Compounded Growth Hormone Secretagogue Products

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Compounded Growth Hormone Secretagogue Products

- Secretagogues belong to two classes: GH releasing hormones (GHRH) or Ghrelin Analogs.
- Sermorelin is a GHRH, all other products mentioned in this document are Ghrelin analogs.
- Ghrelin is a hormone secreted by the stomach lining when the body experiences caloric deficit (hunger). It increases GH and IGF-1 to make use of protein stores until we feed.
- All GH secretagogues mentioned here are produced by several FDA inspected compounded facilities.

Sermorelin Acetate
Description

Sermorelin acetate is a structural analog of naturally occurring, human Growth Hormone-Releasing Hormone (GHRH) consisting of its first 29 amino acids.

Sermorelin stimulates production in and secretion of GH from the pituitary gland by activating GHRH receptors on pituitary somatotrophs. Unlike gene recombinant hGH (rhGH), Sermorelin is less likely to raise serum hGH to unsafe levels because its activity is regulated by negative feedback mechanisms. Thus, Sermorelin simulates more physiologic control over hGH and thereby reduces safety concerns associated with rhGH overdosing.

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Sermorelin Acetate Detail

Type: Growth Hormone Releasing Hormone (GhRh) analog
Available Dosage Form: Lyophilized powder for subcutaneous injection (must be reconstituted)
Strengths: Compounding pharmacies may offer several different strengths and combinations. The most common Sermorelin concentrations offered in a multi-dosed bottle are 3mg, 6mg, and 15mg.
Protocol: 500mcg to 1000mcg qhs for 3 months followed by either a holiday for 30 days or alternate to GHRP/Ipamorelin. Sermorelin can be resumed after the 30-day holiday or a cycle of GHRP/Ipamorelin. Sermorelin should be administered in 12-week cycles followed by a 30-day holiday or alternate medication to mitigate decline in IGF-1 levels that can occur with GhRh supplementation
Uses (off-label): Sermorelin has several clinical indications and applications related to GHRH/GH deficiency (GHD) including diagnostic evaluation of pituitary function and management of age-related, maladaptive changes in body composition such as reduced lean body mass (muscle), increased total and visceral fat, and decreased bone mass. It also may reduce risk for developing metabolic diseases such as diabetes. It also is reported to increase physical performance, benefit sleep, and enhance quality of life.
Patient Type: younger patients (<50) with healthy pituitary function; patients seeking body composition changes without increase in hunger; patients who require improvement in sleep quality

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Sermorelin Acetate
Effects

Benefits:

- Improves sleep by increasing the amount of slow wave sleep (SWS) while augmenting sleep-related GH secretion and reducing cortisol secretion
- Promotes the synthesis and hGH from cells in the pituitary gland, increasing serum concentrations of hGH and subsequently IGF-129
- Can stimulate rhythmic pattern of hGH secretion which mimics healthy, endogenous production
- Anecdotally improves mood and well-being
- Shown to reduce bodyfat in high doses (1mg-2mg daily)

Negatives:

- Low percentage of patients have a reaction to Sermorelin upon administration with symptoms including increased HR, dizziness, rash/wheel at injection site immediately following administration. Symptoms resolve within minutes. Patients should be advised to administer their first injection while sitting down.
- Many patients experience an initial rise in IGF-1 levels followed by a decline which appears to occur over 3-6 months. Patients can be advised to d/c therapy every 12 weeks for 30 days to help mitigate the decline. Alternatively, patients can be switched to a ghrelin peptide (ie. Ipamorelin) monotherapy after 12 weeks of Sermorelin monotherapy.

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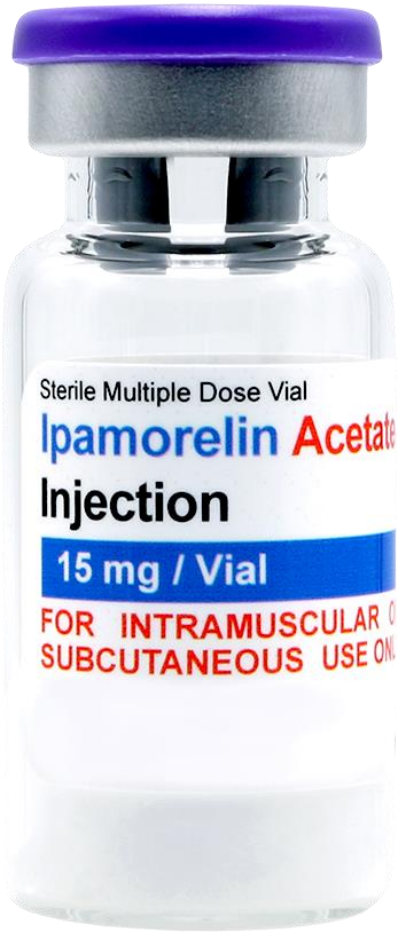
Ipamorelin Acetate

