

# Analysis of somatropin for growth hormone therapy

## Drug utilisation sub-committee (DUSC)

*June 2021*

### **Abstract**

#### ***Purpose***

To analyse the utilisation of growth hormone, somatropin as requested by DUSC at its February 2021 meeting.

#### ***Date of listing on the Pharmaceutical Benefits Scheme (PBS)***

Somatropin was listed on the standard PBS Program on 1 September 2015.

#### ***Data Source / methodology***

Data extracted from the PBS and Authorities database maintained by Department of Health, processed by Services Australia was used for analyses.

#### ***Key Findings***

- There was an average of 2,087 patients treated with somatropin each year. Following restriction changes in 2019 and 2020, this increased to an average of 2,948 patients treated with somatropin each year.
- There was an average of 6,170 somatropin prescriptions dispensed each year. Following restriction changes in 2019 and 2020, this increased to an average of 10,517 prescriptions dispensed each year.
- The most common age group in patients beginning somatropin treatment are those aged between 10-14 years old with 53.2% of initiating patients being male.
- When accounting for treatment breaks, the median treatment duration was 44.6 months (95% confidence interval 42.1 to 46.9 months).
- Paediatric patients were most commonly treated with somatropin for short stature and slow growth whilst adult patients were most commonly treated with somatropin for severe growth hormone deficiency.

## Purpose of analysis

At its February 2021 meeting, DUSC requested a review of the utilisation of growth hormone (somatropin) considering the following main changes to its listing:

- February 2019 to broaden the eligibility criteria for paediatric patients with amendments to the percentile and growth velocity eligibility thresholds, growth velocity measurement intervals and associated growth data requirements; and
- January 2020 amendments to the adult listing in relation to continued access for patients with childhood onset growth hormone deficiency when they reach adulthood.

## Background

### Clinical situation

Growth hormone (GH) is produced by the pituitary gland. GH encourages the liver to synthesise insulin-like growth factor 1 (IGF-1). IGF-1 acts downstream to thicken and elongate bones, grow muscles and reduce fat storage.<sup>1,2,3,4</sup>

Growth hormone deficiency occurs when the pituitary gland does not produce enough growth hormone. Growth hormone deficiency can occur in both children and adults. In some adults, growth hormone deficiency is diagnosed in childhood and is referred to as childhood-onset growth hormone deficiency. In other adults, growth hormone deficiency starts in adulthood and is referred to as adult-onset growth hormone deficiency.<sup>5</sup>

Child-onset growth hormone deficiency can be due to:

- Genetic abnormalities resulting in the inability to produce or respond to growth hormone.
- Abnormal development of the pituitary gland.
- Structural defects of the brain or skull present since birth.

Adult-onset growth hormone deficiency can be due to:

- Pituitary tumours.
- Hypothalamic tumours.
- Damage to the pituitary or hypothalamus following surgery or radiotherapy.

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<sup>1</sup> Ohlsson C, Bengtsson B, Isaksson O.G.P, Andreassen T.T, Słotweg M.C. Growth Hormone and Bone. Endocrine Reviews 1998, 1: 55-79.

<sup>2</sup> Florini J.R, Ewton D.Z, Coolican S.A, Growth hormone and the insulin-like growth factor system in myogenesis. Endocrine Reviews, 1996. 1: 481:517.

<sup>3</sup> Feld S, Hirschberg R. Growth Hormone, the Insulin-Like Growth Factor System, and the Kidney. Endocrine Reviews, 1996. 5: 423-480.

<sup>4</sup> Australian Government Department of Health Therapeutic Goods Administration. Too much of a good thing: the health risks of human growth hormone, 2019. <<https://www.tga.gov.au/blogs/tga-topics/too-much-good-thing-health-risks-human-growth-hormone>>

<sup>5</sup> Hormones Australia- Endocrine Society of Australia. GH Deficiency Fact Sheet, 2009. <<https://www.hormones-australia.org.au/wp-content/uploads/2019/10/Fact-Sheet-GH-Deficiency-20191031.pdf>>

- Brain injury.
- Brain haemorrhage.
- Infections in the brain or nervous system.

Additionally, growth hormone deficiency is associated with several conditions,<sup>6</sup> including:

- Turner syndrome: occurs in females where all or part of one X chromosome is missing.<sup>7</sup>
- Chronic renal disease: Up to one third of children with chronic kidney disease have severe growth delay (below the third percentile for height).<sup>8</sup>
- Prader-Willi syndrome: a complex genetic disorder affecting multiple body systems resulting in hypotonia, hypogonadism and growth hormone insufficiency.<sup>9</sup>
- Small for gestational age (SGA): children who are born with a birth weight or length of at least 2 SD score (SDS) below the mean gestational age.

Prior to 1 September 2015, growth hormone was provided under a special arrangement (subsection 100(1) of the *National Health Act 1953*). The PBS S100 Growth Hormone Program was administered by the Commonwealth Department of Health with guidance from the Growth Hormone Advisory Committee (GHAC). The GHAC comprised of a panel of paediatric endocrinologists and paediatricians who provided clinical advice on specific cases referred to by the Department. Cases referred to the GHAC included instances where the patient did not meet all of the eligibility criteria in the program guidelines.

New GH Program arrangements commenced on 1 September 2015 to align the Program with other Authority-Required PBS subsidised medicines, with the aim of reducing administrative burden and improving access. The GHAC had ceased operation and somatropin was listed as an Authority Required medicine. Pharmacies could directly order from pharmaceutical wholesalers, and pharmacy remuneration, co-payments and safety net provisions were introduced, consistent with usual PBS arrangements.

## Pharmacology

Somatropin is a biosynthetic human growth hormone. It is manufactured using recombinant DNA technology. Somatropin performs the same functions as human growth hormone produced in the human body.

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<sup>6</sup> Ayyar V.S. History of growth hormone therapy. *Indian Journal of Endocrinology and Metabolism* 2011. 15(3): s162-165. doi: [10.4103/2230-8210.84852](https://doi.org/10.4103/2230-8210.84852)

<sup>7</sup> Ross J.L, Long L.M, Loriaux L, Cutler Jr G.B. Growth hormone secretory dynamics in Turner syndrome. *The Journal of Pediatrics* 1985. 106 (2): 202-206 [https://doi.org/10.1016/S0022-3476\(85\)80287-0](https://doi.org/10.1016/S0022-3476(85)80287-0)

<sup>8</sup> Gupta V, Lee M. Growth hormone in chronic renal disease. *Indian Journal of Endocrinology and Metabolism* 2012. 16(2): 195-203. doi: [10.4103/2230-8210.93736](https://doi.org/10.4103/2230-8210.93736)

<sup>9</sup> Cassidy S.B, Driscoll D.J. Prader-Willi syndrome. *European Journal of Human Genetics* 2009. 17: 3-13. <https://doi.org/10.1038/ejhg.2008.165>

## Therapeutic Goods Administration (TGA) approved indications

Somatropin is indicated for:

- Long term treatment of children with growth failure due to inadequate endogenous growth hormone secretion.
- Adults with severe growth hormone deficiency as diagnosed in the insulin tolerance test for growth hormone deficiency and defined by peak GH concentrations of less than 2.5 nanogram/mL.
- Treatment of growth disturbances associated with gonadal dysgenesis (Turner's syndrome).
- Treatment of prepubertal children with growth failure associated with chronic renal insufficiency up to the time of renal transplantation.
- Improvement of body composition and treatment of short stature associated with Prader-Willi syndrome (PWS) in paediatric patients (Genotropin, Pfizer Australia Pty Ltd).
- Growth failure in children born small of gestational age (SGA) who fail to demonstrate catch-up growth by age two to four years (Humatrope, Eli Lilly Australia Pty Ltd).

## Dosage and administration

The recommended dosage of somatropin is individualised and is dependent on the patient's weight or body surface area and adjusted in accordance with therapy response. Somatropin is administered by a subcutaneous injection. The injection site should be rotated to minimise the risk of lipoatrophy. It is administered daily, preferably in the evening, to mimic the body's natural pattern of hormone secretion.<sup>10</sup> Weekly doses are divided into administration 6-7 days per week.

The prescriber is required to calculate each patient's weekly dose and the number of cartridges required for the treatment phase based on the product information for information on indication, usage, dosage and administration. A [Paediatric Dose and Cartridge Quantity Calculator](#) is recommended for use.

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<sup>10</sup> Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2021.

**Table 1: Dosage and administration of somatropin according to indication and brand**

	Paediatric indications					Adult indication
	Growth hormone deficiency	Turner syndrome	Chronic renal disease	Small gestational disease	Prader Willi Syndrome	Growth hormone deficiency
Genotropin <sup>11</sup> Pfizer Australia Pty Ltd	0.175 mg to 0.245 mg/kg/week	0.3 mg to 0.35 mg/kg/week	0.3 mg to 0.35 mg/kg/week		0.245 mg to 0.35 mg/kg/week	0.04 mg to 0.08 mg/kg/week
Humatrope <sup>12</sup> Eli Lilly Australia Pty Ltd	0.177 mg to 0.255 mg/kg/week	0.024 mg to 0.054 mg/kg/day	0.045 mg to 0.05 mg/kg/day	0.033 mg to 0.067 mg/kg/day		0.2 mg/day
Norditropin <sup>13</sup> Novo Nordisk Pharmaceuticals Pty Ltd	0.025 mg to 0.035 mg/kg/day OR 0.7 mg to 1.0 mg/m <sup>2</sup> /day	0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> /day	0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> /day	0.033 to 0.067 mg/kg/day OR 1 mg to 2 mg/m <sup>2</sup> /day		0.15 mg to 0.3 mg/day
Nutritropin <sup>14</sup> Ipsen Pty Ltd	0.025 mg to 0.035 mg/kg/day	Up to 0.05 mg/kg/day	Up to 0.05 mg/kg/day			Initially 0.15 mg to 0.3 mg/day. Adjusted stepwise to max of 1.0 mg/day
Omnitrope <sup>15</sup> Sandoz Pty Ltd	0.025 mg to 0.035 mg/kg/day OR 0.7 to 1.0 mg/m <sup>2</sup> body surface area/day	0.045 mg to 0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> body surface area/day	0.045 mg to 0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> body surface area/day			
Saizen <sup>16</sup> Merck Healthcare Pty Ltd	0.2 mg/kg/week	0.045 mg to 0.05 mg/kg/day	0.045 mg to 0.05 mg/kg/day			0.15 to 0.3 mg/day

<sup>11</sup> Genotropin. Australian Approved Product Information. Sydney: Pfizer Australia Pty Ltd. Approved 2 December 1991, updated 26 February 2020. Available from < <https://www.tga.gov.au/product-information-pi>.>

<sup>12</sup> Humatrope. Australian Approved Product Information. West Ryde: Eli Lilly Australia Pty. Limited. Approved 24 October 1995, updated 9 January 2019. Available from < <https://www.tga.gov.au/product-information-pi>.>

<sup>13</sup> Norditropin. Australian Approved Product Information. Baulkham Hills: Novo Nordisk Pharmaceuticals Pty. Ltd. Approved 17 January 2001 (Norditropin SimpleXx 5 mg, 10 mg, 15 mg presentations), 19 May 2004 (Norditropin NordiFlex 5 mg, 10 mg, 15 mg presentations), 9 May 2011 (Norditropin FlexPro 5 mg, 10 mg, 15 mg presentations), updated 26 August 2020. Available from < <https://www.tga.gov.au/product-information-pi>.>

<sup>14</sup> Nutritropin. Australian Approved Product Information. Glen Waverley: Ipsen Pty Ltd. Approved 10 July 2006, updated 23 April 2019. Available from < <https://www.tga.gov.au/product-information-pi>.>

<sup>15</sup> Omnitrope. Australian Approved Product Information. Macquarie Park: Sandoz Pty Ltd. Approved 11 October 2004 (1.33 mg p.f.i., 5 mg/1.5 mL s.f.i., 10 mg/1.5 mL s.f.i.), 16 December 2013 (15 mg/1.5 mL s.f.i.), 28 October 2014 (5 mg/1.5 mL s.f.i., 10 mg/1.5 mL s.f.u. with pre-assembled cartridge holder), updated 9 June 2020. Available from < <https://www.tga.gov.au/product-information-pi>.>

<sup>16</sup> Saizen. Australian Approved Product Information. Macquarie Park: Merck Healthcare Pty Ltd. Approved 22 August 2011, updated 10 October 2019. Available from < <https://www.tga.gov.au/product-information-pi>.>

	Paediatric indications					Adult indication
	Growth hormone deficiency	Turner syndrome	Chronic renal disease	Small gestational disease	Prader Willi Syndrome	Growth hormone deficiency
SciTropinA <sup>17</sup> SciGen (Australia) Pty Ltd	0.025 mg to 0.035 mg/kg/day OR 0.7 mg to 1.0 mg/m <sup>2</sup> body surface area per day	0.045 mg to 0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> body surface area/day	0.045 mg to 0.05 mg/kg/day OR 1.4 mg/m <sup>2</sup> body surface area/day			

Further details regarding dose and administration can be found in the Appendix A.

