

21 March 2014

## Proposed changes to the brand and distribution of growth hormone

PHARMAC and Sandoz, a Novartis New Zealand Limited company, have reached a provisional agreement to fund Omnitrope, a brand of the human growth hormone somatropin.

This proposal would result in:

- Omnitrope becoming the only subsidised brand of growth hormone from 1 January 2015 to 31 December 2017. This change would mean that there are three strengths of growth hormone listed on the Pharmaceutical Schedule, instead of the current two.
- Genotropin, the currently listed brand of somatropin would be delisted from 1 January 2015.
- Changing the restrictions applying to the prescription of growth hormone for children and adults in Section B and Part II of Section H of the Pharmaceutical Schedule from 1 July 2014. The changes to the restrictions will not affect patient access to growth hormone.
- The disestablishment of the Paediatric and Adult Growth Hormone Panels. Individual patients' physicians would be responsible for applying for and writing prescriptions for somatropin for their patients in accordance with the Special Authority criteria.
- Changes to the current direct distribution model of growth hormone. Patients would collect Omnitrope from their community pharmacy.

### Feedback sought

PHARMAC welcomes feedback on this proposal. To provide feedback, please submit it in writing by **Friday, 4 April 2014** to:

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All feedback received before the closing date will be considered by PHARMAC's Board (or its delegate) prior to making a decision on this proposal.

Feedback we receive is subject to the Official Information Act 1982 (OIA) and we will consider any request to have information withheld in accordance with our obligations under the OIA. Anyone providing feedback, whether on their own account or on behalf of an organisation, and whether in a personal or professional capacity, should be aware that the

content of their feedback and their identity may need to be disclosed in response to an OIA request.

We are not able to treat any part of your feedback as confidential unless you specifically request that we do, and then only to the extent permissible under the OIA and other relevant laws and requirements. If you would like us to withhold any commercially sensitive, confidential proprietary, or personal information included in your submission, please clearly state this in your submission and identify the relevant sections of your submission that you would like it withheld. PHARMAC will give due consideration to any such request.

## Details of the proposal

### Omnitrope sole subsidised supply

- From 1 July 2014 Omnitrope would be listed in Section B and Part II of Section H of the Pharmaceutical Schedule at the following subsidy and price (ex-manufacturer and excluding GST):

Chemical	Presentation	Brand	Pack size	Price and subsidy
Somatropin	Inj 5 mg cartridge	Omnitrope	1	\$109.50
Somatropin	Inj 10 mg cartridge	Omnitrope	1	\$219.00
Somatropin	Inj 15 mg cartridge	Omnitrope	1	\$328.50

- Omnitrope would be subject to confidential rebates, which would reduce its net price to the Funder.
- From 1 July 2014, the Sandoz brand of the human growth hormone somatropin - Omnitrope would be listed in Section B of the Pharmaceutical Schedule subject to a Special Authority (Appendix 1). The restriction applying in Part II of Section H would be broadly similar.
- From 1 July 2014, Omnitrope would be listed in Section B of the Pharmaceutical Schedule subject to a Specialist Prescription rule, limiting funded prescribing to Paediatricians, Endocrinologists or Nephrologists as follows:
  - Retail pharmacy - Specialist Prescription (Specialist must be a Paediatrician, Endocrinologist or Nephrologist)
- Genotropin, the currently listed brand of somatropin would be delisted from Section B (community) and Part II of Section H (hospital) of the Pharmaceutical Schedule from 1 January 2015.
- Omnitrope would be awarded Sole Subsidised Supply Status (the only brand funded in the community) and Hospital Supply Status (the only available brand in DHB hospitals, subject to a 1% discretionary variance limit) from 1 January 2015 until 31 December 2017.
- From 1 July 2014 a six month transition period to change the brands would commence. During this transition period Sandoz would work with patients and clinicians to assist in patients changing from Genotropin to Omnitrope involving direct communication with patients and their treating clinicians.

## Transition timelines

- The implementation process and timelines, should this proposal be approved, would be:
  - **May 2014** - Anticipated notification of a decision on this proposal, depending on consultation responses and approval by PHARMAC's Board or its delegate. We would communicate directly with all patients and provide details about when they should visit their paediatrician, endocrinologist or nephrologist to discuss the brand change, change in distribution arrangements and obtain a prescription for Omnitrope to take to a retail pharmacy.
  - **1 July 2014** - Listing of Omnitrope at the prices and subsidies specified above. There would be no change to the prices and subsidies of the currently listed Genotropin brand.
  - **1 July 2014** – Paediatricians, endocrinologists and nephrologists would be eligible to prescribe growth hormone using the Special Authority criteria that would be included in both Section B and Part II of Section H of the Pharmaceutical Schedule.
  - **1 July 2014 – 31 December 2014** – Two brands of somatropin (Omnitrope and Genotropin) would be listed fully funded. A six month transition period is intended to provide sufficient time for all patients who have been receiving funded Genotropin to be transitioned to the Omnitrope brand. During this transition period, patients currently receiving Genotropin would be educated and supported by Sandoz to manage the change to Omnitrope.
  - **1 January 2015** - The Genotropin brand of somatropin injection 16 iu (5.3 mg) and 36 iu (12 mg) would be delisted from Section B and Part II of Section H of the Pharmaceutical Schedule.
  - **1 January 2015- 31 December 2017** - Omnitrope 5 mg, 10 mg and 15 mg would be the sole subsidised brand of somatropin injection in the community (Sole Subsidised Supply Status) and the only available brand in DHB hospitals subject to a 1% discretionary variance limit (Hospital Supply Status).

## Prescriber changes

Currently applications for growth hormone have been managed by the Paediatric Growth Hormone Panel and the Adult Growth Hormone Panel using specific entry and exit criteria. If the proposal is accepted applications and renewals would be done via Special Authority.

Prescribing of growth hormone for paediatric patients has been managed by the Paediatric Growth Hormone Panel. If this proposal was accepted the patient's specialist would write both the Special Authority application request and growth hormone prescriptions.

Prescribing of growth hormone for adults and older adolescent's patients has been undertaken by the patients treating physician. If this proposal was accepted there would be no change to the prescriber.

For the avoidance of doubt all funded prescriptions would be required to be written by a paediatrician, endocrinologist or nephrologist.

From 1 July 2014 the current Special Authority and restrictions applying to the brand of somatropin injections listed in Section B and Section H Part II of the Pharmaceutical Schedule would be replaced with the proposed criteria outlined on pages 5 to 9 of this document to enable endocrinologists, paediatricians and nephrologists to apply for and prescribe somatropin. Renewal applications could also be made by these prescribers.

## **Distribution**

Currently, patients obtain their supplies of Genotropin via a central pharmacy direct distribution mechanism funded by both PHARMAC and Pfizer, and managed by PHARMAC staff. From 1 July 2014, we are proposing this arrangement would end and somatropin (Omnitrope brand) would be dispensed through community pharmacy on receipt of a prescription in the same way that other pharmaceuticals listed on the Pharmaceutical Schedule are dispensed.

During the transition period (1 July – 31 December 2014) patients with an existing Growth Hormone Special Authority may continue to receive their direct distribution delivery of somatropin (Genotropin) via the current distribution model. Patients would need to obtain a prescription for somatropin (Omnitrope) from their consultant paediatrician, endocrinologist or nephrologist and have their prescription filled at their community retail pharmacy, as happens with other medicines. They would receive follow-up training from a nurse educator about how to use their new device and medication. Once this training had occurred there would be no further direct distribution to the patient. Further information will be sent to patients about when this will occur.

Currently, approximately 80% of patients receiving Genotropin collect the directly distributed product from a retail pharmacy rather than having it sent to their homes.

In order to manage the brand change, retail pharmacists will be paid a brand switch fee. Patients would also be required to pay a patient co-payment.

## **Background**

There is currently one brand of somatropin (growth hormone) listed in the Pharmaceutical Schedule. This is Genotropin supplied by Pfizer and funded under Special Authority (access by application) for patients with the various indications requiring growth hormone.

In October 2013 PHARMAC initiated a competitive process for the supply of somatropin. Following completion of that process PHARMAC has entered into a provisional agreement with Sandoz New Zealand Limited for the sole subsidised supply of its brand of somatropin, Omnitrope.

Currently approximately 250 children and 170 adults requiring growth hormone access funded Genotropin via direct distribution.

## **Managing the proposed brand switch**

Omnitrope is a 'BioSimilar' medicine with the same registered indications as Genotropin. This enables all current patients on Genotropin to change to Omnitrope. Clinical trials have demonstrated that it has comparable safety and efficacy to the Genotropin brand of somatropin. Omnitrope injections have been approved by Medsafe.

