5.18 SOMATROGON, Injection 24 mg in 1.2 mL pre-filled single-use pen, Injection 60 mg in 1.2 mL pre-filled single-use pen, Ngenla®, Pfizer Australia Pty Ltd

1 Purpose of submission

1.1 The submission requested a Section 100 Growth Hormone Program listing for somatrogon for the treatment of growth hormone deficiency (GHD) in the paediatric population.

1.2 The listing was requested based on a cost-minimisation analysis versus somatropin.

Table 1: Key components of the clinical issue addressed by the submission

Component	Description
Population	Paediatric patients with growth hormone deficiency
Intervention	Somatrogon single-use disposable pen 24 mg/1.2 mL or 60 mg/1.2 mL; weekly dosing
Comparator	Somatropin; daily dosing
Outcomes	Annualised height velocity, change in height SDS, absolute IGF-1, IGFBP-3 levels, IGF-1 SDS, IGFP-3 SDS, Quality of life, treatment burden, treatment experience
Clinical claim	Non-inferior effectiveness and safety compared with somatropin

Source: Table 1.1.1, p.29 of the submission.
Abbreviations: IGF-1 insulin-like growth factor; IGFBP-3 IGF binding protein-3; SD standard deviation; SDS standard deviation score

2 Background

Registration status

2.1 Somatrogon was registered in the Australian Register of Therapeutic Goods on 30 November 2021.

3 Requested listing

3.1 The submission requested the listing of somatrogon for the following indications:

- Short stature associated with biochemical growth hormone deficiency (SSABGHD)
- Short stature and slow growth (SSSG)

3.2 The requested abridged listing of somatrogon for the initial and continuing treatment of patients with SSABGHD is presented below. The submission also requested listing of somatrogon for the initial and continuing treatment of SSSG but the restrictions are not presented in the public summary document (PSD)as they were consistent with the current restrictions for the somatropin brand Genotropin.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
SOMATROGON prefilled pen(s) 24 mg/1.2 mL	1	1	$382.03	Ngenla®	Pfizer Australia Pty Ltd
SOMATROGON Prefilled pen(s) 60 mg/1.2 mL	1	1	$943.41	Ngenla®	Pfizer Australia Pty Ltd

Category/Program:	Section 100 Growth Hormone Program
PBS indication:	Short stature associated with biochemical growth hormone deficiency
Treatment phase:	Initial
Restriction:	Authority Required- In Writing
Treatment criteria:	Treated by a specialist or consultant physician in paediatric endocrinology; OR Treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology.
Clinical criteria:	Patient must have evidence of biochemical growth hormone deficiency.
Population criteria:	Patient must have a current height at or below the 1st percentile for age and sex; OR Patient must have a current height above the 1st and at or below the 25th percentiles for age and sex and a growth velocity below the 25th percentile for bone age and sex measured over a 12 month interval (or a 6 month interval for an older child); OR Patient must have a current height above the 1st and at or below the 25th percentiles for age and sex and an annual growth velocity of 8 cm per year or less if the patient has a bone age of 2.5 years or less; AND Patient must be male and must not have a bone age of 15.5 years or more; AND Patient must be female and must not have a bone age of 13.5 or more; AND Patient must be aged 3 years or older
Prescriber instructions:	The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; and (3) Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; and (4) A bone age result performed within the last 12 months; and (5) The final adult height (in cm) of the patient's mother and father (where available).

Category/Program:	Section 100 Growth Hormone Program
PBS indication:	Short stature associated with biochemical growth hormone deficiency
Treatment phase:	Continuing treatment
Restriction:	Authority Required- In writing
Treatment criteria:	Treated by a specialist or consultant physician in paediatric endocrinology; OR Treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology.

Clinical criteria:	Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature associated with biochemical growth hormone deficiency category; AND Patient must have achieved the 50th percentile growth velocity for bone age and sex for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); OR Patient must have achieved an increase in height standard deviation score for chronological age and sex for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); OR Patient must have achieved a minimum growth velocity of 4cm/year for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); OR Patient must have achieved and maintained mid parental height standard deviation score for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); AND Patient must be male and must not have a bone age of 15.5 years or more; OR Patient must be female and must not have a bone age of 13.5 years or more
Population criteria:	Patient must be aged 3 years or older
Prescriber instructions:	The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; and (3) Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; and (4) A bone age result performed within the last 12 months; and (5) The final adult height (in cm) of the patient's mother and father (where available).

3.3 The requested restrictions for somatrogon are consistent with the restrictions for somatropin brand Genotropin, with the exception of prescriber restrictions in the continuing treatment phase, the omission of a maximum dose criterion, and that children must be aged 3 years and older for somatrogon (whereas children must have a bone age more than 2.5 years to be eligible for PBS Genotropin). The age criterion was requested to align with the TGA approved indication. The TGA approved Product Information states "The efficacy and safety of NGENLA have not been established in patients under 3 years of age. Data on the efficacy and safety of NGENLA in patients 12 to under 18 years of age are limited".

3.4 In addition to patients having to have a chronological age of 3 years and above to be eligible for treatment with somatrogon, it was proposed that patients should have a bone age no greater than or equal to 13.5 years for females and 15.5 years for males, which are not the demographics reflected in the clinical trial data. The demographics from the main study 4006 for the total cohorts (somatrogon and Genotropin) reported

a median chronological age of 7.87 years, mean age of 7.72 years, minimum age of 3.01 years, and a maximum age of 11.96 years. The PBAC noted that there was limited data available for the usage of somatrogon in patients aged 12-18, and that there was no data for children under 3 years of age. The PBAC noted the limitations of the data but discussed that it was important that a weekly form of GH injection is available to patients. Therefore, the PBAC considered that patients who do not have a mature skeleton should be eligible for somatrogon.

3.5 The submission requested that the continuing treatment phase be restricted to prescribing 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. The PBAC noted that the continuing treatment phase of the comparator is not restricted to just specialists but to all medical practitioners and considered that somatrogon should likewise be open to prescribing by all medical practitioners.

3.6 The submission requested continuing clinical criteria of achieving the 50th percentile growth velocity for bone age and sex or achieving an increase in height standard deviation score for chronological age and sex or achieving a minimum growth velocity of 4cm/year or achieving and maintaining mid parental height standard deviation score for the most recent treatment period, consistent with that of somatropin. However, somatropin also has the additional criterion of the patient not being on the upper dose limit or greater, such that a patient would need to at least be dosed at the upper limit and not meet any of the other continuing criteria to be deemed to have an inadequate response growth hormone and not continue PBS treatment. Without a specified upper dose limit, a patient who is on a sub-optimal dose of somatrogon that does not meet any of the somatrogon continuing criteria would be deemed to have an inadequate response to growth hormone without having had an opportunity to increase their dose. The PBAC therefore considered that an upper dose limit should be included in the somatrogon restriction and recommended an upper dose limit of 20.73 mg/m^2/week, which was calculated using the upper dose limit of somatropin multiplied by the equi-effective dose ratio of somatrogon to somatropin.

3.7 The submission requested that patients be able to switch from daily somatropin to weekly somatrogon, however, did not present any restriction criteria to this effect. The PBAC considered that switching between somatropin and somatrogon should only be initiated 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. Further the PBAC considered that switching should only occur when the patient is stable, has previously met the initial restriction criteria of somatrogon or somatropin, and is not concurrently taking any other PBS subsidised therapy for the same indication (i.e. is not taking both somatropin and somatrogon). The PBAC noted that the concurrent use of both therapies or frequently interchanging between them may represent a

Quality Use of Medicines (QUM) issue but considered that this should be left to the discretion of the treating endocrinologist.

3.8 The PBAC noted that several updates are expected to be made to all the somatropin restrictions subsequent to the September 2021 PBAC consideration of somatropin. The PBAC considered that the relevant outcomes from its September 2021 consideration of somatropin should apply to somatrogon.

3.9 The submission requested a grandfathering restriction for the treatment of SSABGHD for 3 patients who are still on a somatrogon drug trial and are expected to continue treatment using PBS subsidised therapy. The PBAC noted that a grandfathering restriction would be required as patients on the trial would not be eligible to initiate under the proposed initial restriction. The PBAC considered that patients who initiate under a grandfather restriction must have documented evidence that they have previously met the PBS initial criteria.

3.10 The requested restriction was considered complex in terms of the time required for finalisation.

For more detail on the PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Paediatric growth hormone deficiency (pGHD) is a rare condition. It affects the bone, lipids, protein, and glucose metabolism which results in abnormal growth height in children, and it may be congenital, acquired, or idiopathic. Causes for acquired GHD include brain tumours in the hypothalamic region, traumatic brain injury, infiltrative disease, cranial irradiation, and surgical intervention. The idiopathic origin of GHD is poorly understood but appears to be caused by multiple factors.

