



Sermorelin & Peptides: *Restoring Growth Hormone In Aging*

Prepared & Presented By

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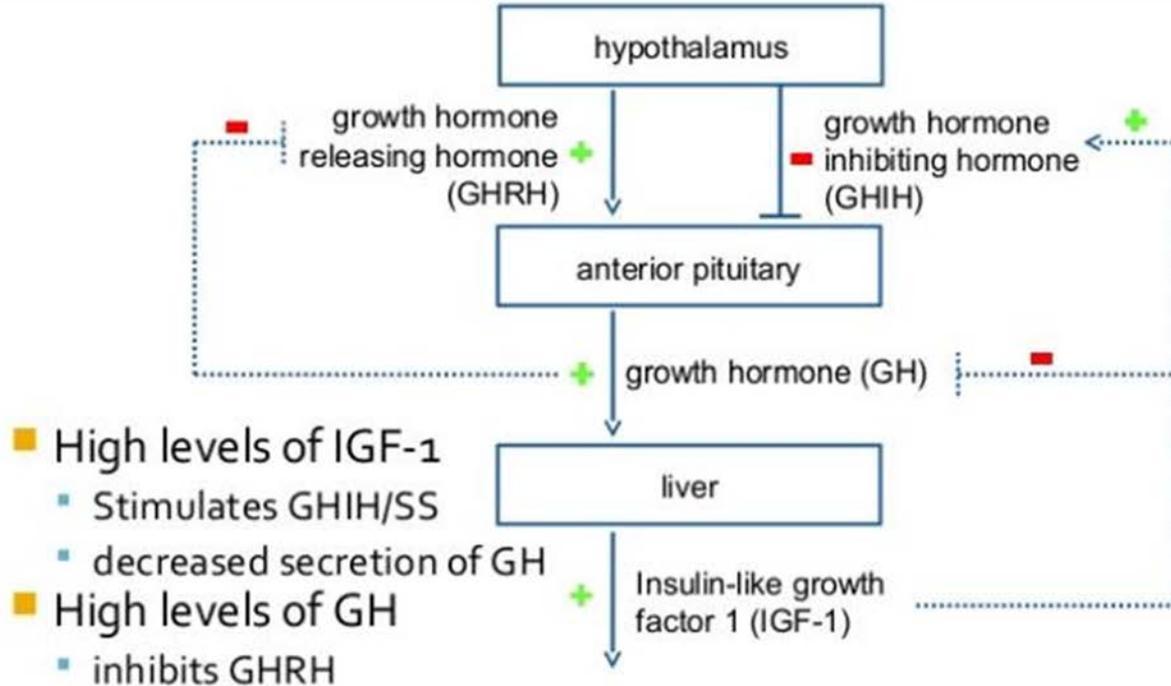
Objectives

- Review physiologic process of how GH is released and how it declines during aging.
- Recognize the effects of aging and the symptoms of somatopause.
- Gain an understanding of what Sermorelin and related peptides are, how they can increase GH output, and how they are most effectively used in clinical practice.
- Become familiar with current dosing protocols using Sermorelin and/or GHRP.
- Answer any questions that remain.

Growth Hormone Secretion

- GH is secreted by the anterior pituitary gland and released into bloodstream in *episodic pulses*
- In the younger, pulses are frequent and strong; however, they begin to decline sharply as aging occurs.
- These pulses, peaking in the evening, promote sleep, healing, exercise recovery, and natural regeneration

