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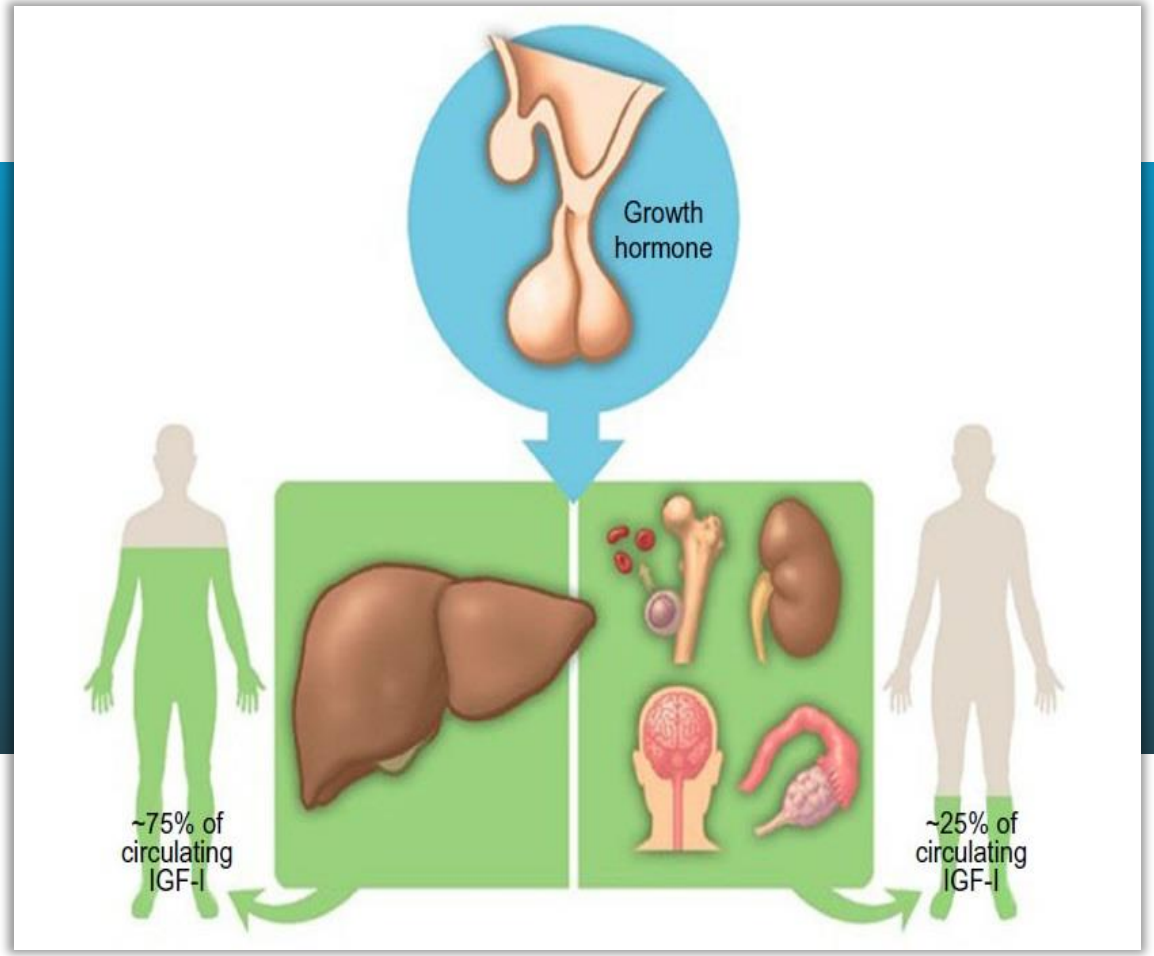
Growth Hormone Secretagogues

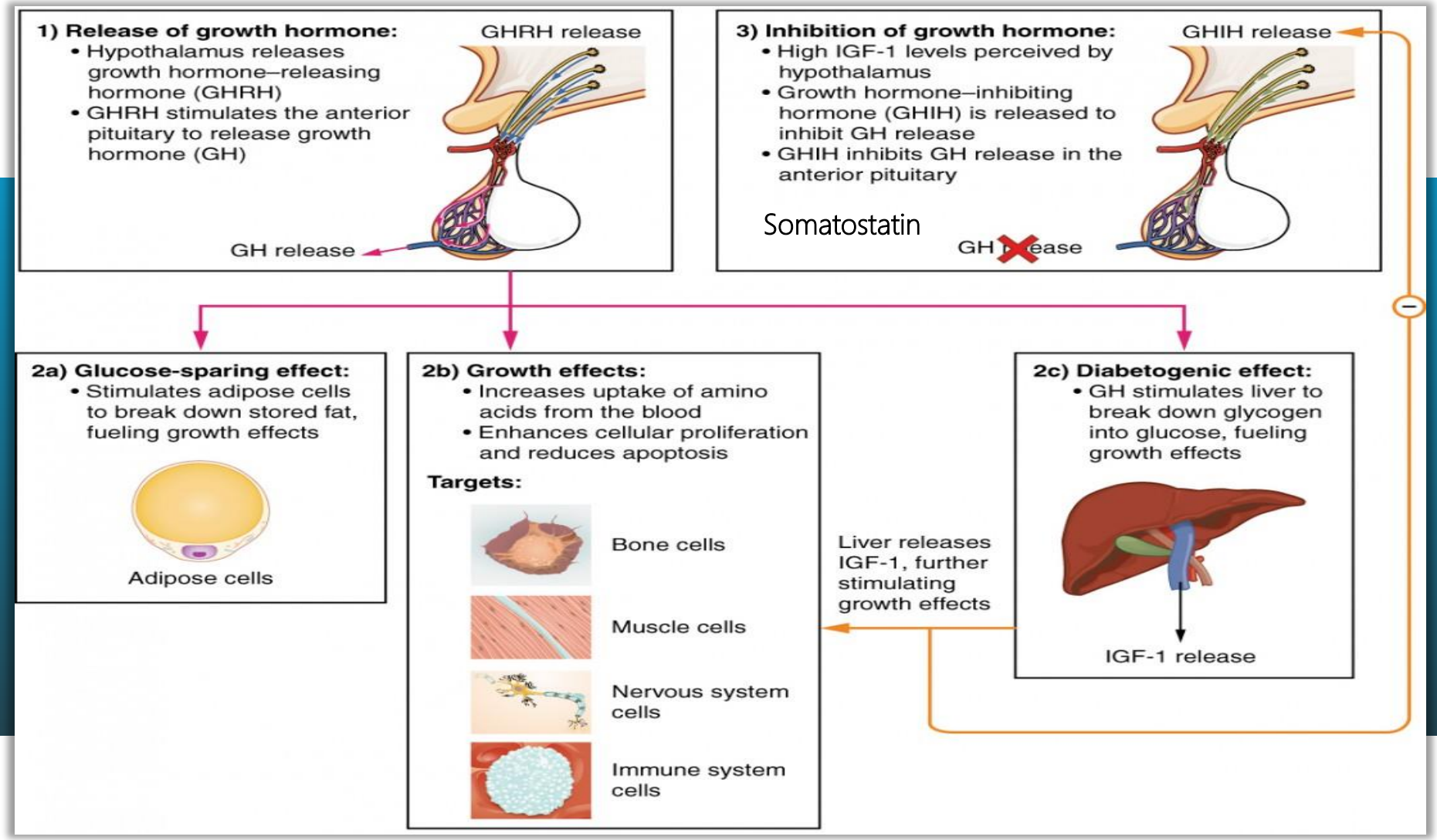
Clinical Uses and Dosing

GH Production Factors



- Growth hormone releasing hormone (GHRH) from the hypothalamus stimulates synthesis of GH in pulsatile fashion- Most of it occurs through sleep cycle
- Ghrelin, produced by endocrine cells in the stomach lining specially in hunger and hypoglycemia states, also has a role in increased GH secretion
- GH exerts its effects directly and via IGF-1 production by the liver and other tissues