4.2 Growth hormone usually increases levels of, the hormone insulin-like growth factor-1 (IGF-1), and IGF binding protein-3 (IGFBP-3), in the blood which results in bone and height growth. Where pGHD is diagnosed this does not occur and the recommended treatment is recombinant human growth hormone (r-hGH) to achieve normalisation of height (GH Research Society, 2000[1]). Growth hormone therapy reduces body fat, reverses insulin insensitivity, and increases bone mineral mass.

4.3 Somatrogon is a glycoprotein that binds to the growth hormone receptor and initiates a transduction cascade culminating in changes in growth and metabolism.

[1] GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone deficiency in childhood and adolescence: summary statement of the GH Research Society. Journal of Clinical Endocrinology and Metabolism, 2000, 85:3990–3.

5 Comparator

5.1 The submission nominated somatropin as the main comparator. The main argument provided in support of this nomination was that somatropin is the formulation of recombinant human GH currently reimbursed via the Section 100 Growth Hormone Program of the PBS for a range of indications including the treatment of short stature due to decreased or failed secretion of pituitary growth hormone. Somatropin is currently subsidised for children and adults who fulfill PBS criteria under Section 100 (Growth Hormone Program). The PBAC considered somatropin as an appropriate comparator.

For more detail on the PBAC's view, see section 7 PBAC outcome.

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (12), health care professionals (2) and organisations (1) via the Consumer Comments facility on the PBS website. The comments from carers described the benefits of a once-weekly GHD treatment, including improved compliance, increased flexibility, fewer injection site effects and reduced damage to skin, and an overall reduced disease burden and improved quality of life. Many comments addressed the notion that weekly dosing would enable children to attend school excursions and camps, have sleep overs, and be able to enjoy a more normal childhood.

6.3 The PBAC noted the advice received from the Australian Pituitary Foundation (APF) clarifying the likely use of somatrogon in clinical practice. The PBAC specifically noted the advice that the use of somatrogon may reduce physical irritation and damage at the injection site, reduce the emotional and psychological burden that both children and their parents/carers experience with daily injections, and minimise the impact on family dynamics. The APF advised that a weekly injection would provide greater flexibility and add a positive impact on quality of life which would flow on to the patient's family.

Clinical trials

6.4 The submission was based on data from four studies: Study 4006 (12 months, N=224); Study 4004 (12 months, N=53 but only used subset of data, n=25); Study 4009 (12 months, N=44); and Study 1002 (6 months, N=87). Study 4006 was the main trial, a direct randomised trial of somatrogon compared with somatropin for prepubertal children with GHD. Study 4004 was a Phase 2 dose-finding study in prepubertal children, Study 4009 was a Phase 3 randomised trial in Japanese pre-pubertal children,

and Study 1002 was a randomised, open-label, 2-period cross-over study that assesses the treatment burden of somatrogon versus somatropin in children aged 3 to 18 years with GHD. Two open label extension (OLE) studies (of Study 4006 and Study 4004) were also identified, which provide longer term efficacy and safety data for somatrogon. The evaluation noted that an OLE was ongoing for Study 4009 but that no results were available at the time of submission.

6.5 The patients in the pivotal clinical trial (Study 3006) had an upper age limit of 12 years. The restriction proposed use in the Australian setting until a bone age of 15.5 years for males and 13.5 years for females. The PBAC noted there was limited evidence regarding whether the drug is beneficial to those > 12 years of age or those who are post-pubertal.

6.6 Three studies (Study 4006, 4004, 4009) included treatment naïve (i.e. no prior exposure to any r-hGH) therapy. Only Study 1002 included children who had been on a stable dose of somatropin for ≥ 3 months and who were compliant on a stable dose for at least 3 months prior to screening. Thus, there was limited evidence for patients "switching" from somatropin to somatrogon compared to the evidence for the treatment naïve population.

6.7 The included clinical trials all had open label study designs so there was a risk of performance and detection bias, particularly for subjective outcomes. This was reasonable as it was not practical to blind participants randomised to somatrogon (dosed weekly) or somatropin (dosed daily).

6.8 Details of the trials presented in the submission are provided in the table below.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
4006	CSR: A phase 3, open-label, randomized, multicenter, 12 months, efficacy and safety study of weekly mod-4023 compared to daily Genotropin® therapy in pre-pubertal children with growth hormone deficiency	24 August 2020
	Deal C et al. Somatrogon growth hormone in the treatment of pediatric growth hormone deficiency: Results of the pivotal pediatric phase 3 clinical trial	Rev Argent Endocrinol Metab, 2021; 58 (Suppl 1) p.247.
	Deal C et al. Pivotal phase 3 results evaluating the non-inferiority of once weekly somatrogon compared to daily somatropin in pediatric patients with growth hormone deficiency (pGHD).	Conference: 2020 Annual Meeting of the Pediatric Endocrine Society, PES 2020. 93(SUPPL 1) (pp 69-70), 2020.
	Loftus J et al. PDB4 Evaluation of Quality of Life in PRE-Pubertal Children Using the Quality of Life in Short Stature Youth (QOLISSY) Questionnaire, Following 12 Months of Growth Hormone Treatment with Either a Weekly Somatrogon or a Daily Genotropin Injection Schedule	Value in Health, 2020,12:S506.
	Fisher et al. Impact of post-dose sampling time on IGF-1 SDS with long-acting somatrogon (human growth hormone-HGH-CTP) therapy.	Conference: 19th International Congress of Endocrinology, 4th Latin American Congress of

		Endocrinology, CONLAEN and 13th Congress of the Argrntine Federation of Endocrinology Societies, FASEN. Virtual. 58(SUPPL 1) (pp 246), 2021
4004	CSR: Safety and dose finding study of different MOD-4023 dose levels compared to daily r-hGH therapy in pre-pubertal growth hormone deficient children.	15 May 2017
	Zelinska N et al. Long-Acting C-Terminal Peptide-Modified hGH (MOD-4023): Results of a Safety and Dose-Finding Study in GHD Children	J Clin Endocrinol Metab. 102(5):1578-1587, 2017 05 01.
	Zelinska N et al. Efficacy of once-weekly administration of CTP-modified human growth hormone (MOD-4023): 24-month complete database results of a phase 2 study in children with growth hormone deficiency	Conference: 55th Annual Meeting of the European Society for Paediatric Endocrinology, ESPE 2016. 86(Suppl 1) (pp 97-98), 2016a
	Zelinska N et al. Safety and tolerability of once-weekly administration of CTP-modified human growth hormone (MOD-4023): Phase 2 study in children with growth hormone deficiency	Conference: 98th Annual Meeting and Expo of the Endocrine Society, ENDO 2016. 37(2 Suppl 1), 2016b.
	Zelinska N et al. 2nd year efficacy results of once-weekly administration of CTP-modified human growth hormone (MOD-4023): A phase 2 study in children with growth hormone deficiency.	Conference: 98th Annual Meeting and Expo of the Endocrine Society, ENDO 2016. 37(2 Suppl 1), 2016c.
	Zadik Z et al. Top line results of 12 months of once-weekly administration of ctp-modified human growth hormone (MOD-4023): Phase 2 dose finding study in children with growth hormone deficiency (GHD).	Conference: 97th Annual Meeting and Expo of the Endocrine Society, ENDO 2015. 36(Suppl 2), 2015a.
	Zadik Z et al. 12-month safety and efficacy of a weekly long-acting GH (MOD-4023) compared to daily recombinant human GH therapy in pre-pubertal GH-deficient children; phase 2 study: Study CP-4-004 summary	Hormone Research in Paediatrics. Conference: 54th Annual Meeting of the European Society for Paediatric Endocrinology, ESPE 2015. 84(SUPPL. 1) (pp 45), 2015b.
	Hart G et al. Pharmacokinetics and pharmacodynamics profile of once-weekly, CTP-modified human growth hormone (MOD-4023): Phase 2 dose finding study in children with GHD deficiency	Conference: 96th Annual Meeting and Expo of the Endocrine Society, ENDO 2014. 35(SUPPL. 3), 2014a.
	Hart G et al. Six months follow-up pharmacokinetics and pharmacodynamics profile of once-weekly, CTP-modified human GH (MOD-4023;): Phase 2 dose finding study in children with GHD deficiency.	Conference: 53rd Annual Meeting of the European Society for Paediatric Endocrinology, ESPE 2014. 82(SUPPL. 1) (pp 135-136), 2014b
	Zadik Z et al. Top line results of once-weekly, CTP-modified human GH (MOD-4023): Phase 2 dose finding study in children with GH deficiency.	Hormone Research in Paediatrics. Conference: 53rd Annual Meeting of the European Society for Paediatric Endocrinology, ESPE 2014. 82(SUPPL. 1) (pp 63), 2014.
	Hart G et al. Metabolic and safety parameters of once-weekly, CTP-modified human growth hormone (MOD-4023): Results of a phase 2 dose and frequency finding study.	Endocrine Reviews. Conference: 95th Annual Meeting and Expo of the Endocrine Society, ENDO 2013. 34(3 SUPPL. 1), 2013.