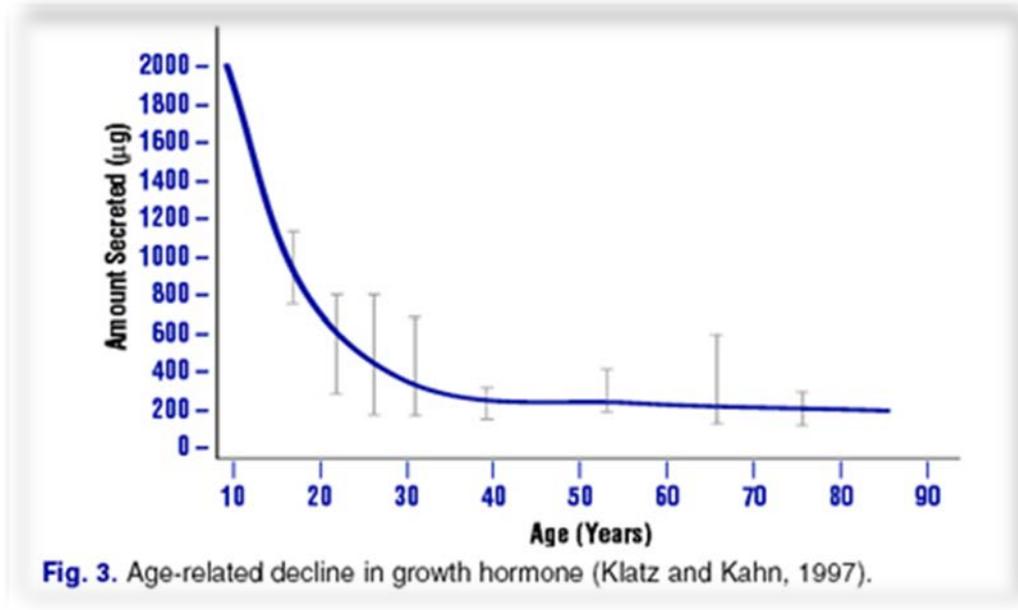
Growth Hormone Regulation



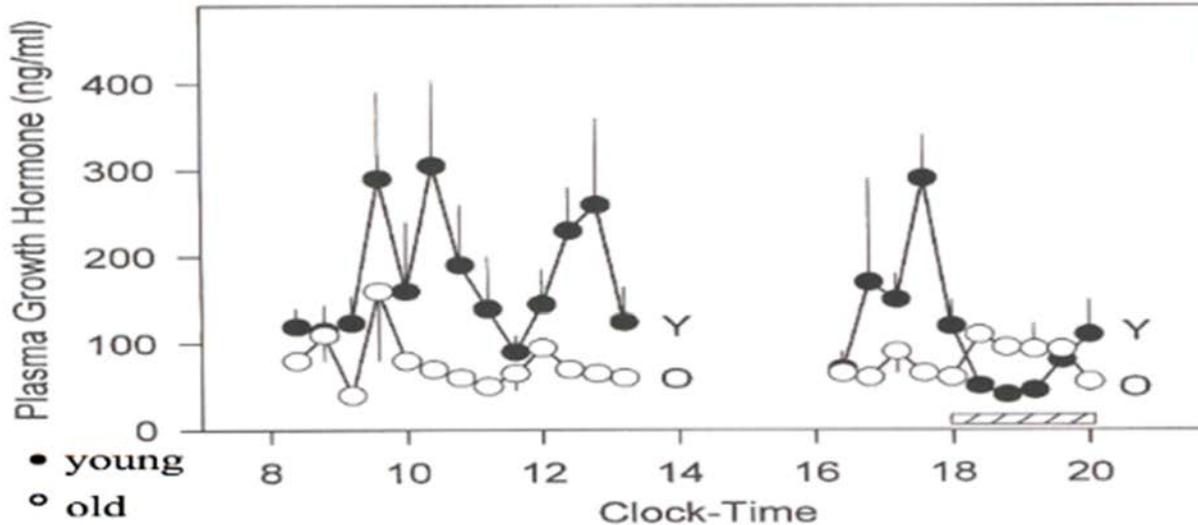
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Growth Hormone Decline with Aging



