



Prior Authorization Approval Criteria

Human growth hormone - children

- Generic name:** Human growth hormone, somatropin
- Brand names:** Tev-Tropin, Humatrope, Nutropin, Genotropin, Norditropin, Saizen, Geref, Omnitrope
- Medication class:** Growth hormone
- FDA-approved uses:** growth hormone deficiency (GHD), short stature associated with Turner syndrome (TS), growth failure due to chronic renal insufficiency (CRI), decreased body growth due to Prader-Willi syndrome (PW), born small for gestational age (SGA), Idiopathic short stature (ISS), Short-stature homeobox-containing gene (SHOX) deficiency, Noonan's syndrome.
- Available dosage forms:** Subcutaneous solution and powder for solution; strength and vial size vary by brand.
Tev-Tropin: One vial of 5mg somatropin with one 5ml vial of diluent
- Usual dose:** GHD: 0.3mg/kg/week divided into 6 or 7 doses
TS: 0.35mg/kg/week divided into daily doses
CRI: 0.35mg/kg/week divided into 6 or 7 doses
SGA: 0.48mg/kg/week divided into daily doses
PW: 0.24mg/kg/week divided into 6 or 7 doses
- Approximate monthly cost:** Tev-Tropin: (5 year old male, 50th weight, 18kg, GHD) \$1154/month (based on AWP 2010)
- Duration of therapy:** Until epiphyseal closure has been documented or patient no longer responds to treatment.
- Criteria** (*bullet points below are all inclusive unless otherwise noted*):
- The indicated diagnosis (including any applicable labs and /or tests) and medication usage must be supported by documentation from the patient's medical records.
 - If patient meets the criteria for growth hormone therapy, FCHP will only approve the preferred formulary product. Other products may be approved if the patient has tried and failed or was intolerant to the FCHP preferred product or if the patient is unable to use a traditional syringe and vial due to physical impairment (including visual impairment).
 - Prescribed by endocrinologist only or pediatric nephrologists (for chronic renal insufficiency)
 - Other reasons for short stature have been ruled out, such as hypothyroidism, chronic system disease, chronic illnesses, skeletal disorders, and medications.
 - Patient must have clinically documented **growth hormone deficiency (GHD)**
 - Must provide documentation of growth failure:
 - Height more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
 - OR**
 - Height velocity more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
 - Must provide documentation of growth hormone deficiency (GHD) confirmed by biochemical diagnosis by means of:

- Subnormal response to at least two provocative stimuli of GH release. Subnormal response is generally accepted to be a peak GH level of less than 10 ng/ml.

OR

- Subnormal response to at least one provocative stimuli of GH release (peak GH level of less than 10 ng/ml) and IGF-1 and IGF-BP-3 more than 2 standard deviations below the mean for age and gender, based on specific lab reference values.

OR

- Patients with clinically documented Multiple Pituitary Hormone Deficiency (MPHD, panhypopituitarism) must have documented deficiency in at least 3 pituitary hormones (In MPHD patients, GHD is nearly universal; GH provocative tests may not be indicated.)
- Documentation of bone age (estimated from a radiograph of left wrist and hand if over 1 year old or knee if under 1 year old) at least 1 standard deviation below the mean for chronological age and gender.
- Documentation that epiphyses are not closed

OR

- Patient must have clinically documented **Turner's Syndrome**
 - Patient must be female with a bone age of less than 14 years
 - Must provide documentation of growth failure:
 - Height more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
- OR**
- Height velocity more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
 - Documentation that epiphyses are not closed

OR

- Patient must have clinically documented **Chronic Renal Insufficiency**
 - Patient must be pre-transplant
 - Must provide documentation of growth failure:
 - Height more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
- OR**
- Height velocity more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
 - Documentation that epiphyses are not closed
 - Before starting therapy, existing metabolic derangements (such as acidosis, secondary hyperparathyroidism, under nutrition) should be corrected.

OR

- Patient must have clinically documented **Small for Gestational Age (SGA) / Intrauterine Growth Retardation**
 - Patient must be over the age of 2
 - Patient's birth weight or length must be more than 2 standard deviations below the mean (or below the 3rd percentile) for gestational age.
 - Must provide documentation of continued growth failure after age 2:
 - Height more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.

