

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY	Growth Disorders	P & T DATE	9/15/2020
THERAPEUTIC CLASS	Endocrine Disorders	REVIEW HISTORY	09/19, 09/18, 12/16,
LOB AFFECTED	Medi-Cal	(MONTH/YEAR)	11/15, 05/14

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Growth hormones (GH) are produced by the cells located in the anterior pituitary known as somatotropes. The predominant action of GH is to stimulate hepatic synthesis and secretion of insulin-like growth factor 1 (IGF-1), a potent growth and differentiation factor that responsible for most of the growth-promoting activities of GH. Growth hormones also play an important role in adult metabolism. A deficiency of GH in adults can affect lipid and bone metabolism, decrease strength and reduce work capacity.¹

Possible causes of growth disorders varies as they can be genetic, constitutional, or as a result of hormonal disorders. This review will examine the variety of growth related disorders and their coverage criteria.

Table 1. Available Somatropin Agents: (Current as of 8/2020)

Growth Hormone Agents	Available Strengths	Formulary Limits	*Average Cost for 28 DS	Notes
Genotropin	5mg/ml, 12mg/ml	PA, SP	\$1,323.92	Reserved for patients with documented growth hormone deficiency, Turner Syndrome, Prader-Willi Syndrome. Restricted to Specialty Pharmacy.
Genotropin Miniquick	0.2mg/0.25ml, 0.4mg/0.25ml, 0.6mg/0.25ml, 0.8mg/0.25ml 1mg/0.25ml, 1.2mg/0.25ml, 1.4mg/0.25ml, 1.6mg/0.25ml, 1.8mg/0.25ml, 2mg/0.25ml	PA, SP	\$2,586.01	
Humatrope	5mg, 6mg, 12mg, 24mg	PA, SP	\$2,819.43	
Norditropin Flexpro	5mg/1.5ml, 10mg/1.5ml, 15mg/1.5ml 30mg/3ml	PA, SP	\$5,104.49	
Nutropin AQ Nuspin	5mg/2ml, 10mg/2ml, 20mg/2mL	PA, SP	\$4,060.27	
Omnitrope	5mg/1.5ml, 10mg/1.5ml, 5.8mg	PA, SP	\$2,391.85	
Saizen	5mg, 8.8mg	PA, SP, NF	\$765.27	
Saizen Click-Easy	8.8mg/1.5ml	NF	\$874.60	
Serostim	4mg, 5mg, 6mg	PA, SP	\$2,286.34	
Zomacton	5mg, 10mg	NF	--	
Zorbitive	8.8mg	NF	\$1,033.98	

PA = Prior Authorization SP = restrict to Specialty Pharmacy NF = Non-Formulary DS = Day Supply

⊞ EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Growth Hormone Agents (Somatropin)

Genotropin, Genotropin Miniquick, Humatrope, Norditropin Flexpro, Nutropin AQ, Nutropin AQ Nuspin, Omnitrope, Saizen, Saizen Click-Easy, Serostim, Zorbitive

Growth Hormone Deficiency (Children)/ Idiopathic Short-Stature/Turner Syndrome/Prader-Willi Syndrome

- Coverage Criteria:** Somatropin is reserved for patients ≤ 18 years old with documented low IGF-1 AND height that is more than 2 standard deviation below the population mean for age and sex.
- Limits:** None
- Required Information for Approval:**
 - Growth charts documenting patient's height and weight
 - Labs showing low IGF-1
- Other Notes:**
 - Therapy is discontinued when bone age exceeds 14 years OR when growth velocity drops below 2.5 cm/year.
 - Growth hormone supplementation are approved for 6 months at a time.
- Non-Formulary:** Saizen, Saizen Click-Easy, Zomacton, and Zorbitive

Growth Hormone Deficiency (Adults)

- Coverage Criteria:** Somatropin is reserved for patients > 18 years old with documented low IGF-1 OR low insulin growth factor binding protein-3 with documented pituitary disease or GH deficiency (GHD) as a result of surgery or radiation therapy.
- Limits:** None
- Required Information for Approval:**
 - Labs showing low IGF-1 (< 5 mcg/L)
 - Clinical documentation of mal-functioning pituitary gland (as a result from surgery, radiation therapy, etc)
- Other Notes:** Growth hormone supplementation are approved for 6 months at a time.
- Non-Formulary:** Saizen, Saizen Click-Easy, Zomacton, and Zorbitive

⊞ CLINICAL JUSTIFICATION

GHD, Turner Syndrome, and idiopathic short stature are treated with growth hormone supplementation, but the treatment approaches vary. In Turner Syndrome or Idiopathic short stature, the 2009 American Academy of Endocrinology Guidelines recommend the discontinuation of growth hormone supplementation when the child reaches their peak height or when their bone age is similar to that of an adult since there is no proven benefit to continuing GH treatment in adulthood.² On the other hand, GHD is confirmed via the Insulin Tolerance Test (ITT). Once growth hormone supplementation is initiated, monitoring of serum IGF-1 levels are recommended every 6-12 months. GH therapy is often long-term in adult patients with GHD.

