



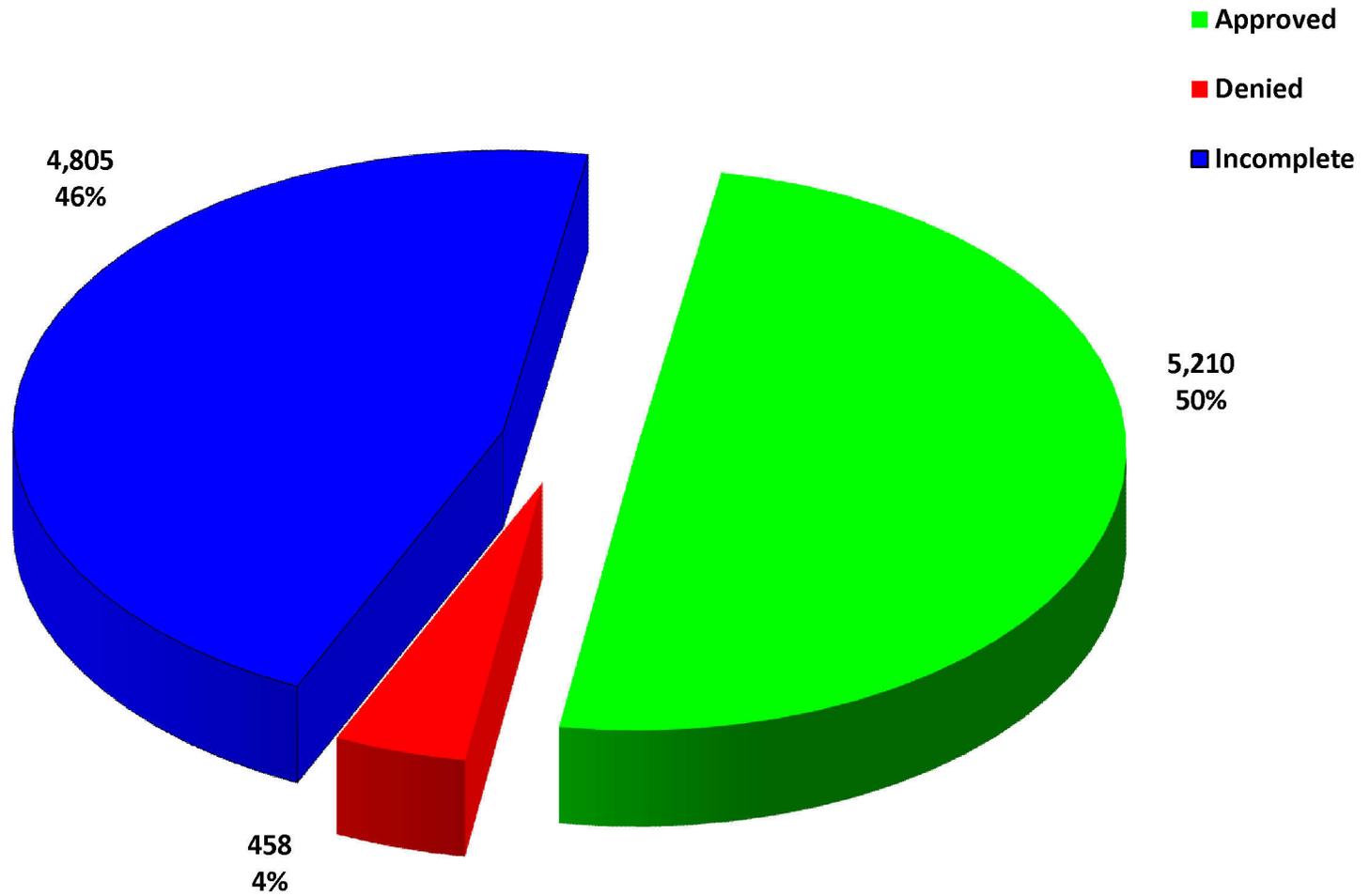
Appendix B

RETROSPECTIVE DRUG UTILIZATION REVIEW REPORT

August 2010

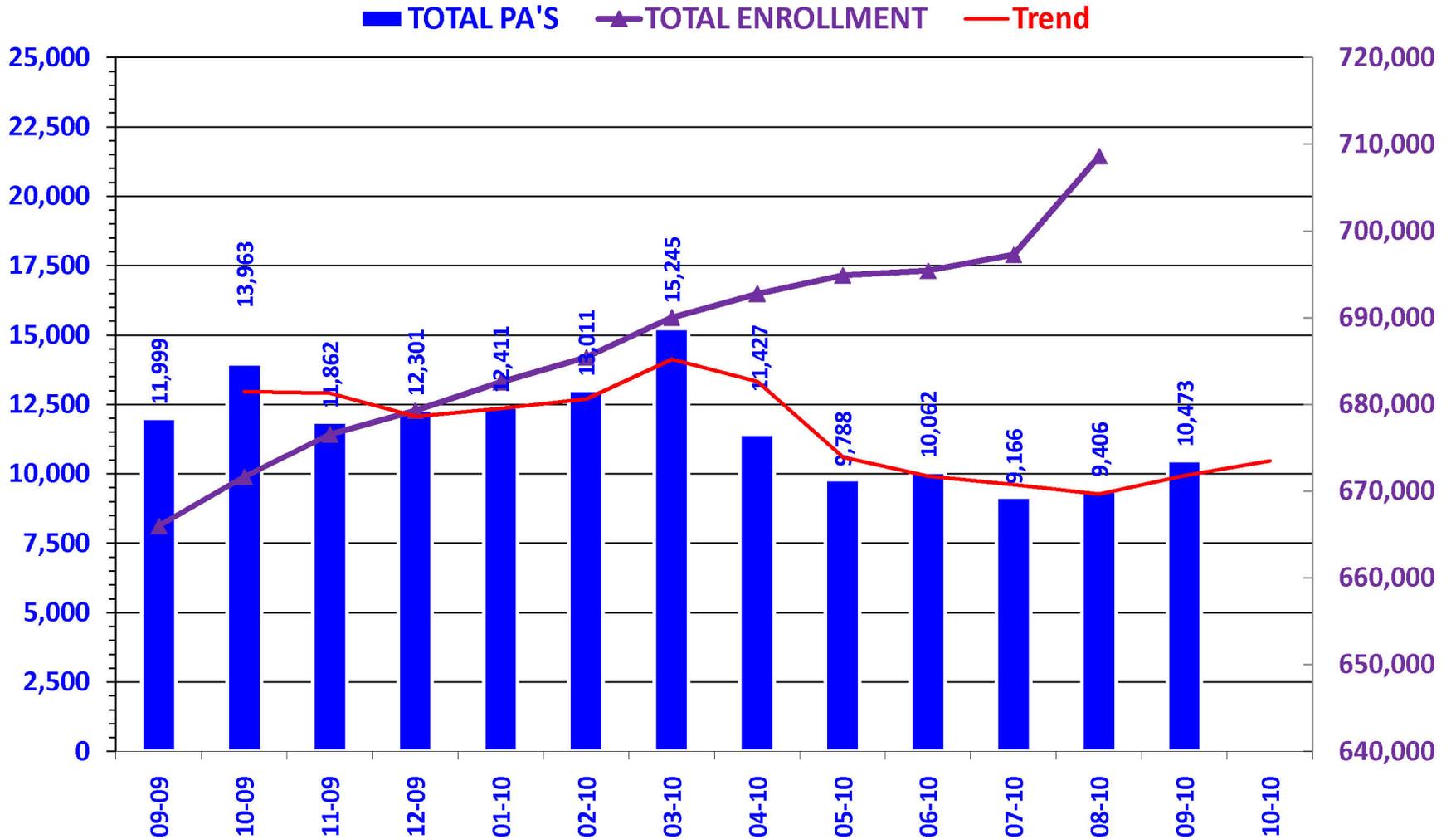
MODULE	DRUG INTERACTION	DUPLICATION OF THERAPY	DRUG-DISEASE PRECAUTIONS	DOSING & DURATION
Total # of <u>messages</u>	51,463	63,940	1,044,192	25,044
<u>Limits</u> applied	Established, Major, Males and Females, Age 19-35	Males and Females, Anorexiants/Stimulants, Age 5-6	Contraindicated, Pregnancy, Males and Females, Age 19-35	High Dose, Males and Females, Age 0-150, Androgens
Total # of <u>messages after limits</u> were applied	53	152	1,129 (229)	13
Total # of <u>members</u> reviewed	53	146	229	13
LETTERS				
Category	Prescribers	Pharmacies	Total Letters	
Drug Interaction	11	6	17	
Duplication of Therapy	21	6	27	
Drug-Disease Precautions	13	11	24	
Dosing & Duration	10	0	10	
Total Letters Sent	55	23	78	