Age Related Decline of GH Secretion



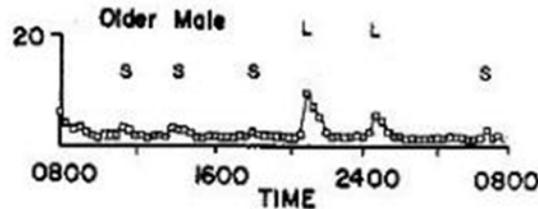
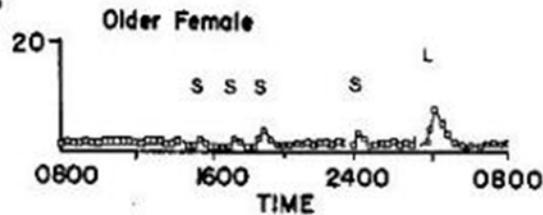
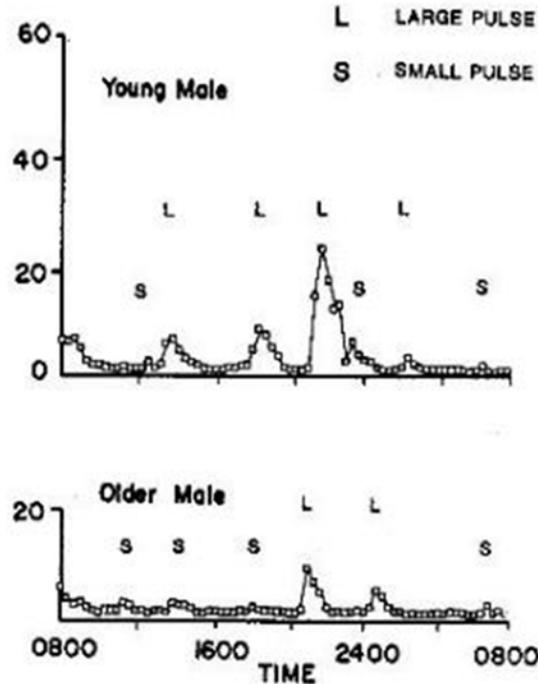
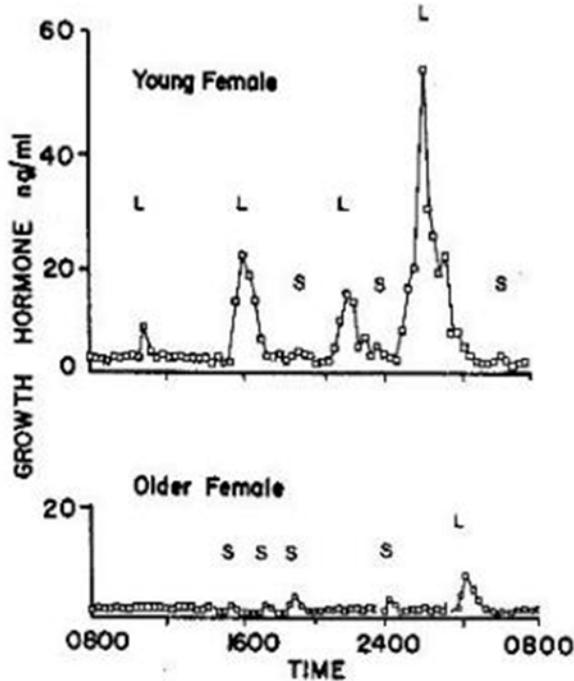
Sonntag et al., 2001 JAAM 4:311



Growth Hormone Secretion

- GH is secreted by the anterior pituitary gland and released into bloodstream in *episodic* pulses
- In the younger, pulses are frequent and strong; however, they begin to decline sharply as aging occurs.
- These pulses, peaking in the early morning hours, promote sleep, healing, exercise recovery, and natural regeneration

Growth Hormone Secretion



Patterns of GH secretion in younger and older women and men.

There is a marked age-related decline in GH secretion in both sexes and a loss of the nighttime enhancement of GH secretion seen during deep (slow-wave) sleep. This decrease is primarily due to a reduction in GH pulse amplitude, with little change in pulse frequency. From Ho et al. 1987 (4).

Somatopause

- SOMA - from Latin soma, from Greek body
 - The entire body of an organism

- PAUSE - from Latin pausa, Greek pausis
 - To halt

Somatopause

- Aging results in reduced production & secretion of GH relative to that which occurs in youth.
- This is the first gross sign of neuroendocrine decline that begins during the mid-to-late thirties.





Somatopause Symptoms

Note that some of these features may have multiple causes or co-factors and may not be solely due to a decline in Growth Hormone.