Growth Hormone (GH) Release, Effects and Inhibition



GH Release Throughout Life

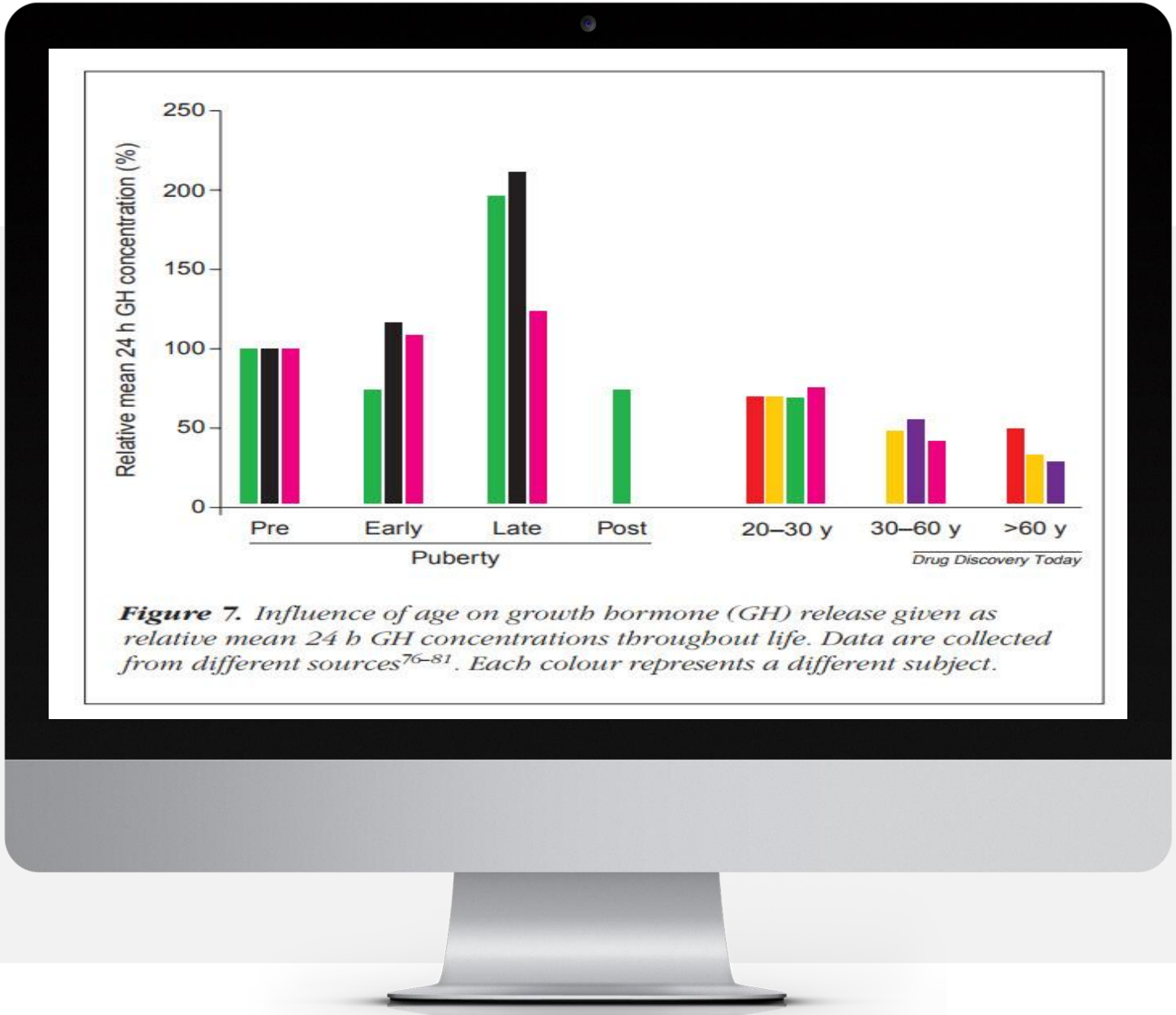


Figure 7. *Influence of age on growth hormone (GH) release given as relative mean 24 h GH concentrations throughout life. Data are collected from different sources[76–81]. Each colour represents a different subject.*

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Stimulators and Inhibitors of GH Release

Factors that stimulate GH secretion:

- Decreased blood glucose
- Starvation or fasting, protein deficiency
- Decreased blood free fatty acids
- Trauma, stress, excitement
- Exercise
- Testosterone, DHEA (women) and estrogen
- Deep sleep (stages II and IV)
- Growth hormone releasing hormone (GHRH)
- Growth hormone secretagogues (GHS)

Factors that inhibit GH secretion:

- Increased blood glucose blood and fatty acids
- Aging, obesity and illness
- Hypogonadism, hypothyrodism and high cortisol
- GH inhibitory hormone (somatostatin)
- Exogenous GH
- Sleep/circadian rhythm disorders

FDA Approved GH Brands and Their Indications

FDA-Approved Indications

Drug	Manufacturer	FDA-Approved Indications				
		GHD (Pediatric/ Adult)	Turner syndrome	CRI	ISS	Other
Genotropin®[1]	Pfizer	X	X		X	PWS, SGA
Humatrope®[2]	Lilly	X	X		X	SHOX, SGA
Norditropin®[3]	Novo Nordisk	X	X			Noonan Syndrome, SGA
Nutropin®[4]	Genentech	X	X	X	X	
Nutropin AQ®[5]	Genentech	X	X	X	X	
Omnitrope®[6]	Sandoz	X				
Saizen®[7]	EMD Serono	X				
Serostim®[8]	EMD Serono					HIV wasting or cachexia
Tev-Tropin™[9]	Gate/Teva	X (pediatric only)				
Zorbtive®[10]	EMD Serono					SBS

GHD = Growth hormone deficiency
PWS = Prader-Willi Syndrome
CRI = Chronic renal insufficiency
SGA = Small for gestational age

ISS = Idiopathic short stature
SHOX = Short stature homeobox gene
SBS = Short bowel syndrome
HIV = Human Immunodeficiency virus

GH Contraindications

- Pregnancy
- Malignancy
- History of Malignancy
- Diabetic proliferative retinopathy
- Sclerosing diseases of the liver and lungs
- Benign intracranial hypertension
- Uncontrolled diabetes

Does GH Increase Cancer Risk?

