Understanding and Treating Acromegaly

SOMAVERT is indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery and/or radiation therapy and/or other medical therapies, or for whom these therapies are not appropriate. The goal of treatment is to normalize serum IGF-I levels.

Important Safety Information
SOMAVERT is contraindicated in patients with a history of hypersensitivity to any of its components.

Patients on opioids often needed higher serum pegvisomant concentrations to achieve appropriate IGF-I suppression compared with patients not receiving opioids.
Incidence and prevalence$^{1,7}$

- The incidence of acromegaly is approximately 3-4 cases per million persons per year
- < 20,000 cases in the United States
- The prevalence is about 60 cases per million
- Men and women are diagnosed equally with acromegaly
- Mean age at diagnosis = 40 years

Types of pituitary tumors$^{1,8,9}$

- Pituitary tumors account for about 15% of intracranial neoplasms
- Four main pituitary tumors are related to:

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The most common adverse events (>10% and at frequencies greater than placebo) in 1 of the 3 active treatment arms in a placebo-controlled study (N=112) included infection, pain, diarrhea, nausea, flu syndrome, abnormal liver function tests, and injection-site reaction.
What is acromegaly?  
- Acromegaly (ack-row-meg-uh-lee) is a rare disease. It happens when there is too much growth hormone and the body tissues and organs grow too much.

What is the pituitary gland?  
- The pituitary gland is a tiny organ in the brain. It makes many hormones, including growth hormone.
- It helps your body maintain normal functions, such as growth in childhood, as well as healthy bones and muscles.

What are pituitary tumors?  
- A pituitary tumor happens when cells in the pituitary gland grow out of control.
- For many patients with acromegaly, the tumor causes their pituitary gland to produce too much growth hormone.

Most pituitary tumors are not malignant.
Patient Tab 1 - Pull Tab

- Side View
  - Brain
  - Optic chiasm
  - Pituitary gland
  - Carotid artery
  - Sphenoid sinus

- Front View
  - Brain
  - Optic chiasm
  - Pituitary gland
  - Carotid artery
  - Sphenoid sinus

- Pituitary gland
- Sphenoid sinus
- Carotid artery
- Optic chiasm
Relationship Between GH and IGF-I

In a fixed-dose pivotal trial
The initial rise in GH levels in patients treated with SOMAVERT® (pegvisomant for injection) stabilized by 2 weeks6

Percent change in serum GH and IGF-I concentrations6

A dose-dependent decrease in serum IGF-I was evident as early as 2 weeks after therapy initiation. As expected, this was accompanied by an adversely proportional rise in serum GH, which was not considered significant6

In the same study, 82% of patients receiving 20 mg/day had normal IGF-I at 12 weeks; 75% at 15 mg; 39% at 10 mg and 10% at placebo

Adapted from Trainer et al.4
Randomized, double-blind, multicenter, placebo-controlled, fixed-dose, 12-week study in 112 patients with acromegaly previously treated with surgery, radiation therapy, and/or medical therapy. Patients received a loading dose of 40 mg at the start of the trial.

Important Safety Information
Functional effects of increased GH are prevented by GH receptor blockade; therefore, patients on SOMAVERT should be carefully observed for the clinical signs and symptoms of a GH-deficient state.

In a long-term dose titration trial
GH levels remained stable with SOMAVERT for 18 months (the duration of the trial)10

Serum concentrations of IGF-I and GH10

The first measurement of GH and IGF-I levels was made at 6 months after initiation of therapy in all cohorts
• The drop in IGF-I mirrors GH rise in this long-term study
• GH levels approximately doubled (an increase from baseline of 12-14 µg/L)

Adapted from van der Lely et al.10
Data from a long-term dose-titration trial in 160 patients treated with SOMAVERT for an average of 425 days. Dosing began at 10 mg/day and was titrated up or down as necessary in 5 mg/day increments until the patient’s serum IGF-I levels were normal or until the maximum dose (in this study) of 40 mg/day was reached (mean dose at 12 months was 18.0 mg/day; mean dose at 18 months was 19.6 mg/day). Data presented are from a cohort of 38 patients in a long-term, open-label, dose-titration extension trial in which patients with acromegaly were treated for at least 18 consecutive months
The maximum indicated daily maintenance dose for SOMAVERT is 30 mg.