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from [the TGA \(Product Information\)](#) and [the TGA \(Consumer Medicines Information\)](#).

### PBS listing details (as at April 2021)

Somatropin is an Authority Required medicine. It is listed under Section 100 Growth Hormone Program on the PBS.

### ***Restriction (abridged)***

Indications:

- Short stature and slow growth
- Short stature associated with biochemical growth hormone deficiency
- Growth retardation secondary to an intracranial lesion, or cranial irradiation
- Risk of hypoglycaemia secondary to growth hormone deficiency in neonates/infants
- Biochemical growth hormone deficiency and precocious puberty
- Hypothalamic-pituitary disease secondary to a structural lesion, with hypothalamic obesity driven growth
- Short stature associated with Turner syndrome
- Short stature due to short stature homeobox (SHOX) gene disorders
- Short stature associated with chronic renal insufficiency

Treatment phases:

- Initial treatment
- Continuing treatment
- Continuing treatment as a reclassified patient

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<sup>17</sup> SciTropinA. Australian Approved Product Information. Billinudgel: SciGen (Australia) Pty Ltd. Approved 8 September, updated 21 October 2020. Available from < <https://www.tga.gov.au/product-information-pi>.>

- Recommencement of treatment
- Recommencement of treatment as a reclassified patient

For the indication severe growth hormone deficiency, the treatment phases are:

- Initial treatment of adult onset growth hormone deficiency
- Initial treatment of childhood onset growth hormone deficiency in a patient who has received PBS-subsidised treatment as a child
- Initial treatment of childhood onset growth hormone deficiency in a patient who has received non-PBS subsidised treatment as a child
- Continuing treatment in a person with a mature skeleton or aged 18 years or older

The prescriber is required to calculate each patient's weekly dose and the number of cartridges required for the treatment phase based on the product information for information on indication, usage, dosage and administration. A [Paediatric Dose and Cartridge Quantity Calculator](#) is recommended for use.

## **Adults**

An adult is defined as a person who:

- Is 18 years of age or older and has adult onset growth hormone deficiency; or
- Has a mature skeleton; or
- Has a diagnosis of Prader-Willi syndrome and is aged 18 years or older.

Initial treatment must be prescribed by an endocrinologist. Continuing treatment must be prescribed by an endocrinologist or in consultation with an endocrinologist.

Provocation tests required to support an authority application:

- Current or historical evidence of an insulin tolerance test with maximum serum growth hormone (GH) less than 2.5 micrograms per litre; or
- Current or historical evidence of an arginine infusion test with maximum serum GH less than 0.4 micrograms per litre; or
- Current or historical evidence of a glucagon provocation test maximum serum GH less than 3 micrograms per litre.

Childhood onset growth hormone deficiency (CO-GHD) patients due to a congenital, genetic or structural cause who have previously received PBS-subsidised therapy as children are no longer required to provide provocation tests to meet the eligibility criteria for adult use somatropin as evidence of growth hormone deficiency was provided in childhood.

## **Children**

A child means a person who:

- Is not an adult; or
- Has a diagnosis of Prader-Willi syndrome and is less than 18 years of age.

Treatment must be prescribed by a specialist or consultant physician in paediatric endocrinology or a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology.

Full restriction details (clinical and treatment criteria) can be found on the [Section 100 Growth Hormone Program](#) on the [PBS website](#).



**Table 2: PBS listing of somatropin as at April 2021**

Item	Name, form & strength, pack size	Max. quant.	Rpts	DPMQ	Brand name and manufacturer
10902T 10891F 10908D	Somatropin 400 microgram injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$128.82	Genotropin Mini Quick Pfizer Australia Pty Ltd
9628R 10456H 10477K	Somatropin 600 microgram injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$189.37	
6313G 10479M 10463Q	Somatropin 800 microgram injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$249.90	
6314H 10480N 10430Y	Somatropin 1 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$310.44	
6315J 10453E 10457J	Somatropin 1.2 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$370.98	
6316K 10488B 10434E	Somatropin 1.4 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$431.52	
6317L 10454F 10498M	Somatropin 1.6 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$492.07	
6318M 10500P 10501Q	Somatropin 1.8 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$552.61	
6319N 10428W 10472E	Somatropin 2 mg injection [1 chamber] (&) inert substance diluent [0.25 mL chamber], 7 dual chamber syringes	7	1	\$613.14	

11895C* 5818F 10432C 10467X	Somatropin 5 mg/1.5 mL injection, 1.5 mL cartridge	1* 1	5* 1	\$217.25* \$217.25	Norditropin FlexPro Novo Nordisk Pharmaceuticals Pty Ltd
6476W 10427T 10484T 10518N 10507B 10512G		1	1	\$223.96	SciTropinA SciGen(Australia) Pty Limited Omnitrope Surepal 5 Sandoz Pty Ltd
6311E 10441M 10481P 5819G 10451C 10496K 10514J 10506Y 10519P	Somatropin 10 mg/1.5 mL injection, 1.5 mL cartridge	1	1	\$440.17	SciTropinA SciGen(Australia) Pty Limited Norditropin FlexPro Novo Nordisk Pharmaceuticals Pty Ltd Omnitrope Surepal 10 Sandoz Pty Ltd
5820H 10449Y 10489C 10446T 10490D 10485W	Somatropin 15 mg/1.5 mL injection, 1.5 mL cartridge	1	1	\$656.39	Norditropin FlexPro Novo Nordisk Pharmaceuticals Pty Ltd Omnitrope Surepal 15 Sandoz Pty Ltd
5822K 10462P 10458K	Somatropin 6 mg/1.03 mL injection, 1.03 mL cartridge	1	1	\$276.20	Saizen Merck Healthcare Pty Ltd
5824M 10483R 10495J	Somatropin 12 mg/1.5 mL injection, 1.5 mL cartridge	1	1	\$526.66	
3388H 10497L 10442N	Somatropin 20 mg/2.5 mL injection, 2.5 mL cartridge	1	1	\$872.60	
11650E* 9604L 10478L 10438J	Somatropin 10 mg/2 mL injection, 2 mL cartridge	1* 1	5* 1	\$426.76* \$426.76	Nutritropin Aq Ispen Pty Ltd

11493X* 9585L 10443P 10435F	Somatropin (recombinant human growth hormone) powder for injection 5 mg (15 i.u.) with diluent in pre-filled pen (with preservative), 1	1* 1	5* 1	\$217.25* \$217.25	Genotropin GoQuick Pfizer Australia Pty Ltd
11495B* 9586M 10431B 10426R	Somatropin (recombinant human growth hormone) powder for injection 12 mg (36 i.u.) with diluent in pre-filled pen (with preservative), 1	1* 1	5* 1	\$510.55* \$510.55	
6266T 10452D 10447W	Somatropin 4 mg injection [1 vial] (& inert substance diluent [1 vial], 1 pack	1	1	\$180.71	Zomacton Ferring Pharmaceuticals Pty Limited
6169Q 10482Q 10429X	Somatropin 6 mg injection [1 cartridge] (& inert substance diluent [3.15 mL syringe], 1 pack	1	1	\$267.20	Humatrope Eli Lilly Australia Pty Ltd
6170R 10487Y 10461N	Somatropin 12 mg injection [1 cartridge] (& inert substance diluent [3.15 mL syringe], 1 pack	1	1	\$526.66	
6345Y 10476J 10502R	Somatropin 24 mg injection [1 cartridge] (& inert substance diluent [3.15 mL syringe], 1 pack	1	1	\$1045.58	

Source: the [PBS website](https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2011-07/pbac-psd-somatropin-july11).

\*Item for adult onset growth hormone deficiency.

### ***Date of listing on PBS***

Somatropin has been subsidised through the PBS under Section 100 Human Growth Hormone Program, in accordance with the “Guidelines for the Availability of Human Growth Hormone (HGH) as a Pharmaceutical Benefit” since 1 August 1993<sup>18</sup>. The program was administered by the Commonwealth Department of Health with guidance from the GHAC. The somatropin listing was changed to align the program with other Authority Required listed medicines on 1 September 2015.

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<sup>18</sup> Public Summary Document, somatropin, July 2011. Accessed at: <https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2011-07/pbac-psd-somatropin-july11>

### ***Changes to listing***

**1 July 2009:** Listing was extended to include improvement of body composition and short stature associated with Prader-Willi Syndrome (PWS) in patients up to 18 years of age.

**1 September 2015:** The listing for somatropin was changed from Restricted to Authority Required to align with other Authority Required medicines. The number of repeats was increased from 0 to 1.

**1 December 2018:** Listing was extended to include treatment of adults with severe growth hormone deficiency. The PBAC recommended the extension of listing at its July 2017 Meeting.

**1 February 2019:** Changes in eligibility restrictions for paediatric growth hormone treatment, relating to:

- Revised height percentile thresholds;
- Growth velocity percentile for bone age and sex;
- Clarification of definitions within the restrictions; and
- Streamlining the way associated growth data requirements are specified within the prescriber instructions.

For further details refer to [PBS Growth Hormone Program \(Paediatric Use\) 1 February 2019 Listing Changes Quick Reference Guide for Prescribers](#).

**1 September 2019:** The Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) was removed. The PBAC recommended its removal at its March 2019 PBAC meeting due to accessibility issues, noting not all endocrinologists in Australia have access to the questionnaire given it is privately owned. The PBAC considered there was uncertainty around the validity and reliability of the questionnaire given it comprises a set of self-administered binary questions.

For further details refer to the [Public Summary Document](#) from the March 2019 PBAC meeting.

**1 January 2020:** The PBAC ratified restriction changes to the adult listing of somatropin to provide additional clarity and improved access to patients with childhood onset growth hormone deficiency (CO-GHD) due to congenital, genetic or structural cause at its August 2019 PBAC Meeting. The changes allow patients with CO-GHD due to congenital, genetic or structural cause to be eligible for adult use somatropin, if they meet the PBS restriction criteria, once they no longer meet the PBS restriction criteria for paediatric growth hormone treatment.

- The majority of patients CO-GHD due to congenital, genetic or structural cause are eligible to access somatropin as adults once skeletal maturity is reached, rather than the age of 18 years.
- Patients with Prader-Willi syndrome, are eligible for adult use somatropin at the age of 18 years.

- CO-GHD patients due to a congenital, genetic or structural cause who have previously received PBS-subsidised therapy as children are no longer required to provide provocation tests to meet the eligibility criteria for adult use somatropin.

For further details refer to [Frequently Asked Questions PBS Growth Hormone Program](#).

Current PBS listing details are available from the [PBS website](#).

**Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)**

Committee-in-confidence

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

End committee-in-confidence

**Table 3: Summary of somatropin submissions to the PBAC**

PBAC meeting	PBAC outcome
November 2006	<p>Somatropin, powder for injection and diluent, 5 mg per mL, 12 mg per mL (with preservative), powder for injection and diluent (single dose syringes) in strengths from 0.8 mg – 2 mg per 0.25 mL, Genotropin® and Genotropin MiniQuick® Pfizer Australia Pty Ltd</p> <p>The resubmission sought an extension to the Section 100 human growth hormone program “Guidelines for the Availability of human Growth Hormone (hGH) as a Pharmaceutical Benefit” to allow treatment for the improvement of body composition and short stature associated with Prader-Willi Syndrome (PWS) in paediatric patients. Overall, whilst the PBAC was sympathetic to this small patient group and acknowledged that some patients with PWS were receiving PBS subsidy for somatropin based on auxological criteria under the current Growth Hormone Program, it did not recommend the requested extension to the listing as the long-term benefit of treatment was highly uncertain resulting in uncertain cost effectiveness.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the November 2006 PBAC meeting.</p>
March 2008	<p>Somatropin, powder for injection and diluent (cartridge), 5 mg per mL, 12 mg per mL (with preservative), powder for injection and diluent (single dose syringes) in strengths from 0.6 mg – 2 mg per 0.25 mL, Genotropin® and Genotropin MiniQuick® Pfizer Australia Pty Ltd</p> <p>The PBAC recommended amending the listing of somatropin on the PBS under the Section 100 Human Growth Hormone Program to include improvement of body composition and short stature associated with Prader-Willi Syndrome (PWS) in patients up to 18 years of age on the basis of high but acceptable cost-effectiveness compared with placebo.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the March 2008 PBAC meeting.</p>
July 2011	<p>Somatropin (Recombinant human growth hormone), injection, 5 mg (15 i.u.) and 12 mg (36 i.u.) in 1 mL cartridge (with preservative), Genotropin®; powder for injection, 5 mg (15 i.u.) and 12 mg (36 i.u.) with diluent in pre-filled pen (with preservative), Genotropin GoQuick®; injection, 0.6 mg (1.8 i.u.), 0.8 mg (2.4 i.u.), 1 mg (3 i.u.), 1.2 mg (3.6 i.u.), 1.4 mg (4.2 i.u.), 1.6 mg (4.8 i.u.), 1.8 mg (5.4 i.u.), and 2 mg (6 i.u.) with diluent in single use syringe (without preservative), Genotropin MiniQuick® Pfizer Australia Pty Ltd</p> <p>The submission requested an extension of the current Section 100 (Human Growth Hormone Program) listing to include treatment of severe adult growth hormone deficiency (AGHD). The PBAC did not recommend to change the listing on the basis of uncertain clinical benefit and highly uncertain cost effectiveness.</p>

PBAC meeting	PBAC outcome
	For further details refer to the <a href="#">Public Summary Document</a> from the July 2011 PBAC meeting
March 2016	<p>SOMATROPIN 0.4 mg (1.2 IU) with diluent in single use syringe, Genotropin® MiniQuick, Pfizer Australia Pty Ltd.</p> <p>The minor submission requested the listing of lower strength of somatropin (Genotropin MiniQuick 0.4 mg (1.2 IU) injection) in the Section 100 (Growth Hormone Programme) on the PBS. The currently listed strengths are 1.8 IU (600 micrograms) and 2.4 IU (800 micrograms). The PBAC recommended listing of the 0.4 mg strength of somatropin under the same circumstances to be consistent with the currently listed strengths of somatropin.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the March 2016 PBAC meeting.</p>
November 2016	<p>Solution for injection 6 mg (18 i.u.) in 1.03 mL cartridge (with preservative), Solution for injection 12 mg (36 i.u.) in 1.5 mL cartridge (with preservative), Solution for injection 20 mg (60 i.u.) in 2.5 mL cartridge (with preservative), Saizen®, Merck Serono Australia Pty Ltd.</p> <p>The PBAC recommended the listing of Saizen® to include an Authority Required listing for the treatment of 'short stature associated with chronic renal insufficiency (CRI)', consistent with the currently listed brands of somatropin, on the basis that it should be available only under special arrangements under Section 100 Human Growth Hormone Program, at an equivalent price per milligram as other brands of somatropin.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the November 2016 PBAC meeting.</p>
November 2016	<p>Multiple forms and strengths, Multiple brands, Endocrine Society of Australia, Australian Paediatric Endocrine Group</p> <p>The resubmission requested a Section 100 (PBS Growth Hormone Program) listing for somatropin for treatment of adults with severe growth hormone deficiency (GHD) and substantially impaired quality of life (QoL) at baseline. This resubmission was based on the submission in July 2011. The first submission was reviewed and rejected in December 2001 (Eli Lilly Australia Pty Ltd). The second resubmission in July 2011 (Pfizer Australia Pty Ltd) was not recommended on the basis of uncertain clinical benefit and highly uncertain cost-effectiveness (paragraph 12, somatropin Public Summary Document (PSD), July 2011).</p> <p>The PBAC decided to defer making its decision on whether to list somatropin on the PBS for the treatment of adults with severe growth hormone deficiency (GHD) and substantially impaired quality of life (QoL) at baseline. In making this decision, the PBAC was of the view that although there was a place for this drug in therapy for adults with severe GHD, the clinical benefit in terms of QoL was uncertain and the magnitude was likely overestimated, and consequently the PBAC was uncertain as to the cost effectiveness of the drug for this indication. The PBAC deferred its decision to seek further comparative analysis on the</p>



PBAC meeting	PBAC outcome
	<p>range of clinical benefits provided by somatropin, to clarify the proposed PBS restriction, and to allow the Department to discuss appropriate pricing in this setting with sponsors of somatropin products registered for use in adults.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the November 2016 PBAC meeting.</p>
July 2017	<p>SOMATROPIN multiple forms and strengths, multiple brands, Endocrine Society of Australia and Australian Paediatric Endocrine Group</p> <p>The minor resubmission requested a Section 100 (Growth Hormone) Authority Required listing for the treatment of adults with severe growth hormone deficiency (GHD) and substantially impaired quality of life (QoL) at baseline. The PBAC recommended the listing of somatropin for the treatment of adults with severe GHD, and substantially impaired QoL at baseline, on the basis that it should be available only under special arrangements under Section 100 (Growth Hormone Program). The PBAC was satisfied that somatropin provided, for some patients, a significant improvement in efficacy over standard care.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the July 2017 PBAC meeting.</p>
July 2018	<p>Solution for injection 5 mg (15 i.u.) in 1.5 mL cartridge (with preservative), SciTropin A™, SciGen (Australia) Pty Ltd</p> <p>The PBAC recommended the re-listing of 5 mg (15 i.u.) in 1.5 mL form of somatropin under the SciTropin A brand in the Section 100 Growth Hormone Programme under the same conditions under the same conditions for which the Omnitrope® brand was listed. The PBAC noted that this brand of somatropin sought the same listing as the previously listed product, Omnitrope®, which was removed from the PBS on 1 September 2017, and is now re-marketed by SciGen (Australia) Pty Ltd under a new brand name, SciTropin A.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the July 2018 PBAC meeting.</p>
March 2019	<p>SOMATROPIN,  Powder for injection 5 mg (15 i.u.) with diluent in pre-filled pen (with preservative)  Powder for injection 12 mg (36 i.u.) with diluent in pre-filled pen (with preservative)  Genotropin GoQuick®, Pfizer Australia Pty Ltd  Solution for injection 10 mg (30 i.u.) in 2 mL cartridge (with preservative)  NutropinAq®, Ipsen Pty Ltd</p> <p>The PBAC recommended the removal of the requirement for prescribers to use the Quality of Life in Adult Growth Hormone Deficiency Assessment (QoL-AGHDA) questionnaire from the current somatropin restrictions for the treatment of adults with severe growth hormone deficiency due to issues with accessibility and the uncertain validity and reliability of the questionnaire.</p>

PBAC meeting	PBAC outcome
	For further details refer to the <a href="#">Public Summary Document</a> from the March 2019 PBAC meeting.
August 2019	<p>SOMATROPIN All forms and strengths, All brands, Endocrine Society of Australia and Australian Paediatric Endocrine Group</p> <p>The PBAC ratified amendments to eligibility criteria for the Section 100 (Growth Hormone) Authority Required listing of adult use somatropin arising from Endocrine Society of Australia (ESA) feedback following the July 2019 PBAC meeting regarding clarification of PBAC intent around Childhood Onset Growth Hormone Deficiency (CO-GHD) patients transitioning to the adult growth hormone (GH) program. The adult-use somatropin restrictions were amended for CO-GHD patients with a congenital, genetic or structural cause to commence from when this cohort reaches skeletal maturity rather than the chronological age of 18 years. The PBAC noted that this would remove the potential of a lapse in PBS funded access for patients after reaching skeletal maturity until the age of 18 years.</p> <p>For further details refer to the <a href="#">Public Summary Document</a> from the August 2019 PBAC meeting.</p>

## Methods

Data extracted from the PBS claims database maintained by the Department of Health and processed by Services Australia was used for the analyses. Prescription data was extracted from 1 September 2015, where changes were made to the Growth Hormone Programme to align with the rest of the PBS, up to and including 31 December 2020. Data was extracted on 19 April 2021 based on the date of supply.

The PBS data was used to determine the number of incident and prevalent patients, number of prescriptions supplied and to analyse patient demographics such as age, gender and prescriber type. Initiating and prevalent patients were counted by quarter of supply. An initiating patient was defined based on their first date of supply of somatropin.

The treatment duration of somatropin was ascertained and median supply days for somatropin were calculated. A Kaplan-Meier curve was generated to examine the treatment duration, and patients that were identified as still continuing treatment at the analysis end date were censored. Initiating patients were selected from 1 September 2015 and were followed until 31 December 2020.

Another Kaplan-Meier curve was generated accounting for breaks in treatment. A patient was considered to be on a treatment break if they did not receive a supply in more than two sets of standard treatment days. The median standard treatment days was calculated to be 97 days. Typically, patients are considered to be on a break in therapy if they missed more than three sets of standard treatment days. However, as a growth hormone treatment, it was assumed that patients taking somatropin would be more closely managed by their prescribers, increasing treatment adherence and reducing the likelihood for breaks.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Department of Human Services (DHS) Medicare date of processing data.<sup>19</sup> The publicly available DHS Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included. The DHS Medicare data used in this report includes under co-payment prescriptions from 1 April 2012.

Additional data was extracted from the Authorities database maintained by Department of Health and processed by Services Australia. Processed authorities data was extracted from 1 September 2015 up to and including 30 December 2020. Data was extracted on 19 April 2021. Authority applications according to indication were analysed.

Data manipulation was undertaken using SAS.

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<sup>19</sup> PBS statistics. Australian Government Department of Human Services Medicare. Canberra. Available from <<http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>>.

## Results

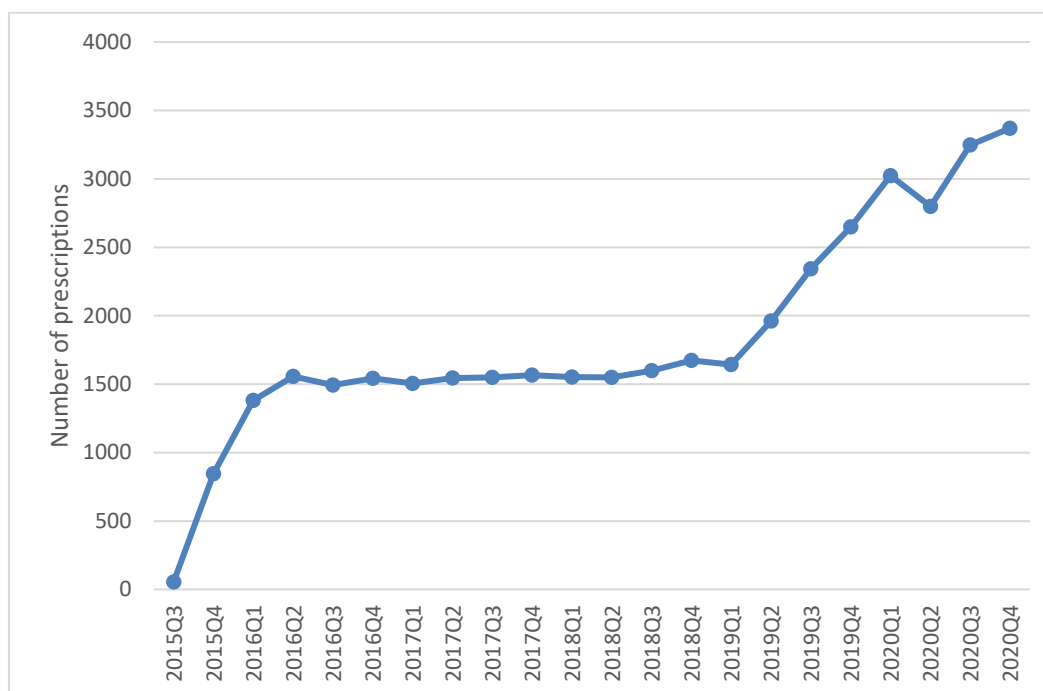
### Analysis of drug utilisation

#### Overall utilisation

**Table 4: Somatropin utilisation according to year**

	2016	2017	2018	2019	2020
Incident patients	1,231	345	391	851	730
Prevalent patients	2,011	2,076	2,174	2,717	3,178
Prescriptions	5,973	6,163	6,373	8,595	12,439
Expenditure <sup>1</sup>	\$24,384,835	\$25,991,412	\$27,588,536	\$29,889,145	\$33,568,012

Note: <sup>1</sup>Based on the published prices.



