THE USE OF
GROWTH HORMONE IN CHILDREN AND ADULTS

QUICK REFERENCE FOR HEALTHCARE PROVIDERS

7. Adults with normal GH status (burns, critically ill patients, ageing, sports,)
6. In adults, rhGH should only be given to patients with GHD symptoms with proven
5. All rhGH-treated patients should be re-evaluated during transition period.
3. Early recognition and early referral is important for optimal outcome.

However, it may be considered as an adjuvant in low IGF-1 patients. rhGH

GH deficiency should be excluded in adult patients with any of the following:
• Reduced vitality and energy
• Reduced physical stamina
• Anxiety
• Impaired psychological well-being

rhGH should only be prescribed to patients with clinical features suggestive of adult GH
deficiency should
do this before the age of 12 years.

Alcohol use and smoking cessation before the age of 12 years.

The use of rhGH is recommended in adults with burns, critically ill patients, elderly

• Traumatic brain injury (accidental or
• Surgery to the hypothalamic pituitary region
• Visual impairment and optic nerve hypoplasia)
• Midline craniofacial defects (such as cleft

in adults with burns, critically ill patients, elderly

• Diabetes mellitus
• Overweight
• Increased adiposity especially

Maintenance dose based on clinical response and IGF-1

Normalisation of height during childhood and attainment of

DURING TRANSITION PERIOD

Period of adolescence/young adulthood after attainment of final

Stage 3 in girls and genital stage 3 in boys

Alternative

DEXA scan should be performed prior to starting GH

MH minus 10 cm

FH in GH-treated childhood onset GHD (COGHD) patients

Abbreviations:

ITT: Insulin tolerance test
GST: Glucose tolerance test
AST: Actinostat test

SGA children who remained short (<3rd percentile) after 4 years

Downward deviation of height ≥1 centile band over at

Height below target height (TH) range i.e. mid parental

≥

Adults with symptoms and signs of GH deficiency

Children with acquired hypothalamic-pituitary disease are

Either ITT, GST or AST are needed.

Children with acquired hypothalamic-pituitary disease are

Evaluation for GH

Hormone replacement before biochemical evaluation.

1. Baseline growth hormone test
2. Serum IGF-1: 3-monthly in the first year, then yearly

of these:

Early recognition and early referral is important for optimal outcome.

Diagnosing GH Deficiency

Diagnosis of GH deficiency is based on GH response to provocative tests:

Testing: The most widely used test is an intravenous glucose tolerance test (ITT).

A minimum of 2 IGF-1 concentrations below the 3rd centile for age and sex

The diagnosis of GH deficiency in adults should be based on the same criteria as for children,

the diagnosis of GH deficiency is based on the same criteria as for children,
I. USE OF GH IN CHILDREN

WHO SHOULD BE INVESTIGATED FOR GH DEFICIENCY IN CHILDREN?

<table>
<thead>
<tr>
<th>In neonates/infants</th>
<th>Evaluation for GH deficiency should be conducted if they manifest persistent, intractable hypoglycaemia ± convulsions associated with any of these:</th>
</tr>
</thead>
</table>
|                     | • Micropenis in a male infant  
                        • Prolonged neonatal jaundice  
                        • Midline craniofacial defects (such as cleft palate, cleft lip, nasal or frontal encephalocele, single central incisor, visual impairment and optic nerve hypoplasia)  
                        • Traumatic delivery (breech) or perinatal asphyxia  
                        • Post-natal failure to thrive (affecting both length and weight) |

<table>
<thead>
<tr>
<th>In order children</th>
<th>Evaluation for GH deficiency should be conducted if history is positive for any of these:</th>
</tr>
</thead>
</table>
|                     | • Surgery to the hypothalamic pituitary region  
                        • Cranial irradiation  
                        • Intracranial tumour such as craniopharyngioma  
                        • Traumatic brain injury (accidental or non-accidental)  
                        • Central nervous system infection  
                        • Signs and symptoms of multiple pituitary hormones deficiency (MPHD)  
                        • Signs indicative of intracranial lesion  
                        • Parental consanguinity ± an affected family member (genetic cause)  
                        • Failure to show normal growth spurt by breast stage 3 in girls and genital stage 3 in boys |
DIAGNOSIS OF GH DEFICIENCY IN CHILDREN

All of the following criteria must be fulfilled to confirm the diagnosis of GH deficiency:

| Clinical and auxological criteria | • Short stature as defined by:  
| | ➢ Height <3rd centile on the NCHS chart **AND/OR**  
| | ➢ Height below target height (TH) range i.e. mid parental height (MPH) minus 10 cm **AND**  
| | • Slow growth as defined by:  
| | ➢ Downward deviation of height ≥1 centile band over at least 12 months  
| | Children with acquired hypothalamic-pituitary disease are considered to have fulfilled the above criteria if they have slow growth even in the absence of short stature. |

| Biochemical criteria | A minimum of **TWO** growth hormone stimulation tests using either ITT, GST or AST are needed.  
| | • Peak GH level of <10 mcg/L is diagnostic  
| | Sex steroid priming is useful for peripubertal children. Children with MPHD should have received adequate adrenal and thyroid hormone replacement before biochemical evaluation. |

| Radiological criteria | • Delayed bone age |

After confirmation of GH deficiency, subsequent investigations should include MRI of hypothalamic-pituitary region and genetic study (if facilities are available).

