dose*
>55 kg	6 mg SC daily
45-55 kg	5 mg SC daily
35-45 kg	4 mg SC daily

* Based on an approximate daily dosage of 0.1 mg/kg.

In patients who weigh less than 35 kg, Serostim® should be administered at a dose of 0.1 mg/kg subcutaneously daily at bedtime. Serostim® 8.8 mg with Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol) should be administered at a dose of 0.1 mg/kg subcutaneously at bedtime.

Dose reductions for side effects felt to be related to treatment with Serostim®, which are unresponsive to symptomatic treatment, may be effected by reducing the total daily dose or the number of doses given per week.

In patients who continue to lose weight at week 2, reevaluate for concurrent opportunistic infections or other clinical events.

Injection sites should be rotated.

Safety and effectiveness in pediatric patients with AIDS have not been established.

Each vial of Serostim® 4 mg, 5 mg or 6 mg is reconstituted with 0.5-1 mL Sterile Water for Injection, USP. Each vial of Serostim® 8.8 mg is reconstituted in 1 mL to 2 mL of Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol preserved). For patients sensitive to this diluent see "WARNINGS".

To reconstitute Serostim®, inject the diluent into the vial of Serostim® aiming the liquid against the glass vial wall. Swirl the vial with a gentle rotary motion until contents are dissolved completely. The Serostim® solution should be clear immediately after reconstitution. **DO NOT INJECT** Serostim® if the reconstituted product is cloudy immediately after reconstitution or refrigeration. Occasionally, after refrigeration, small colorless particles may be present in the Serostim® solution. This is not unusual for proteins like Serostim®.

STABILITY AND STORAGE

Before reconstitution: Vials of Serostim® and diluent should be stored at room temperature (15°-30°C/59°-86°F). Expiration dates are stated on product labels.

After reconstitution with Sterile Water for Injection, USP: When Serostim® is reconstituted with Sterile Water for Injection, USP, the reconstituted solution should be used immediately and any unused portion should be discarded.

After reconstitution with Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol): When Serostim® is reconstituted with Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol), the reconstituted solution should be stored under refrigeration (2°-8°C/36°-46°F) for up to 14 days.

Avoid freezing reconstituted vials of Serostim®.

HOW SUPPLIED

Serostim® [somatropin (rDNA origin) for injection] is available in the following forms:

Serostim® vials containing 4 mg (approximately 12 IU) somatropin (mammalian-cell) with Sterile Water for Injection, USP. Package of 7 vials. NDC 44087-0004-7

Serostim® vials containing 5 mg (approximately 15 IU) somatropin (mammalian-cell) with Sterile Water for Injection, USP. Package of 7 vials. NDC 44087-0005-7

Serostim® vials containing 6 mg (approximately 18 IU) somatropin (mammalian-cell) with Sterile Water for Injection, USP. Package of 7 vials. NDC 44087-0006-7

Serostim® vial containing 8.8 mg (approximately 26.4 IU) somatropin (mammalian-cell) with Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol). Package of 1 vial. NDC 44087-0088-1

Manufactured for: Serono, Inc., Randolph, MA 02368

Rx Only BX Rated

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Serostim®

[somatropin (rDNA origin) for injection]

Serono

DESCRIPTION

Serostim® [somatropin (rDNA origin) for injection] is a human growth hormone produced by recombinant DNA technology. Serostim® has 191 amino acid residues and a molecular weight of 22,125 daltons. Its amino acid sequence and structure are identical to the dominant form of human pituitary growth hormone. Serostim® is produced by a mammalian cell line (mouse C127) that has been modified by the addition of the human growth hormone gene. Serostim® is secreted directly through the cell membrane into the cell-culture medium for collection and purification.

Serostim® is a highly purified preparation. Biological potency is determined by measuring the increase in the body weight induced in hypophysectomized rats.

Serostim® is available in 4 mg, 5 mg and 6 mg vials for single dose administration. Serostim® is also available in 8.8 mg vials for multi-dose administration. Each 4 mg vial contains 4.0 mg (approximately 12 IU) somatropin, 27.3 mg sucrose, 0.9 mg phosphoric acid. Each 5 mg vial contains 5.0 mg (approximately 15 IU) somatropin, 34.2 mg sucrose and 1.2 mg phosphoric acid. Each 6 mg vial contains 6.0 mg (approximately 18 IU) somatropin, 41.0 mg sucrose and 1.4 mg phosphoric acid. Each 8.8 mg vial contains 8.8 mg (approximately 26.4 IU) somatropin, 60.2 mg sucrose and 2.05 mg phosphoric acid. The pH is adjusted with sodium hydroxide or phosphoric acid to give a pH of 7.4 to 8.5 after reconstitution.