OR

- Height velocity more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
- Documentation that epiphyses are not closed

OR

- Patient must have clinically documented **Prader-Willi Syndrome**
 - Must provide documentation of growth failure:
 - Height more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
- OR**
- Height velocity more than 2 standard deviations below the mean (or below the 3rd percentile) for age and gender.
 - Must not be severely obese (must not be greater than 225% of ideal body weight)
 - Must be evaluated for upper airway obstruction or apnea; Growth hormone treatment should not proceed until the sleep disordered breathing is effectively treated
 - Documentation that epiphyses are not closed

Criteria for continuation of therapy in children:

- Epiphysis must not be closed (evidenced by x-ray)
- First year of therapy: height velocity must be double the pre-treatment rate or an increase of 3cm/yr or more
- Therapy past the first year: height velocity must be greater than 2.5cm/year.
- In addition to above:
 - For Turner Syndrome: bone age less than 14 years
 - For chronic renal insufficiency: patient is not post renal transplant.
 - For PW: GH treatment should be interrupted if patients develop signs of upper respiratory obstruction (including onset of or increased snoring) and/or new onset of sleep apnea.

Monitoring:

- Thyroid function tests about every 6 months
- Glucose tolerance/diabetes testing
- periodic monitoring for intracranial hypertension
- monitor for malignant transformation of skin lesion
- If patient has history of scoliosis, then monitor for progression of scoliosis
- For TS: scoliosis, ear disorders (including otitis media), cardiovascular disorders, thyroid test, intracranial hypertension
- For PW: Co-morbid conditions (such as scoliosis, hypogonadism, osteoporosis, adrenal insufficiency, obesity, apnea, diabetes) must be effectively managed

Contraindications:

- Sensitivity to product or diluent
- Active malignant disease. (If GHD is attributable to an intracranial tumor, absence of tumor growth or recurrence should be documented for 6 to 12 months before initiation of GH treatment.)
- Acute illness
- Closed epiphysis in children
- Benign intracranial hypertension (pseudotumor cerebri), proliferative or preproliferative diabetic retinopathy

Not approved if:

- Short stature/growth failure without growth hormone deficiency (except as indicated in criteria)
- Patients with Down Syndrome, Fanconi's Syndrome, or Bloom Syndrome (These conditions have high risk of malignant tumor or leukemia, so it is recommended that GH therapy not be used since the occurrence of a malignant condition may be linked to GH.)
- Patients with Idiopathic short stature (ISS) or SHOX Deficiency
- Patients with Familial short stature
- Patients with constitutional delays
- Patients with Noonan Syndrome
- Patients with GH insensitivity (Laron Syndrome)
- Diagnosis of growth hormone deficiency not confirmed by biochemical test.
- Growth hormone use for patients with non-specific symptomology such as lipidemia, depression and weight gain.
- Patients with acute catabolism (including preoperative and postoperative patients), critically ill patients and burn patients. (Unless otherwise FDA approved)
- Pregnancy: GH therapy should be discontinued if pregnancy is confirmed
- Use for Antiaging
- Performance enhancement for athletes
- Patient has any contraindications to the use of growth hormone.

Note:

- Provocative tests of growth hormone stimulation include arginine, clonidine, glucagon, insulin, and levodopa.
- Peak GH level must be adjusted if monoclonal-based assay or recombinant human GH reference preparations are used, based upon specific lab reference values.
- In neonate with hypoglycemia, but no metabolic disorder, a peak GH level less than 20 ng/ml is usually diagnostic of GHD.
- IGF-1 levels are low early in life. IGF-1 can be low due to other conditions such as psychosocial deprivation, malnutrition, diabetes, renal failure or hypothyroidism. IGF may be normally low in infants and young children. IGF-1 is less nutrition dependent than IGF.
- During puberty, normal growth is about 7-10 cm/year and after puberty about 1-3 cm/year.
- Normal height velocity ranges from 10cm/yr between ages 1 and 4 to 5cm/yr between ages 4 and 12.
- TS: TS patients usually do not have low GH levels. Obtain bone age before starting therapy. Note: Estrogen should not be started too early, as it may interfere with adult height (estrogen usually started age 12-15).
- ng/ml = mcg/L
- Dosing conversion: IU or mU to mg is 3:1
- Due to variations in normal growth hormone secretion, assays, and labs, the clinician should evaluate clinical, auxologic, radiologic, and biochemical factors.
- There is no evidence that one commercial product is more advantageous over another, except for differences in pen devices, dose increments/decrements, and whether refrigeration is required. (from *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Growth Hormone-Deficient Adults and Transition Patients – 2009 Update.*)