All of the currently available growth hormone agents are somatotropins. Although direct comparisons between different GH products have not been published and some differences exist in recommended doses, all GH products are generally considered to be equally efficacious. The guidelines do not recommend the use of one commercial product over another.²

✚ MEDI-CAL UTILIZATION SUMMARY

Table 2. Medi-Cal Utilization Summary (7/2019 - 6/2020)

Growth Hormone Agents	Total Fills	Total Utilizers	Total Cost	Total Qty	Average DS	Cost/Rx	Cost/Unit
GENOTROPIN	47	8	\$98,330.16	81	21	\$1,954.97	\$416.60
10554 - 12 MG/ML CARTRIDGE	25	3	\$49,648.27	1	22	\$1,985.93	\$1,551.51
21454 - 2MG/0.25ML SYRINGE	0	0	0	0	0	0	0
63408 - 5 MG/ML CARTRIDGE	16	2	\$31,773.39	3	25	\$1,985.84	\$635.47
50187- MINQUICK 0.4 MG	1	1	\$1,591.42	28	28	\$1,591.42	\$56.84
50207- MINQUICK 0.8 MG	2	1	\$6,365.44	28	28	\$3,182.72	\$113.67
50217- MINQUICK 1 MG	3	1	\$8,951.64	21	21	\$2,983.88	\$142.09
HUMATROPE	19	3	\$57,342.77	6	22	\$2,819.43	\$1,802.72
25957 - 24 MG CARTRIDGE	13	1	\$40,566.95	1	22	\$3,120.53	\$3,120.53
575 - 12 MG CARTRIDGE	4	1	\$12,200.60	2	24	\$3,050.15	\$1,525.08
25969 - 6 MG CARTRIDGE	2	1	\$4,575.22	3	20	\$2,287.61	\$762.54
NORDITROPIN FLEXPRO	60	13	\$226,447.46	22	26	\$5,104.49	\$931.93
24145 - 5 MG/1.5ML PEN INJCTR	1	1	\$2,424.75	6	25	\$2,424.75	\$404.13
24146 - 10MG/1.5ML PEN INJCTR	12	3	\$39,759.55	4	26	\$3,313.30	\$855.04
24147 - 15MG/1.5ML PEN INJCTR	46	8	\$173,351.78	3	23	\$3,768.52	\$1,256.17
25816 - 30 MG/3 ML PEN INJCTR	1	1	\$10,911.38	9	30	\$10,911.38	\$1,212.38
NUTROPIN AQ NUSPIN	78	12	\$315,492.98	18	28	\$4,060.27	\$748.12
27846 - 5 MG/2 ML PEN INJCTR	6	2	\$15,389.84	8	33	\$2,564.97	\$320.62
39695 - 10 MG/2 ML PEN INJCTR	49	7	\$148,769.68	5	25	\$3,036.12	\$641.25
39698 - 20 MG/2 ML PEN INJCTR	23	3	\$151,333.46	5	25	\$6,579.72	\$1,282.49
OMNITROPE	12	3	\$14,581.67	7	25	\$2,391.85	\$633.99
92366 - 10MG/1.5ML CARTRIDGE	1	1	\$3,803.90	5	25	\$3,803.90	\$845.31
92386 - 5 MG/1.5ML CARTRIDGE	11	2	\$10,777.77	2	25	\$979.80	\$422.66
SEROSTIM	0	0	0	0	0	0	0
63405 - 4 MG VIAL	0	0	0	0	0	0	0
Grand Total	216	39	\$712,195.04	8	25	\$3,386.50	\$891.04

Table 3. Last Year's Medi-Cal Utilization Summary (8/2018 - 7/2019)