Table 2: Majority view of the effect of GH treatment for approved indications on cancer risk in children and adults (including those with a childhood-onset of GH deficiency).

Age at onset of GH treatment	New Primary Cancer	Recurrence of the Primary Cancer in Survivors	Second or Subsequent Neoplasm in Survivors
Child	No evidence for GH treatment effect Level: robust	No evidence for GH treatment effect Level: robust	Risk present but diminishes with time from onset of GH treatment Level: suggestive
Adult	No evidence for GH treatment effect Level: suggestive	Insufficient data available	Insufficient data available

History of GH FDA Approved Indications

Year	Condition
1985	Growth hormone therapy
1993	Chronic renal insufficiency
1996	Adult growth hormone deficiency
1997	Turner syndrome
2000	Prader-Willi Syndrome
2001	Small for gestational age
2003	Idiopathic short stature
2006	Short stature homeobox-containing gene deficiency
2007	Noonan syndrome

GH Side Effects

- The use of GH is associated with several adverse effects including: edema, hyperglycemia, carpal tunnel syndrome, gynecomastia, joint pain, muscle pain, and abnormal skin sensations (e.g., numbness and tingling).
- It may also increase the possibility of developing diabetes.
- Exogenous GH shuts down endogenous GH and GHRH production.
- GH injections produce unphysiologic sustained elevations in GH levels

GH Legalities

- Human growth hormone **is not controlled** under the Controlled Substances Act (CSA).
- However, as part of the 1990 Anabolic Steroids Control Act,

  the distribution and possession, with the intent to distribute, of GH "*for any use… other than the treatment of a disease or other recognized medical condition, where such use has been authorized by the Secretary of Health and Human Services… and pursuant to the order of a physician…*" was criminalized as a five-year felony under the penalties chapter of the Food, Drug, and Cosmetics Act of the FDA.
- Prescribing GH for adult growth hormone deficiency has to be based on strict GH stimulation tests to justify it. Many insurance companies refuse reimbursement and the cash price is prohibiting to most patients.
- GH secretagogues are also not controlled and can be used without the requirements imposed on GH use. They provide physiologic GH levels.

Proving GH Deficiency- GH Stimulation Tests: Labor Intensive

- A GH level by itself is meaningless in the evaluation of GH deficiency
- Provocative agents include clomidine, L-dopa, arginine, insulin, glucagon, and GHRH
- Fasting 8-12 hours
- 5 blood samples, first between 6-8 am, then the provocative agent is administered via IV. 30 minutes after that another blood sample, repeated every 30 minutes
  - Normal peak value, at least 10 nanogram per milliliter (ng/mL) or 10 microgram/L
  - Indeterminate, 5 to 10 ng/mL or 5 to 10 microgram/L
  - Subnormal, 5 ng/mL or 5 microgram/L

  (A normal value rules out GH deficiency; in some laboratories, the normal level is 7 ng/mL or 7 microgram/L.)

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Available Products Involved in GH Release

Hormones involved and related analog drugs

1

Growth Hormone Releasing Hormones:

1. Sermorelin
2. Tesamorelin

2

Ghrelin Agonists:

1. GHRP 2 & 6
2. Ipamorelin
3. Ibutamoren

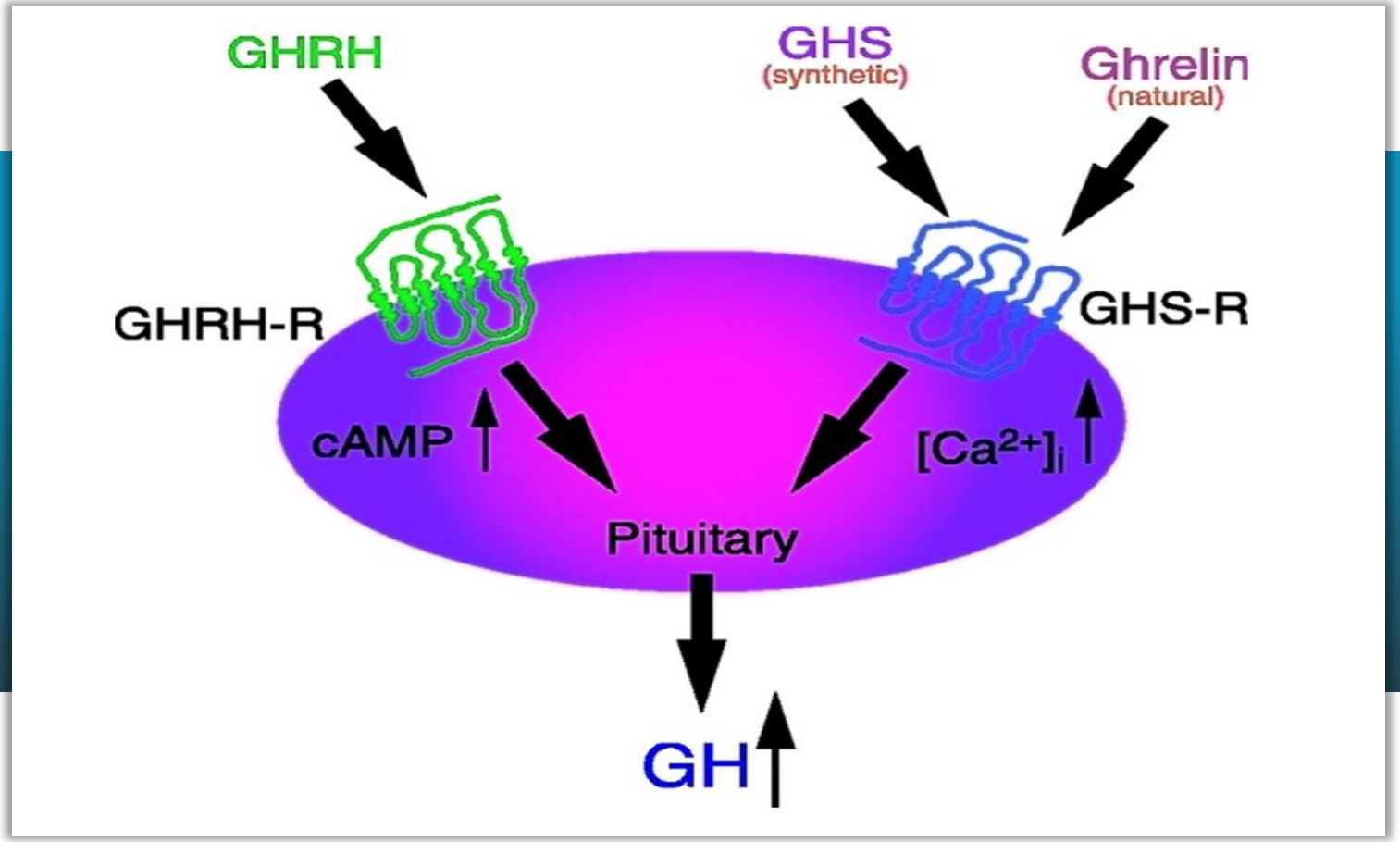
3

Somatostatin

4

Growth Hormone

1. Synthetic human growth hormone (rHGH)



GH Releasing Hormone (GHRH), GH Secretagogues (GHS) and Ghrelin's Effect on Pituitary GH Output