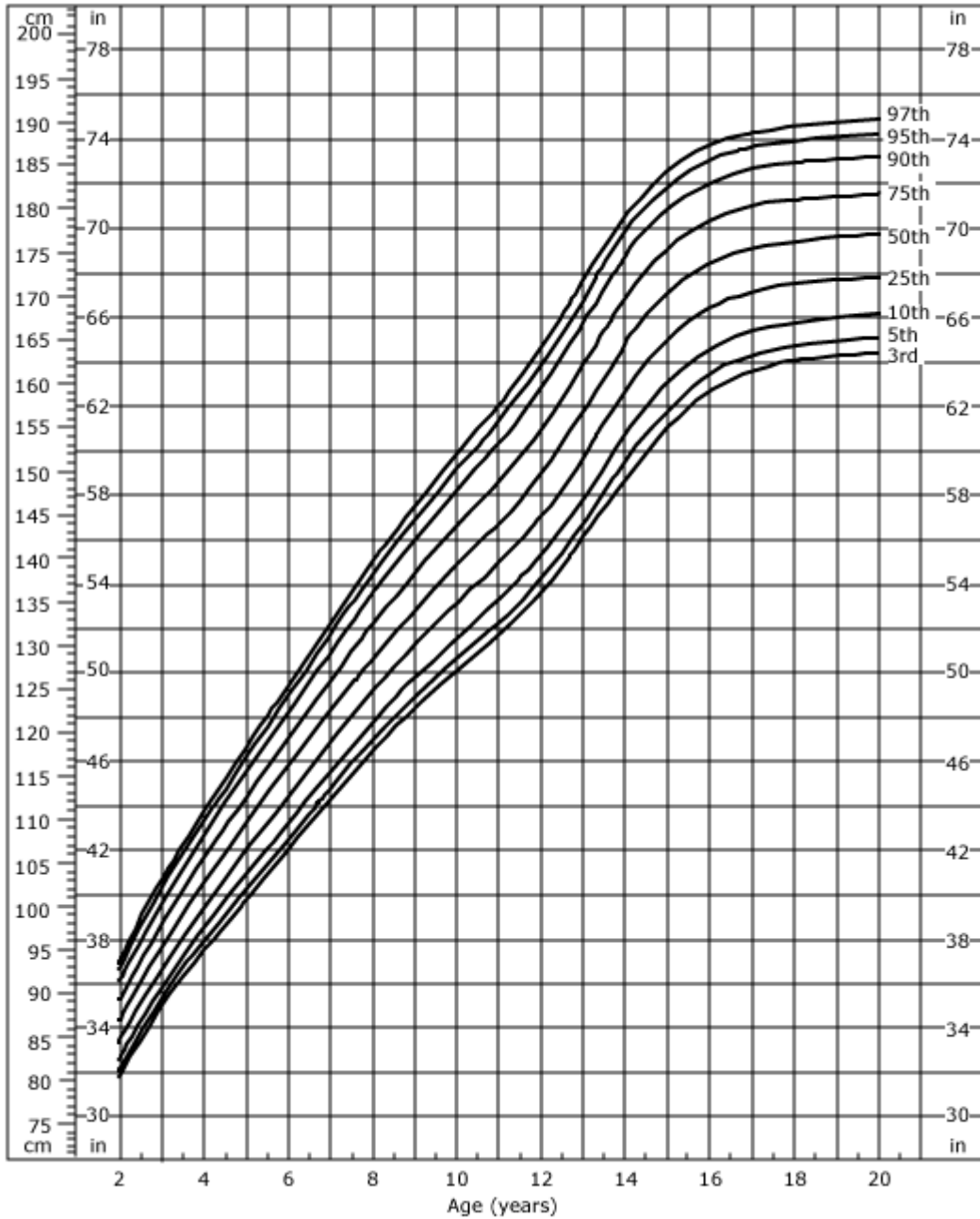
Criteria based in part on *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Adults and Children – 2003 Update*