4009	CSR: A phase 3, open-label, randomized, multicenter, 12-month, efficacy and safety study of weekly mod-4023 compared to daily Genotropin® therapy in Japanese pre-pubertal children with growth hormone deficiency.	10 December 2020.
1002	CSR: A phase 3, randomized, multicenter, open-label, crossover study assessing subject perception of treatment burden with use of weekly growth hormone (Somatrogon) versus daily growth hormone (Genotropin®) injections in children with growth hormone deficiency.	17 December 2020.
4006 OLE	Wajnrajch et al. Poster 7129: Switch Data From the Open-Label Extension of the Pivotal Phase 3 Study of Once Weekly Somatrogon Compared With Daily Somatropin in Pediatric Patients With Growth Hormone Deficiency (GHD).	Presented at the Annual Meeting of the Endocrine Society (ENDO 2021); March 20–23, 2021.
4004 OLE	Pastrak et al. Long Term Safety and Efficacy of a once-weekly Somatrogon (hGH-CTP): A 5-year Phase 2 Extension Study in Children with Growth Hormone Deficiency. Zadik et al. Poster 6887: Results From an Open-Label Extension of the Phase 2 Dose-Finding Study of Once Weekly Somatrogon vs Daily Genotropin in Pediatric Patients With Growth Hormone Deficiency (GHD). Zielinska et al. Long-term Safety of a once-weekly Somatrogon (hGH-CTP): 4-Year Results: of a Phase 2 Extension Study in Children with Growth Hormone Deficiency	Horm Res Paediatr 2020; 93 (suppl 1): p68. Presented at the Annual Meeting of the Endocrine Society (ENDO 2021); March 20–23, 2021. Horm Res Paediatr 2019: 91 (suppl 1): p309.

Source: Table 2.2.1, pp50-51 of the submission.
OLE, Open Label Extension, GHD = growth hormone deficiency, CSR = clinical study report, pGHD = paediatric growth hormone deficiency, GH = growth hormone, CTP = carboxy-terminal peptide, hGH = human growth hormone, SDS = standard deviation score.

6.9 The key features of the trials are summarised in the table below.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Somatrogon versus somatropin						
Study 4006	224	R, OL 12 mths	Low	Prepubertal children with GHD	Annual HV	Used
Study 4004	25	R, OL 12 mths	Low	Prepubertal children with GHD	Annual HV	Not used
Study 4009	44	R, OL 12 mths	Low	Japanese prepubertal children with GHD	Annual HV	Not used
Study 1002	87	R, OL 6 mths	Moderate*	Prepubertal children with GHD	Treatment burden	Not used

Source: Compiled during the evaluation
GHD = growth hormone deficiency; HV = height velocity OL = open label; R = randomised.
* Risk of performance and detection bias due to open-label study design and use of subjective outcome measures.

Comparative effectiveness

6.10 The primary endpoint of the main trial (Study 4006) and the two supportive trials (Study 4004, 4009) was annual height velocity (HV) (cm/year) after 12 months of treatment. This was reasonable and consistent with the primary endpoint of the trials that established the effectiveness of the comparator somatropin. The evaluation noted there was no evidence of a mortality benefit from somatrogon or somatropin.

6.11 For Study 4006 and 4009, the submission stated that the lower bound of the two-sided 95% CI for mean HV was greater than the prespecified non-inferiority margin of -1.8 cm/year, supporting non-inferiority. This was reasonable; however, no mean difference was calculated for Study 4004. The submission stated that the 95% confidence intervals overlapped, indicating no significant difference between the treatment groups. This was not an appropriate method to determine non-inferiority. The results of Study 4004 may not support a clinical claim of non-inferiority as the trial was not powered to detect non-inferiority.

Table 4: Results of annual height velocity at 12 months across the trials

Trial ID	Somatrogon			Somatropin			Mean difference (95%CI)[d]
	Mean	95% CI of mean	SD	Mean	95% CI of mean	SD	
4006[a]	10.10	-	-	9.78	-	-	0.33 (-0.24, 0.89)
4004[b]	11.4	(9.2, 13.7)	3.9	12.5	(11.0, 13.9)	2.1	-
4009[c]	9.654	-	-	7.868	-	-	1.786 (0.966, 2.605)

Source: Tables 2.5.1, 2.5.2, 2.5.4, pp85, 88, 89 of the submission.
CI = confidence interval; SD = standard deviation
a Somatrogon (N=109), somatropin (N=115)
b Somatrogon (N=14), somatropin (N=11), using full analysis set
c Somatrogon (N=22), somatropin (N=22), using full analysis set
d based on least squares means estimate

6.12 Several secondary efficacy endpoints were presented: annualized height velocity at 6 months, change in height standard deviation scores at 6 and 12 months, and change in bone maturation. The results for annualised HV favour somatrogon, although the clinical significance and support for a non-inferiority claim were unclear. The results for change in height standard deviation and change in bone maturation were mixed.

6.13 The submission also presented evidence of biochemical changes. The biochemical evidence tends to favour somatrogon although the clinical significance and support for a non-inferiority claim were unclear.

6.14 The long-term efficacy data from two studies were presented for Study 4006 (additional 12 months) and Study 4004 (additional 5 years). For Study 4006, of 222 patients who completed the main study, 212 (95.5%) entered the OLE phase. For Study 4004, of 53 patients who completed the main study, 48 (90.6%) entered the OLE phase. These results favoured somatrogon. However, the clinical significance and support for non-inferiority claim based on OLE HV and height standard deviation score (SDS) outcomes was unclear.

6.15 The primary endpoint of Study 1002 was treatment burden, assessed using the Patient Life Interference Questionnaire component of the Dyad Clinical Outcomes Assessment 1 (DCOA 1). This was completed by the participant/caregiver, consisted of 7 questions and used a 5-point scale ranging from never (1) to always (5). This questionnaire was validated for use among children with GHD; however, using a subjective outcome in an unblinded trial is problematic. In addition, there was no definition provided for non-inferiority, and no definition of a clinically significant difference.

6.16 The secondary endpoint of Study 1002 was treatment burden, assessed using the remaining items on the DCOA 1, the DCOA 2 and the Patient Global Assessment Severity - Impact on Daily Activities (PGIS-IDA) questionnaires. The PGIS-IDA consists of one question with a 7-point scale in which the participant/caregiver rated the impact of treatment administration on daily activities during the past 4 weeks. A score of 1 indicated no impact while 7 indicated an extremely severe impact. This questionnaire was not validated for use among children with GHD.

6.17 The evidence presented in the submission for switching from somatropin to somatrogon (Study 4006 OLE, Study 4004 OLE, Study 1002) showed that there were no significant differences in effectiveness and safety.

6.18 The submission provided additional information from a literature review regarding switching from daily to weekly injections. Only one study evaluated paediatric patients with GHD. This was a stated preference study using a discrete choice experiment (McNamara et al, 2020) that reported that the frequency of injections was the most important treatment attribute. Three studies specifically evaluated switching from daily to weekly injections among adults with GHD (Johannson et al, 2018; Johannson et al, 2020; McNamara et al, 2020). Overall, these additional studies (mainly for adults, and for conditions other than GHD) provided supportive evidence regarding the preference for weekly over daily injections as a better treatment experience that could increase compliance and therefore result in better health outcomes. Whilst there was lack of additional data for pGHD, children are likely to prefer once weekly versus once daily injections.

Comparative harms

6.19 Although the overall incidence of serious or severe adverse events (AEs) are comparable between somatrogon and somatropin, there was a higher incidence of injection site reactions (erythema, pain, pruritus) for somatrogon across all studies. For example, in Study 4006, the report of at least one injection site reaction was 43.1% (somatrogon) versus 25.2% (somatropin). Discontinuations were low in both study arms.

6.20 Among the participants of Study 4006, there was a higher risk of IGF-1 having a standard deviation >2; 26 (somatrogon) versus 3 (somatropin); with the incidence of patients in the somatrogon group with an IGF-1 SDS >2 increasing over time. In Study 4009, there was an increasing number of patients with an IGF-1 SDS >2 in the somatrogon group. IGF-1 is not routinely monitored as part of ongoing clinical care so the clinical significance of this finding was uncertain.

6.21 Among the participants of Study 4006, 84/109 (77%) patients using somatrogon tested positive for anti-drug antibodies compared with 18/115 (16%) who were using somatropin. Of these, two patients using somatrogon had neutralizing antibodies compared with zero patients using somatropin. In Study 4004, anti-drug antibodies were detected in 24% of patients using somatrogon versus 18% of patients using somatropin, but none had neutralizing activity. In Study 4009, anti-drug antibodies

were detected in 18/22 patients using somatrogon versus 4/22 patients using somatropin. Among these, 2/77 somatrogon samples had neutralizing antibodies versus zero somatropin samples. Anti-drug antibodies are not routinely tested in the clinical setting, thus the long-term significance (beyond 1 year) of this was uncertain.