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Growth Hormone Secretagogues (GHS)

- GHRS belong to a broader class of compounds all of which share the common trait of being able to bind to the Growth Hormone Secretagogue Receptor (GHS-R) and effect GH release.
- These compounds include the synthetic peptides (GHRP-6, GHRP-1, GHRP-2, Ipamorelin) and smaller synthetic non-peptide molecular compounds such as Ibutamoren as well as the natural ligand Ghrelin.
- This broad class which includes all of the above but not Growth Hormone Releasing Hormone (GHRH) is termed Growth Hormone Secretagogues (GHSs). Sometimes people use the term “peptides” online.

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hGH vs GHRH / GHRS

- GHRH / GHRS significantly **less expensive** than rHGH
- HGH **overdosing is minimized** or completely avoided with GHRH / GHRS
- Tissue exposure to hGH released by the pituitary under the influence of GHRH / GHRS is episodic not "square wave", **preventing diminished response** by mimicking normal physiology
- By stimulating the pituitary, GHRH / GHRS **preserves more of the growth hormone neuroendocrine axis** which fails first during aging
- GHRH / GHRS **blocks the cascade of hypophyseal (hypothalamus to pituitary) hormone failure** that occurs during aging, thereby **preserving youthful anatomy and physiology**
- GHRH / GHRS provides all the benefits of hGH replacement therapy , <u>YET ITS OFF LABEL USE IS NOT PROHIBITED BY FEDERAL LAW</u>

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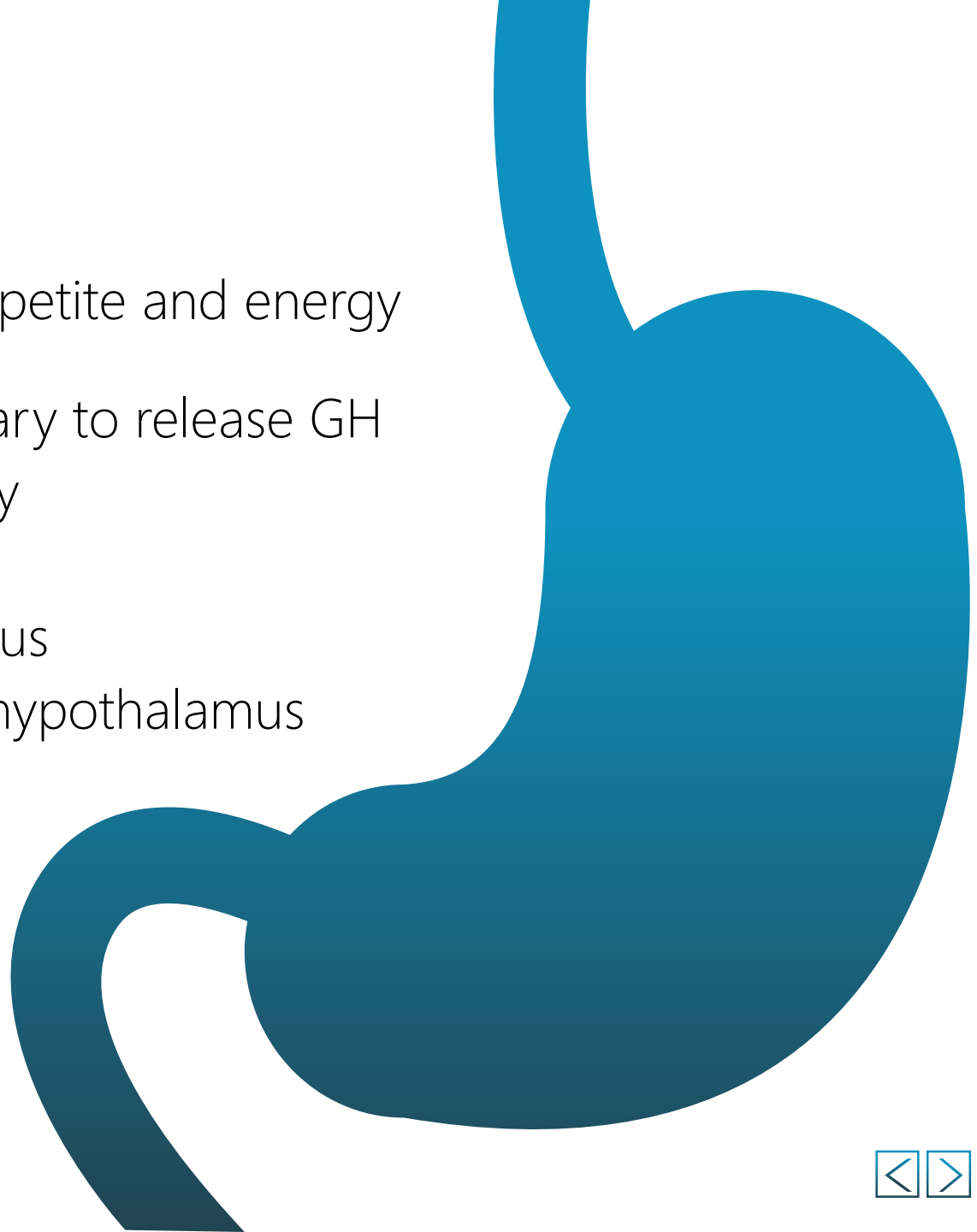
Dates of selected clinical studies with growth hormone secretagogues in various indications