CLINICAL PHARMACOLOGY

Serostim® [somatropin (rDNA origin) for injection] is an anabolic and anticatabolic agent which exerts its influence by interacting with specific receptors on a variety of cell types including myocytes, hepatocytes, adipocytes, lymphocytes, and hematopoietic cells. Some, but not all, of its effects are mediated by another class of hormones known as somatomedins (IGF-1 and IGF-2).

AIDS-associated wasting is a metabolic disorder characterized by abnormalities of intermediary metabolism resulting in weight loss, inappropriate depletion of lean body mass (LBM), and paradoxical preservation of body fat. LBM includes primarily skeletal muscle, organ tissue, blood and blood constituents, and both intracellular and extracellular water. Depletion of LBM results in muscle weakness, organ failure, and death. Unlike nutritional intervention for AIDS-associated wasting, in which supplemental calories are converted predominantly to body fat, Serostim® treatment resulted in an increase in LBM and a decrease in body fat with a significant increase in body weight due to the dominant effect of LBM gain.

Effects on Protein, Lipid, and Carbohydrate Metabolism:

A one-week study in 6 patients with HIV associated wasting has shown that treatment with Serostim® improves nitrogen balance, increases protein-sparing lipid oxidation, and has little effect on overall carbohydrate metabolism.

Lean Body Mass Accrual:

In the same study, treatment with Serostim® resulted in the retention of phosphorus, potassium, nitrogen, and sodium. The ratio of retained potassium and nitrogen during Serostim® therapy was consistent with retention of these elements in lean tissue. In clinical studies (12 weeks), Serostim® significantly increased lean body mass. There was also a proportionate increase in intracellular and extracellular fluid during Serostim® therapy suggesting accretion of normally hydrated lean body tissue.

Physical Performance:

Treadmill performance was examined in a 12-week placebo-controlled study. Work output improved significantly in the Serostim®-treated group after 12 weeks of therapy and was correlated with LBM. No such correlation was seen with body fat. Isometric muscle performance, as measured by grip strength dynamometry, declined, probably as a result of a transient increase in tissue turgor known to occur with r-hGH therapy.

PHARMACOKINETICS

Subcutaneous Absorption: The absolute bioavailability of Serostim® [somatropin (rDNA origin) for injection] after subcutaneous administration of a formulation not equivalent to the marketed formulation was determined to be 70-90%. The $t_{1/2}$ (Mean \pm SD) after subcutaneous administration is significantly longer than that seen after intravenous administration to normal male volunteers, down-regulated with somatostatin (3.94 ± 3.44 hrs. vs. 0.58 ± 0.08 hrs.), indicating that the subcutaneous absorption of the clinically tested formulation of the compound is slow and rate-limiting.

Distribution: The steady-state volume of distribution (Mean \pm SD) following IV administration of Serostim® in healthy volunteers is 12.0 ± 1.08 L.

Metabolism: Although the liver plays a role in the metabolism of growth hormone, GH is primarily cleaved in the kidney. GH undergoes glomerular filtration and after cleavage within the renal cells, the peptides and amino acids are returned to the systemic circulation.



Elimination: The $t_{1/2}$ (Mean \pm SD) in nine patients with AIDS related wasting with an average weight of 56.7 ± 6.8 kg, given a fixed dose of 6.0 mg r-hGH subcutaneously was 4.28 ± 2.15 hrs. The renal clearance of r-hGH after subcutaneous administration in nine patients with AIDS related wasting was 0.0015 ± 0.0037 L/h. No significant accumulation of r-hGH appears to occur after 6 weeks of dosing as indicated.

Special Populations:

Pediatric: Available evidence suggests that r-hGH clearances are similar in adults and children, but no clinical studies were conducted in children with acquired immune deficiency syndrome or AIDS-related complex.

Gender: Biomedical literature indicates that a gender related difference in the mean clearance of r-hGH could exist (Clearance of r-hGH in males > Clearance of r-hGH in females). However, no gender-based analysis is available on Serostim[®] in normal volunteers or patients infected with HIV.

Race: No data are available.

Renal Insufficiency: It has been reported that individuals with chronic renal failure tend to have decreased hGH clearance compared to normals, but there are no data on Serostim[®] use in the presence of renal insufficiency.

