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Prior Authorization Criteria Update: Growth Hormones

Purpose of Update:

The purpose of this prior authorization (PA) update is to align fee-for-service PA criteria with the current Health Evidence Review Commission (HERC) guidance for use of growth hormones (GH) and their FDA-approved indications. Growth hormones are indicated for a variety of childhood and adult conditions. HERC guidance restricts use of GH to funded diagnoses where there is medical evidence of effectiveness and safety. FDA-approved indications for GH vary by brand name product and are presented in **Table 1**. HERC guidance continues to specify that treatment with GH for children with conditions such as gonadal dysfunction, panhypopituitarism, iatrogenic and other pituitary disorders should only continue until adult height, as determined by bone age, is achieved.[1] Treatment for adult human growth hormone deficiency is currently not listed as a funded condition on the prioritized list.[1] However, funded conditions such as HIV associated with cachexia and short bowel syndrome are covered for adults by FDA-approved GH agents.

Table 1. Pediatric and Adults FDA Approved Indications for Growth Hormone[2,3]

	somatropin									somapacitan
	Genotropin®	**Humatrope®**	**Norditropin®**	**Nutropin AQ®**	**Omnitrope®**	**Saizen®**	**Serostim®**	**Zorbtive®**	**Zomacton®**	**Sogroya®**
Pediatric Indications										
GHD	X	X	X	X	X	X			X	
Prader-Willi Syndrome	X		X		X					
Noonan Syndrome			X							
Turner Syndrome	X	X	X	X	X				X	
Idiopathic Short Stature	X	X	X	X	X				X	
SHOX Deficiency		X							X	
CKD with Growth Failure				X						
Small for Gestational Age	X	X	X		X				X	

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HIV Associated Cachexia							X			
Adult Indications										
GHD	X	X	X	X	X	X			X	X
HIV Associated Cachexia							X			
Short Bowel Syndrome								X		

Abbreviations: CKD = chronic kidney disease; FDA = Food and Drug Administration; GHD = growth hormone deficiency; HIV = human immunodeficiency virus; SHOX = Short stature homeobox-containing gene

Recommendation:

- Add somapacitan-beco to Growth Hormone PDL class and make non-preferred.
- Update the prior authorization criteria to align with HERC coverage guidance and FDA-approved indications.

References:

1. Health Evidence Review Commission. HERC Prioritized List of Health Services. February 1, 2021. https://www.oregon.gov/oha/HPA/DSI-HERC/PrioritizedList/2-1-2021%20Prioritized%20List%20of%20Health%20Services.pdf. Accessed March 10, 2021.
2. Somatropin, E-Coli Derived. In: IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. https://www-micromedexsolutions-com.liboff.ohsu.edu/ Accessed March 10, 2021.
3. Somatropin. In: Lexicomp (electronic database). Wolters Kluwer. Hudson, OH. http://online.lexi.com.liboff.ohsu.edu/action/home. Accessed March 10, 2021.

Growth Hormones

Goal(s):
- Restrict use of growth hormone (GH) for funded diagnoses where there is medical evidence of effectiveness and safety.

NOTE: Treatment with GH in children should continue only until adult height as determined by bone age is achieved. Treatment is not included for isolated deficiency of human growth hormone in adults.

Length of Authorization:
- Up to 12 months

Requires PA:
- All GH products require prior authorization for OHP coverage. Treatment of human growth hormone deficiency for adults is not funded by the OHP.

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Initial Approval Criteria		
1. What is the diagnosis being treated?	Record ICD10 code	
2. Is the request for an FDA approved indication?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Is this a request for initiation of growth hormone?	**Yes:** Go to #4	**No:** Go to **Renewal Criteria**
4. Is the patient an adult (>18 years of age)?	**Yes:** Go to #10	**No:** Go to #5
5. Is the agent being prescribed by, or in consultation with, a pediatric endocrinologist or pediatric nephrologist?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness

Initial Approval Criteria		
6. Is the diagnosis funded?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
7. Is the diagnosis promotion of growth delay in a child with 3rd degree burns?	**Yes:** Document and send to DHS Medical Director for review and pending approval	**No:** Go to #8
8. If male, is bone age <16 years? If female, is bone age <14 years?	**Yes:** Go to #9	**No:** Pass to RPh. Deny; medical appropriateness
9. Is there evidence of non-closure of epiphyseal plate?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness
10. Is the request for the treatment of isolated human growth hormone deficiency in an adult (E23.0) or short stature due to an endocrine disorder (E34.3), or another unfunded condition? Per Guideline Note 74, treatment with GH for children with conditions such as panhypopituitarism, iatrogenic and other pituitary disorders, as well as gonadal dysfunction, should only continue until adult height, as determined by bone age, is achieved.	**Yes:** Pass to RPh. Deny; not funded by the OHP.	**No:** Go to #11
11. Is the requested product preferred?	**Yes:** Approve for up to 12 months	**No:** Go to #12
12. Will the prescriber consider a change to a preferred product that is FDA-approved for the condition? <u>Message</u>: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class and approve for up to 12 months.	**No:** Approve for up to 12 months

Renewal Criteria		
1. Document approximate date of initiation of therapy and diagnosis (if not already done).		
2. Was treatment with this agent initiated in patient prior to reaching adulthood (<18 years of age)?	**Yes:** Go to #3	**No:** Go to #5
3. Is growth velocity greater than 2.5 cm per year?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is male bone age <16 years or female bone age <14 years?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the request for isolated human growth hormone deficiency in an adult (E23.0), short stature due to an endocrine disorder (E34.3), or another unfunded condition?	**Yes:** Pass to RPh. Deny; not funded by the OHP.	**No:** Go to #6
6. Is the product requested preferred?	**Yes:** Approve for up to 12 months	**No:** Go to #7
7. Will the prescriber consider a change to a preferred product? <u>Message</u>: • Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class and approve for up to 12 months	**No:** Approve for up to 12 months