Table 5: Summary of key adverse events in the trials

Trial ID	Somatrogon n with event/N (%)	Somatropin n with event/N (%)	RR (95% CI)*
Study 4006			
Serious adverse event	3/109 (2.8)	2/115 (1.7)	1.583 (0.27 to 9.29)
Severe adverse event	9/109 (8.3)	6/115 (5.2)	1.583 (0.583 to 4.299)
Discontinued from study due to adverse event	1 (0.9)	0 (0)	NA
Study 4004			
Serious adverse event	0 (0)	0 (0)	NA
Severe adverse event	2/42 (4.8)	0 (0)	NA
Discontinued from study due to adverse event	0 (0)	0 (0)	NA
Study 4009			
Serious adverse event	2/22 (9.1)	2 (9.1)	1 (0.154 to 6.48)
Severe adverse event	2 (9.1)	2 (9.1)	1 (0.154 to 6.48)
Discontinued from study due to adverse event	0 (0)	1 (4.5)	NA
Study 1002			
Serious adverse event	0 (0)	0 (0)	NA
Severe adverse event	0 (0)	0 (0)	NA
Discontinued from study due to adverse event	1 (1.1)	0 (0)	NA

Source: Table 2.5.32, p116 of the submission.
NA=Not able to be calculated due to zero value.
* Risk difference (RD) and relative risk (RR) were not presented in the submission. Calculated during the evaluation.

Benefits/harms

6.22 As the submission claimed non-inferior comparative effectiveness and safety, a benefit and harms table has not been presented.

6.23 The submission claimed the benefit of somatrogon is to improve the growth (in terms of HV) of pre-pubertal children with GHD. The weekly dosing of somatrogon compared with daily dosing of somatropin could improve treatment satisfaction, patient adherence and potentially, their quality of life.

6.24 Although the overall incidence of serious or severe AEs are comparable between somatrogon and somatropin, there was higher incidence of injection site reactions (erythema, pain, pruritus) with the use of somatrogon across all studies.

6.25 Based on the direct evidence presented by the submission for the main clinical trial (Study 4006), for every 100 patients treated with somatrogon in comparison with somatropin:

- Approximately 18 additional patients will have an injection site reaction.
- Approximately 3 additional patients will have a severe AE.

- Approximately 5 additional patients will have a severe AE (Study 4004).
- Approximately 1 additional patient will have a serious AE.

Clinical claim

6.26 The submission described somatrogon as non-inferior in terms of effectiveness and safety when compared to somatropin. This claim was mostly supported by the evidence presented in the submission. The key issues included:

- The clinical trial evidence was that of pre-pubertal children (Study 4004: <11 years for girls and <12 for boys; Studies 4006 and 4009: <10 years for girls and <11 years for boys) whereas the proposed PBS restrictions are for patients with a bone age (up to 13.5 for girls and 15.5 years for boys).
- The pivotal trial, Study 4006 together with two supportive trials (Study 4004 and Study 4009) demonstrated non-inferiority in terms of annualized HV at 12 months. However, Study 4004's reliance on overlapping 95% confidence intervals to determine non-inferiority may not be appropriate.
- Study 1002 provided data demonstrating improvements in the treatment burden and treatment experience of somatrogon versus somatropin. These data are informative but need to be interpreted with caution as the PGIS-IDA is not validated for children with GHD.
- Two OLE studies provided further evidence for longer-term safety and efficacy; the Study 4006 OLE and the Study 4004 OLE. The Study 4006 OLE likely provides 1 additional year of data and support for a non-inferior clinical effectiveness claim. The Study 4004 OLE provides information on secondary outcomes at 5 years but the clinical significance and support for non-inferiority was unclear.
- Safety data presented showed no significant difference in serious or severe AEs between somatrogon and somatropin. There was a higher incidence of injection site reactions for somatrogon at 12 months, but this rarely led to discontinuation of the drug. Injection site reactions may decrease over time, but the evidence of this was limited.

6.27 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Economic analysis

6.28 The submission presented a cost-minimisation analysis of once-weekly somatrogon compared to daily somatropin in paediatric patients for the treatment of SSABGHD, and SSSG. The submission assumed non-inferior effectiveness to somatropin in terms of annual HV at 12 months, and non-inferior safety in terms of AEs at 12 months. The use of a cost-minimisation was appropriate considering that the claim of non-inferiority was mostly supported by the evidence.

Table 6: Key components and assumptions of the cost-minimisation analysis

Component	Claim or assumption
Therapeutic claim: effectiveness	Somatrogon was assumed to be non-inferior to somatropin for the treatment of pGHD with respect to annual height velocity at 12 months.
Therapeutic claim: safety	Somatrogon was assumed to be non-inferior to somatropin for the treatment of pGHD with respect to AEs at 12 months.
Evidence base	Direct comparison of somatrogon and somatropin using the pivotal Phase 3 randomised trial (Study 4006).
Equi-effective doses	0.66 mg/kg/week of somatrogon is equi-effective to 0.034 mg/kg/day (0.238 mg/kg/week) of somatropin. The use of the median treatment doses of somatrogon and somatropin to derive the equi-effective doses may not provide a robust comparison of steady-state doses. The mean treatment doses of somatrogon and somatropin were more appropriate. The equi-effective doses derived from the mean treatment doses from Study 4006 are 0.655 mg/kg/week of somatropin is equi-effective to 0.034 mg/kg/day (0.237 mg/kg/week) of somatropin.
Direct medicine costs	Based upon the effective AEMP of somatropin ($41.58 per mg) across all branded products for the pGHD indication and the equi-effective doses of somatrogon and somatropin, the calculated cost of somatropin per kilogram of body weight per week was $9.90. The calculated cost of somatropin per kilogram of body weight per week ($9.90) was apportioned to the unit costs of somatrogon using the equi-effective doses of somatrogon and somatropin, to arrive at an equivalent weekly treatment cost of somatrogon per kilogram of body weight ($9.90). The submission presented a cost-minimisation analysis using the equi-effective doses derived from the median treatment doses of Study 4006. The results of the cost-minimisation analysis according to equi-effective doses based on the mean treatment doses were $9.85 per kilogram of body weight for somatrogon versus $9.85 per kilogram of body weight for somatropin.
Other costs or cost offsets	No additional costs or cost offsets were included in the cost minimisation analysis.

Source: Table 3.1.1, p172 of the submission

AE = adverse events; AEMP = approved ex-manufacturer price; pGHD = paediatric growth hormone deficiency; kg = kilograms; mg = milligrams

6.29 The results of the cost minimisation analysis are presented in the table below. The results based on mean doses were added during the evaluation and corrected in the Pre-Sub-Committee Response (PSCR).

Table 7: Results of the cost-minimisation analysis; corrected in the Pre-Sub-Committee Response

Component	Somatrogon		Somatropin	
	Median	Mean	Median	Mean
Treatment dose per week	0.66 mg	0.655	0.238 mg	0.237
Cost per mg (AEMP)	$14.99	$15.04	$14.58	$41.58
Total medicine cost/kg/week	$9.90	$9.85	$9.90	$9.85
Incremental cost	$0.00	$0.00	$0.00	$0.00

Source: Table 3.4.1, p175 of the submission and added during the evaluation and corrected in the Pre-Sub-Committee Response

AEMP = approved ex-manufacturer price; kg = kilograms; mg = milligrams

6.30 The equi-effective doses were estimated from Study 4006 at 12 months as somatrogon 0.66 mg/kg/week and somatropin 0.238 mg/kg/week based on median doses. The use of median treatment doses for somatrogon and somatropin to

determine the equi-effective doses may not provide a robust comparison of steady-state doses between the two medicines among patients with pGHD. The treatment dosing data reported in Study 4006 was not likely to be normally distributed (i.e. the median values were greater than the mean values for both somatrogon and somatropin). The mean treatment doses for somatrogon and somatropin were likely more conservative in accounting for the range of doses observed in Study 4006, which may reflect the likely range within clinical practice. The equi-effective doses derived using the mean treatment doses from Study 4006 are somatrogon 0.655 mg/kg/week and somatropin 0.237 mg/kg/week. The treatment is expected to be ongoing with discontinuation expected when children near adult height or when height is in the adult range. The recommended dosing of somatrogon (0.66 mg/kg/week) is slightly higher than the mean treatment dose for somatrogon (0.655 mg/kg/week).

6.31 The submission suggested no additional costs and/or cost offsets in the cost-minimisation analysis. The trials did report more injection site reactions with somatrogon compared to somatropin although these were mostly mild.

6.32 The requested AEMP for somatrogon 24 mg was $359.86 and for somatrogon 60 mg was $899.64 based on median doses. The equivalent AEMP based on mean doses for somatrogon 24 mg was $361.08 and for somatrogon 60 mg was $902.70.

Drug cost/patient/year

6.33 The estimated of cost per patient per year in this paediatric population is dependent on patient weight. The cost per week was presented during the submission and calculated for additional child weights during the evaluation as presented in Table 8. The calculations are shown for 20-kilograms of body weight.