Hepatic Insufficiency: A reduction in r-hGH clearance has been noted in patients with severe liver dysfunction. However, the clinical significance of this in HIV+ patients is unknown.

CLINICAL STUDIES

The clinical efficacy of Serostim[®] [somatotropin (rDNA origin) for injection] was assessed in two placebo-controlled clinical trials. Of the 205 AIDS subjects exposed to GH, only 5 were women. All study subjects received concomitant anti-HIV therapy.

Clinical Trial 1: A multicenter, double-blind, placebo-controlled study compared Serostim[®] at an average daily dose of 0.1 mg/kg/day administered subcutaneously to placebo in 178 patients with AIDS wasting. The study participants had unintentional weight loss of at least 10% or weighed less than 90% of the lower limit of ideal body weight. In the 140 evaluable patients (those completing a 12-week course of treatment and who were at least 80% compliant with study drug; Serostim[®] = 69, Placebo = 71), the mean difference in weight increase in the Serostim[®]-treated group was 1.6 kg (3.5 lb.). For those patients that had a week two assessment, 76% had weight gain. After 12 weeks of treatment, 74% of the patients treated with Serostim[®] gained weight while only 48% of the placebo-treated patients gained weight ($p=0.002$). Mean differences in lean body mass change between the Serostim[®] treated group and the placebo treated group was 3.1 kg (6.8 lbs) as measured by DEXA. Significant lean body mass gain ($p<0.05$) was achieved in 70% of the patients treated with Serostim[®] after 12 weeks (see Table 1). No change in LBM was observed in placebo-treated patients. Mean increase in weight and lean body mass and mean decrease in body fat (see Figure 1) were significantly greater in the Serostim[®] treated group than in the placebo group ($p=0.011$, $p<0.001$, $p<0.001$, respectively). While depletion of body weight and lean body mass has been associated with increased morbidity and mortality, the clinical significance of treatment-induced weight gain and LBM accrual has yet to be established.

Treatment with Serostim[®] resulted in a significant increase of physical function as assessed by treadmill exercise testing. The median treadmill work output increased by 13% ($p=0.039$) at 12 weeks in the group receiving Serostim[®] (see Figure 2). There was no improvement in the placebo treated group at 12 weeks. Changes in treadmill performance were significantly correlated with changes of lean body mass.

The most common reason for patient drop-out was concurrent medical events including opportunistic infections. There were decreases in serum albumin in both Serostim[®] and placebo groups. There was up to a 2.7 fold increase in serum IGF-1 levels. No patients developed antibodies to growth hormone.

Patients completing the 12-week placebo-controlled portion of the study were eligible to receive open-label Serostim[®] therapy, and 96% ($n=136$) chose to participate. Since this phase of the trial was open-label, and due to limited numbers of evaluable patients, it is difficult to interpret weight and LBM changes. The patients who initially received placebo had significant increases in median weight (1.4 kg, $p=0.012$) and lean body mass (2.4 kg, $p<0.001$) compared to baseline, during their first 12-weeks on Serostim[®]. These changes were similar in magnitude to those observed in patients initially treated with Serostim[®]. For those patients who had initially received Serostim[®] in the placebo-controlled trials, the median weight change during 12-weeks of open label treatment with Serostim[®] (-0.2 kg) and LBM change (-0.3 kg) were not significant ($p=0.700$ and $p=0.661$, respectively), suggesting that the gains of weight and LBM were not lost.

Figure 1: Trial 1: Mean Changes in Body Composition

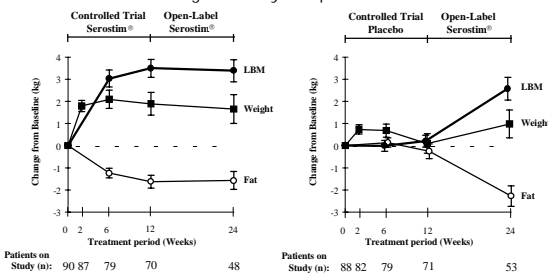


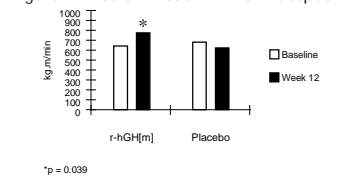
Table 1: Trial 1: Change from Baseline of LBM 12-Week Efficacy Results

	Serostim [®]		Placebo	
	n	Results	n	Results
Lean Body Mass (kg)	69	+3.1*	69	-0.1
LBM Responders†	69	70%*	69	12%