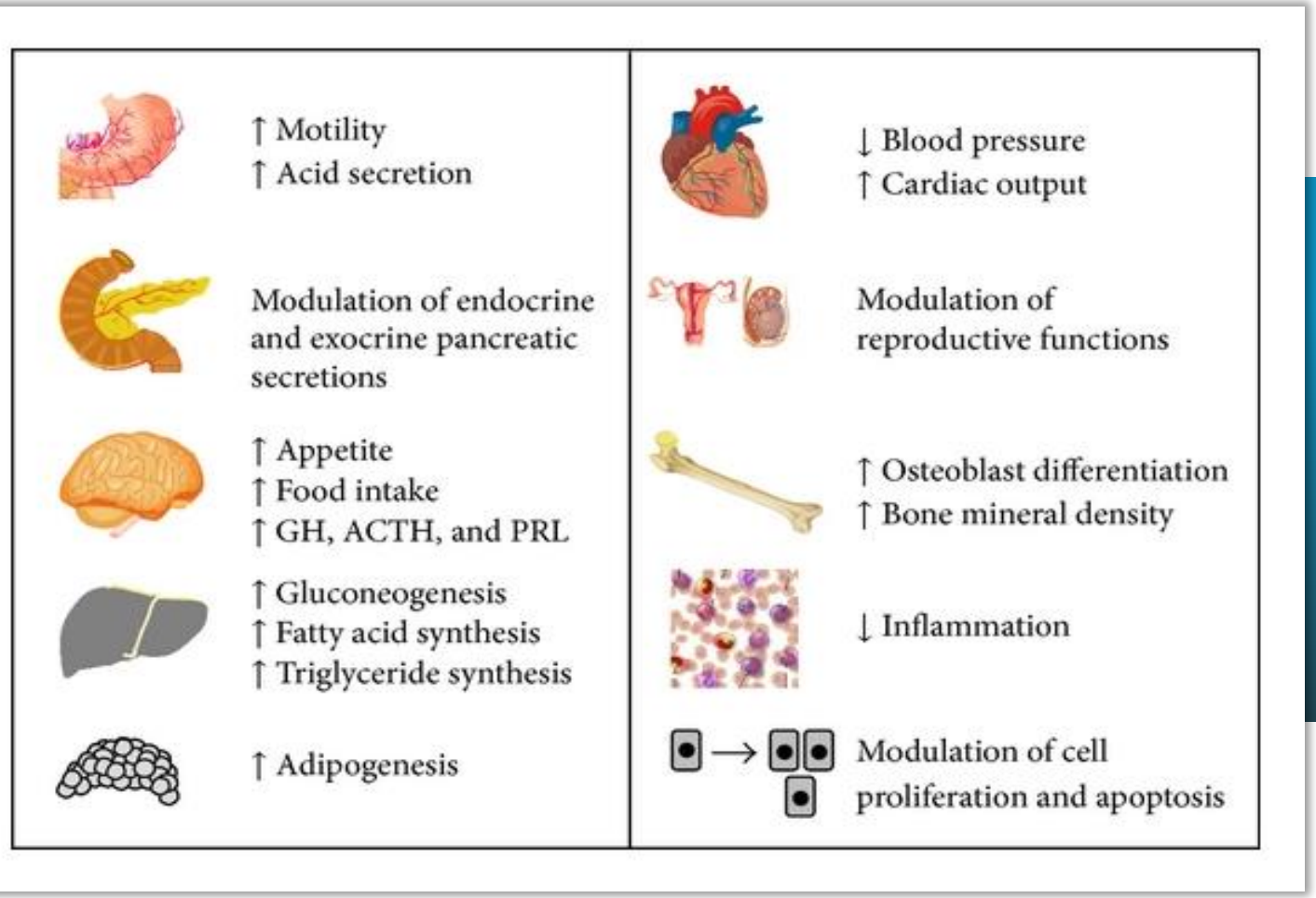
Compound	Acute GH response	GHD in children	GHD in adults	Elderly	Obese	Catabolic states	Insomnia
GHRP-1	Bowers[38,39] 1992, 1993 Robinson[40] 1993	Laron[41] 1993 Mericq[42] 1995	–	–	–	–	–
GHRP-2	Bowers[39] 1993	Pihoker[43,44] 1995, 1997 Tuilpakov[45] 1995 Mericq[46] 1996	–	–	–	Van der Berghe[47–49] 1996, 1997, 1998	–
GHRP-6	Ilson[50] 1989 Penalva[51] 1993 Maccario[52] 1995	Pombo[53] 1995	Leal-Cerro[54] 1995	–	Cordido[55] 1993	–	Frieboes[33] 1995
Hexarelin	Ghigo[56] 1994	Laron[57,58] 1995, 1997 Loche[59] 1995 Klinger[60] 1996	–	Rahim[61] 1998	–	–	Korbonits[62] 1995
L692429	Gertz[63] 1993	–	–	Aloi[64] 1994	Kirk[65] 1997	Gertz[66] 1994	–
MK0677	Chapman[67] 1996	Yu[68] 1998	Chapman[69] 1997	Chapman[67] 1996 Plotkin[70] 1996	Svensson[71] 1998	Murphy[72] 1998	Copinshi[73] 1997

Ghrelin

- Produced by stomach mucosa. Involved in appetite and energy balance.
- Binds to GHRP-R (“Ghrelin receptor”) in pituitary to release GH
- Reduces inhibition by Somatostatin at pituitary
- Distinct and separate path than GHRH
- Stimulate GHRH production from hypothalamus
- It also inhibits Somatostatin production from hypothalamus



Extra-Pituitary/GH Effects of Ghrelin and its Analogs (GHRPs)



VAN DER LELY et al. Biological, Physiological, Pathophysiological, and Pharmacological Aspects of Ghrelin. Endocrine Reviews 25(3):426–457

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Compounded GHS Products

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Commonly Available Compounded Formulations

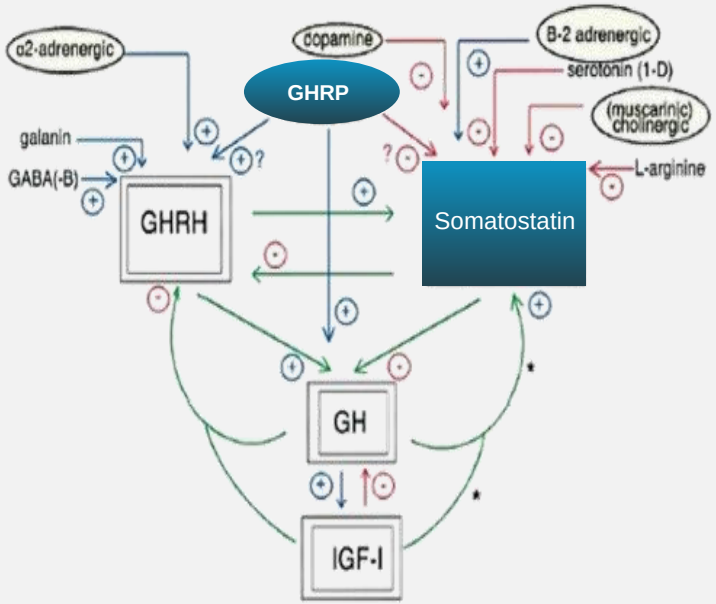
- Sermorelin 6 mg, 9 mg, 15 mg vials
- Ipamorelin 6 mg and 15 mg vials
- Sermorelin/GHRP-2/GHRP-6: 20mg/6mg/15mg
- Ibutamoren, 20 mg capsules

Summary of effects of GHRP favoring GHRH activity

GHRP also suppresses somatostatin which increases during aging and is thus, partially responsible for reduced GH secretion in the elderly.
On the other hand, GHRH stimulates SIRF and thus is lowered by it.