PRIOR AUTHORIZATION ACTIVITY REPORT: September 2010



PA totals include overrides

PRIOR AUTHORIZATION REPORT: September 2009 – September 2010



PA totals include overrides

Prior Authorization Activity September 2010

	Total	Approved	Denied	Incomplete	Average Length of Approvals in Days
Advair/Symbicort	467	219	10	238	358
Amitiza	26	6	2	18	183
Anti-Ulcer	463	118	35	310	126
Antidepressant	321	114	9	198	339
Antihistamine	393	204	10	179	334
Antihypertensives	122	46	3	73	347
Antimigraine	71	8	5	58	182
Atypical Antipsychotics	754	373	10	371	346
Benzodiazepines	102	34	6	62	283
Bladder Control	74	18	3	53	360
Brovana (Arformoterol)	2	1	0	1	361
Byetta	13	5	0	8	343
Elidel/Protopic	56	20	7	29	106
ESA	189	139	6	44	63
Fibric Acid Derivatives	22	1	3	18	358
Fibromyalgia	115	50	3	62	344
Forteo	4	2	0	2	355
Glaucoma	14	4	0	10	360
Growth Hormones	63	49	5	9	170
HFA Rescue Inhalers	107	35	7	65	283
Insomnia	110	29	5	76	178
Misc Analgesics	35	3	16	16	209
Muscle Relaxant	138	39	45	54	98
Nasal Allergy	324	111	27	186	139
NSAIDS	161	32	17	112	284
Ocular Allergy	26	5	1	20	134
Ocular Antibiotics	88	51	1	36	14
Opioid Analgesic	290	121	12	157	216
Other	705	197	57	451	177
Otic Antibiotic	124	86	0	38	15
Pediculicides	129	71	5	53	16
Plavix	206	131	2	73	330
Quaalun (Quinine)	1	0	1	0	0
Singular	965	499	25	441	274
Smoking Cessation	59	19	4	36	59
Statins	371	72	12	287	330
Stimulant	1,471	921	39	511	241
Symlin	2	0	1	1	0
Synagis	18	0	0	18	0
Topical Antibiotics	22	7	0	15	40
Topical Antifungals	19	2	2	15	103
Ultram ER and ODT	7	0	0	7	0
Xopenex Nebs	35	18	3	14	326
Zetia (Ezetimibe)	17	9	1	7	361
Emergency PAs	9	9	0	0	
Total	8,710	3,878	400	4,432	

Overrides

Brand	52	26	5	21	295
Dosage Change	538	502	7	29	9
High Dose	4	4	0	0	217
IHS-Brand	49	46	0	3	176
Ingredient Duplication	3	3	0	0	13
Lost/Broken Rx	128	120	2	6	8
NDC vs Age	23	23	0	0	225
Nursing Home Issue	101	87	0	14	9
Other	32	26	3	3	36
Quantity vs. Days Supply	829	490	41	298	273
Stolen	6	6	0	0	3
Wrong D.S. on Previous Rx	1	1	0	0	3
Overrides Total	1,766	1,334	58	374	
Total Regular PAs + Overrides	10,476	5,212	458	4,806	

Denial Reasons

Unable to verify required trials.	3,289
Lack required information to process request.	1,459
Does not meet established criteria.	482
Not an FDA approved indication/diagnosis.	3
Drug Not Deemed Medically Necessary	1
Considered duplicate therapy. Member has a prior authorization for similar medication.	1

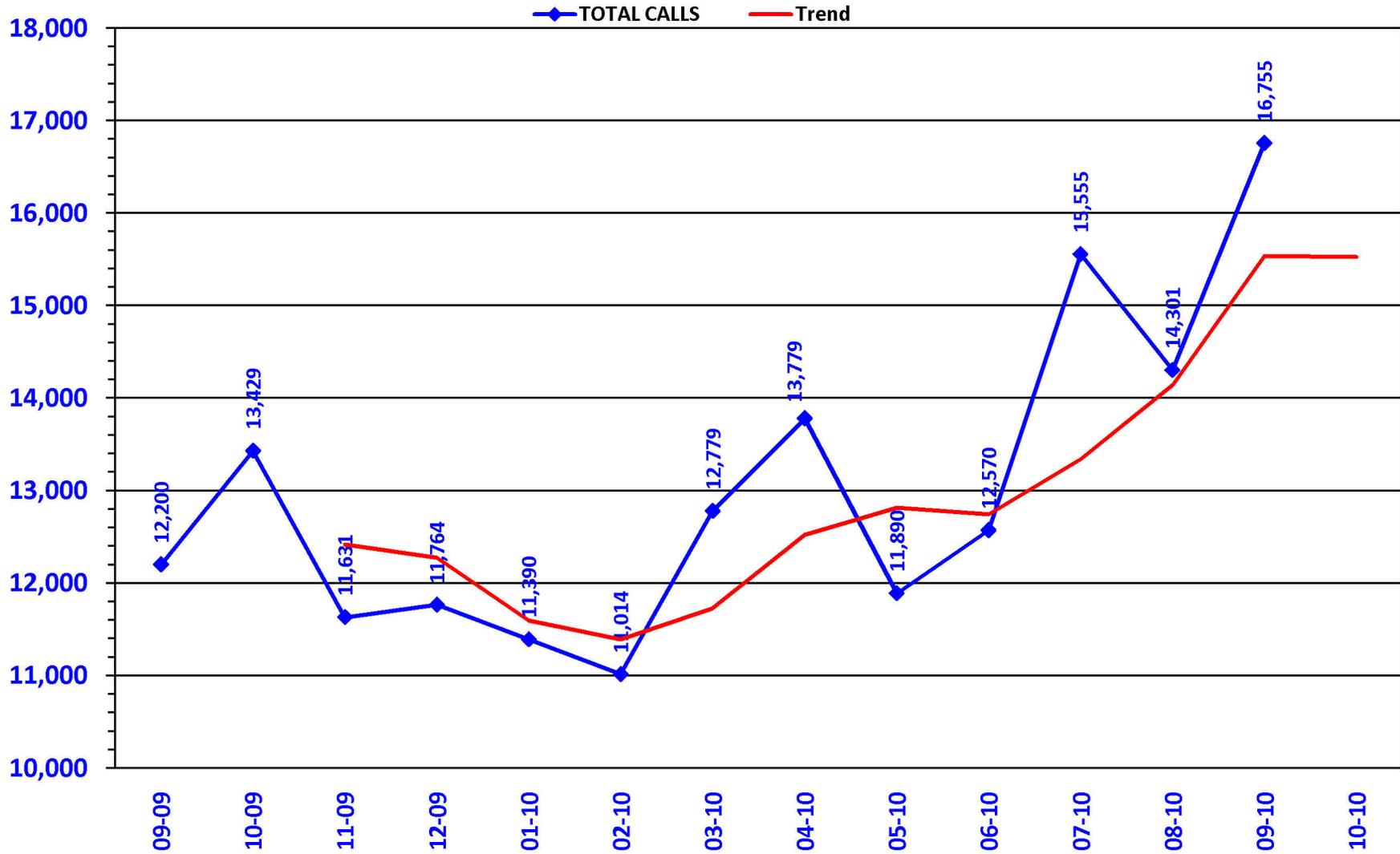
Duplicate Requests: 995

Letters: 1,111

No Process: 1,107

Changes to existing PAs: 506

CALL VOLUME MONTHLY REPORT: September 2009 – September 2010





Appendix C

FY2010 Annual Review of Growth Hormones

Oklahoma Health Care Authority
October 2010

Current Indications for Growth Hormone

COVERED INDICATIONS

- Classic hGH Deficiency
- Short Stature (including Prader-Willi Syndrome)
- Short Stature associated with Chronic Renal Insufficiency
- Small for Gestational Age (SGA)
- Turner's Syndrome or 45 X, 46 XY Mosaicism in males
- Hypoglycemia associated with hGH Insufficiency
- AIDS Wasting (Serostim only)
- SHOX (short stature homeobox-containing gene) Deficiency

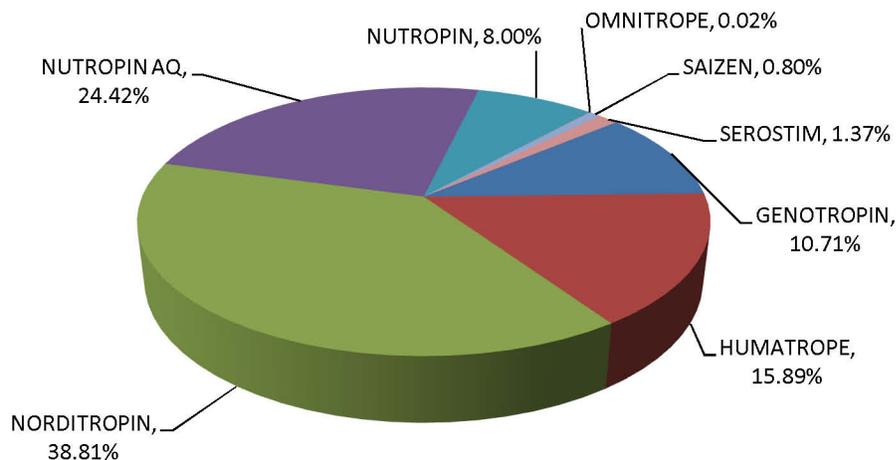
Trends in Utilization of Growth Hormones