† Major LBM response defined as >4% increase of LBM

* Statistically significantly different from placebo at $p<0.05$

Figure 2: Median Treadmill Work Output



* $p=0.039$

Clinical Trial 2: Additional efficacy and safety parameters were evaluated in a second multicenter, double-blind, placebo-controlled study comparing Serostim[®], 6 mg/day administered subcutaneously vs. placebo, in AIDS patients with wasting enrolled 177 patients who were randomized in a 2:1 ratio, to receive Serostim[®] or placebo. In the 78 evaluable patients (those completing a 12-week course of treatment and who were at least 80% compliant with study drug), there was a mean increase in body weight of 1.6 kg, but this change was not significant compared to placebo ($p=0.110$). The most common reason for patient drop-out was concurrent medical events including opportunistic infections.

Patients were asked to respond to a nine item survey that measured subjective assessments of treatment. Positive findings at 6 and 12 weeks were observed in two of the nine items (change in appearance and overall benefit of treatment). Results of other measures were inconclusive.

Survival Analyses: The two placebo-controlled clinical trials of Serostim[®] in patients with AIDS wasting up to 12 weeks in length found no difference in survival between groups.

Clinical Trial 3: A third open-label, baseline-controlled, multicenter study conducted in Europe administering Serostim[®], 6 mg/day subcutaneously, enrolled 24 patients with AIDS wasting. Twenty patients completed the 12-week treatment regimen and had body composition measurements using bioimpedance analysis. The mean increase over baseline for body weight was 1.6 kg ($p=0.137$, NS) and for lean body mass was 2.3 kg ($p=0.037$).

INDICATIONS AND USAGE

Serostim[®] [somatotropin (rDNA origin) for injection] is indicated for the treatment of AIDS wasting or cachexia. This indication is based on analyses of surrogate endpoints in studies of up to 12 weeks in duration. For patients treated in open-label extension studies, no significant additional efficacy was observed beyond 12 weeks. There are no data available from controlled studies for patients that start, stop, and re-start treatment. Concomitant anti-viral therapy is necessary (see PRECAUTIONS: GENERAL). The continued use of Serostim[®] treatment should be reevaluated in patients who continue to lose weight in the first two weeks of treatment.

CONTRAINDICATIONS

Growth hormone should not be initiated to treat patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or to patients having acute respiratory failure. Two placebo-controlled clinical trials in non-growth hormone deficient adult patients ($n=522$) with these conditions revealed a significant increase in mortality (41.9% vs. 19.3%) among somatotropin treated patients (doses 5.3-8 mg/day) compared to those receiving placebo (see WARNINGS).

Serostim[®] reconstituted with Bacteriostatic Water for Injection, USP (0.9% Benzyl Alcohol) should not be administered to patients with a known sensitivity to Benzyl Alcohol. (See "WARNINGS").

Serostim[®] [somatotropin (rDNA origin) for injection] is contraindicated in patients with a known hypersensitivity to growth hormone.

WARNING

Benzyl Alcohol as a preservative in Bacteriostatic Water for Injection, USP has been associated with toxicity in newborns. If sensitivity to the diluent occurs, Serostim[®] [somatotropin (rDNA origin) for injection] may be reconstituted with Sterile Water for Injection, USP. When Serostim[®] is reconstituted in this manner, the reconstituted solution should be used immediately and any unused portion should be discarded.

See CONTRAINDICATIONS for information on increased mortality in patients with acute critical illnesses in intensive care units due to complications following open heart or abdominal surgery, multiple accidental trauma or with acute respiratory failure. The safety of continuing growth hormone treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with growth hormone in patients having acute critical illnesses should be weighed against the potential risk.

PRECAUTIONS

General: Serostim[®] [somatotropin (rDNA origin) for injection] therapy should be carried out under the regular guidance of

a physician who is experienced in the diagnosis and management of AIDS. Inadequate nutritional intake, malabsorption and hypogonadism, which are common in individuals with AIDS and which may contribute to catabolism and weight loss, should also be monitored and treated.

HIV and Growth Hormone Considerations: In some experimental systems, recombinant human Growth Hormone (r-hGH) has been shown to potentiate HIV replication in vitro at concentrations ranging from 50-250 ng/ml. There was no increase in virus production when the antiretroviral agents, zidovudine, didanosine or lamivudine were added to the culture medium. Additional in vitro studies have shown that r-hGH does not interfere with the antiviral activity of zalcitabine or stavudine. In the controlled clinical trials, no significant growth hormone-associated increase in viral burden was observed. However, the protocol required all participants to be on concomitant nucleoside analogue therapy for the duration of the study. In view of the potential for acceleration of virus replication, it is recommended that HIV+ patients be maintained on nucleoside analogue therapy for the duration of Serostim[®] treatment.