**Figure 1: Number of somatropin prescriptions supplied according to supply quarter**

Note: Quarter 3 of 2015 only includes the month of September.

In Figure 1, the number of prescriptions dispensed averaged approximately 1,540 prescriptions per supply quarter from quarter 3 of 2015 to quarter 4 of 2018. The number of prescriptions supplied appeared to stabilise between quarter 1 2016 to quarter 4 2018. However, from the quarter 1 of 2019, the number of prescriptions have increased with the highest, 3,370 prescriptions being supplied in the fourth quarter of 2020.

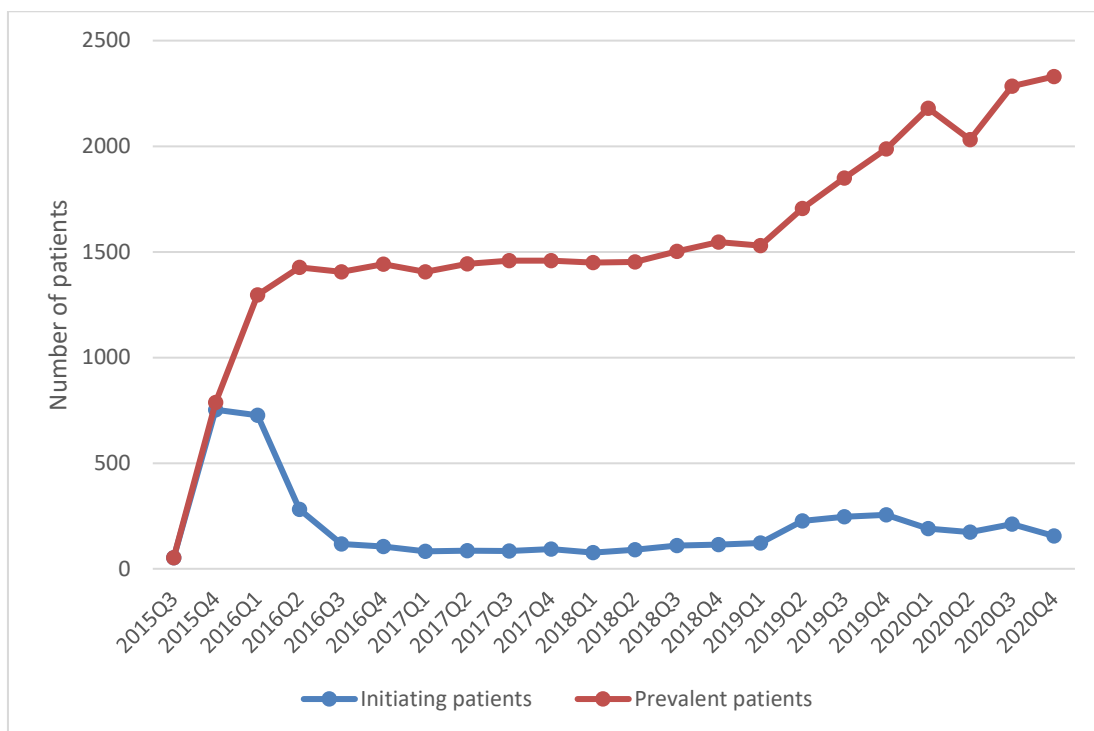
Committee-in-confidence

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End committee-in-confidence

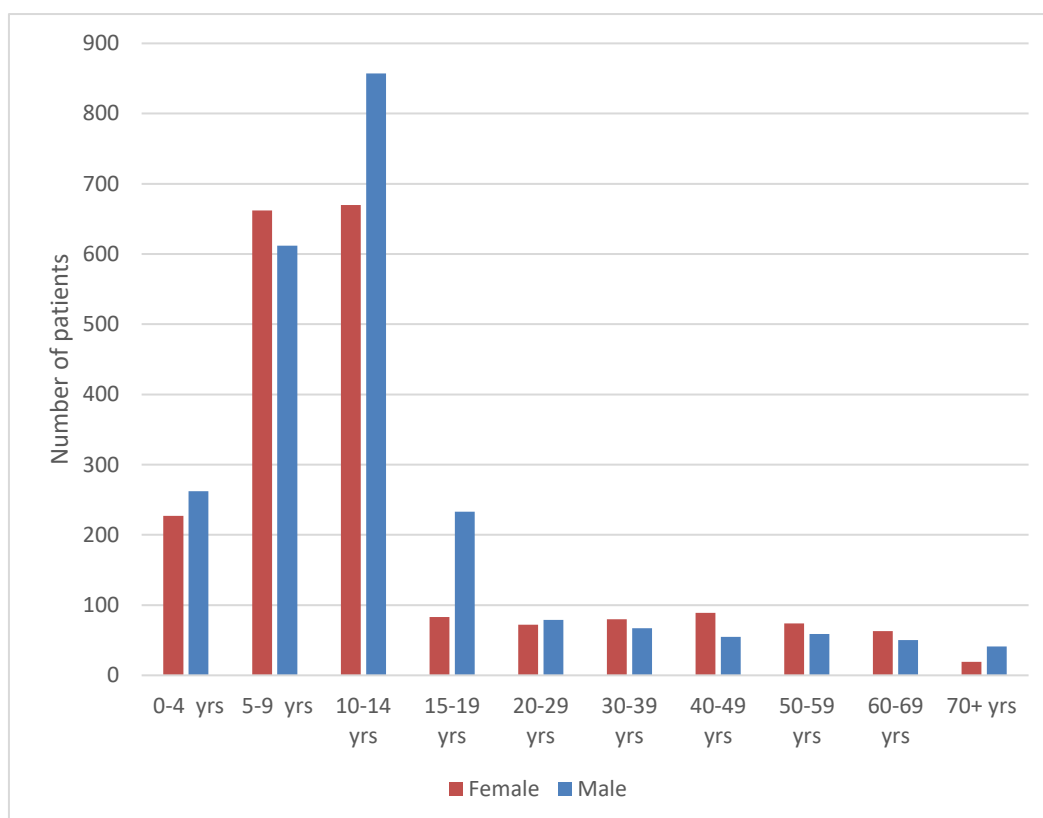


**Figure 3: Number of incident and prevalent somatropin patients according to supply quarter**

Note: Quarter 3 of 2015 only includes the month of September.

Overall in Figure 3, the number of initiating and prevalent patients appeared to stabilise from quarter 3 of 2016 to quarter 4 of 2018 with an average of approximately 113 patients initiating treatment and 1,391 prevalent patients each supply quarter. There was an increase in the number of initiating and prevalent patients from 2019 onwards. The number of initiating patients and the number of prevalent patients increased to an average of approximately 198 patients and 1,988 patients, respectively.

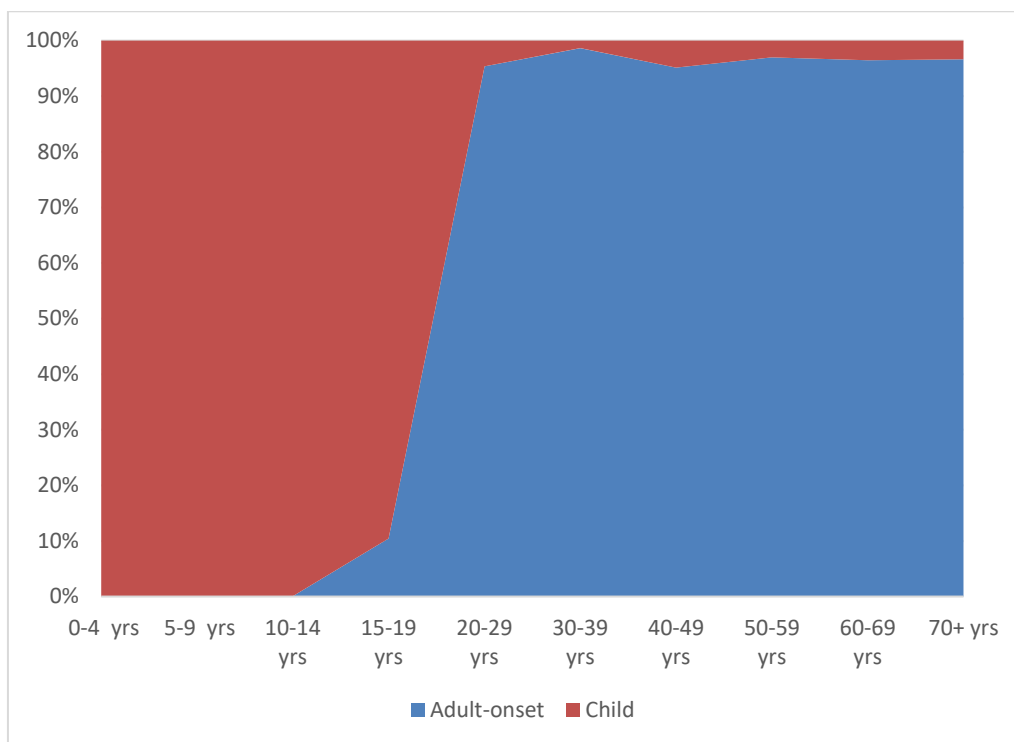
### Utilisation by relevant sub-populations/regions or patient level analysis



**Figure 4: Age and gender distribution of initiating somatropin patients**

In Figure 4, the age distribution of initiating somatropin patients is positively skewed, with the majority of patients (83%) initiating somatropin treatment aged less than 19 years. The most common age group that initiate on somatropin are those aged between 10 and 14 years (36% of patients).

Overall, there was a similar ratio of male and female initiating patients. The mean age of initiating patients was 16 years and a median age of 11 years. The age of patients ranged from 0 to 89 years.

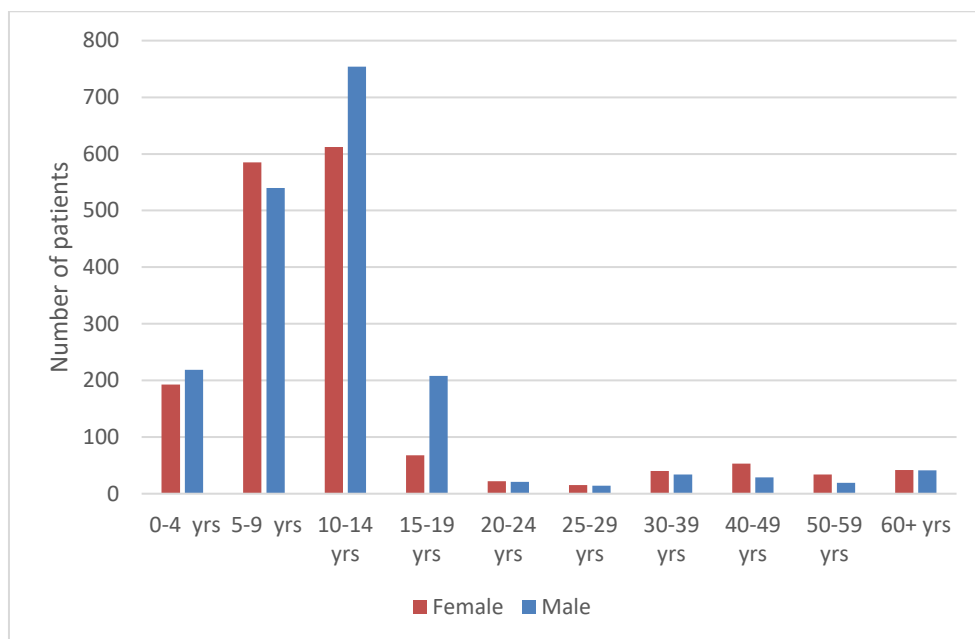


**Figure 5: Age of initiating somatropin patients according to item code for child vs. adult onset**

Note: Item codes for the treatment of adult onset severe growth hormone deficiency include 11895C, 11650E, 11493X, 11495B, 11491T.

In Figure 5, the majority of patients (99%) aged 0-19 years are initiating somatropin treatment according to item codes for paediatric somatropin treatment. The majority of patients aged 20 years and over (96.5%) are initiating somatropin treatment according to item codes for the treatment of adult onset severe growth hormone deficiency.





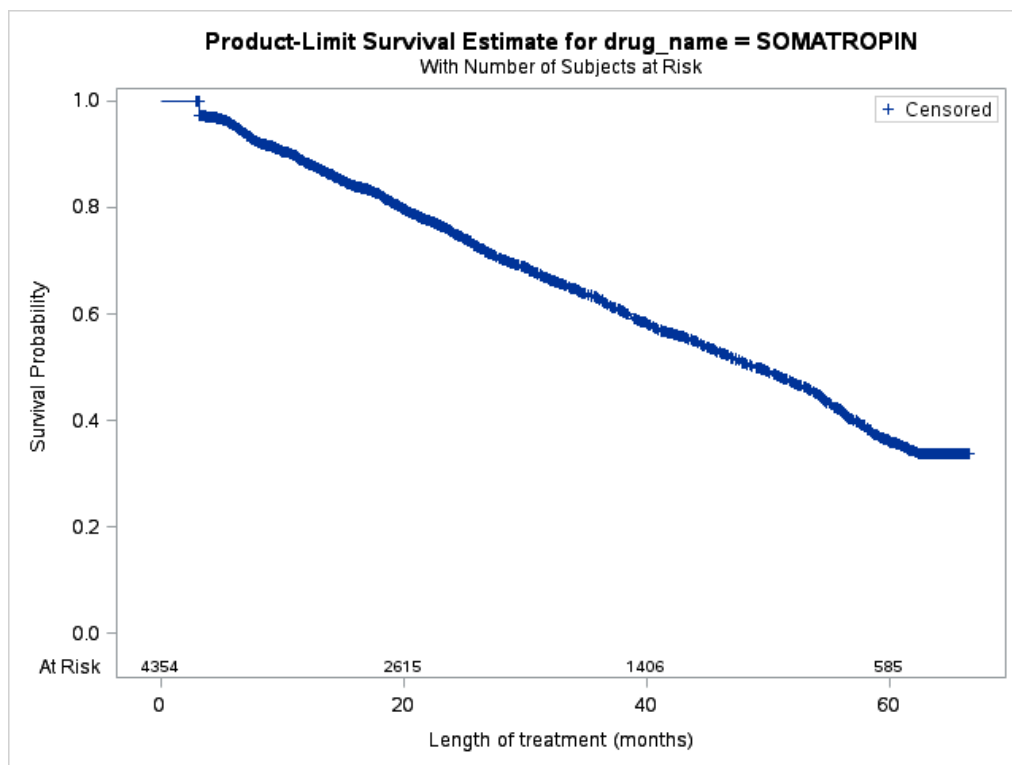
**Figure 6: Age and gender distribution of patients who initiated somatropin treatment before the somatropin listing was extended to include with adult onset growth hormone deficiency**

Similar to Figure 4, in Figure 6 the age distribution of patients initiating somatropin treatment is positively skewed, with the majority of patients initiating somatropin treatment aged up to 19 years.

The mean age of initiating patients was 14 years and a median age of 10 years. The age of patients ranged from 0 to 89 years.

**Table 5: Estimated length of treatment in patients who began somatropin treatment from 1 September 2015 and followed to 31 December 2020**

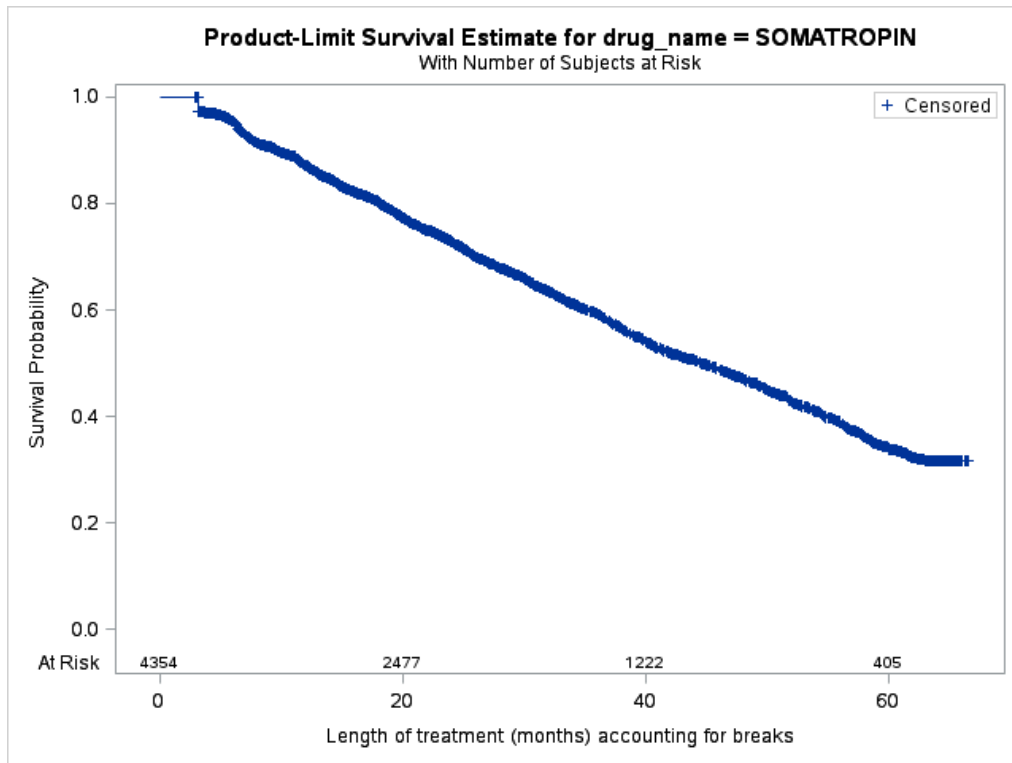
Number of patients	Censored	Median (months)	95% confidence interval (months)	
			Lower Limit	Upper Limit
4,354	2,482	48.82	46.91	51.02



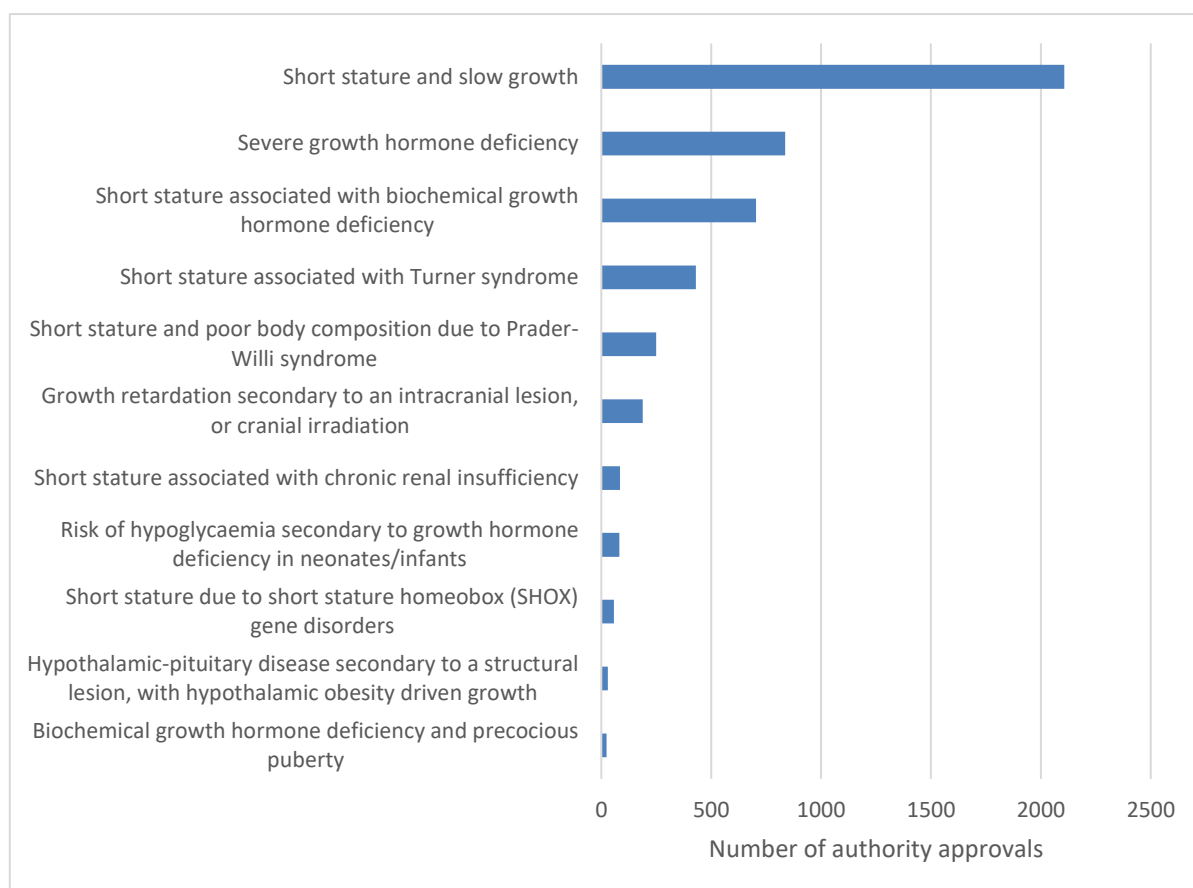
**Figure 7: Kaplan-Meier curve of somatropin treatment duration without accounting for breaks in patients who initiated from 1 September 2015 and followed to 31 December 2020**

**Table 6: Estimated length of treatment from in patients who began somatropin treatment from 1 September 2015 and followed to 31 December 2020, accounting for breaks**

Number of patients	Censored	Median (months)	95% confidence interval (months)	
			Lower Limit	Upper Limit
4,354	2,482	44.58	42.11	46.91



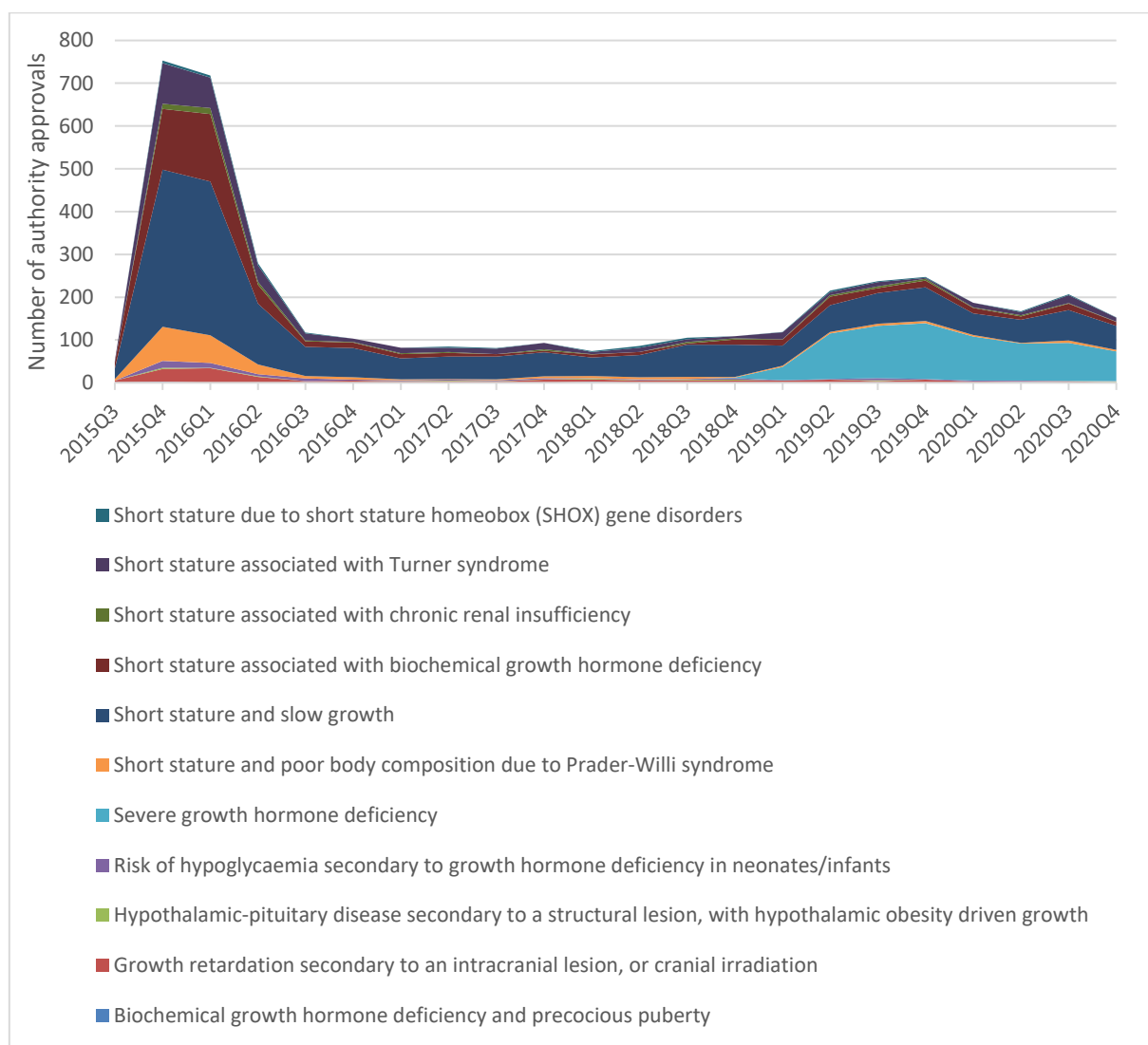
**Figure 8: Kaplan-Meier curve of somatropin treatment duration accounting for breaks in patients who initiated from 1 September 2015 followed to 31 December 2020**



**Figure 9: Number of unique authority approvals according to indication from 1 September 2015 followed to 30 December 2020**

Note: 0.73% of authority applications did not have an indication.

From Figure 9 based on unique patient's authority approvals, somatropin was most commonly used as treatment for short stature and slow growth.

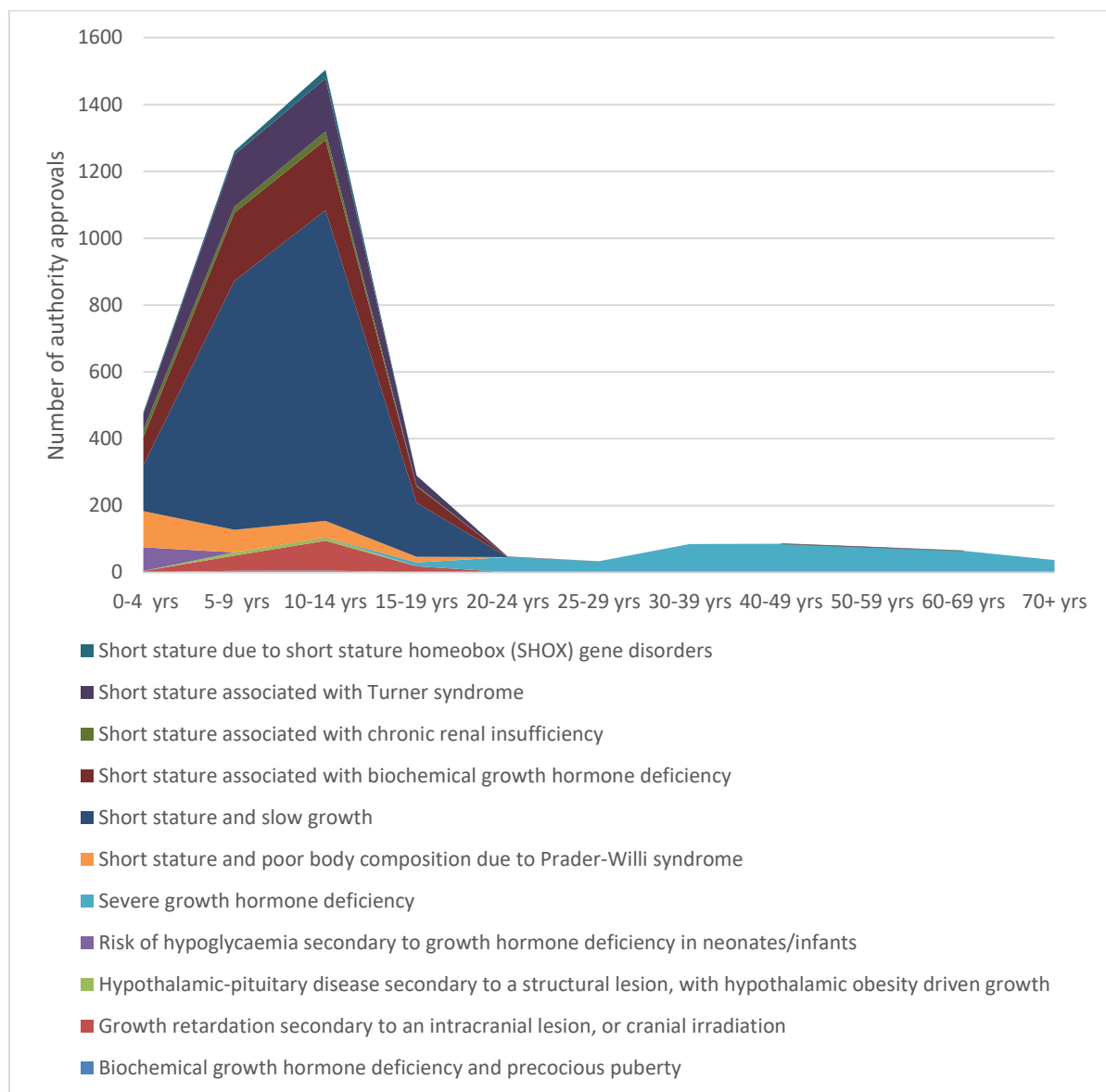


**Figure 10: Number of patients with authority approvals for initiating patients according to indication and supply quarter**

Note: Quarter 3 of 2015 only includes the month of September.

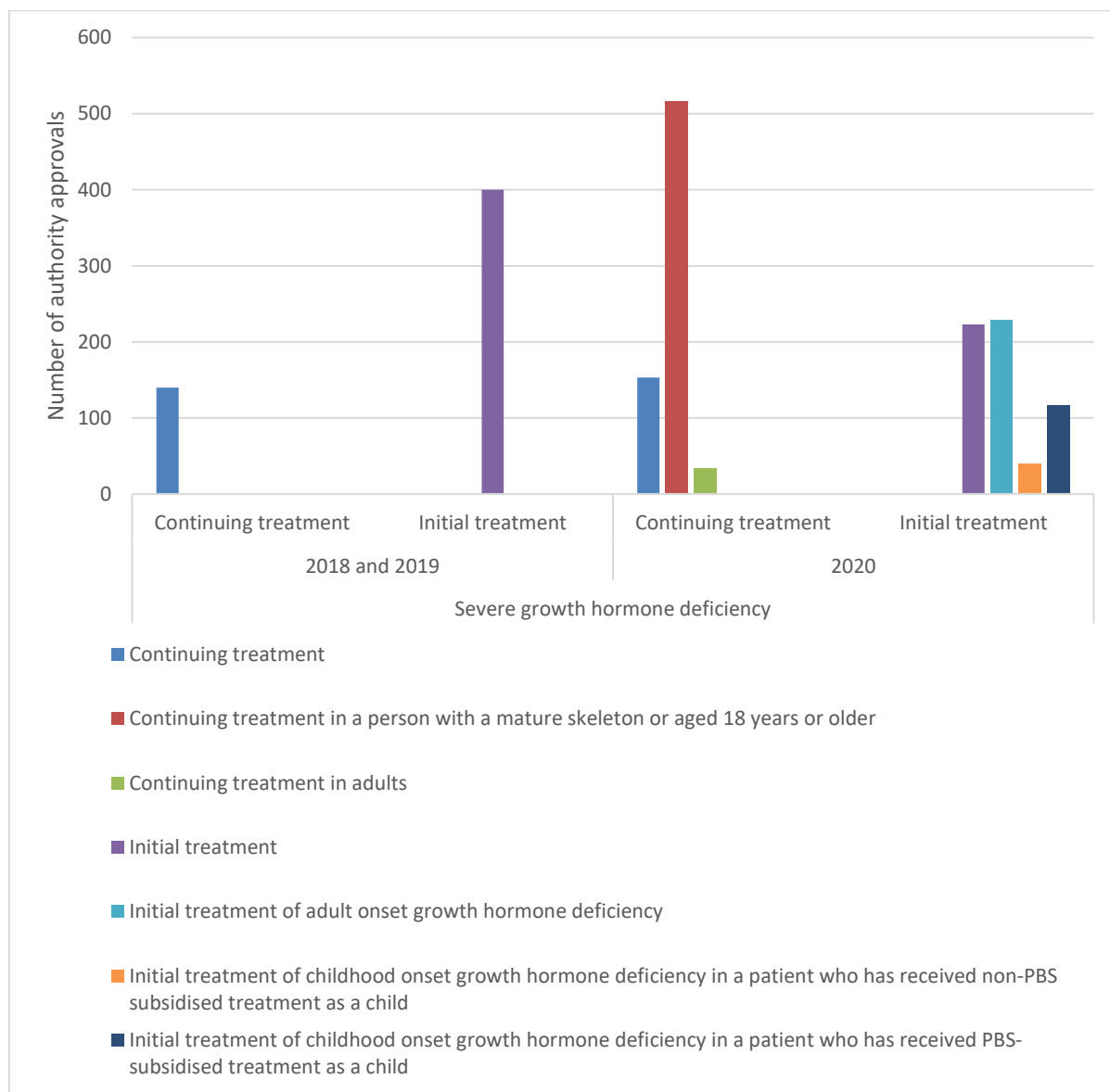
Note: 1.98% of initiating applications did not have an indication.

In Figure 10, based on patients initiating somatropin treatment, most patients initiated somatropin treatment between 2015 and 2016 for short stature and slow growth, short stature associated with biochemical growth hormone deficiency and short stature and poor body composition due to Prader-Willi syndrome. Following on, most patients initiated somatropin treatment for short stature and slow growth. From 2019 onwards, most patient initiated somatropin treatment for short stature and slow growth and severe growth hormone deficiency.