Description



Functioning as a GH secretagogue (Ghrelin analog), Ipamorelin binds to receptors in the brain and pituitary cells to cause the production and release of growth hormone. Not only does it stimulate the pituitary gland to release growth hormone, it also inhibits the release of somatostatin. Ipamorelin creates a more steady slow release of growth hormone and as such mimics the natural release of GH. In laboratory studies it is shown that Ipamorelin has a more stable release of GH than most other GHRPs. In studies previously done on animal test subjects, it was found that Ipamorelin has the ability to strengthen connective tissue and joints, bone strength, and metabolism.

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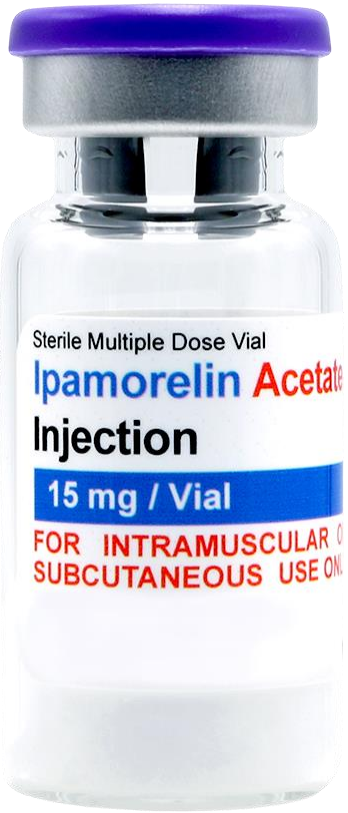
Ipamorelin Acetate Detail

- Type: Ghrelin agonist
- Available Dosage Form: Lyophilized powder for subcutaneous injection (must be reconstituted)
- Strengths: Compounding pharmacies may offer several different strengths and combinations. The most common Ipamorelin concentrations offered as a multi-dosed injection are 6mg, and 15mg. Compounded ipamorelin 500mg tablets (ODTs) remain pending until the investigation is completed in 2018
- Protocol: 250mcg-1000mcg qhs for 3-6 months to reach short term goals. Ipamorelin can also be taken chronically at 250-500mcg qhs for age-management/wellness in aging patients. Dr. Saya recommends between 250-600mg as an effective dose.
- Uses (off-label): Ipamorelin has similar uses as Sermorelin. It is most commonly used in aging patients and/or patients who are undergoing body composition changes including loss of bodyfat. Ipamorelin is used to reverse age-related, maladaptive changes in body composition such as reduced lean body mass (muscle), increased total and visceral fat, and decreased bone mass. It also is reported to increase physical performance, benefit sleep, and enhance quality of life.
- Patient Type: Elderly patients who may not have optimal pituitary function due to aging; younger patients who can optimize hGH output; Patients on a weight-management program; patients requiring long term chronic treatment of GH



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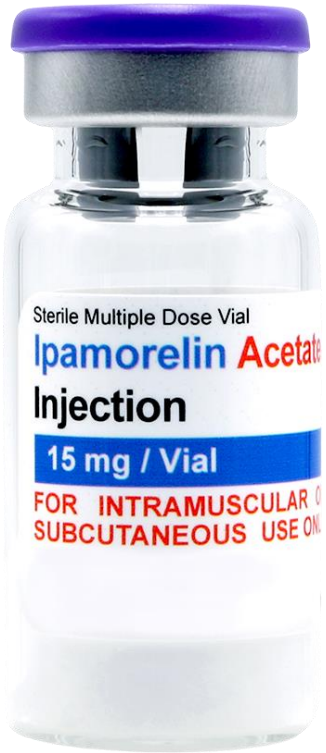
Ipamorelin Acetate Effects

Benefits:

- Appears to be more effective than Sermorelin at increasing IGF-1
- Does not increase hunger unlike other ghrelin peptides
- Reduced risk of increasing cortisol and prolactin unlike other ghrelin peptides
- It does not shut down endogenous GH production upon cessation, unlike Sermorelin.
- Commonly prescribed by physicians who report positive outcomes in patients who want to lose weight and/or who do not respond adequately to Sermorelin
- Safe and effective in elderly patients who have decreased hGH production
- In studies done on animal test subjects, Ipamorelin has been found to increase the amount of lean muscle with the development of new muscle cells.
- It has also shown to possibly have influence on the immune system. This positive effect is due to secondary actions of ghrelin on the body.
- In a few studies, ipamorelin has also been found to increase the natural sleep patterns of test animals.



