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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	April 8, 2008
Subject:	Growth Hormone – Adult	**Page:**	1 of 7

Last Review Date: March 12, 2021

Growth Hormone – Adult Therapy

Description

Genotropin, Humatrope, **Norditropin**, Nutropin, Nutropin AQ, Omnitrope, Saizen, Sogroya*, Zomacton

Bolded medications are the preferred products
*This medication is included in this policy but is not available in the market as of yet

Background
Growth hormone deficiency (GHD) in adulthood, associated with hypothalamic-pituitary dysfunction is now widely accepted as a distinct clinical syndrome, and is linked to a substantial number of significant co-morbidities, many of which can be ameliorated with growth hormone replacement therapy (1).

The FDA has approved growth hormone replacement for use in adult patients with growth hormone deficiency. Approved indications are for the treatment of adults with either adult onset or childhood onset GHD. With the exception of idiopathic adult onset GHD, GHD should be confirmed as due to pituitary disease from known causes, including pituitary tumor, pituitary surgical damage, hypothalamic disease, irradiation, trauma, or reconfirmed childhood GHD. Growth hormone should only be prescribed to patients with clinical features suggestive of adult GHD and biochemically proven evidence of adult GHD (1-9).

Regulatory Status
FDA approved indications: Human growth hormone is indicated for treatment of adult patients with either childhood-onset or adult-onset GH deficiency (2-9).

The laboratory diagnosis of GHD in adults is determined by dynamic endocrine testing. Because growth hormone has a short half-life in blood, growth hormone levels frequently are undetectable in blood samples obtained at random from normal subjects. For this reason, a stimulation test is needed to confirm the diagnosis. American Association of Clinical Endocrinologists (AACE) does not recommend growth hormone stimulation testing in patients with three or more pituitary hormone deficiencies *and* low IGF1 (2-9).

Use of any growth hormone in adults can cause a number of potentially serious adverse effects; therefore regular and routine monitoring is required. Sometimes treatment may need to be permanently stopped. These adverse effects include the development of impaired glucose tolerance and diabetes mellitus, upper airway obstruction and sleep apnea in patients with Prader-Willi syndrome, progression or recurrence of tumors in patients with preexisting tumors, intracranial hypertension, the worsening of hypothyroidism, and the worsening of pre-existing scoliosis, and pancreatitis (1-9).

The usefulness of growth hormone treatment in adults who have completed their structural growth derives from the role of growth hormone in the following processes: increasing bone density, increasing lean tissue, decreasing adipose tissue, bolstering cardiac contractility, improving mood and motivation and enhancing exercise capacity (2-9).

Growth hormone (GH) is used off-label for cosmetic, anti-aging and performance enhancing purposes. These indications are not approved by the FDA and are not a covered benefit under the Service Benefit Plan.

Related policies
Growth Hormone Pediatric, Serostim, Zorbtive

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Adult growth hormone may be considered **medically necessary** for patients 18 years of age or older for wound healing in burn patients, for growth hormone deficiency due to hypothalamic disease, pituitary disease, radiation therapy, surgery, trauma, panhypopituitarism, idiopathic adult onset deficiency and if the conditions below are met.

Adult growth hormone is considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Burn wounds (used for promotion of wound healing in burn patients)

2. Growth hormone deficiency due to at least **ONE** of the following:
    a. Hypothalamic disease
    b. Pituitary disease
    c. Radiation therapy
    d. Surgery
    e. Trauma
    f. Idiopathic adult-onset growth hormone deficiency

    AND the following:

    Documentation of GH stimulation test result from **ONE** of the following:
    a. Insulin tolerance test peak GH ≤ 5 ng/ml
    b. Glucagon, peak GH ≤ 3 ng/ml
    c. Arginine/L-Dopa, peak GH ≤ 1.5 ng/ml
    d. Arginine, peak GH ≤ 0.4 ng/ml

3. Documented IGF-1 level below the age and sex appropriate reference range **AND** panhypopituitarism (defined as a deficiency of three or more pituitary hormones such as gonadotropin [LH and/or FSH], adrenocorticotropic hormone [ACTH], thyroid-stimulation hormone [TSH], arginine vasopressin [AVP])

AND ALL of the following:

1. Confirmation that GH is not being used for cosmetic, anti-aging or athletic performance enhancement
2. Not being used in combination with another somatropin agent (such as Serostim, Zorbtive or any other GH)
3. **Non-preferred medications only:** Patient **MUST** have tried the preferred product (Norditropin) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

All requests are subject to approval by a secondary review by a clinical specialist for final coverage determination

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Burn wounds (used for promotion of wound healing in burn patients)