P&T Review: 6/21 (DE); 11/18 ; 9/17; 9/16; 9/15; 9/14; 9/10; 5/10; 9/08; 2/06; 11/03; 9/03
Implementation: 1/1/19; 10/13/16; 1/1/11, 7/1/10, 4/15/09, 10/1/03, 9/1/06; 10/1/03

Abbreviated Drug Review

Trade Name (generic)

Sogroya (somapacitan-beco)

Indications

- Human growth hormone for the replacement of endogenous growth hormone (GH) in adults with growth hormone deficiency (GHD).
- This indication is an unfunded condition based on Oregon Health Plan (OHP) prioritized list (line 653; guideline note 74)

Dosage

- Initiation: 1.5 mg subcutaneously (SUBQ) once weekly for treatment naïve patients and patients switching from daily GH; 1 mg once weekly in patients aged 65 and older; 2 mg once weekly in women receiving oral estrogen
- Increase weekly dosage by 0.5 mg to 1.5 mg increments every 2 to 4 weeks until desired response has been achieved; Maximum dose is 8 mg once weekly
- Supplied as a 10 mg/1.5 ml (6.7 mg/ml) single-patient-use prefilled pen; pen delivers doses from 0.05 mg to 4.0 mg, in increments of 0.05 mg.

Background

- Binds to a dimeric growth hormone receptor in the cell membrane of target cells resulting in intracellular signal transduction.
- Pharmacodynamic effects aim to mimic action of endogenous GH leading to increase in insulin-like growth factor 1 (IGF-1) levels and improvement in body composition.

Efficacy

FDA-approval was based on a 35-week, phase 3, double-blind, placebo-controlled study [NCT02229851]. The trial enrolled 300 treatment naïve adult growth hormone-deficient patients (AGHD) randomized (2:1:2) to receive somapacitan SUBQ once-weekly injection (n=120), once-weekly placebo (n=61), or an open-label daily dose of somatropin SUBQ injection (n=119). Trial completers were enrolled in a 52-week open-label extension period where placebo group patients were switched to somapacitan while the daily somatropin group was randomized 1:1 to continue once daily somatropin or once weekly somapacitan. Participants were mostly white (67%) or Asian (29%) with a mean age of 45 years and evenly divided by sex. The mean baseline body mass index (BMI) was 27.4 kg/m^2. The primary efficacy outcome was change from baseline to week 34 in truncal fat percentage* as assessed by dual X-ray absorptiometry. The manufacturer did not prespecify thresholds for changes in body composition as evidence GH effectiveness. Although statistical significance was reached for the primary endpoint, the FDA noted that none of the observed improvements in body composition in patients with GHD have been directly linked to an outcome of morbidity/mortality reduction and none of the trials established that use of GH in patients with AGHD reduce cardiovascular risk or mortality.

FDA Results for Primary Outcome Measures	Weekly Placebo	Weekly Somapacitan	Daily Somatropin
Number of subjects in full analysis (N)	61	120	119
Truncal fat % change at 34 weeks from baseline	+0.31	-1.10	-2.38
Absolute Treatment Difference vs Placebo (%) 95% [Confidence Interval]; p-value		-1.41 [-2.61 to -0.22]; 0.02	
Absolute Treatment Difference vs Daily Somatropin (%) 95% [Confidence Interval]; p-value		+1.28% (95% CI: 0.29%, 2.26%); 0.011	

*Truncal fat % = (truncal fat mass)/(truncal fat mass + truncal lean body mass) x 100

Safety

Common adverse reactions: back pain (10%), arthralgia (7%), dyspepsia (5%), sleep disorder (4%), dizziness (4%), tonsillitis (3%), peripheral edema (3%), vomiting (3%), adrenal insufficiency (3%), hypertension (3%), blood creatine phosphokinase increase (3%), weight increased (3%), anemia (3%)
Contraindications: acute critical illness after open-heart or abdominal surgery, multiple accidental trauma, or those with acute respiratory failure; active malignancy; active proliferative or severe non-proliferative diabetic retinopathy
Warnings and Precautions: Increased mortality in patients with acute critical illness, increased risk of neoplasms, glucose intolerance and diabetes mellitus, intracranial hypertension, severe hypersensitivity including anaphylaxis and angioedema, fluid retention, hypoadrenalism, hypothyroidism, pancreatitis, lipohypertrophy/lipoatrophy
Special Populations: Reduce initial dose in elderly (≥65 years) and those with moderate hepatic impairment; avoid use in severe hepatic impairment

Evidence Gaps/Limitations

- There is no evidence that GH treatments affect mortality or major morbidity.
- Although no statistical non-inferiority was pre-specified or required, somapacitan found to be inferior to daily somatropin with the magnitude of difference almost as much as the difference between somapacitan and placebo.

Recommendation

Restrict use for OHP-covered conditions through Prior Authorization

References

1. Sogroya (somapacitan-beco) for subcutaneous injection [Prescribing Information]. Plainsboro, NJ, USA. Novo Nordisk Inc, 2020.
2. FDA Center for Drug Evaluation and Research. Sogroya Sum. Review. Application Number 761156Orig1s000. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761156Orig1s000SumR.pdf