Utilization of Growth Hormones during Fiscal Year 2010

Fiscal Year	Members	Claims	Cost	Cost/Claim	Per-diem	Units	Days
2009	216	1,566	\$3,750,634.44	\$2,395.04	\$83.09	11,403	45,142
2010	213	1,634	\$4,075,790.90	\$2,494.36	\$86.43	11,012	47,157
% Change	-1.40%	4.30%	8.70%	4.10%	4.00%	-3.40%	4.50%
Change	-3	68	\$325,156.46	\$99.32	\$3.34	-391	2,015

There was no use of Zorbitive™, Tev-tropin® or either of the IGF-1 analogs, Iplex™ or Increlex™.

Market Share of Growth Hormone Products

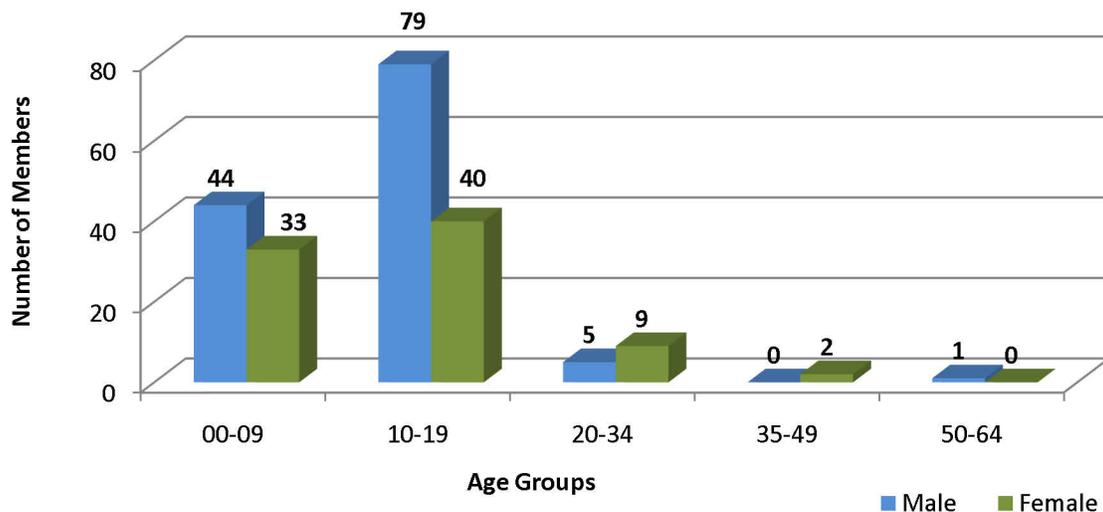


Utilization Details of Growth Hormones during Fiscal Year 2010

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST	CLAIMS/MEMBER	COST/MG
NORDITROPIN INJ 10/1.5ML	260	1,178	7,907	32	\$490,154.44	8.13	65.06
NORDITROPIN INJ 15/1.5ML	216	1,156	6,131	37	\$713,529.71	5.84	65.06
NUTROPIN AQ INJ 10MG/2ML	187	1,286	5,394	25	\$409,890.16	7.48	65.04
NUTROPIN AQ INJ 20MG/2ML	146	898	4,150	19	\$585,371.97	7.68	65.19
HUMATROPE INJ 6MG	109	332	3,095	19	\$129,925.64	5.74	65.22
NORDITROPIN INJ 5/1.5ML	105	617	3,139	15	\$133,893.14	7	65.10
GENOTROPIN INJ 13.8MG	94	276	2,672	11	\$212,142.28	8.55	64.05
NUTROPIN INJ 10MG	86	453	2,480	10	\$272,219.45	8.6	62.87
NORDITROPIN INJ 30/3ML	73	372	1,951	18	\$243,919.95	4.06	65.57
HUMATROPE INJ 12MG	68	165	1,919	10	\$121,105.13	6.8	65.04
HUMATROPE INJ 24MG	49	142	1,445	7	\$222,772.21	7	65.37
NUTROPIN INJ 5MG	46	230	1,272	4	\$53,656.32	11.5	67.35
GENOTROPIN INJ 1MG	36	1,008	1,008	5	\$65,409.46	7.2	64.89
HUMATROPE INJ 5MG	43	533	1278	7	\$173,429.11	6	65.07
GENOTROPIN INJ 5.8MG	23	88	681	3	\$28,544.06	7.67	64.87
GENOTROPIN INJ 2MG	18	504	506	2	\$64,522.36	9	63.76
SAIZEN INJ 8.8MG	13	62	392	2	\$32,482.37	6.5	59.53
GENOTROPIN INJ 0.6MG	13	364	364	3	\$14,079.29	4.33	64.47
GENOTROPIN INJ 1.2MG	12	336	336	3	\$26,057.14	4	64.63
GENOTROPIN INJ 0.8MG	12	336	336	3	\$17,194.53	4	63.89
GENOTROPIN INJ 0.2MG	10	280	280	2	\$3,613.48	5	64.53
GENOTROPIN INJ 0.4MG	7	196	196	2	\$5,212.83	3.5	66.49
SEROSTIM INJ 6MG	7	196	200	1	\$55,871.70	7	47.51
OMNITROPE INJ 5/1.5ML	1	4.5	25	1	\$794.17	1	52.94
Totals	1,634	11,013	47,157	213*	\$4,075,790.90	7.67	63.48**

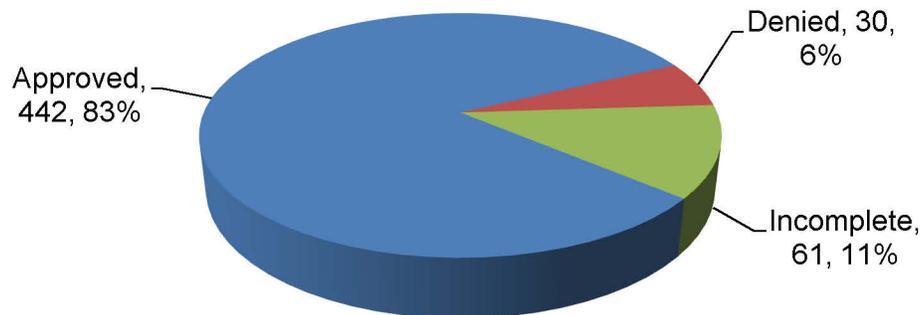
*Unduplicated Members **Average cost/mg

Demographics of Members Utilizing Growth Hormone during Fiscal Year 2010



Prior Authorization of Growth Hormones during Fiscal Year 2010

A total of 533 petitions were submitted for growth hormone in FY10.



Market News

- March 2010 – Novo Nordisk, Inc., introduced Norditropin Flexpro prefilled pen device. The EAC (estimated acquisition cost) of this product is \$69.90/mg, compared with \$65.20 for the previous device.

Trends across the United States

Random review of other states' Medicaid program elicited the following findings that differed from the SoonerCare Criteria:

Alabama – Does not cover Idiopathic Short Stature (ISS) or Small for Gestational Age (SGA); height requirement <5%; clonidine not acceptable as provocative test; growth hormone-releasing hormone (GHRH) is acceptable. Adults are required to take insulin tolerance test (ITT), unless contraindicated. Normal thyroid function required for all indications

Alaska – ISS not covered; height velocity <10th percentile of normal for age/sex and tracked over one year. Prader-Willi confirmed by genetic testing

Arkansas – ISS not covered, septo-optic dysplasia is acceptable diagnosis; no height or velocity requirements. Panhypopituitarism proven by two pituitary hormone replacements (thyroid, hydrocortisone, estrogen, or testosterone)

California – ISS not covered; two provocative tests below 7 ng/ml. If stim results 7-12 ng/ml, have documented delayed growth rate for age 4.5 cm/yr or less for male 0-12 years and female 0-10 years; <8-10 cm/yr if pubertal changes.

Delaware – ISS not covered. Growth velocity <7 cm/yr for 3 years and under, <5 cm/yr for 4 years and up. Height <5th percentile. Covered until final height or epiphyseal closure.