Table 8: Somatrogon and somatropin patient weight, cost per mg, cost per week

Component	Somatrogon	Somatropin
Cost per mg (B)	$14.99	$41.58
Dose (mg) per kg per week (C)	0.66	0.238
20 kg body weight patient (A)		
Dose (mg) per week (A x C)	13.2	4.76
Cost per week ((A x C) x B)	$197.92	$197.92
15kg body weight patient		
Dose (mg) per week	9.9	3.57
Cost per week	$148.40	$148.44
Difference in cost per week compared to 20kg	-$0.04	$-
30kg body weight patient		
Dose (mg) per week	19.8	7.14
Cost per week	$296.80	$296.88
Difference in cost per week compared to 20kg	-$0.08	$-
50kg body weight patient		
Dose (mg) per week	33.0	11.9
Cost per week	$494.67	$494.80
Difference in cost per week compared to 20kg	-$0.13	$-

Source: Somatrogon CMA spreadsheet, sheet 1 "CMA calculations", p176 of the submission and added during the evaluation for additional body weights.
kg = kilograms; mg = milligrams

6.34 These estimates translate into a somatrogon cost per year (cost per week multiplied by 52 weeks) of $7,716.80 for a 15 kg child, $10,291.84 for a 20 kg child, $15,433.60 for a 30 kg child or $25,722.84 for a 50 kg child. The calculations performed during the evaluation rely on the assumption that a child will not change weight for the annual period of the cost calculation.

Estimated PBS usage & financial implications

6.35 This submission was not considered by DUSC.

6.36 The submission proposed a DPMQ for somatrogon of $382.03 for a 24 mg/1.2 mL pre-filled pen (maximum single-dose of 12 mg) and $943.41 for a 60 mg/1.2 mL pre-filled pen (maximum single-dose of 30 mg).

6.37 The submission used a market-share approach to estimate the usage and financial impact of listing weekly somatrogon on the PBS as an alternative to daily somatropin in paediatric patients for the treatment of SSABGHD and SSSG. The data sources within the submission were market data from PBS 1 in 10 data, PBS Statistics, and Centres for Disease Control and Prevention (CDC) growth charts. The market share approach assumed that 20% of the estimated patients in 2022 (year 1) will substitute to weekly somatrogon from daily somatropin and 65% thereafter at 2027 (year 6).

Table 9: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Population	The estimated number of patients treated with daily GH from 2022 to 2027 using a linear extrapolation of PBS 1 in 10 data from 2016 to 2019 Year 1: Age <5: 102; 5-9: 356; 10-14: 999; Total: 1,457 Year 2: 107; 348; 1,046; 1,500 Year 3: 111; 340; 1,092; 1,543 Year 4: 116; 332; 1,139; 1,587 Year 5: 121; 324; 1,185; 1,630 Year 6: 125; 316; 1,232; 1,673	Uncertain. The submission did not provide appropriate justification for the linear market growth of daily GH. The PBS 1 in 10 data was verified. The variation between the PBS 100% dataset and 10% dataset was insignificant and would not likely have an impact on the overall estimates
Uptake rate	The estimated uptake rate multiplied by the eligible population was: Yr 1: 20%, Yr 2: 40%, Yr 3: 50%, Yr 4: 55%, Yr 5: 60%, Yr 6: 65%	The submission did not provide appropriate justification for the assumed somatrogon uptake rate. The uptake rate was uncertain across all 6 years. There was no data to justify the assumed uptake rate, however, the assumption was not critical to the overall cost estimates of the drug.
Number of somatrogon patients	The uptake rate was applied to the estimated number of patients treated with daily GH from 2022 to 2027. Year 1: Age <5: 20; 5-9: 71; 10-14: 200; Total: 291 Year 2: 43; 139; 419; 600 Year 3: 56; 170; 546; 772 Year 4: 64; 182; 626; 783 Year 5: 72; 194; 711; 978 Year 6: 81; 205; 801; 1,087	Uncertain. The linear extrapolation of patient numbers by age and the somatrogon uptake rate were uncertain.
Average weekly dosage of somatrogon	The submission applied the median somatrogon weekly dose of 0.66 mg per kg of body weight per week in the estimation of the equi-effective doses using the average weight of patients (CDC growth charts) Age (weight): mg per week – Males; Females Under 5 (16kg M, 15kg F): 10; 10 5-9 (24kgs): 16; 16 10-14 (44kg M, 45kg F): 29; 30	Mean doses are more appropriate. Although the CDC growth charts are based on US patients, use of the data were reasonable since it was likely to be generalisable to the Australian population.
Somatrogon dosing and pens per patient per month	This was based on a dose of 0.66 mg/kg of body weight per week and the doses listed above Age: Pens per month (rounded) – Males; Females; Pen mg Under 5: 1.9 (2.0); 1.8 (2.0); 24mg 5-9: 1.2 (1.0); 1.2 (1.0); 60mg 10-14: 2.1 (2.0); 2.1 (2.0); 60mg	The rounding may be inappropriate and may account for discrepancies in the net costs within the financial analysis.

Source: Table prepared during the evaluation using Somatrogon utilisation and cost model excel spreadsheet
CDC = Centres for Disease Control and Prevention; GH = growth hormone; mg = milligrams, M = males, F = females, kg = kilograms

6.38 The approach to estimating the market share for somatrogon was reasonable. However, the rounding may be inappropriate and may account for discrepancies in the net costs within the financial analysis. For instance, in the under 5 age cohort, the average monthly number of pens for males was 1.9 and for females was 1.8, but both were rounded up to 2 pens when assessing the total annual usage of somatrogon. There were also differences to these values if the second decimal point was

considered (e.g., in the 5-9 age cohort: males, 1.20 pens; females 1.17 pens). The submission conducted a sensitivity analysis to address the impact of the rounding of daily and weekly treatment units in the financial analysis. The evaluation noted a conservative approach was taken by the sponsor given the assumption that the government would have to pay for 2 injections if the dose required is more than 1.

6.39 The estimated financial implications of listing once weekly somatrogon compared to daily somatropin in paediatric patients for the treatment of SSABGHD and SSSG are presented in the table below.

Table 10: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[1]	[5]	[5]	[5]	[5]	[5]
Number of scripts dispensed	[2]	[6]	[6]	[6]	[8]	[8]
Estimated financial implications of somatrogon						
Cost to PBS/RPBS less co-payments	$[3]	$[7]	$[7]	$[7]	$[7]	$[9]
Estimated financial implications for somatropin						
Cost to PBS/RPBS less co-payments	-$[4]	-$[4]	-$[4]	-$[4]	-$[4]	-$[4]
Net financial implications						
Net cost to PBS/RPBS	-$[4]	-$[4]	-$[4]	-$[4]	-$[4]	-$[4]

Source: Table 4.4.1 p121, Table 4.1.4 p 181, Table 4.2.4 p 187, Table 4.2.2 p 186, Table 4.1.4 p 181 of the submission.
PBS = Pharmaceutical Benefits Scheme, RPBS = Repatriation Pharmaceutical Benefits Scheme
The redacted values correspond to the following ranges:
[1] *< 500*
[2] *5,000 to < 10,000*
[3] *$0 to < $10 million*
[4] *net cost saving*
[5] *500 to < 5,000*
[6] *10,000 to < 20,000*
[7] *$10 million to < $20 million*
[8] *20,000 to < 30,000*
[9] *$20 million to < $30 million*

6.40 The total savings to the PBS/RPBS of listing somatrogon were estimated to be net cost saving in Year 6, and net cost saving in the first 6 years of listing. The submission noted that the PBS listing of somatrogon was likely to be cost-neutral and that the saving shown was a consequence of weight-based dosing estimates and rounding to achieve monthly doses. This statement could not be verified in the submission's model because the values inputted in the spreadsheet could not be cross-referenced as no formulas were provided. It was therefore difficult to assess the potential sources in the financial analysis that had contributed to a net cost saving to the PBS/RPBS when unrounded units of daily and weekly treatment were used, despite the cost-minimised price of somatrogon.

6.41 The estimated financial impact may be understated or overstated for the following reasons:

- The use of a cost minimised price should have led to a net cost to the PBS/RPBS relatively close to zero. The submission stated that the financial estimates presented were because of weight-based dosing estimates and rounding to achieve monthly doses. This could not be verified.
- The financial estimates were sensitive to the assumption of a linear extrapolation of the GH market growth
- The submission did not provide appropriate justification for the somatrogon uptake rate
- The submission used median doses in all calculations rather than mean doses.

6.42 The net financial impact to the PBS had been estimated over six full calendar years.

6.43 Grandfather patients were not counted separately in the submission but should already be covered in the predicted market for somatropin.

Quality Use of Medicines

6.44 The QUM activities planned for somatrogon were outlined in the submission. The submission proposed developing educational activities that help identify patients eligible for treatment, that ensure that the target population is consistent with the evidence presented in the submission, and to minimise the misuse of somatrogon in eligible patients. The submission presented no concerns relating to QUM, and no important issues were omitted. The submission did not propose a post marketing surveillance study.