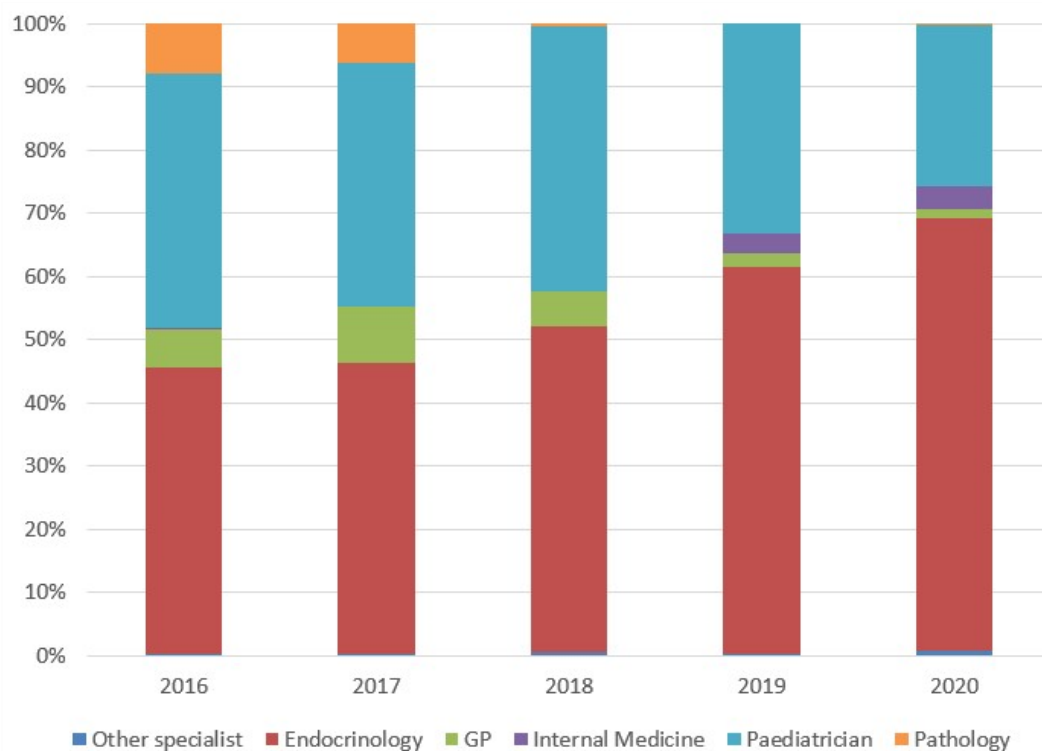


**Figure 11: Number of patients with initial authority approvals according to indication and age**

From Figure 11, initiating patients aged up to 19 years are supplied somatropin for a greater range of indications compared to those aged 20 years and older where severe growth hormone deficiency is the most common indication. Short stature and slow growth was the most common indication among patients aged up to 19 years. Of note, the indication short stature and poor body composition due to Prader-Willi syndrome was most common in those aged 0-4 years.



**Figure 12: Number of authority approvals for unique patients for severe growth hormone deficiency according to treatment phase and year**



**Figure 13: Script prescriber type according to year**

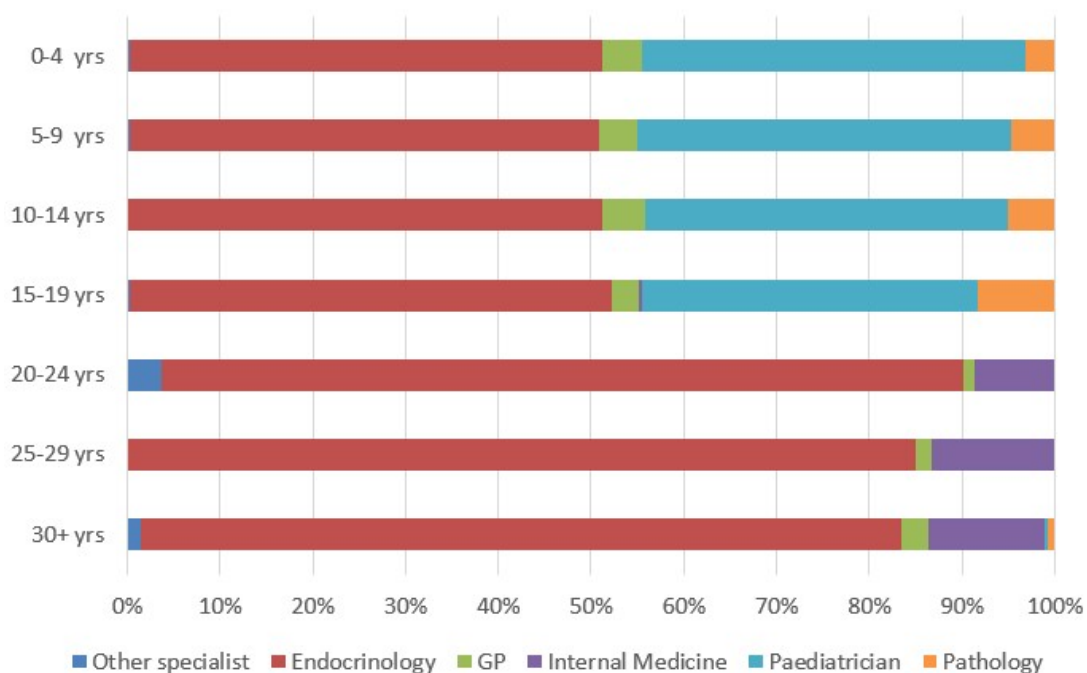
Note: "GP" defined as including non-vocationally registered GP, vocationally registered GP, trainee GP and GP with unclassified registration status.

Note: "Other specialist" defined as including anaesthetics, cardiology, college trainee – physician, dermatology, gastroenterology and hepatology, intensive care, nephrology, nuclear medicine, obstetrics and gynaecology, ophthalmology, optometrist and surgery.

Note: 4.25% of scripts had an unknown prescriber.

From Figure 13, endocrinologists have increasingly accounted for the majority of scripts prescribed, whereas GP and pathology prescribers have decreased in the scripts prescribed over time. From 2019 onwards, internal medicine specialists have emerged as a prescriber type accounting for approximately 5% of scripts prescribed.





**Figure 14: Initiating patient prescriber type according to age**

Note: "GP" defined as including non-vocationally registered GP, vocationally registered GP, trainee GP and GP with unclassified registration status.

Note: "Other specialist" defined as including college trainee – physician, gastroenterology and hepatology, intensive care, nephrology, nuclear medicine, obstetrics and gynaecology and surgeon.

Note: 2.85% of initiating patients had an unknown prescriber.

From Figure 14, there is a difference in the prescriber types between children and adult patients. Across all age groups, endocrinologists account for at least 50% and GPs account for approximately 5% of prescribers. In patients aged up to 19 years paediatricians and pathology specialists are also included as prescriber types. In contrast, in patients 20 years and over, internal medicine and other specialist prescribers are potential prescribers.

## Discussion

Somatropin utilisation remained stable from September 2015 to the end of 2018. There was an average of approximately 1,489 prescriptions, 113 patients initiating treatment and 1,391 prevalent patients per supply quarter during this time.

A number of changes were made to the Growth Hormone Program in December 2018, February 2019 and January 2020. On 1 December 2018, the somatropin listing was extended to include the treatment of adults with severe growth hormone deficiency. On 1 February 2019, changes were made to the eligibility restrictions in paediatric growth hormone treatment relating to: revised height percentile thresholds, growth velocity percentile for bone age and sex, clarification of definitions within the restrictions and streamlining the way associated growth data requires are specified within the prescriber instructions. These changes translated to an increase in somatropin utilisation. From 2019 there was an increase from an average per supply quarter of 1,489 to 2,630 prescriptions, 113 to 198 patients initiating somatropin treatment and 1,391 to 1,988 prevalent patients.

The annual expenditure over the life of the program has increased from approximately \$24.4 million in 2016 to \$33.6 million in 2020, based on the published listing prices. Expenditure increased steadily between 2016 and 2019 with a large increase observed between 2019 and 2020 of \$29 million to \$33 million.

In Figure 9, patients are most commonly supplied somatropin for short stature and slow growth, with 2,107 unique authority applications approved for this indication from September 2015 to December 2020. From 2019 onwards following the restriction changes, the treatment of severe growth hormone deficiency has become increasingly prevalent becoming the second most common indication at the end of 2020. In adults initiating somatropin treatment, treatment for severe growth hormone deficiency was the most common indication.

The median treatment duration of somatropin treatment was 48.2 months (95%CI 46.9 to 51 months). When accounting for breaks in the supply of somatropin, this decreased to 44.6 months (95%CI 42.1 to 46.9 months). On 1 January 2020, changes were made to the restriction allowing continued access for patients with childhood onset GHD due to congenital, genetic or structural cause into adulthood. Due to these restriction changes, additional treatment phases for the severe growth hormone deficiency indication were included, as shown in Figure 13. There was a large increase in the number of approvals for continuing treatment, with the majority for patients continuing treatment with a mature skeleton or aged 18 years or older. Additional authority approvals were made for adult patients initiating treatment for childhood onset growth hormone deficiency who received non-PBS and PBS subsidised treatment as a child. These changes indicate additional patients eligible for ongoing access into adulthood may lead to longer therapy time in future analyses.

Somatropin utilisation was most common in those aged up to 19 years, with the highest utilisation observed in those aged 10-14 years. However, 2.57% of those who initiated somatropin treatment were aged 65 years and over. A number of side effects have found to

be associated with somatropin in adults, with older patients more susceptible to adverse events. These include fluid retention with peripheral oedema, joint pain, carpal tunnel syndrome, paraesthesia, and worsening of glucose intolerance.<sup>20</sup> These side effects can be managed with vigilant dose titration.<sup>21</sup>

A range of specialists are involved in prescribing somatropin to patients. Across all age groups, somatropin is most commonly prescribed by endocrinologists. In patients aged up to 19 years, paediatricians and pathology specialists are also included as prescribers. In contrast, in patients 20 years and over, internal medicine and other specialist prescribers are included as prescribers. In patients aged 70 years and over, internal medicine physicians account for a greater proportion of prescribers compared to other age groups.

## DUSC consideration

DUSC noted that between 2016 and 2020 the number of treated patients increased from 2,011 to 3,178 patients, the number of prescriptions supplied increased from 5,973 to 12,439 prescriptions and expenditure (based on published prices) increased from \$24.4 million to \$33.6 million. DUSC noted the changes to listing in 2019 and 2020 which involved broadening the eligibility criteria for paediatric patients and amendments to the adult listing in relation to continued access for patients when they reach adulthood. DUSC considered the increased utilisation reflects the changes made to the listing with the addition of new clinical subgroups.

DUSC noted the majority of patients who initiated somatropin treatment were aged up to 19 years. DUSC noted the majority of initiating patients were supplied somatropin with the appropriate item code, with 99% of patients aged up to 19 years supplied item codes for paediatric somatropin treatment and 96.5% of patients aged 20 years and over initiating somatropin treatment with item codes for adult onset growth hormone deficiency. DUSC noted the small proportion of patients who initiated somatropin treatment were aged over 60 years.

DUSC noted the requirement for prescribers to use the Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) questionnaire for the treatment of adults with severe growth hormone deficiency was removed from the somatropin restrictions in September 2019 due to issues with accessibility and uncertain validity and reliability of the questionnaire. DUSC considered how quality of life could be measured as the lack of information on patient's quality of life could affect cost effectiveness.

DUSC noted weight-based dosing and flat dosing regimens were available for adults with growth hormone deficiency. DUSC considered the script per patient ratio between children

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<sup>20</sup> Reed M.L, Merriam G.R, Kargi A.Y. Adult growth hormone deficiency-benefits, side effects, and risks of growth hormone replacement. *Frontiers of Endocrinology*. 2013, 4(64) doi: 10.3389/fendo.2013.00064

<sup>21</sup> Garcia JM, Merriam GR, Kargi AY. Growth Hormone in Aging. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc. 2019. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK279163/>

and adults over time. DUSC commented that the script ratio for children remained relatively stable over time. However, the script ratio for adults appeared to be increasing, particularly between 2019 and 2020 when the restriction changes were made. DUSC considered the different dosing regimens of flat and weight-based dosing may have contributed to the increased script ratio in adult patients.

DUSC noted paediatric patients were most commonly treated with somatropin for short stature and slow growth whilst adults were most commonly treated with somatropin for severe growth hormone deficiency. DUSC noted the provocation tests required to support an authority application to initiate somatropin treatment. DUSC considered adult patients receiving somatropin treatment would likely be appropriately indicated for treatment. DUSC sought endocrinologist input. The response did not raise concern of use in adults outside of expectations.

## **DUSC actions**

DUSC requested that the report be provided to the PBAC for consideration.

## **Context for analysis**

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

## **Sponsors' comments**

Eli Lilly Australia Pty Ltd: The sponsor has no comment.

Ferring Pharmaceuticals Pty Ltd: The sponsor has no comment.

Ispen Pty Ltd: The sponsor has no comment.

Merck Healthcare Pty Ltd: The sponsor has no comment.

Novo Nordisk Pharmaceuticals Pty Ltd: The sponsor has no comment.

Pfizer Australia Pty Ltd: The sponsor has no comment.

Sandoz Pty Ltd: The sponsor has no comment.

SciGen (Australia) Pty Ltd: The sponsor has no comment.

## **Disclaimer**

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

To the extent provided by law, DoH makes no warranties or representations as to accuracy or completeness of information contained in this report.

To the fullest extent permitted by law, neither the DoH nor any DoH employee is liable for any liability, loss, claim, damage, expense, injury or personal injury (including death), whether direct or indirect (including consequential loss and loss of profits) and however incurred (including in tort), caused or contributed to by any person's use or misuse of the information available from this report or contained on any third party website referred to in this report.

## Appendices

### Appendix A: Dosage and administration of somatropin according to indication and brand

Indication	Brand name, sponsor	Dosage and administration
Growth hormone deficiency	Genotropin Pfizer Australia Pty Ltd	The diagnosis of growth hormone deficiency should be verified before the preparation is administered. This requires a thorough investigation of the pituitary function, including proper provocation tests. The dosage is individual and gradually titrated, generally an initial dose of 0.175 to 0.245 mg/kg body weight per week is recommended.
	Humatrope Eli Lilly Australia Pty Ltd	The dosage and administration schedule should be individualised for each patient. Generally, the recommended weekly dosage is 0.177-0.255 mg/kg (0.53-0.765 IU/kg) of body weight. The maximal replacement weekly dosage is 0.26 mg/kg (0.78 IU/kg) of bodyweight. It should be divided into equal doses given on 3 alternate days, 6 times per week or daily. The subcutaneous route of administration is preferable; intramuscular injection is also acceptable.
	Norditropin Novo Nordisk Pharmaceuticals Pty Ltd	25-35 µg/kg/day Equal to: 0.7 – 1.0 mg/m <sup>2</sup> /day
	Nutritropin Ispen Pty Ltd	0.025 - 0.035 mg/kg bodyweight given as a daily subcutaneous injection.
	Omnitrope Sandoz Pty Ltd	Generally, a dose of 0.025 to 0.035mg/kg body weight per day or 0.7 to 1.0 mg/m <sup>2</sup> body surface area per day is recommended. If the response to therapy is not satisfactory in the following years, the dose can be increased, as higher doses have been used.
	Saizen Merck Healthcare Pty Ltd	The recommended weekly dose is as follows: 0.2 mg/kg body weight or 4 mg/m <sup>2</sup> BSA (Body Surface Area) The weekly dose may be divided as shown below and is expressed per injection: <div style="display: flex; justify-content: space-between;"> <div>3 single doses</div> <div>0.07 mg/kg body weight 1.3 mg/m<sup>2</sup> BSA</div> </div> <div style="display: flex; justify-content: space-between;"> <div>6 single doses</div> <div>0.03 mg/kg body weight 0.7 mg/m<sup>2</sup> BSA</div> </div> <div style="display: flex; justify-content: space-between;"> <div>7 single doses</div> <div>0.03 mg/kg body weight 0.6 mg/m<sup>2</sup> BSA</div> </div>
	SciTropinA SciGen (Australia) Pty Ltd	Generally, a dose of 0.025 to 0.035 mg/kg body weight per day or 0.7 to 1.0 mg/m <sup>2</sup> body surface area per day is recommended. If the response to therapy is not satisfactory in the following years, the dose can be increased, as higher doses have been used.
Turner syndrome	Genotropin Pfizer Australia Pty Ltd	A dose of 0.3 to 0.35 mg/kg body weight per week is recommended
	Humatrope Eli Lilly Australia Pty Ltd	<i>Weekly Dosing</i> <div style="display: flex; justify-content: space-between;"> <div>mg/kg/week</div> <div>0.17 to 0.375</div> </div> <div style="display: flex; justify-content: space-between;"> <div>IU/kg/week</div> <div>0.5 to 1.125</div> </div> <div style="display: flex; justify-content: space-between;"> <div>mg/M<sup>2</sup>/week</div> <div>5 to 11</div> </div> <div style="display: flex; justify-content: space-between;"> <div>IU/M<sup>2</sup>/week</div> <div>15 to 34</div> </div> <i>Daily Dosing</i> <div style="display: flex; justify-content: space-between;"> <div>Mg/kg/day</div> <div>0.024 to 0.054</div> </div>
	Norditropin Novo Nordisk Pharmaceuticals Pty Ltd	50 µg/kg/day Equal to: 1.4 mg/m <sup>2</sup> /day

Indication	Brand name, sponsor	Dosage and administration
	Nutritropin Ispen Pty Ltd	Up to 0.05 mg/kg bodyweight given as a daily subcutaneous injection.
	Omnitrope Sandoz Pty Ltd	A dose of 0.045 to 0.05 mg/kg body weight per day or 1.4 mg/m <sup>2</sup> body surface area per day is recommended. If the response to therapy is not satisfactory in the following years, the dose can be increased.
	Saizen Merck Healthcare Pty Ltd	The recommended daily dose is: 0.045 – 0.05 mg/kg body weight or 1.4 mg/m <sup>2</sup> body surface area
	SciTropinA SciGen (Australia) Pty Ltd	A dose of 0.045 to 0.05 mg/kg body weight per day or 1.4 mg/m <sup>2</sup> body surface area per day is recommended. If the response to therapy is not satisfactory in the following years, the dose can be increased.
Chronic renal disease	Genotropin Pfizer Australia Pty Ltd	A dose of 0.3 to 0.35 mg/kg body weight per week is recommended
	Humatrope Eli Lilly Australia Pty Ltd	The recommended dose is 0.045 mg/kg – 0.050 mg/kg (approximately 0.14 IU/kg) of body weight per day, given as a daily subcutaneous injection.
	Norditropin Novo Nordisk Pharmaceuticals Pty Ltd	50 µg/kg/day Equal to: 1.4 mg/m <sup>2</sup> /day
	Nutritropin Ispen Pty Ltd	Up to 0.05 mg/kg bodyweight given as a daily subcutaneous injection. Somatropin therapy may be continued up to the time of renal transplantation.
	Omnitrope Sandoz Pty Ltd	A dose of 0.045 to 0.05 mg/kg body weight per day or 1.4 mg/m <sup>2</sup> body surface area per day is recommended. A dosage adjustment may be necessary after 6 months. If the response to therapy is not satisfactory, the dose can be increased.
	Saizen Merck Healthcare Pty Ltd	The recommended daily dose is: 0.045 – 0.05 mg/kg body weight 1.4 mg/m <sup>2</sup> body surface area
	SciTropinA SciGen (Australia) Pty Ltd	A dose of 0.045 to 0.05 mg/kg body weight per day or 1.4 mg/m <sup>2</sup> body surface area per day is recommended. A dosage adjustment may be necessary after 6 months. If the response to therapy is not satisfactory, the dose can be increased.
Small for gestational age	Humatrope Eli Lilly Australia Pty Ltd	The recommended dosage is 0.033 to 0.067 mg/kg body weight per day given as a subcutaneous injection. Very short children (i.e., height SDS < -3) and/or older pubertal children: it is recommended to start treatment with larger doses of somatropin (e.g 0.067 mg/kg/day), and to reduce the dosage gradually towards 0.033 mg/kg/day if substantial catch-up growth is observed during the first few years of therapy. Younger SGA children (e.g, approximately <4 years) with less severe short stature (baseline height SDS values between -2 and -3): it is recommended to start treatment at a lower dose (e.g, 0.033 mg/kg/day) and titrate the dose as needed over time. In all children, clinicians should carefully monitor the growth response, and adjust the somatropin dose as necessary.

Indication	Brand name, sponsor	Dosage and administration
	Norditropin Novo Nordisk Pharmaceuticals Pty Ltd	<p>33-67 µg/kg/day Equal to: 1-2 mg/m<sup>2</sup>/day</p> <p>The dosage must be adjusted to the need of the individual patient. It is recommended to start treatment with 33µg/kg/day. If catch-up growth has not commenced after 6 months of observation (and verification of compliance by increase in IGF1 and/or IGFBP3) then the physician may increase the dose up to 67µg/kg/day according to the patient's needs. It is recommended that the treating physician advise the parents/guardians that their children are not being treated for growth hormone deficiency, and that treatment with Norditropin induces catch-up growth during childhood and increases adult height. It is also recommended that parents/guardians be advised that long term treatment with somatropin has been associated with impaired glucose tolerance and malignancies. However, causality has not been established and there is no evidence that somatropin treatment is associated with an increased incidence of persistent impaired glucose tolerance or malignancies.</p>
Prader Willi syndrome	Genotropin Pfizer Australia Pty Ltd	The diagnosis of PWS should be confirmed by appropriate genetic testing. Generally a dose of 0.245 to 0.35 mg/kg body weight per week is recommended.
Adult growth hormone deficiency	Genotropin Pfizer Australia Pty Ltd	The recommended dosage at the start of therapy is 0.04 mg/kg/week divided into 7 daily subcutaneous injections. This dose should be gradually increased according to individual patient requirements to a maximum of 0.08 mg/kg/week. Women may require higher doses than men. This means that there is a risk that women, especially those on oral oestrogen replacement may be under-treated. Dose titration is based on the development of side effects and determination of serum levels of insulin-like growth factor-I (IGF-I). Dose requirements may decline with increasing age.
	Humatrope Eli Lilly Australia Pty Ltd	<p>Either a non-weight based or a weight-based dosing regimen may be followed, with doses adjusted based on treatment response, side effects and serum insulin-like growth factor I (IGF-I) concentrations. Dose requirements may decline with increasing age and may differ between male and female patients.</p> <p>The dosage of somatropin should be decreased in cases of persistent oedema or severe paraesthesia, in order to avoid the development of carpal tunnel syndrome.</p> <p>Non-weight based dosing: A starting dose of approximately 0.2 mg/day (range, 0.15 – 0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1 – 2 months by increments of approximately 0.1 - 0.2 mg/day.</p> <p>Weight-based dosing: The recommended starting dosage is not more than 0.006 mg/kg (6 µg/kg) daily. The dosage may be increased according to individual patient requirements to a maximum of 0.0125 mg/kg (12.5 µg/kg) daily.</p>
	Norditropin Novo Nordisk Pharmaceuticals Pty Ltd	<p>The dosage must be adjusted to the need of the individual patient. It is recommended to start treatment with a low dose of 0.15-0.3 mg/day and to increase the dosage gradually at monthly intervals based on clinical response. Serum insulin-like growth factor 1 (IGF-1) can be used to guide dose titration.</p> <p>Dose requirements decline with age. Maintenance dosages vary from patient to patient, but seldom exceeds 1.0 mg.</p>



Indication	Brand name, sponsor	Dosage and administration
	Nutritropin Ispen Pty Ltd	<p>At the start of somatropin therapy, low initial doses of 0.15 - 0.3 mg are recommended, given as a daily subcutaneous injection. The dose should be adjusted stepwise, controlled by serum Insulin-Like Growth Factor-1 (IGF-1) values. The recommended final dose seldom exceeds 1.0 mg/day. In general, the lowest efficacious dose should be administered. In older or overweight patients, lower doses may be necessary.</p> <p>Women may require higher doses than men, with men showing an increasing IGF-I sensitivity over time. This means that there is a risk that women, especially those on oral oestrogen therapy are under-treated while men are over-treated.</p> <p>In women on oral oestrogen replacement, a higher dose of growth hormone may be required to achieve the treatment goal</p>
	Saizen Merck Healthcare Pty Ltd	<p>At the start of therapy, low doses of 0.15 – 0.3 mg are recommended, given as a daily subcutaneous injection. The dose should be titrated carefully guided by IGF-1 age-adjusted normal values and on the basis of clinical effect and adverse events. The recommended final dose seldom exceeds 1.0 mg/day. In general, the lowest efficacious dose should be administered. With women showing an increasing IGF-1 sensitivity over time, dose adjustment may be required for women, especially for those on oral oestrogen replacement. In older or overweight patients, lower doses may be necessary.</p>