If this proposal is approved PHARMAC will work with clinicians, pharmacists and patients to manage the brand change. PHARMAC would keep patients directly informed of the proposal and any decisions made in order for them to schedule appointments with their paediatrician, endocrinologist or nephrologist to discuss the brand change.

Sandoz will also commit resources to ensure existing and new patients are fully trained in using the Omnitrope injector device (which differs from the current one used with Genotropin) and prescribing clinicians are well informed about the medicine. The training will include comprehensive education for patients taking Omnitrope so that they know how to use the injector device appropriately.

## Appendix 1

### Special Authority for Subsidy

**Initial application (growth hormone deficiency in children)** from a paediatrician or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:

Either:

1. Growth hormone deficiency diagnosed on at least two random blood samples in the first 2 weeks of life, or from samples during established hypoglycaemia (whole blood glucose  $<2$  mmol/l using a laboratory device), with symptomatic hypoglycaemia, or other significant growth hormone deficient sequelae (e.g. cardiomyopathy, hepatic dysfunction); or
2. All of the following:
  - 2.1 Height velocity  $< 25$ th percentile for age; and
  - 2.2 Bone age if there is marked growth acceleration or delay over 6 or 12 months using the standards of Tanner and Davies; and
  - 2.3 Peak growth hormone value of  $< 5.0$  mcg per litre in response to two different growth hormone stimulation tests as specified in the application form. In children who are 5 years or older, GH testing with sex steroid priming is one of the two tests required; and
  - 2.4 If the patient has been treated for a malignancy, they should be disease free for at least one year based upon follow-up laboratory and radiological imaging appropriate for the malignancy; and
  - 2.5 If growth hormone deficiency is not congenital, then appropriate imaging of the pituitary gland has been obtained.

**Renewal application (growth hormone deficiency in children)** from a paediatrician or endocrinologist. Approvals valid for 12 months for applications meeting the following criteria:

All of the following:

1. The patient has achieved a height at or near adult height ( as defined in 4. below); and
2. In children more than 5 years of age, the patient's current bone age is  $\leq 14$  years (female patients) or  $\leq 16$  years (male patients); and
3. Growth velocity is  $>$ the 50th percentile while on growth hormone treatment, as calculated over six months; and
4. The patient is maintaining a height velocity of at least 2.0 cm per year while on growth hormone treatment, as calculated over six months with a bone age of  $<14$  years in girls and  $<16$  years in boys.

**Initial application (Turner syndrome)** from a paediatrician or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:

All of the following:

1. The patient has a diagnosis consistent with proven Turner Syndrome; and

2. The patient has poor growth velocity (< 25th percentile for normal girls) measured over 6-12 months; and
3. The patient is being monitored or treated for hypothyroidism; and
4. The patient's bone age is <14 years.

**Renewal application (Turner syndrome)** from a paediatrician or endocrinologist. Approvals valid for 12 months for applications meeting the following criteria:

All of the following:

1. Growth velocity  $\geq$  50<sup>th</sup> percentile for age (based upon Ranke's Turner Syndrome growth velocity charts); and
2. A current bone age  $\leq$ 14 years; and
3. Growth velocity is at least 2 cm per year, calculated over six months; and
4. No serious adverse reaction or complication of growth hormone treatment and
5. No malignancy has developed since starting growth hormone.

**Initial application (short stature without growth hormone deficiency)** from a paediatrician or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:

All of the following:

1. The patient's height is more than 3 standard deviations below the mean for age; and
2. The patient has an absence of severe chronic disease (including recognised skeletal dysplasia's) and is not receiving medications known to impair height velocity; and
3. The patient is not treated for and does not have evidence of a malignancy; and
4. The patient has a growth velocity below the 25th percentile calculated over 6-12 months; and
5. The patient's bone age is  $\leq$ 14 years (female patients) or  $\leq$ 16 years (male patients); and
6. The patient does not have >1 standard deviation discordance between standing and sitting height standard deviation scores, to exclude unrecognised skeletal dysplasias.

**Renewal application (short stature without growth hormone deficiency)** from a paediatrician or endocrinologist. Approvals valid for 12 months for applications meeting the following criteria:

Both of the following:

1. Either:
  - 1.1 The patient has been treated with somatropin for less than 12 months, and height velocity has increased by at least 2 cm per year from the pre-treatment records; or
  - 1.2 The patient has been treated with somatropin for more than 12 months, and growth velocity (adjusted for bone age/pubertal status if appropriate) is > 50th percentile for bone age; and
2. All of the following:
  - 2.1 The patient's bone age is  $\leq$  14 years (female patients) or  $\leq$  16 years (male patients); and
  - 2.2 The patient's growth velocity is at least 2 cm per year as calculated over six months; and
  - 2.3 No malignancy has developed after growth hormone therapy was commenced; and
  - 2.4 No serious adverse reaction or complication that the patient's specialist considers is likely to be attributable to growth hormone treatment has occurred; and
  - 2.5 In patients with very delayed bone ages (more than 2 years), height velocity has been assessed in relationship to age and change in bone age.

Note:

- Short patients with very delayed bone age may have an increase in height velocity which can be offset by acceleration in skeletal maturity as reflected by a rapid change in bone age (e.g. bone age advancement by 2-3 years in a one year interval).

**Initial application (short stature due to chronic renal insufficiency)** from a paediatrician, endocrinologist or nephrologist. Approvals valid for 9 months for applications meeting the following criteria:

All of the following:

1. The patient's height is <2 standard deviations below the mean, with poor growth velocity (below the 25th percentile, measured over 6-12 months); and
2. The patient's bone age is  $\leq$  to 14 years (female patients) or  $\leq$  to 16 years (male patients); and
3. The patient is metabolically stable, has no evidence of metabolic bone disease and absence of any other severe chronic disease; and
4. The patient is under the supervision of a specialist with expertise in renal medicine; and
5. Either:
  - 5.1 The patient has a GFR  $\leq$  30 ml/min/1.73 m<sup>2</sup> as measured by the Schwartz method in a child who may or may not be receiving dialysis; or
  - 5.2 The patient has received a renal transplant and is not receiving glucocorticoid therapy.

**Renewal application (short stature due to chronic renal insufficiency)** from a paediatrician, endocrinologist or nephrologist. Approvals valid for 12 months for applications meeting the following criteria:

Any of the following:

1. All of the following:
  - 1.1 The patient has not received renal transplantation; and
  - 1.2 Either:
    - 1.2.1 The patient has been treated with somatropin for less than 12 months, and height velocity has increased by at least 2 cm per year compared with pretreatment measurements with a bone age  $\leq$ 14 in girls and  $\leq$  16 in boys; or
    - 1.2.2 Patient has been treated with somatropin for more than 12 months, and growth velocity (adjusted for bone age/pubertal status if appropriate) is at or above the 50th percentile; and
  - 1.3 The patient has a bone age of less than or equal to 14 years (female patients) or less than or equal to 16 years (male patients); and
  - 1.4 The patient has not experienced significant biochemical or metabolic deterioration confirmed by diagnostic results; and
  - 1.5 No malignancy has developed after growth hormone therapy was commenced and
  - 1.6 The patient has not experienced a major adverse effect of growth hormone since starting growth hormone treatment; or
2. Both:
  - 2.1 The patient has received a renal transplant in the last 12 months; and
  - 2.2 The patient has demonstrated a growth velocity below the 50th percentile in the 6 months following prednisone reduction to less than 5mg/m<sup>2</sup>/day, or to alternate-day steroids; or
3. All of the following:
  - 3.1 The patient received a renal transplant more than 12 months ago and is under the supervision of a specialist with expertise in renal medicine; and
  - 3.2 Either:
    - 3.2.1 The patient has been treated with somatropin for less than 12 months, and growth velocity has increased by at least 2 cm per year; or
    - 3.2.2 The patient has been treated with somatropin for more than 12 months, and growth velocity (adjusted for bone age/pubertal status if appropriate) is above the 50th percentile; and
  - 3.3 Either:

- 3.3.1 The patient's bone age is  $\leq 14$  years (female patients) or  $\leq 16$  years (male patients); or
- 3.3.2 The patient's growth velocity is at least 2 cm per year as calculated over six months; and
- 3.4 The patient has not experienced significant biochemical or metabolic deterioration confirmed by diagnostic results; and
- 3.5 The patient has not developed diabetes mellitus that has not resolved with manipulation of immunosuppressive therapy; and
- 3.6 No malignancy has developed after growth hormone therapy was commenced and
- 3.7 The patient has not experienced a major adverse effect of growth hormone since starting growth hormone treatment.

**Initial application (Prader-Willi syndrome)** from a paediatrician or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:

All of the following:

- 1. The patient has a diagnosis of Prader-Willi syndrome that has been confirmed by genetic testing; and
- 2. The patient's growth velocity is less than the 25th percentile for bone age or pubertal status over 6 to 12 months; and
- 3. Either:
  - 3.1 The patient is aged two years or older; or
  - 3.2 growth velocity if patient is under two years of age has been assessed over a minimum six month period from the age of 12 months, with at least three supine length measurements over this period demonstrating clear and consistent evidence of linear growth failure (growth velocity  $< 25$ th percentile); and
- 4. The patient's current bone age is  $< 14$  years (female patients) or  $< 16$  years (male patients); and
- 5. Sleep studies or overnight oximetry have been performed and there is no obstructive sleep disorder requiring treatment, or if an obstructive sleep disorder is found, it has been adequately treated under the care of a sleep physician and/or ENT surgeon; and
- 6. There is no evidence of type II diabetes or uncontrolled obesity defined as a BMI that has increased by more than 0.5 standard deviations in the preceding 12 months.

**Renewal application (Prader-Willi syndrome)** from a paediatrician or endocrinologist, Approvals valid for 12 months for applications meeting the following criteria:

All of the following:

- 1. Either:
  - 1.1 The patient has been treated with somatropin for less than 12 months, and growth velocity has increased by at least 2 cm per year; or
  - 1.2 The patient has been treated with somatropin for more than 12 months, and growth velocity (adjusted for bone age/pubertal status if appropriate) is  $<$  the 50th percentile for children with Prader-Willi syndrome; and
- 2. Either;
  - 2.1 The patient's bone age is  $\leq 14$  years (female patients) or  $\leq 16$  years (male patients); or
  - 2.2 both
    - 2.2.1 The patient's growth velocity is at least 2 cm per year as calculated over six months; and
    - 2.2.2 The patient's BMI has increased by less than 0.5 standard deviations in the last 12 months.



**Initial application (adults and adolescents)** from a paediatrician or endocrinologist. Approvals valid for 9 months for applications meeting the following criteria:

All of the following:

1. The patient has a medical condition that is known to cause growth hormone deficiency (e.g. surgical removal of the pituitary for treatment of a pituitary tumour); and
2. The patient has undergone appropriate treatment of other hormonal deficiencies and psychological illnesses; and
3. The patient has severe growth hormone deficiency (see notes); and
4. The patient's serum IGF-1 is more than 1 standard deviation below the mean for age and sex; and
5. The patient has poor quality of life, as defined by a score of 16 or more using the disease-specific quality of life questionnaire for adult growth hormone deficiency (QoL-AGHDA).

Notes:

- For the purposes of adults and adolescents, severe growth hormone deficiency is defined as a peak serum growth hormone level of  $\leq 3$  mcg per litre during an adequately performed insulin tolerance test (ITT) or glucagon stimulation test.
- Patients with one or more additional anterior pituitary hormone deficiencies and a known structural pituitary lesion only require one test. Patients with isolated growth hormone deficiency require two growth hormone stimulation tests, of which, one should be ITT unless otherwise contraindicated. Where an additional test is required, an arginine provocation test can be used with a peak serum growth hormone level of  $\leq 0.4$  mcg per litre.
- The dose of somatropin should be started at 0.2 mg daily and be titrated by 0.1 mg monthly until it is within 1 standard deviation of the mean normal value for age and sex; and
- Dose of somatropin not to exceed 0.7 mg per day for male patients, or 1 mg per day for female patients.
- At the commencement of treatment patients with hypo-pituitary disorders must be monitored for any required adjustment in replacement doses of corticosteroid and levothyroxine.

**Renewal application (adults and adolescents)** from a paediatrician or endocrinologist. Approvals valid for 12 months for applications meeting the following criteria:

Either:

1. All of the following:
  - 1.1 The patient has been treated with somatropin for  $< 12$  months; and
  - 1.2 There has been an reduction of at least 8 points on the Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) score from baseline; and
  - 1.3 Serum IGF-I levels have been maintained within  $\pm 1$ SD of the mean of the normal range for age and sex; and
  - 1.4 The dose of somatropin does not to exceed 0.7 mg per day for male patients, or 1 mg per day for female patients; or
2. All of the following:
  - 2.1 The patient has been treated with somatropin for more than 12 months; and
  - 2.2 The patient has not had a 6 point or greater increase from their lowest QoL-AGHDA score on treatment (other than due to obvious external factors such as external stressors); and
  - 2.3 Serum IGF-I levels have been maintained within  $\pm 1$ SD of the mean of the normal range for age and sex (other than for obvious external factors); and
  - 2.4 The dose of somatropin does not exceed 0.7 mg per day for male patients or 1 mg per day for female patients.