6.45 The submission claimed that the weekly dosing of somatrogon, compared with the daily dosing of somatropin, could improve treatment satisfaction, patient adherence, and potentially, quality of life. The proposed multi-dose pre-filled pen is to be used with a new needle for each injection site. The same pre-filled pen should be discarded after being used 5 times or 28 days after the first use. If more than one injection is required to deliver a complete dose, each injection should be administered at a different site, but it was unclear how many injections would be required for a weekly dose. The PBAC considered that the administration of multiple injections to achieve a complete dose may pose a QUM issue but could be managed with appropriate education and training of how to use the device.

For more detail on the PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the Section 100 Growth Hormone Program listing of somatrogon for the treatment of SSABGHD and SSSG in patients who do not have a mature skeleton (i.e. a bone age of less than 13.5 years in females or less than 15.5 years in males). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of somatrogon would be acceptable if it were cost-minimised to somatropin for the same indications.

7.2 The PBAC advised that the equi-effective doses were 0.655 mg/kg/week of somatrogon and 0.237 mg/kg/week (0.034 mg/kg/day) of somatropin. This was derived from the mean treatment doses of the Study 4006 which the PBAC considered to represent the steady-state doses for somatrogon and somatropin.

7.3 The PBAC noted the consumer comments which noted the improved patient satisfaction and treatment convenience of weekly dosing with somatrogon compared to daily dosing with somatropin. The PBAC agreed with the consumer comments that there is clinical need for a once-weekly growth hormone treatment for patients with paediatric GHD.

7.4 The PBAC considered that somatrogon was non-inferior to somatropin in terms of effectiveness and safety. The PBAC accepted annual height velocity (HV) as the primary measure of non-inferiority. The PBAC noted the submission relied on the overlapping 95% confidence intervals in Study 4004 to support non-inferiority. The PBAC considered that Study 4006 together with two supportive trials (Study 4004 and Study 4009) demonstrated non-inferiority in terms of annualised HV at 12 months. The PBAC considered that the safety data presented showed no significant difference in serious or severe AEs between somatrogon and somatropin. The PBAC noted that there was a higher incidence of injection site reactions for somatrogon at 12 months and that it rarely led to discontinuation of the drug and considered this AE would be manageable in clinical practice.

7.5 The PBAC considered that the listing of somatrogon should result in a nil cost to Government since it is likely that patients currently using daily somatropin would switch to weekly somatrogon and the submission requested the same weekly cost as that of somatropin. The PBAC noted that there may be potential additional costs due to wastage if pens are discarded with drug remaining.

7.6 The PBAC noted that there were limited data available for the usage of somatrogon in patients aged 12-18, and that there were no data for children under 3 years of age but discussed that it was important that a weekly form of growth hormone injection was available to patients. Therefore, the PBAC considered that patients who do not have a mature skeleton should be eligible for somatrogon. The PBAC considered that the removal of the population criterion for children aged 3 years should be flowed-on to other PBS listed GH products for these indications.

7.7 The PBAC noted that switching from a once daily injection to a once weekly injection may pose QUM risks if the patients use somatropin concurrently with somatrogon or if there is frequent interchange between the therapies. The PBAC considered this risk to be low. However, to prevent treatment discontinuation in these circumstances, the PBAC considered that patients who initiate on somatropin or somatrogon for the treatment of SSABGHD or SSSG would not need to meet the initial restriction criteria again for those indications if they had previously met these criteria for either somatropin or somatrogon. The PBAC considered that the following criteria should be included in somatrogon for the respective indications, under the continuing

restriction, to allow patients to switch from daily to weekly treatment for GHD. The PBAC noted similar criteria were included in the restrictions for the other PBS listed GH products for these indications.

- [17596] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature and slow growth category
- [17603] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature associated with biochemical growth hormone deficiency category.

7.8 The PBAC considered that the relevant outcomes from its September 2021 consideration of somatropin should apply to somatrogon for these two indications.

7.9 The PBAC noted that the Early Supply Rule cannot currently be applied to Growth Hormone program listings and therefore considered that it should not apply to somatrogon.

7.10 The PBAC considered that somatrogon is not suitable for inclusion in the PBS medicines for prescribing by nurse practitioners, noting that somatropin can only be prescribed by an endocrinologist for this indication.

7.11 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because somatrogon is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over somatropin, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.

7.12 The PBAC advised, under section 101 (3BA) of the Act, that somatrogon should not be treated as interchangeable on an individual patient basis with any other drugs.

7.13 The PBAC noted that this submission is not eligible for an Independent Review as it was recommended for listing.

Outcome:
Recommended

8 Recommended listing

8.1 Add new medicinal products as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
SOMATROGON					
somatrogon 24 mg/1.2 mL injection, 1.2 mL pen device	NEW	1	1	1	Ngenla
somatrogon 60 mg/1.2 mL injection, 1.2 mL pen device	NEW	1	1	1	Ngenla

Benefit Type	53229
Restriction Number	11792
Treatment of Code (ToC)	8342
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Initial treatment
Restriction Level / Method	Authority required
Treatment criteria	[15885] [15685] Must be treated by a specialist or consultant physician in paediatric endocrinology; or [15884] Must be treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[23361] [23363] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 2 pharmacological growth hormone stimulation tests (e.g. arginine, clonidine, glucagon, insulin); or [23364] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 pharmacological growth hormone stimulation test (e.g. arginine, clonidine, glucagon, insulin) and 1 physiological growth hormone stimulation test (e.g. sleep, exercise); or [23365] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) with other evidence of growth hormone deficiency, including septo-optic dysplasia (absent corpus callosum and/or septum pellucidum), midline abnormality including optic nerve hypoplasia, cleft lip and palate, midfacial hypoplasia and central incisor, ectopic and/or absent posterior pituitary bright spot, absent empty sella syndrome, hypoplastic anterior pituitary gland and/or pituitary stalk/infundibulum, and genetically proven biochemical growth hormone deficiency either isolated or as part of hypopituitarism in association with pituitary deficits (ACTH, TSH, GnRH or vasopressin/ADH deficiency); or [23366] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1

	growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGF-1 levels; or [23367] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGFBP-3 levels AND [23429] [15859] Patient must have a current height at or below the 1st percentile for age and sex; or [23426] Patient must have a current height above the 1st and at or below the 25th percentiles for age and sex and a growth velocity below the 25th percentile for bone age and sex measured over a 12 month interval (or a 6 month interval for an older child); or [23428] Patient must have a current height above the 1st and at or below the 25th percentiles for age and sex and an annual growth velocity of 8 cm per year or less if the patient has a bone age of 2.5 years or less AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [17583] [17582] Patient must not have previously received treatment under the PBS S100 Growth Hormone Program AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16075] The maximum duration of the initial treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23443] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for initial treatment; AND, 3. (a) A minimum of 12 months of recent growth data (height and weight measurements) or a minimum of 6 months of recent growth data for an older child. The most recent data must not be more than three months old at the time of application; OR, (b) Height and weight measurements, not more than three months old at the time of application, for a patient whose current height is at or below the 1st percentile for age and sex; AND, 4. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less); AND, 5. Evidence of biochemical growth hormone deficiency, including the type of tests performed and peak growth hormone concentrations; AND, 6. The proprietary name (brand), form and strength

	of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [15905] Biochemical growth hormone deficiency should not be secondary to an intracranial lesion or cranial irradiation for applications under this category. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[28584] Any queries concerning the arrangements to prescribe may be directed to the Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001 [NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50395
Restriction Number	11649
Treatment of Code (ToC)	8378
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Continuing treatment with this drug
Restriction Level / Method	Authority required
Treatment criteria	[NEW TC2] Patient must be undergoing continuing PBS-subsidised treatment with this drug AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[17604] [17603] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature associated with biochemical growth hormone deficiency category AND

	[NEW CC1] Patient must have been treated with PBS-subsidised growth hormone for the most recent treatment period (either: (i) 32 weeks for an initial/recommencement treatment period, (ii) 26 weeks for a continuing treatment period) AND [NEW CC2] Patient must have been assessed for growth for the most recent treatment period where either: (i) the assessment demonstrates an adequate response to treatment irrespective of dose, (ii) the assessment demonstrates an inadequate response to treatment dosed less than the upper dose limit AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[NEW PI1] Definition of an adequate response to treatment: Patient must have either: (i) achieved the 50th percentile growth velocity for bone age and sex, (ii) achieved an increase in height standard deviation score for chronological age and sex, (iii) achieved a minimum growth velocity of 4cm/year, (iv) achieved and maintained mid parental height standard deviation score. Prescribers must assess if there is an adequate response to growth hormone treatment. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23360] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; AND, 3. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 4. A bone age result performed within the last 12 months; AND, 5. The final adult height (in cm) of the patient's mother and father (where available); AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week

Cautions	
Benefit Type	50395
Restriction Number	11669
Treatment of Code (ToC)	8463
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Continuing treatment as a reclassified patient
Restriction Level / Method	Authority required
Treatment criteria	[16426] [16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[23452] [23451] Patient must have previously received treatment under the PBS S100 Growth Hormone Program (treatment) under a category other than short stature associated with biochemical growth hormone deficiency AND [17237] [17232] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [17233] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [17234] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [17235] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [17236] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [23453]