Growth Hormone Agents	Total Fills	Total Utilizers	Total Cost	Total Qty	Average DS	Cost/Rx	Cost/Unit
GENOTROPIN	23	3	\$67,334.78	149	26.22	\$2,927.60	\$451.91
10554 - 12 MG/ML CARTRIDGE	4	1	\$6,116.34	4	20.00	\$1,529.09	\$1,529.09
21454 - 2MG/0.25ML SYRINGE	3	1	\$22,671.66	84	28.00	\$7,557.22	\$269.90
63408 - 5 MG/ML CARTRIDGE	16	1	\$38,546.78	61	27.44	\$2,409.17	\$631.91
HUMATROPE	30	3	\$101,837.42	55	23.40	\$3,394.58	\$1,851.59
25957 - 24 MG CARTRIDGE	13	1	\$39,029.27	13	22.00	\$3,002.25	\$3,002.25
575 - 12 MG CARTRIDGE	17	2	\$62,808.15	42	24.47	\$3,694.60	\$1,495.43
NORDITROPIN FLEXPRO	66	9	\$323,103.33	327	23.21	\$4,895.51	\$988.08
24145 - 5 MG/1.5ML PEN INJCTR	1	1	\$2,897.39	7.5	25.00	\$2,897.39	\$386.32
24146 - 10MG/1.5ML PEN INJCTR	20	1	\$119,015.64	150	20.30	\$5,950.78	\$793.44
24147 - 15MG/1.5ML PEN INJCTR	44	6	\$190,278.92	160.5	24.34	\$4,324.52	\$1,185.54
25816 - 30 MG/3 ML PEN INJCTR	1	1	\$10,911.38	9	30.00	\$10,911.38	\$1,212.38
NUTROPIN AQ NUSPIN	120	14	\$547,608.58	772	26.12	\$4,563.40	\$709.34
27846 - 5 MG/2 ML PEN INJCTR	32	4	\$73,101.85	228	24.34	\$2,284.43	\$320.62
39695 - 10 MG/2 ML PEN INJCTR	59	8	\$223,139.38	348	26.31	\$3,782.02	\$641.21
39698 - 20 MG/2 ML PEN INJCTR	29	3	\$251,367.35	196	27.69	\$8,667.84	\$1,282.49

OMNITROPE	24	5	\$51,478.77	91.5	21.83	\$2,144.95	\$562.61
92366 - 10MG/1.5ML CARTRIDGE	7	3	\$28,098.46	34.5	27.14	\$4,014.07	\$814.45
92386 - 5 MG/1.5ML CARTRIDGE	17	2	\$23,380.31	57	19.65	\$1,375.31	\$410.18
SEROSTIM	2	1	\$4,572.68	14	30.00	\$2,286.34	\$326.62
63405 - 4 MG VIAL	2	1	\$4,572.68	14	30.00	\$2,286.34	\$326.62
Grand Total	265	35	\$1,095,935.56	1408.5	24.74	\$4,135.61	\$778.09

UTILIZATION ANALYSIS

Growth hormone agents solely consist of the active ingredient of Somatropin. Brand names differentiate the various formulations available for use. Non-formulary Somatropin options are Saizen, Zomacton, and Zorbtive which have no utilization in the past two years. The total drug spend for growth hormone agents decreased from \$1,085,935 to \$712,195 from the previous year (34.4% decrease). Although the number of utilizers is similar, there was a decrease in claims from the previous year (265 to 215). Most of the decreased spend was contributed by Nutropin AQ Nuspin. The spend for the medication decreased from \$547,000 to \$315,000 because of the decreased utilization.. Current utilization is appropriate and review of growth hormone utilization will continue to occur on an annual basis.

NEWLY APPROVED MEDICATIONS NOT ON FORMULARY

None

GUIDELINE & LITERATURE REVIEW

- American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care 2019 AACE Growth Hormone Task Force³
 - Insulin tolerance test remains gold-standard test to establish diagnosis of adult GHD using peak GH cut-point of 5 ug/L. The glucagon-stimulation test and macimorelin test could also be used as an alternative test.
 - With the macimorelin-stimulation test, the GH cut-point of 2.8 ug/L is used to differentiate patients with normal GH secretion from those with GHD.
 - The use of one commercial rhGH product is not suggested over another, as there is no evidence that one rhGH product is more advantageous

CRITERIA REVIEW FOR UNNECESSARY BARRIERS

Current requirements are appropriate

RECOMMENDATIONS

Review on an annual cycle

REFERENCES

1. HPSJ Growth Hormone Class Review—May 2014. Guidelines for use of growth hormone in clinical practice. *Endocr. Pract.* 2009;15(Suppl 2).
2. Grimberg A, Divall S, Polychronakos C, et al. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. *Horm Res Paediatr.* 2016;86:361-397.
3. Yuen KCJ, Biller BMK, Radovick S, et al. American Association of Clinical Endocrinologists and American College of Endocrinology guidelines for management of growth hormone deficiency in adults and patients transitioning from pediatric to adult care. *Endocr Pract.* 2019;25(11):1191-1232.

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Growth Hormone Class Review 05-2015.doc	05/2014	Jonathan Szkotak, PharmD, BCACP
Update to Policy	HPSJ Coverage Policy - Endocrine - Growth Hormone 2015-10.docx	11/2015	Johnathan Yeh, PharmD

Update to Policy	HPSJ Coverage Policy - Endocrine - Growth Hormone 2016-12.docx	12/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy - Endocrine - Growth Hormone 2018-09.docx	09/2018	Johnathan Yeh, PharmD
Update to Policy	Growth Hormone	09/2019	Matthew Garrett, PharmD
Update to Policy	Growth Hormone	09/2020	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy