Spedizione abb. post. - art. 1, comma 1
Legge 27-02-2004, n. 46 - Filiale di Roma
GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA

Agenzia Italiana del Farmaco
AIFA

## 18-11-2010: Serie generale - n. 270

## *NOTE 39: Growth Hormone (GH, somatotropin)*

- ***Prescription of GH by Italian National Health System (SSN) is possible in specialized centres, University Departments, Hospitals, Scientific Research Institutes (IRCCS) identified by the Regions and the autonome Districts of Trento and Bolzano.***
- ***Prescription is limited to some specific conditions, individuated according to specific diagnostic criteria for age.***

Spedizione abb. post. - art. 1, comma 1
Legge 27-02-2004, n. 46 - Filiale di Roma
GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA

Agenzia Italiana del Farmaco
AIFA

**18-11-2010: Serie generale - n. 270**

***NOTE 39: Growth Hormone (GH, somatotropin)***

***Considered periods of life:***

1. ***Neonatal period;***
2. ***Childhood;***
3. ***Transition phase;***
4. ***Adulthood.***

# Note 39: (1) Neonatal Period

- Evidence (MRI) of malformations/lesions of hypothalamus-pituitary region, plus clinical and laboratory data suggesting the diagnosis of congenital isolated or multiple hypopituitarism.

(GH treatment should be administered for at lest 2 years; then, after no more than 3-month stop, auxological and laboratory parameters should be re-evaluated to determine if GH treatment should be continued and the therapy scheme).

# Note 39: (2) Childhood

- Short stature due to GH deficiency,
- Turner syndrome (certainty by karyotype),
- Short stature in chronic renal insufficiency,
- Prebubertal individuals with Prader-Willi syndrome (certainty by genetics; BMI < 95° centile; normal respiratory function; no sleep apnea);
- Children born small for gestational age.

---

*Addendum*: Italian GU (AIFA): n. 42 (*21-02-2011*)

- Short stature in individuals with SHOX gene insufficiency (certainty by DNA analysis).

# Note 39 - GH Treatment: Growth Hormone Deficiency

## I - Clinical parameters:

a. stature < -3 SD or stature < -2 SD plus growth velocity (GV)/year < -1 SD vs normal mean for age and sex; GV should be measured at least 6 months apart with the same procedures;

or

b. GV/year < -2.0 SD or < -1.5 SD after 2 consecutive years, also without short stature; in the first 2 years of life may be adequate (sufficient) a progressive decrease of GV (due to the inadequate literature data to calculate SD in this age period);

or

c. Hypothalamic-pituitary malformations/lesions demonstrated by neuroradiological techniques (MR, TC) or multiple pituitary defects associated with GH deficiency assessed by a modality of point (II).

# Note 39 - GH Treatment: Growth Hormone Deficiency

## II - Laboratory parameters:

a. GH peak < 10 µg/L after two pharmacological tests performed in different days (*GH peak* > 10 µg/L *in one test exclude the diagnosis of GH deficiency*);

or

b. GH peak < 20 µg/L if one test is represented by GHRH + arginine or GHRH + piridostigmine.

**- IGF1?**

# GH Treatment: Pediatric International Indications

## European Medicine Agency (*Europe*)

- Growth hormone deficiency.
- Chronic kidney disease.
- Turner syndrome.
- Small-for-gestational age infants (who fail to catch up to the normal growth percentiles).
- Prader-Willi syndrome.
- SHOX gene haplo-insufficiency.

## US Food & Drug Administration (*USA*)

- Growth hormone deficiency.
- Chronic kidney disease.
- Turner syndrome.
- Small-for-gestational age infants (who fail to catch up to the normal growth percentiles by 2-4 years).
- Prader-Willi syndrome.
- SHOX gene haplo-insufficiency.
- Idiopathic short stature (height >2.25 SD below the mean who are unlikely to catch up in height).
- Noonan syndrome.

*Richmond & Rogol, Endocr Dev. 2010*

## Note 39: (3) Transition phase (age at Final Height to 25 yrs)

At final height, GH treatment must be discontinued in:

- Turner syndrome;
- CRI;
- SGA;
- SHOX;
- Prader Willi syndrome.

## **Note 39 (3): Transition phase** (age at Final Height to 25 yrs)

At final height, GH treatment can be continued without any re-evaluation in:

- GH deficiency due to proven genetic mutation;
- Multiple pituitary deficiency with involvment of at least 3 pituitary hormones.

## **Note 39 (3): Transition phase** (age at Final Height to 25 yrs)

At final height, GH treatment can be continued if after at least 1 month from rGH discontinuation the patient shows:

- a GH peak <6 µg/L after insulin tolerance test (ITT);

or

- a GH peak <19 µg/L after GHRH + Arginine test.

# Note 39 (4): Adulthood

***E' indicata la terapia con GH in soggetti adulti, di età superiore a 25 anni, con livelli di GH allo stimolo con ipoglicemia insulinica < 3 µg/L ,***

**oppure**

**(in presenza di controindicazioni al test dell'ipoglicemia)**

- **con *picco inadeguato di GH dopo stimoli alternativi*** **(Il test con GHRH + arginina viene ad oggi ritenuto l'alternativa di prima scelta e, dopo questo stimolo, un severo deficit di GH è dimostrato da un picco dei livelli circolanti di GH < 9 µg/L.)**

***nei casi di:***

- ***ipofisectomia totale o parziale*** **(chirurgica o da radiazioni)**
- ***ipopituitarismo idiopatico, post-traumatico, da neoplasie sellari o parasellari*.**

# Terapia con rhGH nelle diverse fasi della vita: dosi sostitutive appropriate