	[16429] Patient must have previously received treatment under the indication risk of hypoglycaemia secondary to growth hormone deficiency in neonates/infants and have reached or surpassed 5 years of age (chronological); or [23410] Patient must have had a height at or below the 1st percentile for age and sex immediately prior to commencing treatment; or [23454] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and a growth velocity below the 25th percentile for bone age and sex measured over the 12 month interval immediately prior to commencement of treatment (or the 6 month interval immediately prior to commencement of treatment if the patient was an older child at commencement of treatment); or [23455] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and an annual growth velocity of 14 cm per year or less in the 12 month period immediately prior to commencement of treatment, if the patient had a chronological age of 2 years or less at commencement of treatment; or [23456] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and an annual growth velocity of 8 cm per year or less in the 12 month period immediately prior to commencement of treatment, if the patient had a bone or chronological age of 2.5 years or less at commencement of treatment AND [23361] [23363] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 2 pharmacological growth hormone stimulation tests (e.g. arginine, clonidine, glucagon, insulin); or [23364] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 pharmacological growth hormone stimulation test (e.g. arginine, clonidine, glucagon, insulin) and 1 physiological growth hormone stimulation test (e.g. sleep, exercise); or [23365] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) with other evidence of growth hormone deficiency, including septo-optic dysplasia (absent corpus callosum and/or septum pellucidum), midline abnormality including optic nerve hypoplasia, cleft lip and palate, midfacial hypoplasia and central incisor, ectopic and/or absent posterior pituitary bright spot, absent empty sella syndrome, hypoplastic anterior pituitary gland and/or pituitary stalk/infundibulum, and genetically proven biochemical growth hormone deficiency either isolated or as part of hypopituitarism in association with pituitary deficits (ACTH, TSH, GnRH or vasopressin/ADH deficiency); or [23366] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGF-1 levels; or [23367] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGFBP-3 levels AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity

	AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23459] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment as a reclassified patient; AND, 3. (a) A minimum of 12 months of growth data (height and weight measurements) from immediately prior to commencement of treatment, or a minimum of 6 months of growth data from immediately prior to commencement of treatment if the patient was an older child at commencement of treatment; and the result of a bone age assessment performed within the 12 months immediately prior to commencement of treatment (except for a patient whose chronological age was 2.5 years or less at commencement of treatment); OR, (b) Height and weight measurements from within three months prior to commencement of treatment for a patient whose height was at or below the 1st percentile for age and sex immediately prior to commencing treatment; OR, (c) Confirmation that the patient has previously received treatment under the indication risk of hypoglycaemia secondary to growth hormone deficiency in neonates/infants and has reached or surpassed 5 years of age (chronological); AND, 4. Evidence of biochemical growth hormone deficiency, including the type of tests performed and peak growth hormone concentrations; AND, 5. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 6. A bone age result performed within the last 12 months; AND, 7. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [15905] Biochemical growth hormone deficiency should not be secondary to an intracranial lesion or cranial irradiation for applications under this category. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50438
Restriction Number	11657
Treatment of Code (ToC)	8469
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)

Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Recommencement of treatment
Restriction Level / Method	Authority required
Treatment criteria	[16426] [16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[17604] [17603] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature associated with biochemical growth hormone deficiency category AND [16128] [16127] Patient must have had a lapse in growth hormone treatment AND [17237] [17232] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [17233] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [17234] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [17235] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [17236] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711]

	[15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[16142] The maximum duration of each recommencement treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23493] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for recommencement of treatment; AND, 3. Recent growth data (height and weight, not older than three months); AND, 4. A bone age result performed within the last 12 months; AND, 5. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy
Administrative Advice	[16513] If recommencement of treatment is sought under a different indication than that under which the patient was previously receiving treatment an application for recommencement of treatment as a reclassified patient should be submitted. [NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50438
Restriction Number	11675
Treatment of Code (ToC)	8429
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Recommencement of treatment as a reclassified patient
Restriction Level / Method	Authority required
Treatment criteria	[16426] [16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics

	AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[23452] [23451] Patient must have previously received treatment under the PBS S100 Growth Hormone Program (treatment) under a category other than short stature associated with biochemical growth hormone deficiency AND [23398] [23400] Patient must have had a lapse in treatment AND [17237] [17232] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [17233] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [17234] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [17235] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [17236] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [23453] [16429] Patient must have previously received treatment under the indication risk of hypoglycaemia secondary to growth hormone deficiency in neonates/infants and have reached or surpassed 5 years of age (chronological); or [23410] Patient must have had a height at or below the 1st percentile for age and sex immediately prior to commencing treatment; or [23454] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and a growth velocity below the 25th percentile for bone age and sex measured over the 12 month interval immediately prior to commencement of treatment (or the 6 month interval immediately prior to commencement of treatment if the patient was an older child at commencement of treatment); or [23455] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and an annual growth velocity of 14 cm per year or less in the 12 month period immediately prior to commencement of treatment, if the patient had a chronological age of 2 years or less at commencement of treatment; or [23456] Patient must have had both a height above the 1st and at or below the 25th percentiles for age and sex immediately prior to commencing treatment and an annual growth velocity of 8 cm per year or less in the 12 month period immediately prior to commencement of treatment, if the patient had a bone or chronological age of 2.5 years or less at commencement of treatment

	AND [23361] [23363] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 2 pharmacological growth hormone stimulation tests (e.g. arginine, clonidine, glucagon, insulin); or [23364] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 pharmacological growth hormone stimulation test (e.g. arginine, clonidine, glucagon, insulin) and 1 physiological growth hormone stimulation test (e.g. sleep, exercise); or [23365] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) with other evidence of growth hormone deficiency, including septo-optic dysplasia (absent corpus callosum and/or septum pellucidum), midline abnormality including optic nerve hypoplasia, cleft lip and palate, midfacial hypoplasia and central incisor, ectopic and/or absent posterior pituitary bright spot, absent empty sella syndrome, hypoplastic anterior pituitary gland and/or pituitary stalk/infundibulum, and genetically proven biochemical growth hormone deficiency either isolated or as part of hypopituitarism in association with pituitary deficits (ACTH, TSH, GnRH or vasopressin/ADH deficiency); or [23366] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGF-1 levels; or [23367] Patient must have evidence of biochemical growth hormone deficiency, with a peak serum growth hormone concentration less than 10 mU/L or less than or equal to 3.3 micrograms per litre in response to 1 growth hormone stimulation test (pharmacological or physiological e.g. arginine, clonidine, glucagon, insulin, sleep, exercise) and low plasma IGFBP-3 levels AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16142] The maximum duration of each recommencement treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed).

	[amend 23495] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for recommencement of treatment as a reclassified patient; AND, 3. (a) A minimum of 12 months of growth data (height and weight measurements) from immediately prior to commencement of treatment, or a minimum of 6 months of growth data from immediately prior to commencement of treatment if the patient was an older child at commencement of treatment; and the result of a bone age assessment performed within the 12 months immediately prior to commencement of treatment (except for a patient whose chronological age was 2.5 years or less at commencement of treatment); OR, (b) Height and weight measurements from within three months prior to commencement of treatment for a patient whose height was at or below the 1st percentile for age and sex immediately prior to commencing treatment; OR, (c) Confirmation that the patient has previously received treatment under the indication risk of hypoglycaemia secondary to growth hormone deficiency in neonates/infants and has reached or surpassed 5 years of age (chronological); AND, 4. Evidence of biochemical growth hormone deficiency, including the type of tests performed and peak growth hormone concentrations; AND, 5. Recent growth data (height and weight, not older than three months); AND, 6. A bone age result performed within the last 12 months; AND, 7. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [15905] Biochemical growth hormone deficiency should not be secondary to an intracranial lesion or cranial irradiation for applications under this category. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	NEW
Restriction Number	NEW
Treatment of Code (ToC)	NEW
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15745] Short stature associated with biochemical growth hormone deficiency
Treatment phase	Changing drug treatment of this PBS-indication
Restriction Level / Method	Authority required
Treatment criteria	[15885] [15685] Must be treated by a specialist or consultant physician in paediatric endocrinology; or [15884] Must be treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology AND [NEW TC3] Patient must be undergoing PBS-subsidised treatment of this indication where each of the following applies: (i) the drug is changing, (ii) a Continuing treatment authority application for growth hormone has not been rejected in the past AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone

Clinical criteria	[17604] [17603] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature associated with biochemical growth hormone deficiency category AND [NEW CC3] Patient must have been treated with PBS-subsidised growth hormone for less than 32 weeks; or [NEW CC4] Patient must have been treated with PBS-subsidised growth hormone for the most recent treatment period (either: (i) 32 weeks for an initial/recommencement treatment period, (ii) 26 weeks for a continuing treatment period) where each of the following applies: (i) has been treated for at least 32 weeks, (ii) has been assessed for growth for the most recent treatment period where either: (a) the assessment demonstrates adequate growth irrespective of dose, (b) the assessment demonstrates an inadequate response to treatment dosed less than the upper dose limit of the previous growth hormone AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[NEW PI1] Definition of an adequate response to treatment: Patient must have either: (i) achieved the 50th percentile growth velocity for bone age and sex, (ii) achieved an increase in height standard deviation score for chronological age and sex, (iii) achieved a minimum growth velocity of 4cm/year, (iv) achieved and maintained mid parental height standard deviation score. Prescribers must assess if there is an adequate response to growth hormone treatment. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23360] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; AND, 3. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 4. A bone age result performed within the last 12 months; AND, 5. The final adult height (in cm) of the patient's mother and father (where available); AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written.