Negatives:

- While few side effects have been reported, below are some that have been mentioned anecdotally. These if real, are undoubtedly related to excessive hGH exposure and thus, dosage should be reduced.
- Headache/light headedness
- Water retention
- Numbness in extremities
- Tiredness
- Decreased Insulin sensitivity
- Carpal tunnel symptoms

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Rotating/Cycling Sermorelin and Ipamorelin

- Sermorelin monotherapy is commonly prescribed for relatively younger patients who have significant pituitary reserve and only need treatment for a few months, to increase exposure to endogenous hGH.
- Since Sermorelin eventually down regulates its pituitary receptors and actually "turns off" production of endogenous GHRH due to ultra-short feedback and activation of somatostatin neurons in the hypothalamus, its efficacy of slowly lost and recovery is often required for restoration of function.
- Recovery may be facilitated by subsequent monotherapy with Ipamorelin which will restore GHRH function and suppress somatostatin activity that is enhanced by Sermorelin therapy.
- Ipamorelin monotherapy is also beneficial when provocative testing reveals that pituitary reserve is low, possibly due to hypothalamic deficiency of GHRH and enhancement of somatostatin influence. This condition often occurs at early somatopause and can be treated well with ipamorelin alone.

Protocol:

- Administer Sermorelin at 500mcg mcg qhs for weeks 1-12 followed by ipamorelin at 500mcg qhs for 12 weeks . An alternative would be to just use Ipamorelin for 12 weeks on and 12 weeks off.

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Rationale for Prescribing Sermorelin + Ipamorelin Combination Therapy

- Severe GHD that is relatively unresponsive to monotherapy of either peptide can be best treated by taking advantage of synergy between both families of peptides. In this case, combinations of Sermorelin and Ipamorelin in a ratio generally representing 2:1 (more or less) will be effective and most appropriate, especially for the older patient. Thus, because of the different properties of Ipamorelin and Sermorelin they are often used as monotherapies after identifying the condition to be best treated. However, under certain conditions of relatively severe growth hormone insufficiency, combination therapies are indicated.

Protocol:

- Order Sermorelin 15mg and Ipamorelin 6mg strengths
- Patients must reconstitute both bottles and store them separately (do not combine them into the same bottle otherwise it becomes unstable)
- Using a single 1mL insulin syringe, draw ipamorelin then Sermorelin followed by administering by SubQ injection
- Rec. dosages:
  - High dose: 1000mcg Sermorelin + 500mcg Ipamorelin qhs
  - Low/Maintenance dose: 500mcg Sermorelin + 250mcg Ipamorelin qhs

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Ibutamoren
Description

Ibutamoren, also called MK-677, is an orally-active, non-peptidic, long-acting, and selective agonist of the body's ghrelin receptor. It is also a potent growth hormone secretagogue. A secretagogue is a substance that promotes secretion; in this case, Ibutamoren may be a way to stimulate the pituitary gland to secrete growth hormone. Ibutamoren can increase appetite and weight in many patients. Lower doses under 25 mg qd can improve GH output without excessive appetite.

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Ibutamoren
Detail

Available Dosage Form: Capsule (gelatin)

Strengths: commonly available as a 12.5mg and 25mg capsule

Protocol:

Start with 12.5mg po qd for 1-3 months
Follow up with fasting serum IGF-1 and review patient's subjective improvements
If IGF-1 have not significantly and/or the patient is not receiving the desired response increase to 25mg po qd

Uses (off-label): Various studies have found statistically significant differences between subjects treated with ibutamoren versus those on placebo for the purposes of stimulating the secretion of GH, increasing serum levels of IGF-1, reversing diet or illness induced lean mass catabolism (wasting), increasing lean body mass, and decreasing fat mass

Patient Type: Patients seeking significant increase in lean body mass and bone density; Patients wanting to improve physical performance and stamina; patients who require an increase in appetite and feed efficiency; surgical/injury recovery; patients who are averse to injections

Ibutamoren
Effects

Benefits:

- Orally bioavailable which provides an alternative method of administration for patients adverse to injections
- Provides 24 hours of activity after administration by optimizing GH secretion over this time
- Human studies support Ibutamoren's positive benefits towards improving body composition by increasing muscle and reducing bodyfat levels.
- One study conducted in elderly patients receiving once-daily treatment with oral ibutamoren for up to 4 weeks significantly enhanced pulsatile GH release, serum GH, and IGF-I concentrations. Furthermore, at a dose of 25 mg per day, effectively restored serum IGF-I concentrations to the levels of young adults
- It does not shut down endogenous GH production.
- Dose of 12.5mg per day may work for many patients

Negatives:

The only side effects observed in several studies in subjects taking ibutamoren have been

- a transient increase in appetite
- some initial water weight gain
- symptoms typically resolved within a period of days to weeks, specially if dosing frequency or amount is reduced
- Some patients may gain too much weight initially and decide to stop it without dose/frequency adjustment

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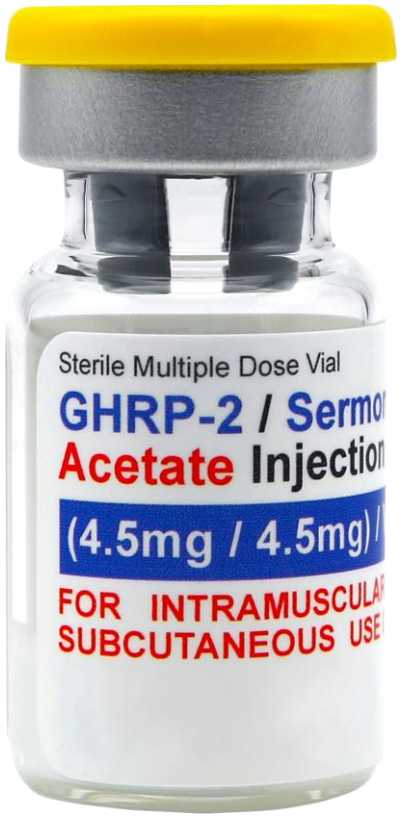
Sermorelin/GHRP-2 Combo Description



Description:
GHRP-2, a Ghrelin hexapeptide analog containing six amino acid residues, is one of the most potent members of the GHS drug class. It can significantly promote the release of growth hormone (GH), improving the serum concentrations of GH and subsequently insulin-like growth factor 1 (IGF-1) in animals and humans. GHRP-2 is readily degraded after reaching the bloodstream, its biological half-life is approximately 30 min. Peak GH concentration occur at approximately 15 min after administration. Due to the biological half-life and bioavailability of GHRP-2, administration must occur periodically several times a day, in multiple subcutaneous-injections

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Sermorelin/GHRP-2 Combo Detail

Type: Ghrelin agonist combined with a Growth Hormone Releasing Hormone analog
Available Dosage Form: Lyophilized powder for subcutaneous injection (must be reconstituted)

Strengths: Compounding pharmacies may offer several different strengths and combinations. The most common GHRP2/Sermorelin combo concentrations offered as a multi-dosed injection is 4.5mg/4.5mg and 15mg/9mg

Protocol: Currently the ratio of GHRP-2 and Sermorelin that Empower Pharmacy offers is not per the recommended 2:1 ratio of Sermorelin to GHRP. Until a new product is available that allows for 2:1 dosing, prescribe this combination as if it where GHRP-2 by itself. The usual dosage of GHRP-2 is 250mcg to 500mcg qhs or 100mcg BID prior to means (breakfast/lunch)*. When using the 15mg/9mg, this would mean that for every 250mcg of GHRP-2 administered there is 150mcg of Sermorelin co-administered.