Georgia – predicted height <3rd percentile based on bone age. Continue if growth velocity doubled or increased by 3 cm/yr in the first year,

Idaho – ISS, SGA, SHOX not covered; levodopa and arginine <7 ng/ml, ITT <7 ng/ml “an equivalent diagnostic test” for documentation of deficiency; Height velocity <10th percentile for age/sex tracked over at least one year; increase in height velocity of at least 2 cm/yr over one year

Iowa – ISS not covered

Kansas – ISS, SGA not covered; normal thyroid functions before testing; height velocity <25th percentile for age for all indications, height <5th percentile for Turner, Noonan, or Prader-Willi also acceptable. Discontinue if growth velocity <2 cm, noncompliant, or failure to show changes in body composition, lipid profile, or growth rate in PWS

Maryland – ISS not covered. Adults with childhood onset GHD or additional pituitary hormone deficits require 1 stim test, all others (adults and children) require 2. ITT required unless contraindicated. Arginine, glucagon, GHRH, L-dopa and combinations of them acceptable; not clonidine. Adults require bone density testing. For chronic renal insufficiency, only IGF-1 required. Continue until 25th percentile achieved, Height velocity >2.5 cm/yr over pretreatment rate

Minnesota – ISS, SGA not covered, “decreasing velocity relative to physical and chronological age”, height <5th percentile for age or absolute height -2.25 SD, ISS not covered, but may be reconsidered if the patient undergoes a 6 month trial of GH supplied by manufacturer and shows restoration of normal growth and development. Continue if growth velocity increases by 2 cm/yr in first year and >2.5 cm/yr. Covered height 5’6” for males, 5’1” for females.

Montana – ISS, SGA not covered

Nebraska – ISS, SGA not covered; growth velocity <4 cm/yr, thyroid and cortical normal or replaced, bone age >2 SD delayed

Nevada – height <5th percentile, bone age >2 years delayed.

New Hampshire – height velocity over 1 year >1 SD below the mean for chronological age; if >2 years old, -0.5SD height loss over a year.

North Carolina – ISS, SGA not covered; bone age -2SD below mean for age/sex; accept two provocative test or IGF-1 or IGFBP-3 level. Cont if height velocity >4.5 cm/yr (prepubertal) or >2,5 cm/yr (postpubertal)

Oregon – Adults not covered. No lab or height requirements. Epiphyses open. Continue tx if height velocity >2.5 cm/yr.

Pennsylvania – Growth velocity -2-3SD below age related mean, bone age -2SD delay; SGA if no catch up by 3 years of age with height -2SD below the mean; Cont if height velocity >4.5 cm/yr (prepubertal) or >2,5 cm/yr (postpubertal)

Vermont – ISS not covered. Propranolol included as provocative test. All available provocative tests acceptable for children and adults – children x2, adults x1

West Virginia – ISS, SGA not covered. Neurosecretory growth retardation included with mixed or normal provocative test and IGF-1 levels <50th percentile for chronological age.

Wyoming – ISS, short stature of chronic renal insufficiency not covered

Discussion of Growth Hormone Criteria

The following is the current growth hormone coverage criteria. The black type is the current criteria, the red sections are the recommended changes or additions to the current criteria received after consultation with an adult and pediatric endocrinologist. \$ indicates increased expenditures may occur if changes are implemented.

COVERED INDICATIONS

- Classic hGH Deficiency
- Short Stature (including Prader-Willi Syndrome)
- Short Stature associated with chronic renal insufficiency
- Small for Gestational Age (SGA)
- Turner's Syndrome or 45 X, 46 XY mosaicism in males
- Hypoglycemia associated with hGH insufficiency
- AIDS wasting (Serostim only)
- SHOX (short stature homeobox-containing gene) deficiency

Covered indications

Childhood indications (prior to epiphyseal closure\$)

Classic hGH deficiency as determined by childhood hGH stimulation tests outlined below

- 1) History of pituitary or hypothalamic injury due to tumor, trauma, surgery, irradiation, hemorrhage or infarction or a congenital anomaly and
 - a. ≥ 3 pituitary hormones deficient and IGF-1 ≤ 2.5 percentile
 - b. 0,1,or 2 hormones deficient and IGF-1 $< 50^{\text{th}}$ percentile failure of a growth hormone stimulation test as outlined below
- 2) Children with height < 2.25 SD for mean for age and MRI evidence for pituitary stalk agenesis, empty sella, pituitary stalk agenesis or ectopic posterior pituitary "bright spot"
- 3) Short stature from Prader-Willi Syndrome
- 4) Short stature associated with chronic renal insufficiency (pre-transplantation)
- 5) History of intrauterine growth restriction who have not reached a normal height (≥ 2.25 SD below mean for age/gender) by age 2 years
- 6) Children with idiopathic short stature who are ≥ 2.25 SD below mean for height and are unlikely to catch up in height.
- 7) Turner's syndrome or 45X, 46XY mosaicism
- 8) Hypoglycemia with evidence for hGH deficiency
- 9) SHOX deficiency (with genetic evidence for short stature homeobox-containing gene deficiency)
- 10) AIDS wasting syndrome (12 weeks therapy only.)
- 11) Other evidence for hGH deficiency submitted for panel review and decision

Transitional indications for clients on childhood hGH therapy (after reaching target height or epiphyseal closure\$.)

Transitional patients must be phased down to adult hGH doses over a year.

- 1) Classic childhood hGH deficiency who fail an adult hGH stimulation tests after a month or more withholding hGH therapy.
- 2) Persons who have initiated growth hormone therapy in childhood because of pituitary damage, agenesis or anomaly.

Adult indications

- 1) Persons with other childhood indications for hGH therapy who fail an adult hGH stimulation test.
- 2) Persons who have initiated growth hormone therapy in childhood because of pituitary damage, agenesis or anomaly.

- 3) History of pituitary or hypothalamic injury due to tumor, trauma, surgery, irradiation, hemorrhage or infarction
 - a. ≥ 3 pituitary hormones deficient and IGF-1 ≤ 2.5 percentile
 - b. 0,1, or 2 hormones deficient and IGF-1 $< 50^{\text{th}}$ percentile failure of an adult growth hormone stimulation test as outlined below
- 4) AIDS wasting syndrome (12 weeks therapy only.)

FOR INITIATION OF hGH THERAPY

A member must be evaluated by an Endocrinologist, Pediatric Nephrologist, or an Infectious Disease Specialist before consideration will be given for coverage of Growth Hormone therapy.

The following information must be provided

- PROJECTED HEIGHT: final adult height without hGH therapy with hGH therapy
- TARGET HEIGHT: [Calculation – (Total of father’s and mother’s height in cm, divided by 2) plus 6.5cm for boys and minus 6.5cm for girls]
- COVERED HEIGHT - height to which coverage of hGH therapy will be provided [152.4cm for girls, 165.1cm for boys].

For continuation of hGH therapy

Client must be evaluated by an endocrinologist at least once a year, with monitoring for adverse effects and compliance and documentation of indications for continuation of therapy.

Contraindications to therapy

Presence of active malignancy or diabetes out of control or intracranial hypertension

Dose of hGH (doses must be individualized and titrated)

- 1) Children – 25 to 100 mcg/kg/day (in 3 to 7 doses per week) according to current pediatric guidelines.
- 2) Adults - 0.1 to 0.5 mg per day – lower doses in older clients. Doses should be evaluated and titrated at 1 to 2 month intervals targeting an IGF-1 level at or below the mean reference value for age and gender.

DIAGNOSIS OF CLASSIC hGH DEFICIENCY

A. Criteria for Initiation of Therapy

Pediatric Members

- Height below the third percentile on growth chart
- Subnormal growth velocity: current height more than two standard deviations below the mean and/or growth velocity of less than 5cm/yr
- Evidence of delayed bone age and open epiphysis.
- No contributing medical condition, i.e. chronic diseases (cystic fibrosis, chronic renal failure), malnutrition, psychosocial deprivation, etc
- Subnormal response of 10ng/ml or less on two provocative growth hormone stimulation tests
Note: this criterion may be waived when a clinical diagnosis of panhypopituitarism, based on diagnostic radiographic and clinical findings (see below*) is made. In addition, children with a profoundly low growth velocity who are at high risk for GHD due to CNS radiation or other organic causes (termed “neurosecretory dysfunction”) may demonstrate “normal” responses to provocative tests, often for several years, yet often benefit from GH treatment. \$

Panhypopituitarism is defined as a condition in which the secretion of anterior pituitary hormones, including growth hormone, is inadequate or absent. This condition can be acquired as a result of surgery or irradiation of the hypothalamus or pituitary, head trauma or central nervous system infections, or may be congenital. Furthermore,

radiological studies such as a MRI, may reveal pituitary stalk agenesis, empty sella, an underdeveloped anterior pituitary, or midbrain abnormalities that may indicate a diagnosis of GHD or multiple pituitary hormone deficiencies. These patients with organic GHD, or GHD secondary to major brain malformations tend to be the most profoundly deficient of all patients with GHD, and tend to have a very robust response to GH therapy. Many of these patients with multiple pituitary hormone deficiencies have severe hypoglycemia and seizures, and when treated with growth hormone, often have a dramatic response with rapid resolution of hypoglycemia. For these patients, a formal GH stimulation test usually is unnecessary in making the definitive diagnosis.

Adult Members

- Childhood or Adult onset of hGH deficiency
 - Age < 60 years
 - No evidence of active malignancy
 - Other hormone deficiencies have been ruled out or stabilized with adequate replacement
 - Subnormal response of 5ng/ml or less to insulin hypoglycemia growth hormone stimulation test
- Note, it is appropriate that the criteria for GHD in adults are much tighter, and stipulate the use of insulin. Most advocate that the max response should be less than 3 ng/ml, but some use 5....Bidlingmaier M, Strasburger CJ. What endocrinologists should know about growth hormone Measurements. *Endocrinol Metab Clin North Am.* Mar 2007;36(1):101-8.

B. Accepted Pharmacologic GH Stimulation Tests for children

- Propranolol with exercise
- Levodopa
- Insulin hypoglycemia test
- Arginine HCl infusion
- Clonidine

Accepted childhood pharmacological hGH stimulation tests:

- Insulin tolerance test: 0.1 units per Kg insulin IV, with hGH samples at baseline and every 30 minutes to 120 minutes. hGH response of <10 ng/ml is evidence for hGH deficiency.\$
- OTHER (PENDING)

Accepted adult pharmacological hGH stimulation tests:

- Insulin tolerance test: 0.1 units per Kg insulin IV, with hGH samples at baseline and every 30 minutes to 120 minutes. hGH response of <5 ng/ml is evidence for hGH deficiency.
- Glucagon stimulation test: 1 mg glucagon IM with hGH samples at baseline and every 30 minutes to 180 minutes. hGH response of <3 ng/ml is evidence for hGH deficiency.

C. Accepted GH Screening Test

- Insulin-like growth factor 1 (IGF-1)
- Insulin-like growth factor – binding protein 3 (IGFBP-3)

D. Continuation of Therapy

Pediatric Members

- Members should be evaluated every 6 months to determine increase in growth velocity and monitor for adverse effects and compliance
- Client must be evaluated by an endocrinologist at least once a year, with monitoring for adverse effects and compliance and documentation of indications for continuation of therapy.
- Members should be evaluated every 4 months to determine growth velocity and monitor for adverse effects and compliance.

Adult Members

- Members should be evaluated every 6 months to monitor for adverse effects and compliance

E. Discontinuation of Therapy

Member therapy may be discontinued when one of the following criteria is met:

Pediatric Members

- Growth velocity less than 2.5cm/yr **unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism), and indicated by fused epiphyses by bone age determination. \$**
- Covered height has been reached
- Inadequate compliance
- Significant adverse effects

Adult Members

- Inadequate compliance
- Significant adverse effects

DIAGNOSIS OF SHORT STATURE (INCLUDING PRADER-WILLI SYNDROME)

A. Initiation of Therapy

The member should meet three of the criteria listed:

- Delayed bone age and open epiphysis.
- Subnormal growth velocity: current height more than two standard deviations below the mean and/or growth velocity of less than 5cm/yr
This needs to be modified, since newborns with congenital GHD will USUALLY have GV >>> 5 cm/year within the first few years of life, but still require treatment. \$
- Subnormal response of 10ng/ml or less on two provocative growth hormone stimulation tests
“GH stimulation test responses are extremely poor in discriminating between normal and GHD children. This observation has led to a recommendation of the Stanford group (Wilson, et al. Journal of Pediatrics Oct 2003, 415-421) to declare GH stimulation tests as optional for prescribing therapy, especially in the context of growth failure, additional pituitary hormone deficiencies, and/or a history of surgery or irradiation in the region of the hypothalamus.”
- Projected height below Target height and Covered height

B. Continuation of Therapy

Members should be evaluated every six months to determine the increase in growth velocity. **(See above)**

C. Discontinuation of Therapy

Member therapy may be discontinued when one of the following criteria is met:

- Target height or Covered height has been reached
- Bone age of 15 or epiphyseal fusion for girls
- Bone age of 16 or epiphyseal fusion for boys
- Slow growth rate (< 5cm in the previous year) **unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism) \$**
- Inadequate compliance
- Significant adverse effects

DIAGNOSIS OF SHORT STATURE ASSOCIATED WITH RENAL INSUFFICIENCY

A. Initiation of Therapy

The member should meet the following criteria:

- Documented chronic renal insufficiency with an estimated creatinine clearance less than 50ml/min

- Subnormal growth velocity: current height more than two standard deviations below the mean and/or growth velocity of less than 5cm/yr
- Projected height below Target height and Covered Height

B. Continuation of Therapy

Members should be evaluated every six months to determine the increase in growth velocity. (See above)

C. Discontinuation of Therapy

Member therapy may be discontinued when one of the following criteria is met:

- Target height or Covered height has been reached
- Bone age of 15 or epiphyseal fusion for girls
- Bone age of 16 or epiphyseal fusion for boys
- Slow growth rate (< 5cm in the previous year) unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism) \$
- Inadequate compliance
- Significant adverse effects
- Transplantation

DIAGNOSIS OF SMALL FOR GESTATIONAL AGE (SGA)

A. Initiation of Therapy

The member should meet the following criteria:

- Diagnosis of Small for Gestational Age
- Member over 2 years of age
- Subnormal growth velocity: current height more than two standard deviations below the mean and/or growth velocity of less than 5cm/yr
Subnormal growth velocity: current height more than two standard deviations below the mean and/or growth velocity subnormal for age

B. Continuation of Therapy

Members should be evaluated every six months to determine the increase in growth velocity. (See above)

C. Discontinuation of Therapy

Member therapy may be discontinued when one of the following criteria is met:

- Target height or Covered height has been reached
- Bone age of 15 or epiphyseal fusion for girls
- Bone age of 16 or epiphyseal fusion for boys
- Slow growth rate (< 5cm in the previous year) unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism) \$
- Inadequate compliance
- Significant adverse effects

DIAGNOSIS OF TURNER'S SYNDROME OR 45X, 46XY MOSAICISM

A. Initiation of Therapy

The member should meet the following criteria:

- Chromosome analysis diagnosing either Turner's syndrome in female members or 45X, 46XY mosaicism in males
- Height below the third percentile on growth charts

B. Continuation of Therapy

Members should be evaluated every six months to determine the increase in growth velocity. (See above)

C. Discontinuation of Therapy

Member therapy may be discontinued when one of the following criteria is met:

- Target height or Covered height has been reached
- Bone age of 15 or epiphyseal fusion for girls
- Bone age of 16 or epiphyseal fusion for boys
- Slow growth rate (< 5cm in the previous year) **unless associated with another growth-limiting and treatable medical condition (i.e. hypothyroidism) §**
- Inadequate compliance
- Significant adverse effects

DIAGNOSIS OF HYPOGLYCEMIA ASSOCIATED WITH hGH INSUFFICIENCY

Hypoglycemia is a symptom that is present in some members as a result of low growth hormone levels. Because of the severity of problems related to this form of hypoglycemia (permanent neurologic morbidity, septo-optic dysplasia), it will be given separate consideration from short stature issues. Coverage will not be provided for growth hormone used to treat members with normal hGH levels who happen to be hypoglycemic.

A. Initiation of Therapy

Due to the severity of this condition, initial doses may be administered without receiving a medication coverage authorization first. However, appropriate information must be provided within 30 days for coverage consideration. When all member information has been received, a retroactive authorization will be given for any emergency doses dispensed.

B. Continuation and Discontinuation of Therapy

Members should be evaluated every six months to monitor for efficacy and side effects. Therapy should not be discontinued if there is a probability of the hypoglycemic condition reoccurring once hGH replacement therapy is withdrawn.

DIAGNOSIS OF AIDS-RELATED WASTING SYNDROME (SEROSTIM ONLY)

A. Initiation of Therapy

Members must have documentation showing that they fulfill all of the following criteria. Members meeting the criteria will be approved for an initial 4 week course of therapy.

- Unintentional weight loss of more than 10% if baseline pre-morbid weight was <120% of Ideal Body Weight OR unintentional weight loss of more than 20% if baseline pre-morbid weight was > 120% of Ideal Body Weight
- Member is receiving optimal antiretroviral therapy
- Member does not have a reversible cause of weight loss (e.g. infection, GI bleed or obstruction, or malnutrition)
- Member is receiving aggressive nutritional intake or supplementation
- Member does not have an active malignancy (except localized Kaposi's Sarcoma)
- Member has had a poor response to therapy with megestrol acetate and/or dronabinol
- Male members have had serum testosterone levels evaluated and treated as needed

B. Continuation of Therapy

- At four weeks, the member will be evaluated for response to therapy (weight gain), side effects, and compliance. If member response is favorable, another 4 weeks of therapy will be authorized.