- *increased fat mass, particularly around the waistline & abdomen*
- *decreased muscle mass, bone density**
- *sleep disorders/irregularities*
- *abnormal blood lipids* (high LDL/decreased HDL)*
- *impaired glucose tolerance and/or insulin resistance**



The Hypothesis

Growth Hormone replacement therapy (intended to restore optimal concentrations of growth hormone) may improve or sustain good youthful anatomy & physiology; thereby, good health and vitality during aging.



rhGH Therapy

ADVANTAGES

- Proven and effective increases in GH and IGF-1
- Widely accepted and researched
- Many studies have shown that long-term administration reduces intrinsic disease and extends life in adults *with pathogenic GHD (however, how this relates to the aging condition has not yet been agreed upon)*.



rhGH Therapy

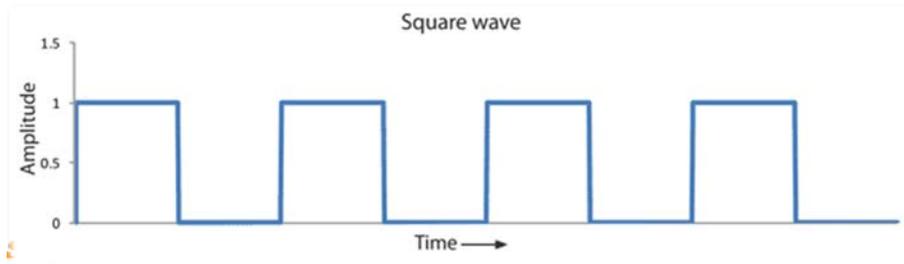
DISADVANTAGES

- Potential risks associated with long-term therapy?
- Creates unnatural exposure to the hormone that may erode normal physiology / exacerbate decline
 - Not controlled by (-)feedback; tachyphylaxis/reduced efficacy
- Use restricted to AIDS wasting or GHD diagnosis
- Mitogenic issues?
- Improper doses may promote metabolic disorders

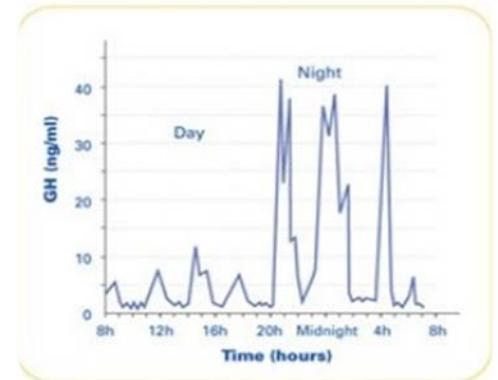
GHRH Therapy

ADVANTAGES

- Pulsatile secretions vs. Prolonged elevation
- Quick bursts vs. Square-wave / prolonged exposure
- More accurately reflects normal physiologic actions
- No supraphysiologic exposure / tachyphylaxis



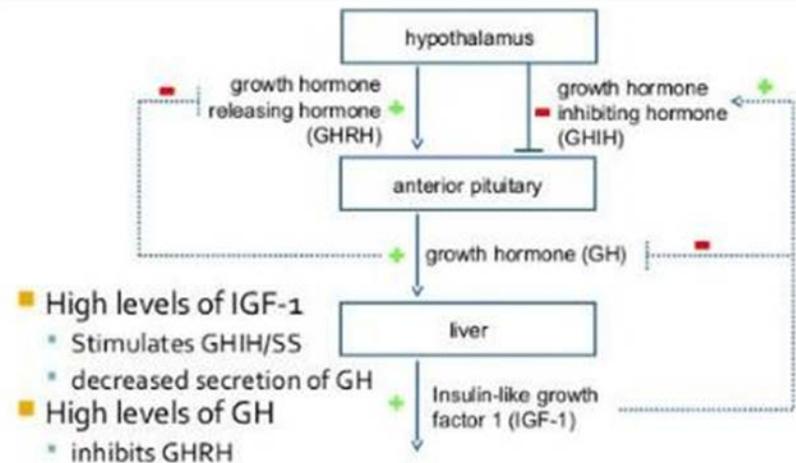
Normal Secretion of Growth Hormone Over 24 Hours



GHRH Therapy

ADVANTAGES

- Normal feedback regulation by IGF-1 is preserved, offering some relative buffering against potential overdosing.