Tumors that secrete GH may expand and cause serious complications. All patients with GH-secreting tumors, including those receiving SOMAVERT, should be carefully monitored for changes in tumor volume.
What causes the signs and symptoms of acromegaly?³

- When there is too much growth hormone (GH) in your body, it triggers the body to make too much insulin-like growth factor I (IGF-I)
- This causes organs and tissues to grow too much
- Other signs and symptoms of acromegaly may also appear

Important Safety Information
Some people who have used SOMAVER® have developed liver problems. These problems generally disappeared when those people stopped taking SOMAVER®.
Managing Signs and Symptoms

In the fixed-dose pivotal trial, **SOMAVERT®** (pegvisomant for injection) provided improvements in signs and symptoms at each dose\(^4\)

**Improvement in total score for signs and symptoms for all dose levels of SOMAVERT vs placebo at week 12**\(^6\)

- Total score for signs and symptoms was defined as the sum of all scores from 0=absent to 8=worst for symptoms including fatigue, perspiration, headache, arthralgia, and soft tissue swelling\(^6\)
- At 12 weeks, mean % change from baseline increased (worsened) 16% for placebo, and decreased (improved) 8% for 10 mg, 20% for 15 mg, and 33% for 20 mg\(^11\)
- At 12 weeks, ring size was smaller (improved) in groups treated with 15 or 20 mg of SOMAVERT, compared with placebo\(^5\)

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**Adapted from Trainer et al.\(^4\)**

Randomized, double-blind, multicenter, placebo-controlled, fixed-dose, 12-week study in 112 patients with acromegaly previously treated with surgery, radiation therapy, and/or medical therapy. Mean baseline total score for signs and symptoms was 15.2

In a post-hoc analysis of the same study,

**91% of patients who achieved normalized IGF-I levels also experienced improvements in their total signs and symptoms score of acromegaly**\(^11\)

Study description: For the post-hoc analysis, a subset of 57 patients was identified as having both IGF-I normalization and reported any signs and symptoms of acromegaly at or after the visit at which IGF-I levels were normalized\(^6\)

**Important Safety Information**

Patients on opioids often needed higher serum pegvisomant concentrations to achieve appropriate IGF-I suppression compared with patients not receiving opioids.
Do you suffer from...\textsuperscript{1, 3}

- Pain in the joints (like knees or hips)
- Headaches
- Fatigue (weak muscles)
- Sweating more than normal
- Swelling in your hands or feet
- Increased ring size

Talk to your health care professional about your signs and symptoms of acromegaly

It is important to monitor your symptoms and discuss them with your health care professional at each visit

Please see the tear pad on the back of the easel
In a long-term dose-titration trial, 92% of patients (35/38) treated with SOMAVERT® (pegvisomant for injection) achieved IGF-I reductions within age-adjusted normal range after a mean of 55 weeks. In these patients, IGF-I levels remained normalized at >90% of office visits for a mean duration of 1 year.

**Important Safety Information**

Tumors that secrete GH may expand and cause serious complications. All patients with GH-secreting tumors, including those receiving SOMAVERT, should be carefully monitored for changes in tumor volume. The maximum indicated daily maintenance dose for SOMAVERT is 30 mg. Injection sites should be rotated daily to help prevent lipohypertrophy.

Adapted from van der Lely et al. Data from a long-term, dose-titration trial in 160 patients treated with SOMAVERT for an average of 425 days. Dosing began at 10 mg/day and was titrated up or down as necessary in 5 mg/day increments until the patient’s serum IGF-I levels were normal or until the maximum dose (in this study) of 40 mg/day was reached (mean dose at 12 months was 18.0 mg/day; mean dose at 18 months was 19.6 mg/day). Data presented are from a cohort of 38 patients in a long-term, open-label, dose-titration extension trial in which patients with acromegaly were treated for at least 18 consecutive months.
What is IGF-I?¹, ³
- IGF-I stands for insulin-like growth factor-I
- In acromegaly, your body makes too much IGF-I and parts of your body grow too much

Why is it important to control my IGF-I levels if I have acromegaly?¹¹
- Keeping IGF-I levels within the normal range for people your age generally:
  - Suggests that your disease is under control
  - Helps to improve the signs and symptoms of acromegaly

What treatments may help me manage the symptoms of acromegaly?⁵
- For most patients, the first treatment is surgery to remove the tumor or reduce its size
- Many patients also need prescription medicines to help control their hormone levels, including IGF-I levels
SOMAVERTR® (pegvisomant for injection) Works

**SOMAVERTR is a growth hormone receptor antagonist (GHRa)**

SOMAVERTR effectively binds to GH receptors on cell surfaces
- Blocks the binding of endogenous GH
- Reduces IGF-I production
- The initial increase in GH levels is attributed to loss of negative feedback inhibition and does not diminish the efficacy of SOMAVERTR

**Important Safety Information**
Functional effects of increased GH are prevented by GH receptor blockade; therefore, patients on SOMAVERTR should be carefully observed for the clinical signs and symptoms of a GH-deficient state. In subjects with systemic hypersensitivity reactions, caution and close monitoring should be exercised when re-initiating SOMAVERTR therapy.
How does SOMAVERT work?6

SOMAVERT is a prescription medicine for acromegaly. It is for patients whose disease has not been controlled by surgery, radiation, and/or other medical therapies, or patients for whom these options are not appropriate. The goal of treatment with SOMAVERT is to have a normal IGF-I level in the blood.