FCHP Pharmacy and Therapeutics Committee approval: _____

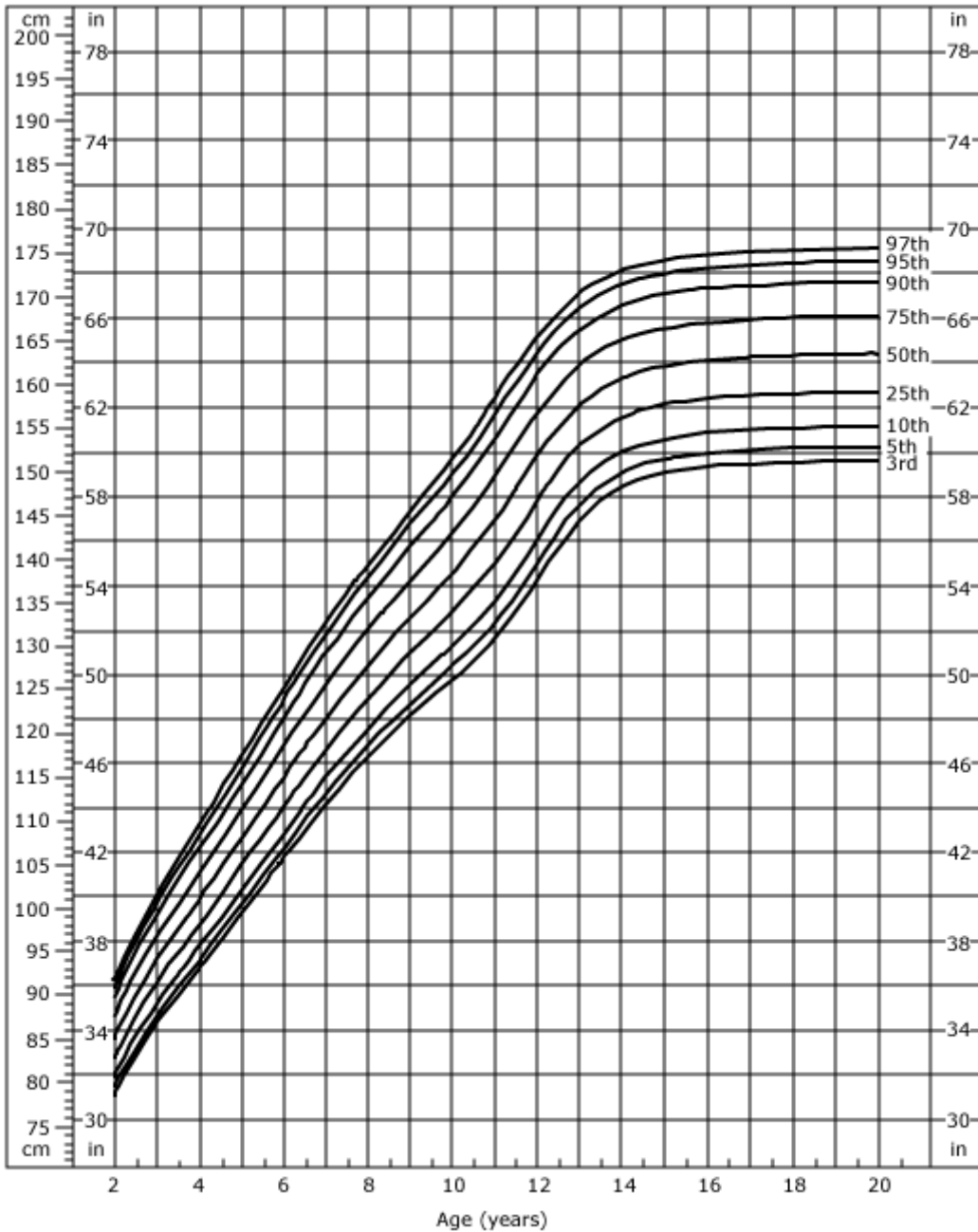
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Adopted: 12/10/2008