- Subsequent follow up evaluations will be required every 4 weeks to assess response, side effects, and compliance. The member may receive another 4 weeks of therapy for a maximum of 12 weeks of continuous therapy.

C. Discontinuation of Therapy

Therapy may be discontinued if the member meets any of the following criteria:

- Completion of the FDA approved 12 weeks of therapy
- Treatment failure as measured by EITHER no weight gain despite 8 weeks of therapy OR continued/resumed weight loss at any time following 8 weeks of therapy when other potential causes have been resolved or ruled out.
- Member non compliance
- Adverse effects that are refractory to dose reduction
- New or progressive Kaposi's Sarcoma
- Member weight exceeds 110% of pre-morbid weight

DIAGNOSIS OF SHOX (short stature homeobox-containing gene) DEFICIENCY

The member should meet the following criteria:

- Chromosomal analysis diagnosing SHOX gene anomaly
- Height below the third percentile on growth chart
- Open epiphyses
- Normal endocrine screen
- No evidence of GH deficiency or insensitivity, tumor activity, diabetes mellitus, history of impaired glucose tolerance, or other serious illness known to interfere with growth

IGF-1 Analog Products

Increlex™ and Iplex™ (mecasermin)

A. Initiation of therapy

- Therapy initiated by an endocrinologist
- Diagnosis of Primary IGF-1 Deficiency with all of the following:
 - Height >3 SD below the mean
 - Basal IGF-1 >3 SD below the mean
 - Normal or elevated GH
- Documentation of mutation in GH receptor (GHR) or mutation in post-GHR signaling pathway or IGF-1 gene defects (Laron Syndrome)
- Not approved for use in secondary IGF-1 deficiencies related to GH deficiency, malnutrition, hypothyroidism, or chronic steroid therapy.

B. Discontinue therapy

Therapy may be discontinued when one of the following criteria is met:

- Epiphyses closed
- Covered height (165.1 cm. in males, 152.4 cm in females) is reached
- Sensitivity to mecasermin
- Member is noncompliant

Questions for discussion by the Board regarding the current criteria:

Diagnosis

- 1) For the diagnosis of panhypopituitarism and growth hormone deficiency, should growth hormone continue to be covered into adulthood? \$
- 2) Should growth hormone continue to be covered for idiopathic short stature as it currently is? \$ If not, then what about short stature of chronic renal insufficiency, Prader-Willi, Turner's syndrome, and Noonan's syndrome?
- 3) At what age should GH therapy for short stature be initiated? \$
- 4) At what age should GH therapy for growth hormone deficiency be initiated? \$
- 5) Should the criteria be modified in the case of panhypopituitarism so that patients with multiple pituitary deficiencies, radiological evidence of absence of pituitary stalk or other pituitary abnormality, hx of irradiation, or surgery do not require stim testing?
- 6) Should the diagnosis of neurosecretory growth hormone deficiency be covered?

Continuation

- 1) Should continuation criteria include improvement parameters, e.g. 2 cm/yr improvement in growth velocity? Currently, criteria do not define required increase in growth velocity for continuation. Should a minimum acceptable increase in growth velocity be defined in the criteria for continuation of GH therapy?

Discontinuing

- 1) Should children with panhypopituitarism or GHD be allowed to stay on GH until their epiphyses seal (\$) or until they reach covered height (165.1 cm (65") for boys, 152.4 cm (60") for girls)?
- 2) Should covered height be increased to 170.2 cm (67") for boys? \$
- 3) Should growth hormone for short stature of chronic renal insufficiency continue to be covered after kidney transplant? Currently, GH therapy is allowed to continue for these patients, even after the kidney transplant.

Recommendation

Since the FDA approved Norditropin for short stature of Noonan syndrome, the College also recommends adding Noonan syndrome as a covered indication. Criteria for this diagnosis would be the same as the other genetic disorders (Turner's syndrome, 45X, 46XY mosaicism).



Appendix D

Fiscal Year 2010 Annual Review of Erythropoietin Stimulating Agents (ESAs)

Oklahoma Health Care Authority
October 2010

Current Prior Authorization Criteria for ESAs

1. FDA approved indication for specific products.
 - a. Treatment of Anemia of Chronic Renal Failure Patients
 - b. Treatment of Anemia in Zidovudine-treated HIV-infected Patients
 - c. Treatment of Anemia in Cancer Patients on Chemotherapy
 - i. Myelosuppressive Chemotherapy-Induced Anemia (Hb 8-10 g/dL) Non-Curative
 - d. Reduction of Allogeneic Blood Transfusion in Surgery Patients
2. Most recent Hb levels (and date obtained) should be included on petition. Each approval will be for 8 weeks in duration. Authorization can be granted for up to 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen. Authorization for surgery patients will be for a maximum of 4 weeks.
3. **Continuation Criteria:**
 - a. Continue dose if Hb is ≤ 12.0 g/dL.
 - b. If Hb is increasing and approaching 12 g/dL then reduce dose by at least 25%.
 - c. If more than 1 g/dL increase (but Hb not greater than upper limits listed below) has occurred in a 2 week period reduce dose by 25 to 50 %.
4. **Discontinuation Criteria:**
 - a. ESRD – Discontinue treatment if **Hb is at or above 13.0 g/dL**.
 - b. All others – Discontinue treatment if **Hb is at or above 12 g/dL**.
 - c. If a minimum increase of 1 g/dL has not been achieved after initial 8 weeks of therapy.
5. **Reinitiation Criteria:**
 - a. If Hb decreases to ≤ 10 g/dL then therapy may be reinitiated at 25 to 50% of the prior dose.

Trends in Utilization of ESAs

Fiscal Year	Members*	Claims	Cost	Cost/ Claim	Units /Claim[†]
2008	722	6,087	\$2,406,084.46	\$395.28	299.5
2009	597	7,835	\$3,395,815.45	\$433.42	205.3
2010	477	9,036	\$2,262,697.86	\$250.41	152.8
% Change[†]	-20.1%	15.3%	-33.4%	-42.2%	-25.6%
Change[†]	-120	1,201	-\$1,133,117.59	-\$183.01	-52.5

*Some members may be duplicated between pharmacy and medical claims.

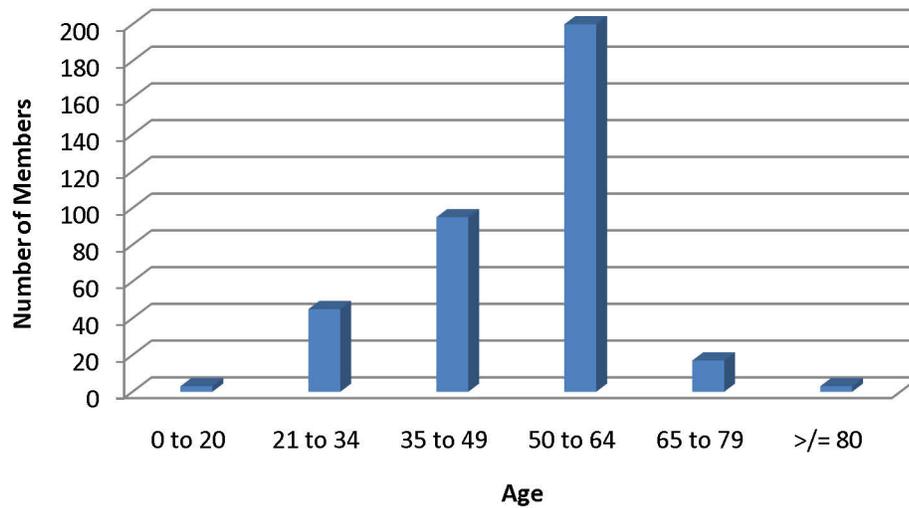
[†]Change from FY09 to FY10.

[‡]For medical billing only, does not include pharmacy claims.

Diagnoses for ESA Members during FY10

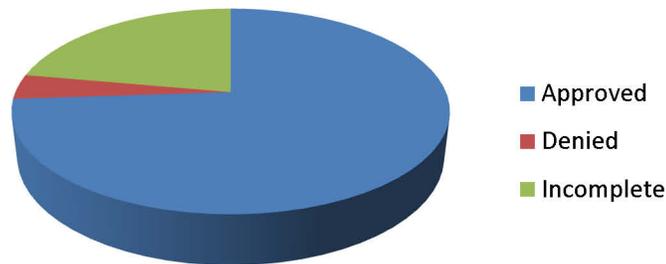
The majority of the claims for FY10 were for End Stage Renal Disease or a similar diagnosis (96.7%) followed by a cancer or chemotherapy related diagnosis (2.6%).