GHRH's

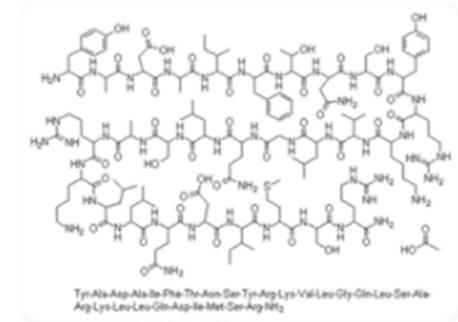
GRF(1-44); $t_{1/2}$ = 5-10 minutes

- Research studies have shown that GHRH helps stimulate the release and synthesis of growth hormone.
- Research has also shown that it helps promote slow-wave sleep.

GRF(1-29); $t_{1/2}$ = 5-10 minutes; MW 3357

- GHRH analogue which is a 29-amino acid polypeptide representing the (1-29) fragment from endogenous hGHRH, and is thought to be the shortest, fully functional fragment of GHRH.

Stages of Healthy Sleep

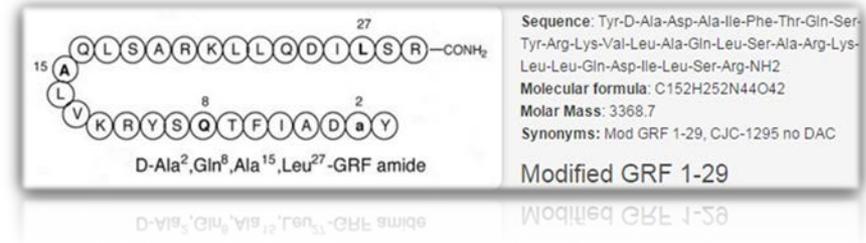


GHRH's

Modified GRF(1-29) or CJC-1295 w/o DAC; $t_{1/2} > 30$ minutes; MW 3368

Tetrasubstituted analog of GRF 1-29

- *D-Ala* at the 2-position
- *Gln* at the 8-position to reduce asparagine rearrangement or hydrolysis to aspartic acid
- *Ala* at position 15 to enhance bioactivity
- *Leu* at position 27 to prevent methionine oxidation



CJC-1295 w/DAC; $t_{1/2} =$ days; MW 3647

Same as above but with *MPA-Lys* at the C terminus.



GHRH Pulses

- GHRH pulses can only last < 30 minutes before the body has used out the potential for a single GH pulse.
- Since another pulse won't be generated for another two to three hours, GHRH's that last more than 30 minutes are not any more beneficial.
- Administration of GHRH creates a pulse or train of GH release
 - Higher pulse if during a rising natural GH wave; lower if during a trough

Sermorelin (GRF1-29)

- $\text{GHRH}(1-29)\text{NH}_2$
- Biological active analog of growth hormone releasing hormone (GHRH) that is produced by the human brain to stimulate production and release of growth hormone by the pituitary gland.
- First 29 amino acids of the complete sequence of hGHRH confer biologic activity.
- Synthetically prepared from highly purified sources; FDA oversight.

Sermorelin Dosing

Doses widely vary; no standardized dose for everyone

TYPICAL DOSING PROTOCOL

- Younger patients with good body composition
 - 200 - 300mcg SC one hour prior to bedtime will sustain youthful characteristics, health, vitality during aging *without* the use of additional hGH supplementation.

IDEAL PATIENT

- 35y - 70y
- Good general health w/baseline IGF-1 > 95 & BMI < 35
- NO known brain lesions or untreated thyroid conditions

Sermorelin Dosing

EXCESSIVE ABDOMINAL FAT/INCREASED WEIGHT

- 1 - 2 IU of hGH QAM x 3-6 months until body composition improved.
- 200 - 300mcg of Sermorelin one hour before HS
- This has been shown to provide the maintenance dose to sustain pituitary function during aging.