2. Growth hormone deficiency due to at least **ONE** of the following:
    a. Hypothalamic disease
    b. Pituitary disease
    c. Radiation therapy
    d. Surgery
    e. Trauma
    f. Idiopathic adult-onset growth hormone deficiency
    g. Panhypopituitarism

AND ALL of the following:

1. Confirmation that GH is not being used for cosmetic, anti-aging or athletic performance enhancement
2. Not being used in combination with another somatropin agent (such as Serostim, Zorbtive or any other GH)
3. **Non-preferred medications only:** Patient **MUST** have tried the preferred product (Norditropin) unless the patient has a valid medical exception (e.g. inadequate treatment response, intolerance, contraindication)

All requests are subject to approval by a secondary review by a clinical specialist for final coverage determination

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Growth hormone deficiency (GHD) in adulthood, associated with hypothalamic-pituitary dysfunction is now widely accepted as a distinct clinical syndrome, and is linked to a substantial number of significant co-morbidities, many of which can be ameliorated with growth hormone replacement therapy. The FDA has approved growth hormone replacement for use in adult patients with growth hormone deficiency (1-9).

Growth hormone is used off-label for cosmetic, anti-aging and performance enhancing purposes. These indications are not approved by the FDA and are not a covered benefit under the Service Benefit Plan.

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of human growth hormone while maintaining optimal therapeutic outcomes.

References

1. Cook DM, Yuen KC, Biller BM, Kemp SF, Vance ML. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients - 2009 update: executive summary of recommendations. Endocr Pract 15:580-586.
2. Norditropin [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; March 2020.
3. Humatrope [package insert]. Indianapolis IN: Eli Lilly and Company Ltd.; October 2019.
4. Nutropin AQ [package insert]. South San Francisco, CA: Genentech Inc.; December 2016.
5. Omnitrope [package insert]. Princeton, NJ: Sandoz Inc.; June 2019.
6. Saizen [package insert]. Rockland, MA: EMD Serono Inc.; February 2020.
7. Sogroya [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; August 2020.
8. Zomacton [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; July 2018.
9. Genotropin [package insert]. New York, NY: Pfizer Inc.; April 2019.

Policy History

Date	Action
April 2008	Criteria modified to include requirement of stimulation test result of peak GH ≤ 5ng/ml.

	Removed the GH stimulation test requirement for a renewal PA.
May 2008	Changed minimum age requirement to 18. Added negative GH stimulation test requirement for PA renewals and confirmation that it is not being used for cosmetic, anti-aging or athletic performance enhancement. AACE does not recommend GH stimulation testing in patients with three or more pituitary hormone deficiencies or when the IGF1 is low. Patients with serum IGF-I less than 84 ug/L do not require GH stimulation testing for the diagnosis of adult GHD.
September 2009	Revised to clarify that low IGF-1 (level < 84 ug/ml) establishes growth hormone deficiency in combination with three pituitary hormone deficiencies (2-4). This corrects 5/13/2009 notation– AACE does not recommend GH stimulation testing in patients with three or more pituitary hormone deficiencies and low IGF1, (rather than three or more pituitary hormone deficiencies or low IGF-1).
August 2010	Removal of Geref; discontinued by the manufacturer. Revised to add specific Growth Hormone stimulation test and approvable levels for each based on American Association of Clinical Endocrinologists (AACE) and Endocrine Society Clinical Practice Guidelines. Inclusion statement to reflect the growth hormone review process and separate initiation of therapy and continuation of therapy criteria. Adding a continuation criterion prevents exclusion of members with previous growth hormone approval from having the new GH stimulation test requirements. This requirement would not be clinically appropriate for members who have been on continuous therapy for years. All requests that met criteria (initiation or continuation) will continue to go through the secondary review by a clinical specialist to prevent misuse and abuse.
September 2012	Annual editorial and reference update
December 2012	Annual editorial and reference update
September 2013	Annual editorial review by PMPC
December 2014	Annual editorial and reference update Removed: stimulation test arginine/GHRH because GHRH is no longer manufactured and available in the US Added: No concurrent use with another somatropin
March 2015	Annual editorial and reference update
September 2016	Annual editorial review and reference update Policy number change from 5.08.11 to 5.30.11
December 2017	Annual editorial review and reference update Change of the requirement from documented IGF-1 less than 84 ug/L to a documented serum IGF-I level below the age and sex appropriate reference range per SME
March 2018	Addition of Zomacton
June 2018	Annual editorial review and reference update

September 2018	Annual review and reference update Updated regulatory status per SME
December 2019	Annual review and reference update. Addition of requirement to trial preferred product
September 2020	Addition of Sogroya
December 2020	Annual review and reference update
March 2021	Annual editorial review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.