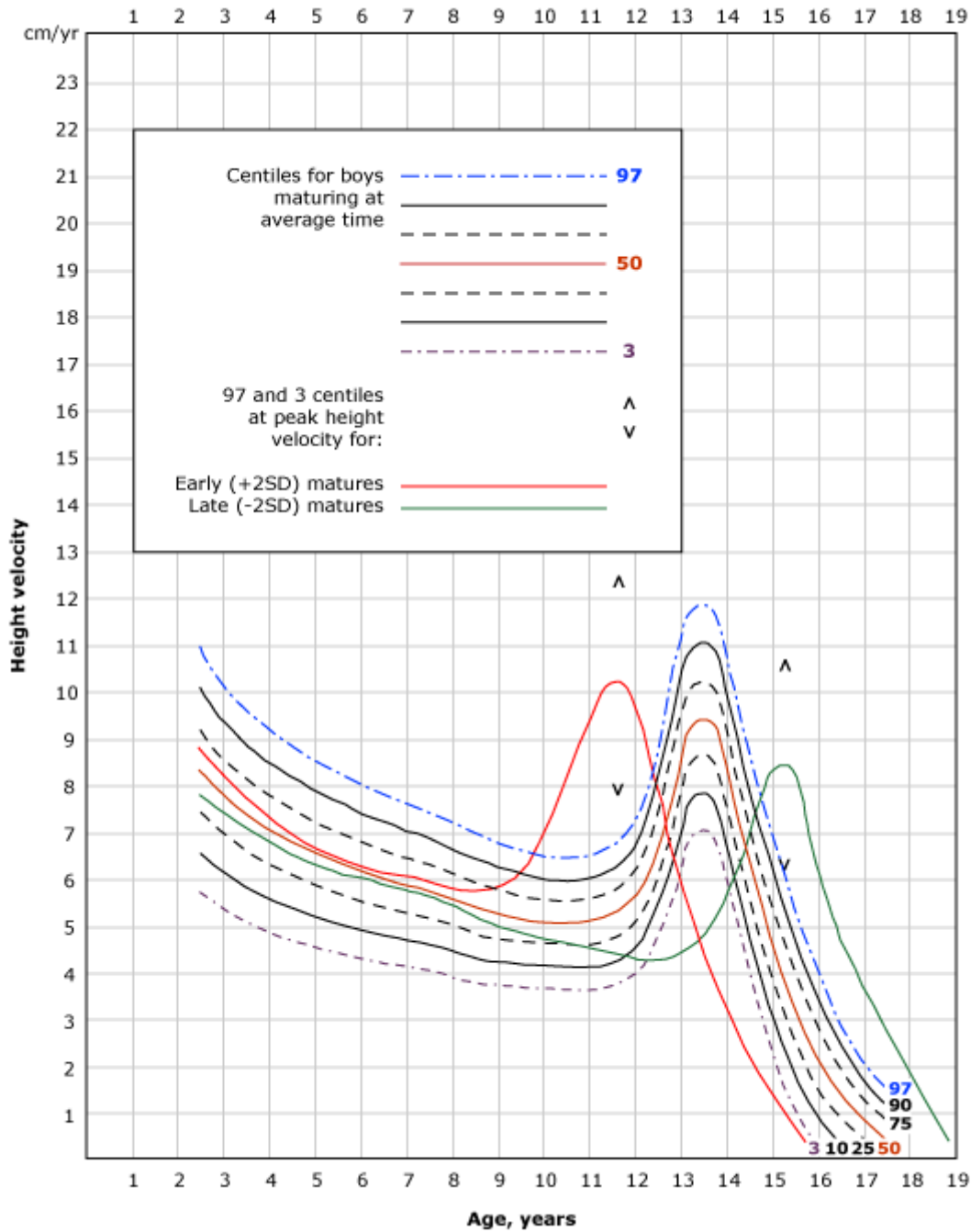
Stature-for-age percentiles, boys, 2 to 20 years, CDC growth charts:
United States (from *UpToDate*, Diagnosis of growth hormone deficiency in children, 2010)



Stature-for-age percentiles, girls, 2 to 20 years, CDC growth charts: United States (from *UpToDate*, Diagnosis of growth hormone deficiency in children, 2010)