Sermorelin Dosing

FOR WOMEN, OR OBESE PATIENTS

- Same as described for excessive abdominal fat or initiate treatment at dosages of 400 - 500mcg per day.
- Women require higher doses because estrogen blunts the effect of hGH upon the liver to produce IGF-1 (oral vs. transdermal)

Sermorelin Dosing Based on BMI

BMI	Men	Women
18 – 24	200mcg	300mcg
25 – 29	400mcg	400-500mcg

Absolute contraindications to begin treatment include:

- Malignancies
- Pregnancy
- Benign Intracranial Hypertension
- Proliferative Retinopathy.

Adverse Reactions

THE MOST COMMON SIDE EFFECTS WITH SC INJECTION:

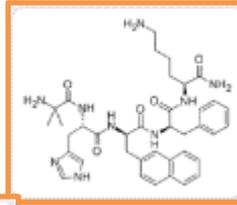
- local injection reactions (occurring in about 16%; pain, swelling or redness)
- < 1% include headache, flushing, dysphagia, dizziness, hyperactivity, somnolence and urticaria.
- Antibody formation to Sermorelin has been reported after chronic SC administration of large doses. The clinical significance is unknown, but antibodies do not appear to be related to a specific ADR profile.
- No generalized allergic reactions have been reported. A temporary allergic reaction described as severe redness, swelling and urticaria at the injection sites has been reported in a few patients who developed antibodies.

-Elsevier; Clinical Pharmacology 2017

GHRPs

IPAMORELIN

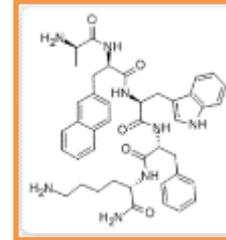
- Potent, but weakest GH releaser
- Does not effect cortisol or prolactin up to 100mcg



IPAMORELIN
MW 711

GHRP6

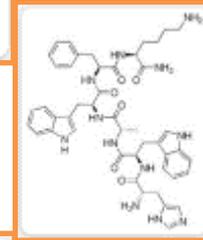
- Very potent GH releaser
- Does not effect cortisol or prolactin up to 100mcg



GHRP6
MW 873

GHRP2

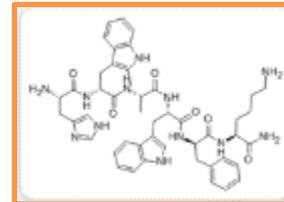
- More potent than GHRP6
- Effect on cortisol & prolactin are slightly higher w/doses >100mcg



GHRP2
MW 817

HEXARELIN

- Strongest; more potent than GHRP2
- Strongest impact on cortisol & prolactin; upper limits of normal



HEXARELIN
MW 887

GHRPs

- Concurrent administration with GHRH (*Sermorelin*) results in synergistic release of GH from pituitary.
- Total GH release is not additive
- GHRP capable of creating larger GH pulse without regard to natural peak/trough



GHRP Dosing

Although most studies have shown that the saturation dose is defined as 100mcg or 1mcg/kg/pulse, it is often recommended to round up to at least 150mcg.

While 100mcg will fully saturate the receptors; another 100mcg to that dose will only be 50% effective; adding yet another 100mcg to that dose will only be 25% more effective, etc.

- 200mcg = 150mcg
- 300mcg = 188mcg

Doses > 100mcg may be susceptible to desensitization → decrease in IGF-1

- Cease administering for several days, then restart to remedy the effect
- Design dosing protocol that involves short breaks (21/7 or 5/2)

GHRP Dosing

TYPICAL CONSERVATIVE DOSING PROTOCOL

- 100 – 200mcg GHRP
- Subcutaneous Injections 5 – 7 days per week
- May be given 1 – 3 times/day ... separate dosing > 3 hours apart if MDD

Most commonly combined with the addition of GHRH to further enhance GH release

F.A.Q.'s

How To Reconstitute Lyophilized Vials

We recommend the following for any size vial to calculate a 30 day supply:

- To Inject 0.2mL nightly; Mix with 6mL
- To Inject 0.3mL nightly; Mix with 9mL
- 15mg vial with 6mL diluent = 2500mcg/mL and a 0.2mL dose = 500mcg Sermorelin
- 15mg vial with 9mL diluent = 1667mcg/mL and a 0.3mL dose = 500mcg Sermorelin

How do I calculate mcg per dose?