**Important Safety Information**

Your doctor may do blood tests before and during your treatment with SOMAVERT. The doctor is checking that the IGF-I levels in your blood are normal and/or that your liver is working correctly. Your dose of SOMAVERT may be changed based on the results of these tests.

If you have stopped SOMAVERT because of an allergic reaction, your doctor will carefully monitor what happens if you start SOMAVERT again.

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**Growth Hormone (GH) with acromegaly**1,3

The pituitary gland receives signals to produce GH. GH signals the body to produce IGF-I. This causes your organs and tissues to grow too much.

**Growth Hormone Receptor antagonist (GHRa)**1,6

SOMAVERT is a GHRa that works by blocking GH action, which lowers the levels of IGF-I in the blood.
In a fixed-dose pivotal trial, SOMAVERT demonstrated a dose-dependent improvement in IGF-I normalization

Percentage of patients achieving a normal serum IGF-I at week 12

The maximum indicated daily maintenance dose for SOMAVERT is 30 mg

- The majority of adverse events were mild to moderate and of limited duration. They did not appear to be dose dependent

Adapted from Trainer et al.

Randomized, double-blind, multicenter, placebo-controlled, fixed-dose, 12-week study in 112 patients with acromegaly previously treated with surgery, radiation therapy, and/or medical therapy

Dosing with SOMAVERT

1. Establish IGF-I baseline
2. Initiate SOMAVERT therapy
   - 40-mg loading dose under physician supervision
   - 10-mg daily self-administered at-home injections
3. Monitor IGF-I levels
   - Every 4-6 weeks until normalized; every 6 months thereafter
4. Titrate if IGF-I is not normalized
   - In 5-mg increments or decrements

Important Safety Information

The most common adverse events (>10% and at frequencies greater than placebo) in 1 of the 3 active treatment arms in a placebo-controlled study (n=112) included infection, pain, diarrhea, nausea, flu syndrome, abnormal liver function tests, and injection-site reaction.

Acromegalic patients with diabetes mellitus being treated with insulin and/or oral hypoglycemic agents may require dose reductions of these therapeutic agents after the initiation of therapy with SOMAVERT.
What can I expect from treatment with SOMAVERT?6

The goal of treatment with SOMAVERT is to reach a normal IGF-I level in the blood

In 2 clinical trials, the majority of patients treated with SOMAVERT achieved normal IGF-I levels for their age

- 92% of patients treated with SOMAVERT achieved normal IGF-I levels in a long–term study (at 55 weeks)
  - This data comes from a part of a study involving 38 of the original 160 patients who received SOMAVERT. Their dose of SOMAVERT was changed until their IGF-I levels were normal

- 82% of patients treated with 20 mg/day of SOMAVERT achieved normal IGF-I levels in a short–term study*
  - In the same short-term study, the overall signs and symptoms of acromegaly improved in patients who took SOMAVERT compared with those who didn’t take any medicine
    — This study showed how patients rated the change in their symptoms, which included joint pain, headaches, fatigue, sweating, and soft tissue swelling

*This data is from a 12-week clinical trial that involved 112 patients with acromegaly: 31 patients received no medicine; 80 were treated with SOMAVERT at one of three doses. Results for patients achieving normal IGF-I levels for their age were as follows: 10% of patients taking no medicine; 39% of those on 10 mg/day of SOMAVERT; 75% of those on 15 mg/day; 82% of those on 20 mg/day.

Important Safety Information
Blood sugar levels may go down when taking SOMAVERT.
Be sure to tell your doctor if you use insulin or other medicines (oral hypoglycemic medicines) for diabetes. The dose of these medicines may need to be reduced when you use SOMAVERT.

The most common side effects with SOMAVERT are pain, infection, reaction at the injection site, flu-like symptoms, nausea, and diarrhea. These are not all of the possible side effects of SOMAVERT. For more information, speak to your doctor.
**Indication**

SOMAVERT is indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery and/or radiation therapy and/or other medical therapies, or for whom these therapies are not appropriate. The goal of treatment is to normalize serum IGF-I levels.