Age for Members Utilizing ESAs during FY10



Prior Authorizations for FY 2010

The total number of petitions for this category was 1,954. A total of 1,445 were approved, 76 were denied, and 433 were incomplete.



Conclusions and Recommendations

Usage of these products appears to have continued to decline over the review period, based on both the available safety information and the use of the prior authorization. The increase in the number of claims appears to be related to a change in billing methods on the part of the providers who are billing more frequently.

The College of Pharmacy recommends continuation of the current ESA Prior Authorization criteria with the following change: increase the length of approval from eight weeks to 16 weeks per petition.



Appendix E

ANNUAL REVIEW OF NARCOTIC ANALGESICS AND
30 DAY NOTICE TO PRIOR AUTHORIZE BUTRANS™,
PRIMLEV™, XOLOX®, EXALGO™ ER, RYBIX™ ODT,
AND SUBOXONE®/SUBUTEX®

OKLAHOMA HEALTH CARE AUTHORITY

OCTOBER 2010

CURRENT PRIOR AUTHORIZATION CRITERIA

Narcotic Analgesics			
<u>Tier-1 products</u> are covered with no prior authorization necessary.			
<u>Tier-2 authorization requires:</u>			
<ul style="list-style-type: none"> ▪ documented 30 day trial/titration period with at least two Tier-1 medications within the last 90 days, or ▪ clinically appropriate pain therapy requiring time-released medication 			
<u>Tier-3 authorization requires:</u>			
<ul style="list-style-type: none"> ▪ documented 30 day trial with at least two Tier-2 medications within the last 90 days, or ▪ documented allergy or contraindication to all Tier-2 medications 			
<ul style="list-style-type: none"> ▪ Members with an oncology-related diagnosis are exempt from the prior authorization process, although quantity and dosage limits still apply. Actiq®, Fentora®, and Onsolis® are approved only for oncology-related diagnoses. 			
<ul style="list-style-type: none"> ▪ Only one long-acting and one short-acting agent can be used concurrently 			
Tier-1	Tier-2	Tier-3	Oncology Only
All immediate release narcotics not listed in a higher tier	Long Acting		
	fentanyl patch (Duragesic®)	oxymorphone (Opana® ER)	
	morphine ER	morphine sulfate (Kadian®)	
		morphine sulfate (Avinza®)	
		oxycodone (OxyContin®)	
		tramadol ER (Ultram ER®, Ryzolt®)	
		morphine and naltrexone (Embeda™)	
	Short Acting		
	Hydrocodone/APAP (Xodol®, Zamicet™)		fentanyl (Actiq®, Onsolis™, Fentora®)
	oxymorphone (Opana®)		
Tapentadol (Nucynta™)			

OTHER PRIOR AUTHORIZED ANALGESICS

Darvocet A500 (propoxyphene napsylate 100mg / acetaminophen 500mg)

Balacet 325 (propoxyphene napsylate 100mg / acetaminophen 325mg)

- Approved for members with documented need to restrict acetaminophen use or documented renal insufficiency or hepatic impairment.
- A quantity limit of 180/30 on each of the products also applies.

Hydrocodone/APAP

- Quantity limit for a maximum of 3,250mg of APAP per day.
- Annual claim limit of 12 per 365 days.
- Ingredient Duplication ProDUR edit for multiple claims from different physicians.

UTILIZATION FOR FISCAL YEAR 2010

TRENDS IN UTILIZATION

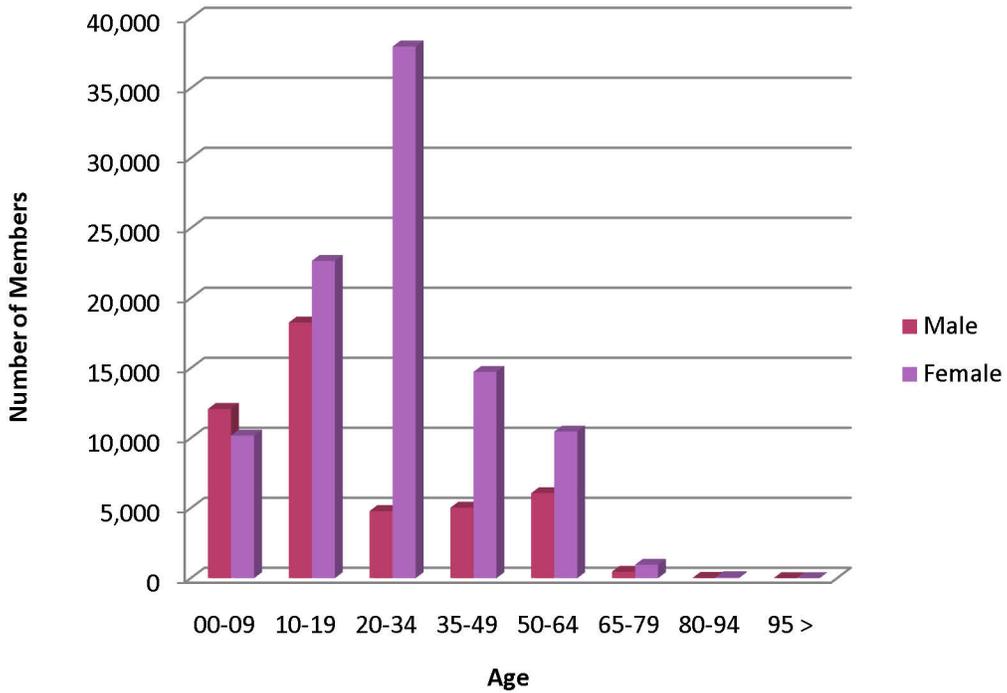
Fiscal Year	Total Members*	Total Claims	Total Cost	Cost/Claim	Cost/Day	Total Units	Total Days
2009							
	131,437	472,661	\$16,844,634.14	\$35.64	\$2.54	30,537,055	6,634,981
2010							
	144,256	515,229	\$17,243,745.82	\$33.47	\$2.29	33,668,641	7,544,467
% Change	9.8%	9.0%	2.4%	-6.1%	-9.8%	10.3%	13.7%
Change	12,819	42,568	\$399,111.68	-\$2.17	-\$0.25	3,131,586	909,486

UTILIZATION DETAILS OF NARCOTIC ANALGESICS BY CLASS

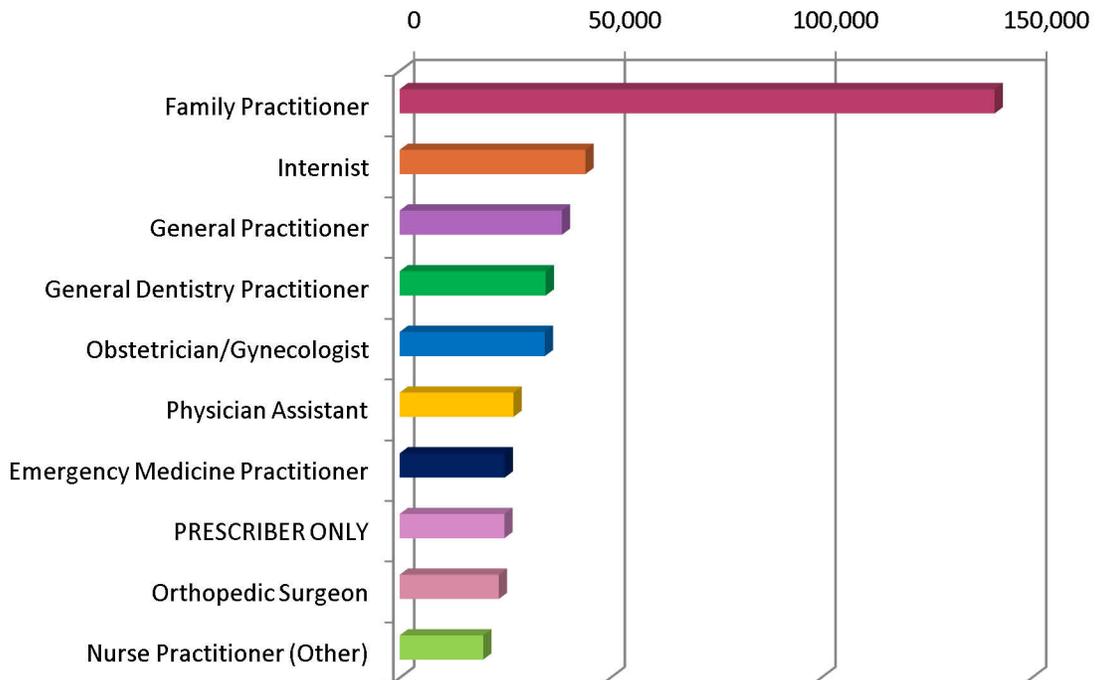
Class	Total Claims	Total Members	Total Cost	Claims/Member	Cost/Day
Hydrocodone Combinations	292,342	82,481	\$3,969,405	3.11	\$0.98
Opioid Agonists	100,449	26,384	\$10,467,061	3.81	\$4.76
Opioid Combinations	45,945	25,435	\$1,074,726	1.81	\$1.96
Codeine Combinations	42,228	32,337	\$360,633	1.31	\$1.34
Propoxyphene Combinations	27,293	15,256	\$259,383	1.79	\$0.78
Opioid Partial Agonist	4,295	999	\$1,036,986	4.30	\$10.66
Tramadol Combinations	2,161	1,201	\$52,756	1.80	\$1.75
Dihydrocodeine Combinations	429	264	\$18,584	1.63	\$3.80
Pentazocine Combinations	87	41	\$4,212	2.12	\$3.02
	515,229	144,256*	\$17,243,746	3.57	\$2.29