Increased tissue turgor (swelling, particularly in the hands and feet) and musculoskeletal discomfort (pain, swelling and/or stiffness) may occur during treatment with Serostim[®], but may resolve spontaneously, with analgesic therapy, or after reducing the frequency of dosing (see DOSAGE AND ADMINISTRATION).

Carpal tunnel syndrome may occur during treatment with Serostim[®]. If the symptoms of carpal tunnel syndrome do not resolve by decreasing the weekly number of doses of Serostim[®], it is recommended that treatment be discontinued.

Patients should be informed that allergic reactions are possible and that prompt medical attention should be sought if an allergic reaction occurs. None of the 188 study participants with AIDS wasting who were evaluable for antibody assessments and who were treated with Serostim[®] for the first time developed detectable antibodies to growth hormone (> 4 pg binding). Patients were not rechallenged.

Recombinant Human Growth Hormone (r-hGH) has been associated with acute pancreatitis. Hyperglycemia may occur in HIV-infected individuals due to a variety of reasons. Serostim[®] use was associated with a minimal increase of mean blood glucose concentration. Patients with other risk factors for glucose intolerance should be monitored closely during Serostim[®] therapy.

During post-marketing surveillance, cases of new onset glucose intolerance, diabetes mellitus and exacerbation of pre-existing diabetes mellitus have been reported in patients receiving Serostim[®]. Some patients developed diabetic ketoacidosis and diabetic coma. In some patients, these conditions improved when Serostim[®] was discontinued while in others the glucose intolerance persisted. Some patients necessitated initiation or adjustment of antidiabetic treatment while on Serostim[®].

No cases of intracranial hypertension (IH) have been observed among patients with AIDS wasting treated with Serostim[®]. The syndrome of IH, with papilledema, visual changes, headache, and nausea and/or vomiting has been reported in a small number of children with growth failure treated with growth hormone products. Nevertheless, fundoscopic evaluation of patients is recommended at the initiation and periodically during the course of Serostim[®] therapy. Kaposi's sarcoma, lymphoma, and other malignancies are common in HIV+ individuals. There was no increase in the incidence of Kaposi's sarcoma, lymphoma, or in the progression of cutaneous Kaposi's sarcoma in clinical studies of Serostim[®]. Patients with internal KS lesions were excluded from the studies. Potential effects on other malignancies are unknown.

Information For Patients: Patients being treated with Serostim[®] should be informed of the potential benefits and risks associated with treatment. Patients should be instructed to contact their physician should they experience any side effects or discomfort during treatment with Serostim[®].

It is recommended that Serostim[®] be administered using sterile, disposable syringes and needles. Patients should be thoroughly instructed in the importance of proper disposal and cautioned against any reuse of needles and syringes. An appropriate container for the disposal of used syringes and needles should be employed.

Patients should be instructed to rotate injection sites to avoid localized tissue atrophy.

Drug Interactions: Formal in vitro drug interaction studies have not been conducted. No data are available on drug interactions between Serostim[®] and HIV protease inhibitors or the non-nucleoside reverse transcriptase inhibitors.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies for carcinogenicity have not been performed with Serostim[®]. There is no evidence from animal studies to date of Serostim[®]-induced mutagenicity or impairment of fertility.

Pregnancy: Pregnancy Category B. Reproduction studies have been performed in rats and rabbits. Doses up to 5 to 10 times the human dose, based on body surface area, have revealed no evidence of impaired fertility or harm to the fetus due to Serostim[®]. 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 Women: It is not known whether Serostim[®] is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Serostim[®] is administered to a nursing woman.

Pediatric Use: In two small studies, 11 children with HIV associated failure to thrive were treated subcutaneously with human growth hormone. In one study, five children (age range, 6 to 17 years) were treated with 0.04 mg/kg/day for 26 weeks. In a second study, six children (age range, 8 to 14 years) were treated with 0.07 mg/kg/day for 4 weeks. Treatment appeared to be well tolerated in both studies. These preliminary data collected on a limited number of patients with HIV associated failure to thrive appear to be consistent with safety observations in growth hormone treated adults with AIDS wasting.

Geriatric Use: Clinical studies with Serostim[®] did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Elderly patients may be more sensitive to growth hormone action, and may be more prone to develop adverse reactions. Thus, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