**Important Safety Information**

SOMAVERT is contraindicated in patients with a history of hypersensitivity to any of its components.

Patients on opioids often needed higher serum pegvisomant concentrations to achieve appropriate IGF-I suppression compared with patients not receiving opioids.

Functional effects of increased GH are prevented by GH receptor blockade; therefore, patients on SOMAVERT should be carefully observed for the clinical signs and symptoms of a GH-deficient state.

Acromegalic patients with diabetes mellitus being treated with insulin and/or oral hypoglycemic agents may require dose reductions of these therapeutic agents after the initiation of therapy with SOMAVERT.

**Important safety information regarding periodic tumor size monitoring**

Tumors that secrete GH may expand and cause serious complications. All patients with GH-secreting tumors, including those receiving SOMAVERT, should be carefully monitored for changes in tumor volume. Overall, mean tumor size was unchanged during the course of treatment in clinical studies. Tumor volume change did not appear to be influenced by whether or not patients had previously received radiation therapy.

**Important safety information regarding liver test monitoring**

Monitor liver tests based on baseline values and changes during therapy according to the schedule in the full prescribing information. In clinical studies with SOMAVERT ALT was >3X but <10X the upper limit of normal (ULN) in patients treated with SOMAVERT (1.2%) vs placebo (2.1%). ALT and AST elevations occurred within 4 to 12 weeks after the start of therapy and did not appear to be related to the dose 2 patients (0.8%) experienced elevations of ALT and AST serum concentrations >10X the upper limit of normal (ULN). In both patients, the elevations normalized after discontinuation of the medicine. If a patient develops liver test elevations, or any other signs or symptoms of liver dysfunction while receiving SOMAVERT, please see Liver Tests section of full Prescribing Information.

In subjects with systemic hypersensitivity reaction, caution and close monitoring should be exercised when re-initiating SOMAVERT therapy.

The most common adverse events (>10% and at frequencies greater than placebo) in 1 of the 3 active treatment arms in a placebo-controlled study (N=112) included infection, pain, diarrhea, nausea, flu syndrome, abnormal liver function tests, and injection-site reaction.

Injection sites should be rotated daily to help prevent lipohypertrophy.

The maximum indicated daily maintenance dose for SOMAVERT is 30 mg.

Rx only
Indication
SOMAVERT is a prescription medicine for acromegaly. It is for patients whose disease has not been controlled by surgery, radiation, and/or other medical therapies, or patients for whom these options are not appropriate. The goal of treatment with SOMAVERT is to have a normal IGF-I level in the blood.

Important Safety Information for Patients
Do not use SOMAVERT if you are allergic to SOMAVERT or anything that is in it.
Be sure to tell your doctor if you use narcotic painkillers (opioid medicines) because the dose of SOMAVERT may need to be changed.
Tumors that make growth hormone may grow in people with acromegaly. Studies have shown that the size of these tumors generally does not change for people who use SOMAVERT. Even so, these tumors need to be watched carefully by your doctor. Your doctor may ask you to have a magnetic resonance imaging (MRI) test to monitor the size of your tumor.
Blood sugar levels may go down when taking SOMAVERT. Be sure to tell your doctor if you use insulin or other medicines (oral hypoglycemic medicines) for diabetes. The dose of these medicines may need to be reduced when you use SOMAVERT.
Some people who have used SOMAVERT have developed liver problems. These problems generally disappeared when those people stopped taking SOMAVERT.
Stop the drug right away and call your doctor if you get any of these symptoms:
• Your skin or the white part of your eyes turns yellow (jaundice)
• Your urine turns dark
• Your bowel movements (stools) turn light in color
• You do not feel like eating for several days
• You feel sick to your stomach (nausea)
• You have unexplained tiredness
• You have pain in the stomach area (abdomen)

Your doctor may do blood tests before and during your treatment with SOMAVERT to check that the IGF-I levels in your blood are normal and/or that your liver is working correctly. Your dose of SOMAVERT may be changed based on the results of these tests.
If you have stopped SOMAVERT because of an allergic reaction, your doctor will carefully monitor what happens if you start SOMAVERT again.
The most common side effects with SOMAVERT are pain, infection, reaction at the injection site, flu-like symptoms, nausea, and diarrhea. These are not all of the possible side effects of SOMAVERT. For more information, speak to your doctor.
A different site should be used each day for injections. This can help prevent skin problems such as lumpiness or soreness.
SOMAVERT has not been studied in pregnant women. It is not known if SOMAVERT passes into the mother’s milk or if it can harm the baby.
If you have questions about the Pfizer Bridge Program, please call toll free at 1-800-645-1280, or visit www.somavert.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088


