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USADA guidelines for a Therapeutic Use Exemption for Growth Hormone (GH) treatment of children and adolescents with idiopathic short stature (ISS)

Background

The common definition of ISS is height that is more than 2 -SD below the mean for that age, sex and population group. The definition approved by the United States Food and Drug Administration (FDA) for therapy with recombinant human GH (rhGH) is -2.25 SD below the appropriate mean (1.2 percentile) without evidence for a systemic, endocrine, nutritional or chromosomal abnormality that might explain the short stature. By definition as new syndromes and causes of short stature are identified, the pool of children defined as ISS will shrink.

Children and adolescents with ISS will have normal birth weight, and sufficient growth hormone as documented by a growth hormone stimulation test (using assay-specific normal ranges)

Included in the ISS group are a heterogeneous group of children consisting of many presently unidentified causes of short stature. It is estimated that approximately 60-80 % of all short children at or below -2 SD for height fit this definition of ISS. The criteria for rhGH therapy in the United States are

- Auxologic: height below – 2.25 SD with a projected adult height of less than 5’3” or 160 cm (in males) and 4’11” or 150 cm (in females)
- Biochemical: there are no specific biochemical criteria; however, by definition all are GH sufficient
- Psychological: The psychological benefits of rhGH therapy in children with ISS have yet to be proven. However, robust measures to prove the psychological value of rhGH therapy in such children remains elusive

The diagnosis is difficult in those under 6 years of age for the projections of adult height are poor.

The evaluation, diagnosis and treatment of children and adolescents with ISS should be performed by a pediatric endocrinologist or an appropriately trained specialist. Since rhGH is a performance-enhancing substance, a TUE for rhGH to treat children and adolescents with ISS will be considered only when the FDA-approved definition of ISS is strictly followed.



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Essential Requirements for TUE applications for this Diagnosis:

In order for a TUE application for this treatment to be considered by USADA, the following medical information must be submitted with the application:

1. Auxologic data documenting short stature and sub-normal growth over at least 1 year;
2. Bone age, mid-parental height, and predicted adult height without treatment;
3. Results of dynamic GH testing;
4. Karyotype in girls;
5. Documentation that an adequate evaluation has excluded short stature due to systemic illness, inflammatory disease, renal disease, and psychosocial causes.

Adequacy of treatment with rhGH should be documented, including adequate height velocity response and IGF-I levels within the age- and laboratory-specific normal range of the assay used. Annual bone age and height velocity are required during therapy, and rhGH must be discontinued when growth velocity slows to <2 cm/yr or bone age is >16 years in boys or 15 years in girls.