GHRP:

1. Stimulates GHRH neurons to sustain their activity
2. Combines with GHRH to stimulate pituitary and amplify the effect of GHRH
3. Inhibits somatostatin to produce greater GHRH neuronal activity.
4. Supports dopamine neurons to enhance GHRH neurons



Sermorelin:

1. Inhibits GHRH neurons reducing endogenous GHRH
2. Acts alone to stimulate pituitary in the absence of endogenous GHRH
3. Stimulates somatostatin to suppress GHRH neurons

Muller Lee, Locatelli V, Cocchi D. Neuroendocrine control of growth hormone secretion. Physiol Rev 1999, 79:511-607

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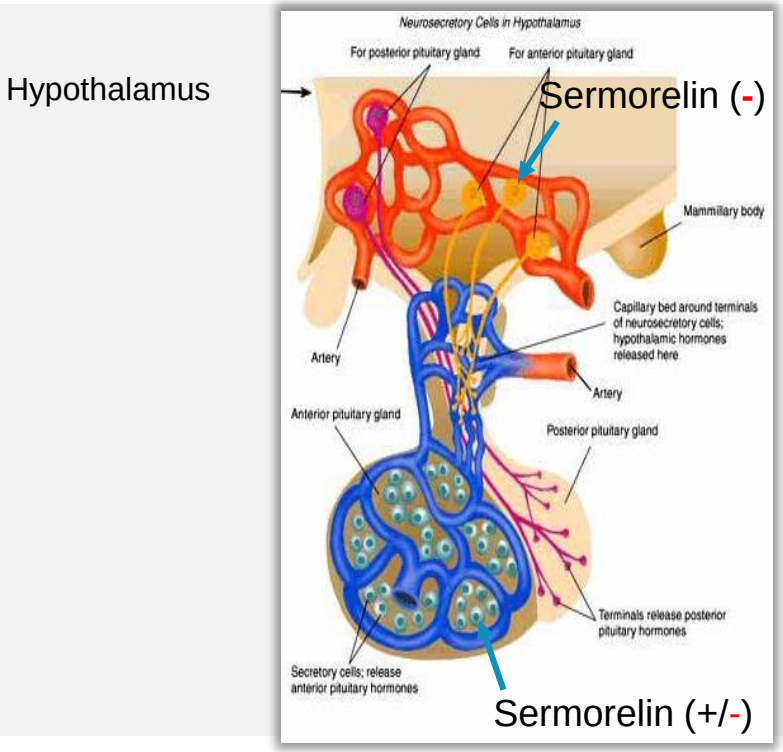
Functional Differences

Sermorelin

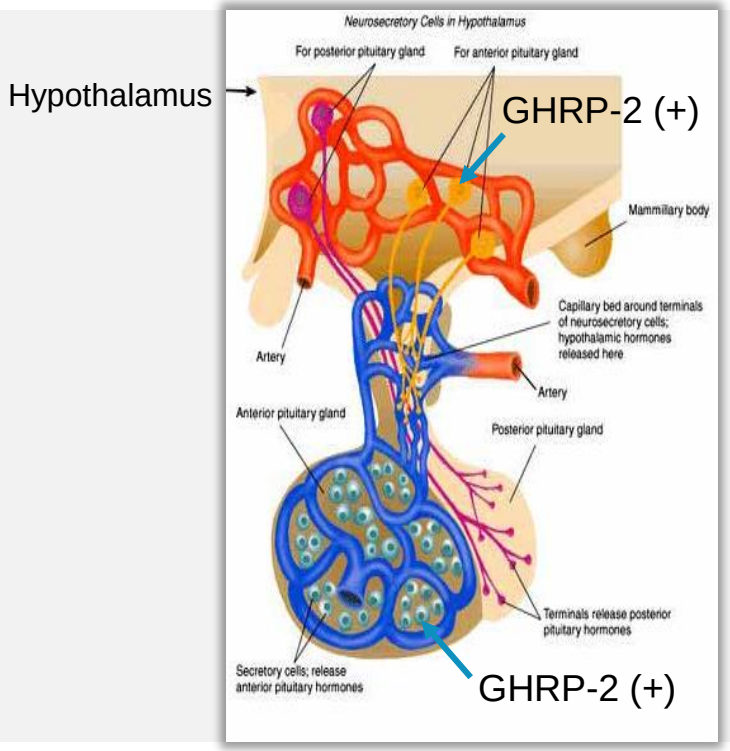
Inhibits production and secretion of endogenous GHRH by direct negative feedback on GHRH neurons. Also Binds to receptors on somatotrophs causing them to produce and secrete GH.



[Endocrinology.](#) 1997 Mar;138(3):1058-65. Homologous down-regulation of growth hormone-releasing hormone receptor messenger ribonucleic acid levels. [Aleppo G](#)[1], [Moskal SF 2nd](#), [De Grandis PA](#), [Kineman RD](#), [Frohman LA](#).

GHRP-2

Stimulates GHRH neurons and also binds to specific receptors on somatotrophs causing them to produce GH



[Life Sci.](#) 1992;50(16):1149-55. Growth hormone-releasing peptide (GHRP) binding to porcine anterior pituitary and hypothalamic membranes. [Veeraragavan K](#)[1], [Sethumadhavan K](#), [Bowers CY](#).

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Sermorelin Acetate

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

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-1
- 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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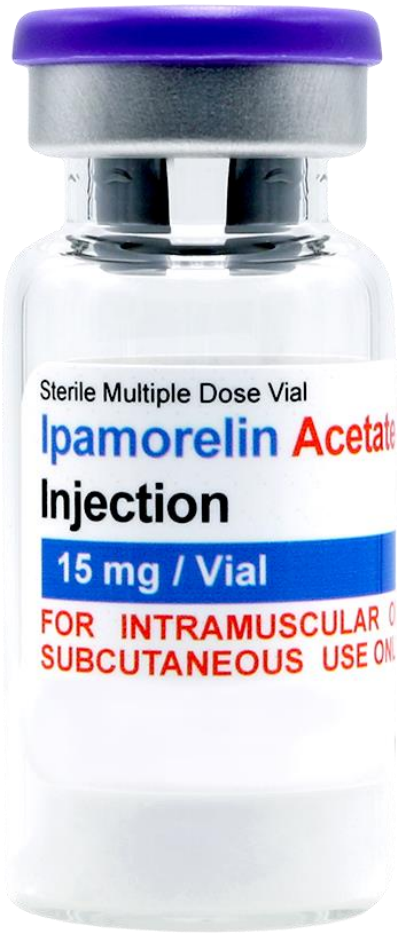
Ipamorelin Acetate