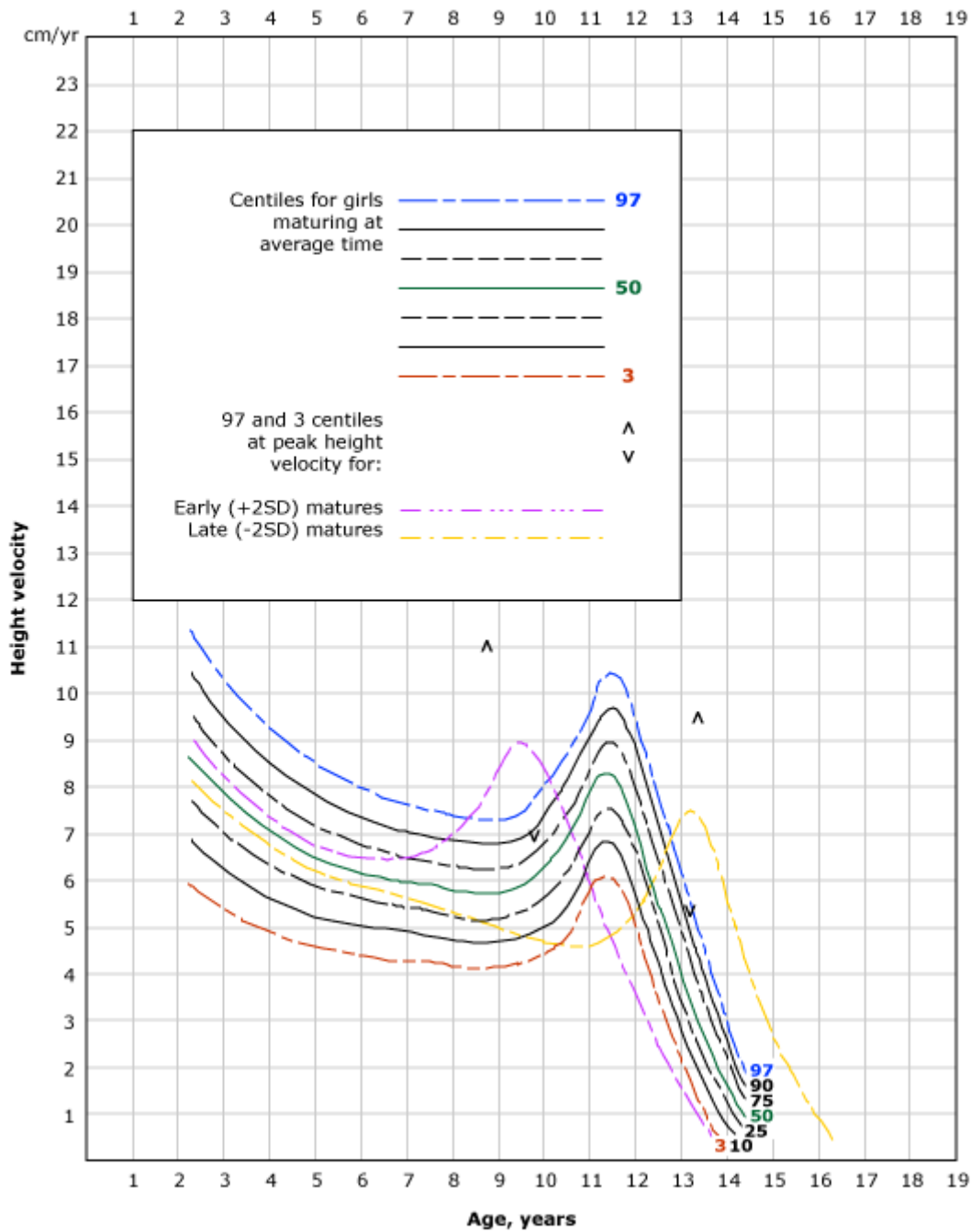


Height velocity for American boys (from *UpToDate*, Diagnosis of growth hormone deficiency in children, 2010)



Red line, 50th centile for boys 2 SD of tempo early; green line, 50th centile for boys 2 SD of tempo late. The 97th and 3rd centiles for peak velocities of early and late maturers, respectively.

Height velocity in American girls (from *UpToDate*, Diagnosis of growth hormone deficiency in children, 2010)



Purple line, 50th centile for girls 2 SD of tempo early; Yellow line, 50th centile for girls 2 SD of tempo late. The 97th and 3rd centiles for peak velocities of early and late maturers, respectively.