When figuring a 30 day supply, the total mgs of the vial would be divided by 30

- Sermorelin 15mg divided by 30 days = 500mcg
- Sermorelin/GHRP-2 (9mg/3mg) divided by 30 days = 300mcg/100mcg
- Sermorelin/GHRP-2 (6mg/4.5mg) divided by 30 days = 200mcg/150mcg

What is included with the shipment?

In each shipment from Wells Pharmacy, the patient will be provided the following for each 30 day supply:

- 1 x 10mL syringe with 1 x 18g needle to reconstitute the powder with the diluent
- #30 insulin syringes of your choice:
 - Gauge 29,30, or 31 - Length 5/16" or 1/2" - Volume 0.3mL, 0.5mL, or 1mL
- #30 alcohol swabs

Current Formulary Items Available

**Doses Shown Assume 6mL or 9mL Reconstitution Unless Otherwise Noted
(30-day Supply)**

- | | | |
|-----|--|----------------------------------|
| 1. | Sermorelin 9mg | (300mcg per dose) |
| 2. | Sermorelin 15mg | (500mcg per dose) |
| 3. | Sermorelin 28mg | (800mcg per dose)* |
| 4. | Sermorelin 6mg/ GHRP2 4.5mg | (200mcg/150mcg per dose) |
| 5. | Sermorelin 9mg/ GHRP2 3mg | (300mcg/100mcg per dose) |
| 6. | Sermorelin 3mg/ GHRP6 3mg | (100mcg/100mcg per dose) |
| 7. | Sermorelin 6mg/ GHRP6 3mg | (200mcg/100mcg per dose) |
| 8. | Sermorelin 5mg/ GHRP2 6mg/ GHRP6 2mg | (150mcg/180mcg/60mcg per dose)** |
| 9. | Sermorelin 6mg/ GHRP2 3mg/ GHRP6 3mg | (200mcg/100mcg/100mcg per dose) |
| 10. | Sermorelin 9mg/ GHRP2 3.15mg/ GHRP6 3.15mg | (300mcg/105mcg/105mcg per dose) |
| 11. | Sermorelin 9mg/ GHRP2 9mg/ GHRP6 6mg | (300mcg/300mcg/200mcg per dose) |
| 12. | Sermorelin 9mg/ GHRP2 9mg/ GHRP6 9mg | (300mcg/300mcg/300mcg per dose) |
| 13. | Sermorelin 15mg/ GHRP2 5.4mg/Theanine 75mg | (500mcg/180mcg/2.5mg per dose) |

3mg Vial = 100mcg
6mg Vial = 200mcg
9mg Vial = 300mcg
15mg Vial = 500mcg

F.A.Q.'s Continued

What is the minimum amount of time a patient should take before they see results?

Most patients will begin to feel sleep changes in the first week. For best results patients should commit to using for a minimum of 90 days to feel the full benefits.

What if my patient did not see the changes they hoped for?

Just as with BHRT therapy, changes in the body are measured in both the labs and in the feedback from your patients. It's important to discuss both as well as their expectations.

The IGF-1 Labs did not change or have begun to decrease

The feedback from the patient in how they are feeling is equally important as the lab testing. Remember, that you are treating a patient and not a number. In some patients the dosage may need to be titrated up or converted to a blend of all 3 (GHRH/GHRP-2/GHRP-6) to experience results. Also, it is important that the labs are measured at the same time every time.

Is Sermorelin FDA Approved?

While no compounded medication is ever FDA approved, Geref[®] (sermorelin) was FDA approved in 1997 to treat pediatric GH deficiency. In 2002, Geref[®] was discontinued.

The chemicals purchased by Wells Pharmacy are strictly from FDA approved facilities and vendors

superior science & service



Thank You!
Other Questions? Email
Info@wellsrx.com

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