*Unduplicated Members

MEMBER DEMOGRAPHICS

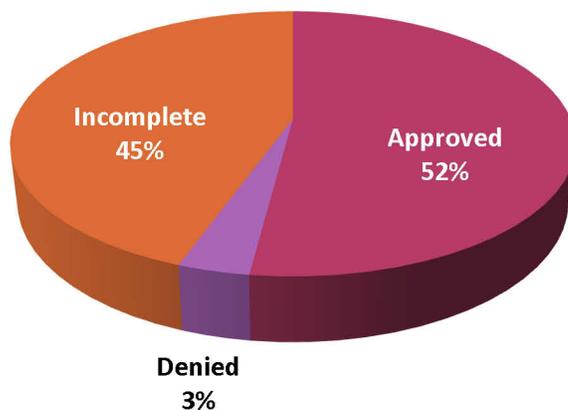


TOP PRESCRIBERS OF NARCOTIC ANALGESICS BY CLAIMS



PRIOR AUTHORIZATION REQUESTS

Most prior authorization requests for this category are handled through the DUR Plus point-of-sale prior authorization system. There were a total of 4,108 manual petitions submitted for Narcotic Analgesics during Fiscal Year 2010. The following chart shows the status of the submitted petitions.



MARKET NEWS AND UPDATES

BUTRANS™ (BUPRENORPHINE) TRANSDERMAL SYSTEM

Butrans™ is indicated for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. The patch is worn continuously for 7 days. Butrans™ transdermal system comes in 5mcg/hour, 10mcg/hour, and 20mcg/hour. The maximum dose is 20mcg/hour.

EXALGO™ (HYDROMORPHONE HCL) EXTENDED-RELEASE

Exalgo™ is an opioid agonist indicated for once daily administration for the management of moderate to severe pain in opioid tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time. Exalgo™ tablets are available in 8mg, 12mg, and 16mg dosage strengths.

PRIMLEV™ (OXYCODONE HCL/ACETAMINOPHEN)

Primlev™ is an opioid analgesic combination medication used for relief of moderate to moderately severe pain. Primlev™ is an oblong shaped tablet that comes in three strengths: 5mg/300mg (yellow), 7.5mg/300mg (red), and 10mg/300mg (orange).

XOLOX® (OXYCODONE HCL/ACETAMINOPHEN)

Xolox® is an opioid analgesic combination medication used to relieve moderate to severe pain. Xolox® is available in 10mg/500mg tablet.

RYBIX™ ODT (TRAMADOL HCL)

Rybix™ ODT is indicated for the management of moderate to moderately severe pain in adults. It is a white orally disintegrating tablet with a mint flavor and is available only in 50mg.

SUBOXONE® (BUPRENORPHINE/ NALOXONE) AND SUBUTEX® (BUPRENORPHINE) REVIEW

According to package labeling, the use of these products in the treatment of opioid dependence is limited to physicians who meet certain qualifying requirements and have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe these products for the treatment of opioid dependence. These products are only FDA indicated for the treatment of opioid dependence. However, they are often used off-label for the treatment of pain. According to the Substance Abuse and Mental Health Services Administration (SAMHSA), there are 81 certified physicians in Oklahoma and 8 treatment programs. A review of the Suboxone claims indicated that 85% of the claims were written by prescribers who are on the SAMHSA listing, however only a handful of the claims were processed by the pharmacies using the correct DEA number therefore it is difficult to tell from claims data whether the products are being used according to the FDA labeling. Medical claims data for the Suboxone members was also reviewed and 71% of the members had a diagnosis that indicated an addiction.

	SAMHSA Certified	Percent	Not SAMHSA Certified	Percent
Suboxone Claims	2,410	85%	419	15%
Prescribers	45	40%	67	60%

Several states and insurance plans currently have criteria in place for the use of these medications. Some of the surrounding states' criteria are listed below.

Arkansas: Requires an ICD-9 for opioid dependence and also has quantity limits in place. Subutex is approved for induction only and no other opioids may be prescribed for members.

Kansas: Requires a copy of the SAMHSA waiver confirmation and diagnosis of opioid dependence.

Missouri: Clinical edit in place which requires an appropriate diagnosis before approval and physician with SAMHSA waiver.

Colorado: Requires a prior authorization and must be for opioid dependency. Physician must have a waiver and the maximum dose is 24 mg daily.

Texas: No prior authorization, but is a part of the opiate overutilization clinical edit.

CONCLUSION AND RECOMENDATIONS

SUBOXONE®/SUBUTEX® RECOMMENDATIONS

The College of Pharmacy recommends all prescriptions for Suboxone® (buprenorphine/naloxone) tablets and film or Subutex® (buprenorphine), and their generic equivalents if available, require prior authorization.

Criteria for coverage are as follows:

- Prescribed by a licensed physician who qualifies for a waiver under the Drug Addiction Treatment Act (DATA) and has notified the Center for Substance Abuse Treatment of the intention to treat addiction patients and has been assigned a DEA (X) number.
- Diagnosis of opiate abuse/dependence.
- Combination with benzodiazepines, hypnotics, and opioids (including tramadol) will be denied.
- Approval will be for 90 days to allow for concurrent medication monitoring.
- The following limitations will apply:
 - **Suboxone**® 2mg/0.5mg and 8mg/2mg tablets and film: A quantity limit of 90 per 30 days.
 - **Subutex**® 2mg tablets and 8mg tablets for induction only: a quantity limit of 15 tablets for up to a 5 day supply allowed (if the member is pregnant, product may be used for the duration of the pregnancy).

NEW TIER RECOMMENDATIONS

The College of Pharmacy recommends continuation of the Narcotic PBPA Category. In addition, the College of Pharmacy recommends placement of the following products in the current Tier structure:

Butrans™: to be placed in Tier 3 of the long-acting products Tier structure, with a quantity limit of 4 patches every 28 days.

Exalgo™: to be placed in Tier 3 of the long-acting products Tier structure, with a quantity limit of 1 tablet daily for the 8mg, 3 tablets daily for the 12mg, and 4 tablets daily for the 16mg.

Primlev™ and Xolox®: to be placed in Tier 3 of the short-acting products Tier structure, with a quantity limit based on 3,250 mg of acetaminophen daily and a clinical reason why member cannot use currently available similar generic products.

Rybix™ ODT: to be placed in Tier 3 of the short-acting products Tier structure, with a quantity limit of 4 tablets per day and a diagnosis indicating the member has a condition that prevents them from swallowing tablets.

Additionally, the College recommends moving the hydrocodone/APAP products, Xodol® and Zamicet™, from Tier 2 to Tier 3 with additional criteria requiring a clinical reason why the member cannot use currently available similar generic products. The College also recommends that any brand-only formulations of currently available generic narcotic products be placed in Tier 3 with similar criteria.

Narcotic Analgesics			
Tier-1	Tier-2	Tier-3	Oncology Only
All immediate release narcotics not listed in a higher tier	Long Acting		
		oxymorphone (Opana® ER)	
	fentanyl patch (Duragesic®)		
	morphine ER	morphine sulfate (Kadian®)	
		morphine sulfate (Avinza®)	
		oxycodone (OxyContin®)	
		tramadol ER (Ultram ER®, Ryzolt®)	
		morphine and naltrexone (Embeda™)	
		buprenorphine transdermal (Butrans™)	
		hydromorphone (Exalgo™)	
	Short Acting		
	Oxymorphone (Opana®)	tramadol ODT (Rybix™)	fentanyl (Actiq®, Onsolis™, Fentora®)
	Tapentadol (Nucynta™)	oxycodone/APAP (Primlev™, Xolox®)	
	hydrocodone/APAP (Xodol®, Zamicet™)		