CRITERIA FOR REFERRAL

• Neonates/infants with features of GH deficiency  
• Children at risk of GH deficiency showing slow growth and/or short stature  
• Children who fulfill clinical and auxological criteria for GH deficiency

TREATMENT OF GROWTH HORMONE DEFICIENCY IN CHILDREN

| Aim | • Normalisation of height during childhood and attainment of normal adult height |
| Dose | • Starting dose 0.025 mg/kg/day and adjusted within the range of 0.025 to 0.05 mg/kg/day based on the growth response and IGF-1 level  
| | • rhGH should be given as a daily SC injection 7 days a week  
| | • rhGH should be given uninterrupted for at least 4 years prior to closure of the epiphyses |

| Monitoring | • Height: 3 - 6-monthly  
| | • Serum IGF-1: 3-monthly in the first year, then yearly  
| | • Free T4, TSH: yearly  
| | • Fasting plasma glucose, HbA1c and insulin: before starting rhGH  
| | • HbA1c: yearly or more frequently in patients at risk for type 2 diabetes mellitus  
| | • Bone age: prior to starting rhGH and yearly thereafter |
**USE OF GROWTH HORMONE IN NON-GHD CHILDREN**

<table>
<thead>
<tr>
<th>Turner Syndrome</th>
<th>Small for Gestational Age (SGA)</th>
</tr>
</thead>
</table>
| • GH should be started early for optimisation of final height (FH).  
• Oestrogen replacement therapy should not be initiated before the age of 12 years. | SGA children who remained short (<3rd percentile) after 4 years of age should be referred to a paediatric endocrinologist for evaluation and consideration of rhGH therapy. |

rhGH should not be used in familial/genetic short stature, idiopathic short stature, chronic renal insufficiency, Prader-Willi syndrome, Noonan syndrome, Russell-Silver syndrome and skeletal dysplasia.

**ALGORITHM FOR GROWTH HORMONE THERAPY IN CHILDREN**

**Suspect GHD**
- Short stature (Ht <3rd percentile or < target height range) AND
- Slow growth AND
- Delayed bone age

**Turner syndrome**
- Short stature (Ht <3rd percentile) AND/OR
- Slow growth AND
- Chronological age <12 years OR bone age <10 years

**Small for Gestational Age**
- > 4 years AND
- Short stature (Ht <3rd percentile) AND
- Slow growth

Refer to paediatric endocrinologist for further evaluation

- **GH stimulation tests (ITT/GST/AST)**
  - Peak GH >10mcg/L
  - History of:
    - Cranial irradiation
    - Hypothalamic-pituitary disease
  - No
  - Yes
  - Monitor growth
  - Slow growth
  - No
  - Yes
  - **GHD**
    - MRI
    - Assess other pituitary hormones deficiency
  - Continue to observe
  - Treatment with rhGH + Replacement of other pituitary hormone deficiency
  - Treatment with rhGH
II. USE OF GH IN TRANSITION PERIOD

<table>
<thead>
<tr>
<th>Definition of transition period</th>
<th>Period of adolescence/young adulthood after attainment of final height (FH) in GH-treated childhood onset GHD (COGHD) patients until 6 to 7 years later (approximately from 17 to 25 years old)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who to be re-evaluated</td>
<td>All COGHD patients who have reached FH</td>
</tr>
</tbody>
</table>
| Who should continue GH therapy  | Those with:  
- ≥3 pituitary hormone deficiencies and serum IGF-1 below −2 SD or  
- Peak GH after ITT <5 mcg/L or after GST <3 mcg/L                                                                 |
| Dose                            | Starting dose 0.0125 – 0.0250 mg/kg/day and the dose of rhGH should be adjusted to maintain normal serum IGF-1 level |