*BID dosing is an attempt to mimic endogenous GH pulses which occur multiple times per day in those with healthy, GH producing pituitary glands. However, mimicking endogenous pulses is based on hypothesis since the GH release process is intricately complex and the perfect timing of each injection would be difficult to achieve. There might be some benefit of twice per day administration due to GHRP-2s short active life once injected

Uses (off-label): GHRP-2 is a drug used to stimulate the pituitary to release growth hormone; Increase lean body mass; Improve athletic recovery; increase appetite and feed-efficiency; improve sleep; reverse sarcopenia

Patient Type: Physically active patients seeking increase in appetite and improvement in muscle performance

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Sermorelin/GHRP-2 Combo Effects

Benefits:

- GH-releasing effect of GHRP-2 has been demonstrated to be several fold higher than baseline growth hormone levels
- As monotherapy GHRP-2 is capable of releasing more GH than the highest effective dose of GHRH
- It has been demonstrated that 1, 3 and 10 mcg/kg SC GHRP-2 administration elicits a dose-related GH response
- New findings strongly suggest that GHRP-2 has significant direct effects on muscle cells (myocytes) in skeletal muscle

Negatives:

- GHRP-2 is often injected multiple times per day (bid) for optimal effect due to short half-life
- GHRP-2 can cause an increase in hunger which can be problematic for individuals seeking weight-management
- GHRP-2 has been shown to increase prolactin and cortisol in some patients.

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Combination Dosing of GHRP/GHRH

Combining Sermorelin with GHRP appears to have synergy, resulting in a more robust release of Growth Hormone. There are several pharmaceutical products that can be combined into a single therapy. Although limited in availability, some compounding pharmacies offer custom combination products in all dosage forms including injectable.

Commercial GHS Products

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EGRIFTA® (Tesamorelin acetate)

Description: EGRIFTA® is an injectable prescription medicine used to reduce the excess in abdominal fat in HIV-infected patients with lipodystrophy. EGRIFTA® contains tesamorelin which is a synthetic analog of growth hormone releasing hormone. EGRIFTA® is the only commercially available GHRH product available in the US. Since it is only indicated for treatment of lipodystrophy, its off-label use will not be covered by insurance. HIV negative patients receiving treatment for age-related growth hormone deficiency can use a compounding pharmacy to source GHRH and GHS products that are not available commercially and usually at a lower, more affordable price

Availability: Lyophilized powder for subcutaneous injection (requires reconstitution)

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Geref® (Sermorelin acetate)

Description: Geref® (sermorelin acetate for injection) increases plasma growth hormone (GH) concentration by stimulating the pituitary gland to release GH. Geref® is similar to the native hormone (GRF [1-44]-NH 2) in its ability to stimulate GH secretion in humans. Geref® (sermorelin acetate for injection) is indicated for the treatment of idiopathic growth hormone deficiency in children with growth failure. Most of these short, slowly growing children retain pituitary responsiveness to growth hormone releasing hormone.

Product update: Geref® was discontinued by the manufacturer in 2008 and is no longer available in the US. The active ingredient, Sermorelin acetate, is available at specific compounding pharmacies who compound sterile products using this ingredient. Thus, a compounding pharmacy is the only source for Sermorelin Acetate and is available in several concentrations depending on the pharmacy.

Geref Reference:

Click here to view Geref data archived on the FDA website

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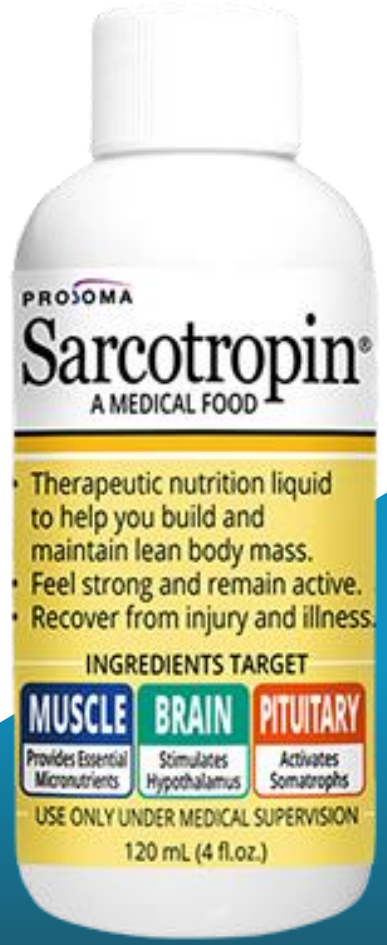
Sarcotropin ® (Proprietary blend containing GHRP-2)

Subtitle: **Medical Food Product**

Description: Sarcotropin® is a manufactured medical food that is available with a doctor's prescription. It is used to reverse muscle loss associated with aging.

Active Ingredients: GHRP-2; β-hydroxy β-methyl butyrate (HMB); Mucuna Pruriens

Available dosage form: Liquid suspension for oral administration
Strength: Proprietary blend



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