- Functioning as a secretagogue, 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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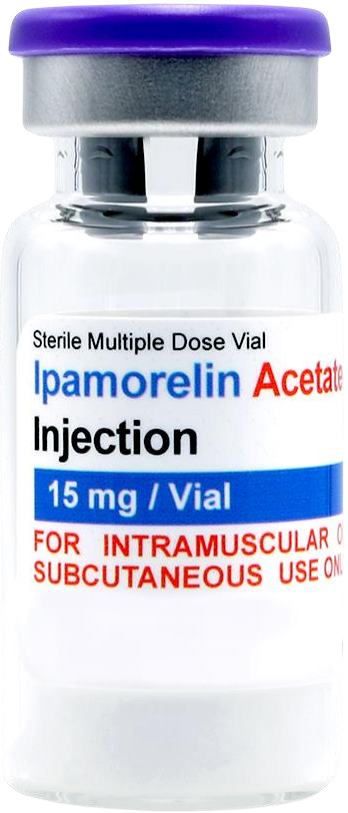
Ipamorelin Acetate

- 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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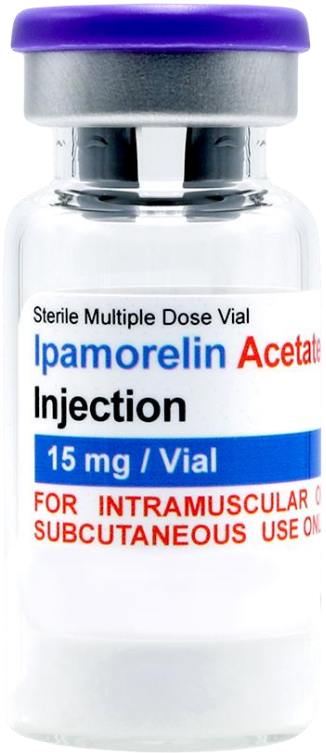
Ipamorelin Acetate

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
- 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-100mcg qhs for weeks 1-12 followed by ipamorelin at 500mcg qhs for 12 weeks

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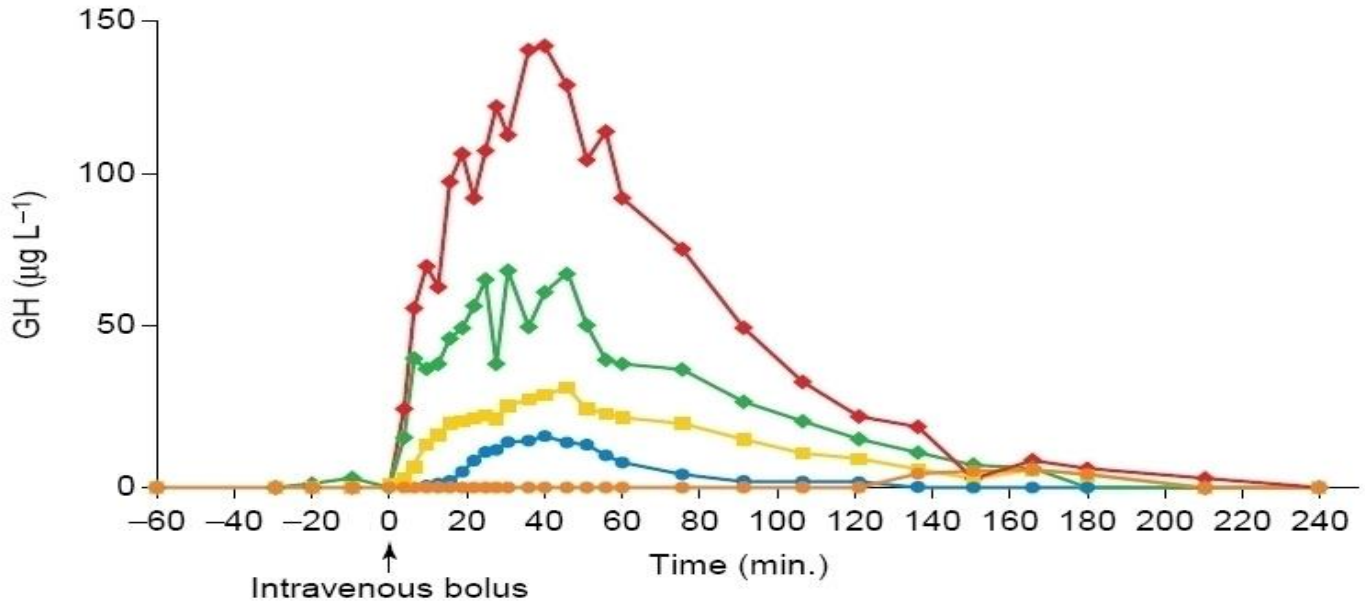
Synergy of GHS + GHRH



Comparative growth hormone (GH) responses in individual subjects. GH responses, together with the area-under-the-curve (in μg L^{-1} after 4 h treatment) is as follows: placebo (orange, 540); 0.1 μg kg^{-1} growth hormone-releasing peptide (GHRP; blue, 916); 1 μg kg^{-1} GHRP (green, 5319); 1 μg kg^{-1} growth hormone-releasing hormone (GHRH; yellow, 2590); 0.1 μg kg^{-1} GHRP plus 1 μg kg^{-1} GHRH (red, 10,065) in two normal men J. Clin. Endocrinol. Metab. 70, 975-982

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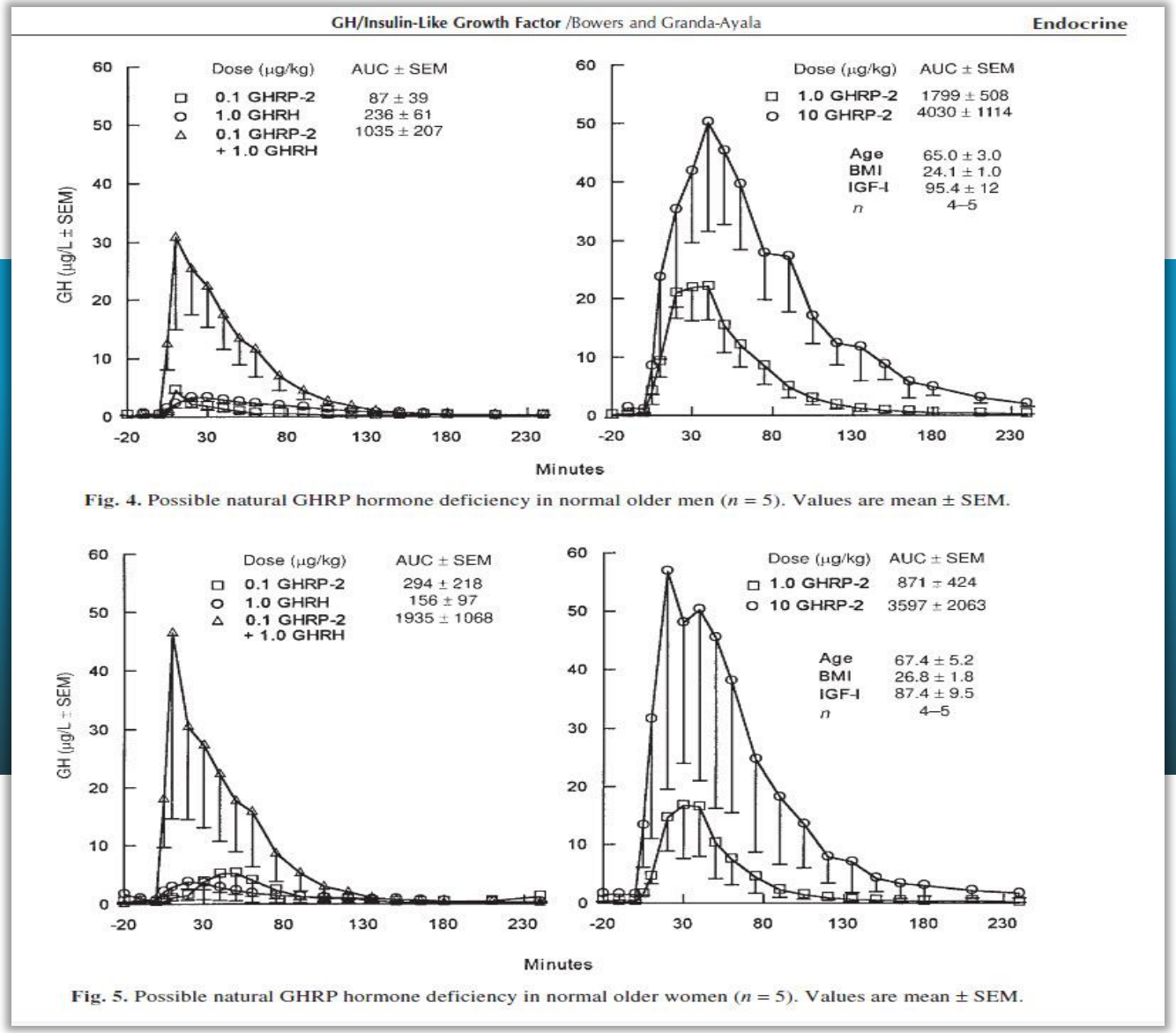