ALGORITHM FOR MANAGEMENT OF GROWTH HORMONE-TREATED CHILDREN DURING TRANSITION PERIOD

1. GH treated children during transition period with possible persistent GH deficiency

2. Organic disease
   - ≥3 pituitary hormones deficient
   - Low IGF-1 (< 2.5 percentile/2SD)

3. Organic disease
   - 0, 1 or 2 pituitary hormones deficient
   - IGF-1 < 50 percentile/2SD

4. Idiopathic GH deficiency in childhood OR suspect hypothalamic origin

5. Stimulation test
   - ITT or GST

6. No further testing
   - Treat

7. ITT
   - Peak GH ≤ 5.0 mcg/L
   - Treat

8. Glucagon
   - Peak GH ≤ 2.0 mcg/L
   - Treat

9. Normal IGF-1 (≥ 2SD) (Low suspicion)

10. Observe
III. USE OF GH IN GH DEFICIENT ADULTS

Whom to screen? In adults with the following symptoms and signs and suspected to have hypothalamic-pituitary disease:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Increased body fat</td>
<td>- Overweight</td>
</tr>
<tr>
<td>- Reduced muscle bulk</td>
<td>- Increased adiposity especially abdominal</td>
</tr>
<tr>
<td>- Reduced strength and physical fitness</td>
<td>- Poor muscular development</td>
</tr>
<tr>
<td>- Reduced sweating</td>
<td>- Reduced exercise performance</td>
</tr>
<tr>
<td>- Impaired psychological well-being</td>
<td>- Thin, dry skin</td>
</tr>
<tr>
<td>- Depressed mood</td>
<td>- Depressed affect</td>
</tr>
<tr>
<td>- Anxiety</td>
<td></td>
</tr>
<tr>
<td>- Reduced physical stamina</td>
<td></td>
</tr>
<tr>
<td>- Reduced vitality and energy</td>
<td></td>
</tr>
<tr>
<td>- Increased social isolation</td>
<td></td>
</tr>
</tbody>
</table>

GH deficiency should be excluded in adult patients with any of the following:
- Hypothalamic-pituitary disease
- Previous cranial irradiation
- Traumatic brain injury

ALGORITHM FOR SCREENING AND DIAGNOSIS FOR ADULT WITH POSSIBLE GROWTH HORMONE DEFICIENCY

Adult with clinical features of GH deficiency

- Organic disease
  - ≥3 hormones deficient
  - Low IGF-1 ≤ 2.5 percentile (< 2SD)

- Organic disease
  - 1 or 2 hormones deficient
  - IGF-1 < 50 percentile (GSD)

- History of:
  - Head injury
  - Cranial irradiation
  - Subarcnoid hemorrhage or hypothalamic disease

Stimulation test ITT or GST

- No further testing
  - Treat

- ITT
  - Peak GH ≤ 5.0 mcg/L
  - Treat

- Glucagon
  - Peak GH ≤ 3.0 mcg/L
  - Treat
5. All rhGH-treated patients should be re-evaluated during transition period.

4. rhGH therapy should not be taken lightly in view of its high cost, the need of

1. All growth hormone deficient (GHD) children should be treated using the

QUICK REFERENCE FOR HEALTHCARE PROVIDERS THE USE OF GROWTH HORMONE IN CHILDREN AND ADULTS

I. USE OF GH IN CHILDREN

7. Adults with normal GH status (burns, critically ill patients, ageing, sports,

3. Early recognition and early referral is important for optimal outcome.

WHO SHOULD BE INVESTIGATED FOR GH DEFICIENCY IN CHILDREN?

• Increased social isolation
• Anxiety
• Depressed mood
• Impaired psychological well-being

Adults with GH deficiency should be excluded in adult patients with any of the following:

- Traumatic brain injury
- Reduced vitality and energy

ALGORITHM FOR MANAGEMENT OF GROWTH HORMONE-TREATED CHILDREN

All of the following criteria must be fulfilled to confirm the diagnosis of adult GH deficiency:

<table>
<thead>
<tr>
<th>Clinical criteria</th>
<th>Adults with symptoms and signs of GH deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemical criteria</td>
<td>Peak GH after ITT ≤5 mcg/L or after GST ≤ 3 mcg/L</td>
</tr>
<tr>
<td>Investigation after confirmation of GH-deficiency</td>
<td>MRI of hypothalamic-pituitary region</td>
</tr>
<tr>
<td></td>
<td>Evaluation of QoL using suitable QoL questionnaire</td>
</tr>
</tbody>
</table>

TREATMENT OF GROWTH HORMONE DEFICIENCY IN ADULTS

rhGH should only be prescribed to patients with clinical features suggestive of adult GH deficiency, biochemically proven GH deficiency and have adverse quality of life.

Aim

• Normalisation of IGF-1 level and improvement in QoL

Dose

• The starting dose of rhGH is 0.1 mg daily for men and 0.2 mg daily for women.
• The dose is increased by 0.1 mg or 0.2 mg to achieve a maintenance dose based on clinical response and IGF-1 levels
• rhGH dose should be individualised independent of body weight

Monitoring

• Serum IGF-1: 3-monthly in the first year and then yearly
• Fasting plasma glucose, HbA1c and insulin: before starting rhGH
rhGH therapy should not be used for routine treatment of fibromyalgia. However, it may be considered as an adjuvant in low IGF-1 patients. rhGH therapy should not be used in adults with burns, critically ill patients, elderly as an anti-ageing therapy, sports to enhance athletic performance, treatment of infertility and simple adult obesity.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) The Use of Growth Hormone in Children and Adults (November 2010).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

- Ministry of Health Malaysia: http://www.moh.gov.my
- Academy of Medicine Malaysia: http://www.academ.org.my

**CLINICAL PRACTICE GUIDELINES SECRETARIAT**

Health Technology Assessment Section, Medical Development Division
Ministry of Health Malaysia, 4th Floor, Block E1, Parcel E, 62590 Putrajaya
Tel: 603-8883 1246  E-mail : htmalaysia@moh.gov.my