GHRP-2 Exhibits Strong Synergy with Sermorelin on GH levels

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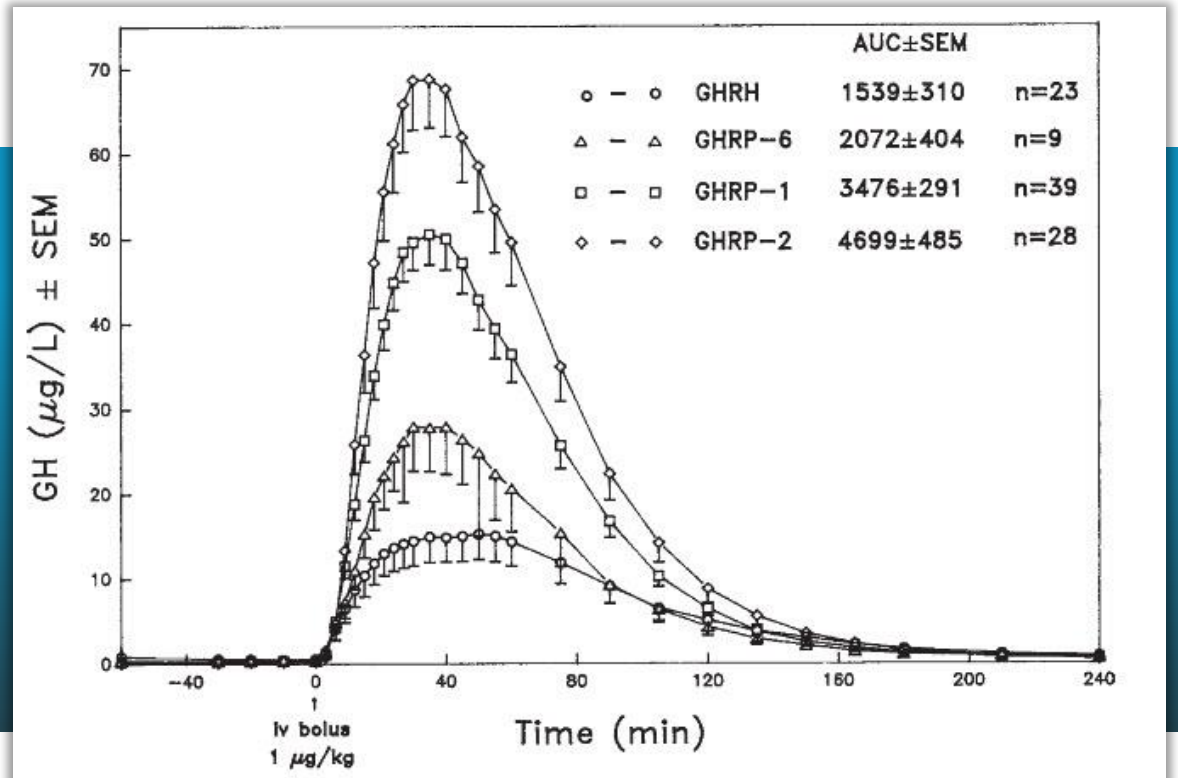
Effect of Monotherapy of GHRH and GRRPs on GH Blood Levels in Young Men



. 4. Comparative mean responses to 1.0 μg/kg GHRH(1-44)NH2, GHRP-6, GHRP-1 and RP-2 in normal young men. Reproduced with permission from ref. *64*.

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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.

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

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

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Ibutamoren

Available Dosage Form: Capsule (gelatin)

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

Protocol:

Start with 12.5mg poqd 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 poqd

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, diet-induced catabolism (wasting), increasing lean body mass, and decreasing fat mass

Patient Type: Patients seeking significant increase in lean body mass and bone density; patients who want to lose bodyfat; 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

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

Negatives:

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

- a transient increase in appetite,
- slight lower extremity edema, and
- muscle pain;
- symptoms typically resolved within a period of days to weeks

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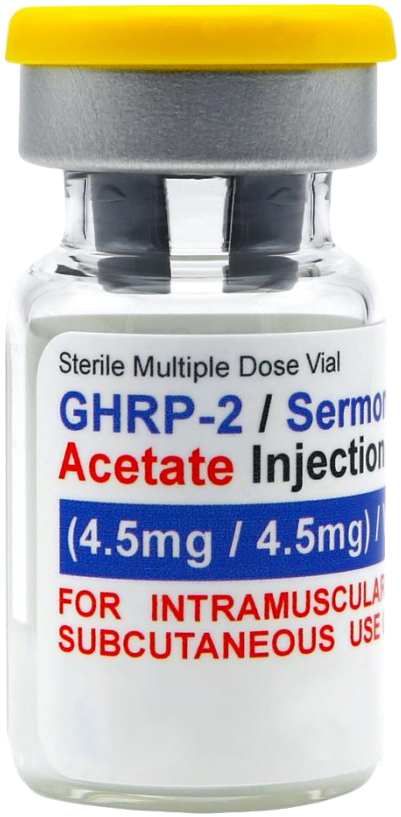
Sermorelin/GHRP-2 Combo



- GHRP-2, a hexapeptide 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

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 some compounding pharmacies offer 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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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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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.

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Thank You!

Clinicians can contact us at ClinicOptimizers.com