	[28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	53229
Restriction Number	11791
Treatment of Code (ToC)	8481
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth
Treatment phase	Initial PBS-subsidised treatment
Restriction Level / Method	Authority required
Treatment criteria	[15885] [15685] Must be treated by a specialist or consultant physician in paediatric endocrinology; or [15884] Must be treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[New CC5] Patient must have/have had a height measurement no greater than the 1st percentile adjusted for age plus sex, at the time of initiating treatment with this drug AND [New CC6] Patient must have/have had a growth velocity measurement below the 25th percentile adjusted for bone age plus sex measured over a 12 month interval (or a 6 month interval for an older child), at the time of initiating treatment with this drug; or [New CC7] Patient must have/have had an annual growth velocity of no greater than 8 cm per year (where the patient has/had a bone/chronological age of no greater than 2.5 years), at the time of initiating treatment with this drug AND [NEW CC8] Patient must have been treated with non-PBS-subsidised growth hormone for the most recent treatment period (either: (i) 32 weeks for an initial/recommencement treatment period, (ii) 26 weeks for a continuing treatment period) if treatment was initiated with non-PBS supply; and [NEW CC2] Patient must have been assessed for growth for the most recent treatment period where either: (i) the assessment demonstrates an adequate response to treatment irrespective of dose, (ii) the assessment demonstrates an inadequate response to treatment dosed less than the upper dose limit AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND

	[15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [17583] [17582] Patient must not have previously received treatment under the PBS S100 Growth Hormone Program AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more AND [16071] [16069] Patient must be male and must not have a height greater than or equal to 167.7 cm; or [16070] Patient must be female and must not have a height greater than or equal to 155.0 cm AND [17223] [17221] Patient must be male and must not have maturational or constitutional delay in combination with an estimated mature height equal to or above 160.1 cm; or [17222] Patient must be female and must not have maturational or constitutional delay in combination with an estimated mature height equal to or above 148.0 cm
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[NEW PI1] Definition of an adequate response to treatment: Patient must have either: (i) achieved the 50th percentile growth velocity for bone age and sex, (ii) achieved an increase in height standard deviation score for chronological age and sex, (iii) achieved a minimum growth velocity of 4cm/year, (iv) achieved and maintained mid parental height standard deviation score. Prescribers must assess if there is an adequate response to growth hormone treatment. [23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16075] The maximum duration of the initial treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [NEW PI2] The authority application must be in writing and must include: 1. A completed authority prescription form; AND 2. A completed Growth Hormone Authority Application Supporting Information Form for initial treatment; AND 3. A minimum of 12 months of recent growth data (height and weight measurements) or a minimum of 6 months of recent growth data for an older child. The most recent data must not be more than three months old at the time of application; or where treatment was initiated as non-PBS subsidised supply, documented evidence of a minimum of 12 months of growth data (height and weight measurements) or a minimum of 6 months of growth data for an older child, prior to the initiation of non-PBS subsidised therapy. The most recent of that data must not have be more than three months old at the time of initiating non-PBS subsidised therapy; AND

	4. Where treatment was initiated as non-PBS subsidised supply, growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND 5. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less), and, where treatment was initiated as non-PBS subsidised supply, within the preceding 12 months (except for a patient whose chronological age was 2.5 years or less) of initiating that non-PBS subsidised supply; AND 6. Confirmation of the patient's maturational or constitutional delay status; AND 7. If the patient has maturational or constitutional delay, confirmation that the patient has an estimated mature height below the 1st adult height percentile; AND 8. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). 9. The final adult height (in cm) of the patient's mother and father (where available) [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[28584] Any queries concerning the arrangements to prescribe may be directed to the Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001 [NEW AA2] A patient who is transitioning from non-PBS to PBS-subsidised supply of this drug for this condition must have met all the initial restriction criteria prior to initiating non-PBS subsidised treatment. A patient may qualify for PBS-subsidised treatment under this restriction once only. [NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Benefit Type	55212
Restriction Number	12863
Treatment of Code (ToC)	12787
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth

Treatment phase	Continuing treatment with this drug
Restriction Level / Method	Authority required
Treatment criteria	[NEW TC] Patient must be undergoing continuing PBS-subsidised treatment with this drug AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[17597] [17596] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature and slow growth category AND [NEW CC1] Patient must have been treated with PBS-subsidised growth hormone for the most recent treatment period (either: (i) 32 weeks for an initial/recommencement treatment period, (ii) 26 weeks for a continuing treatment period) AND [NEW CC2] Patient must have been assessed for growth for the most recent treatment period where either: (i) the assessment demonstrates an adequate response to treatment irrespective of dose, (ii) the assessment demonstrates an inadequate response to treatment dosed less than the upper dose limit AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more AND [16136] [16134] Patient must be male and must not have a height greater than or equal to 167.7cm; or [16135] Patient must be female and must not have a height greater than or equal to 155.0cm
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[NEW PI1] Definition of an adequate response to treatment: Patient must have either: (i) achieved the 50th percentile growth velocity for bone age and sex, (ii) achieved an increase in height standard deviation score for chronological age and sex, (iii) achieved a minimum growth velocity of 4cm/year, (iv) achieved and maintained mid parental height standard deviation score. Prescribers must assess if there is an adequate response to growth hormone treatment. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth

	Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23360] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; AND, 3. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 4. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less); AND, 5. The final adult height (in cm) of the patient's mother and father (where available); AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50395
Restriction Number	11668
Treatment of Code (ToC)	8389
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth
Treatment phase	Continuing treatment as a reclassified patient
Restriction Level / Method	Authority required
Treatment criteria	[16426] [16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[23446] [23445] Patient must have previously received treatment under the PBS S100 Growth Hormone Program (treatment) under a category other than short stature and slow growth AND [17237]

	[17232] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [17233] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [17234] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [17235] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [17236] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [23447] [17279] Patient must have previously received treatment under the indication short stature associated with chronic renal insufficiency, have undergone a renal transplant and a 12 month period of observation following the transplant, and have an estimated glomerular filtration rate of greater than or equal to 30mL/minute/1.73m2 measured by creatinine clearance, excretion of radionuclides such as DTPA, or by the height/creatinine formula; or [23448] Patient must have had a height at or below the 1st percentile for age and sex immediately prior to commencing treatment and a growth velocity below the 25th percentile for bone age and sex measured over the 12 month interval immediately prior to commencement of treatment (or the 6 month interval immediately prior to commencement of treatment if the patient was an older child at commencement of treatment) AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more AND [16071] [16069] Patient must be male and must not have a height greater than or equal to 167.7 cm; or [16070] Patient must be female and must not have a height greater than or equal to 155.0 cm
Population criteria	
Foreword	

Definitions	
Prescriber Instructions	[23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23449] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment as a reclassified patient; AND, 3. (a) A minimum of 12 months of growth data (height and weight measurements) from immediately prior to commencement of treatment, or a minimum of 6 months of growth data from immediately prior to commencement of treatment if the patient was an older child at commencement of treatment; and the result of a bone age assessment performed within the 12 months immediately prior to commencement of treatment; OR, (b) Confirmation that the patient has previously received treatment under the indication short stature associated with chronic renal insufficiency, has undergone a renal transplant and a 12 month period of observation following the transplant, and has an estimated glomerular filtration rate of greater than or equal to 30mL/minute/1.73m2 measured by creatinine clearance, excretion of radionuclides such as DTPA, or by the height/creatinine formula; AND, 4. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 5. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less);; AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[11698] Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). , Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au, Applications for authority to prescribe should be forwarded to:, Department of Human Services , Prior Written Approval of Complex Drugs, Reply Paid 9826, HOBART TAS 7001 [NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50438
Restriction Number	11665
Treatment of Code (ToC)	5352
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth
Treatment phase	Recommencement of treatment
Restriction Level / Method	Authority required

Treatment criteria	[16426] [16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[17597] [17596] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature and slow growth category AND [16128] [16127] Patient must have had a lapse in growth hormone treatment AND [17237] [17232] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [17233] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [17234] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [17235] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [17236] – [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more

	AND [16136] [16134] Patient must be male and must not have a height greater than or equal to 167.7cm; or [16135] Patient must be female and must not have a height greater than or equal to 155.0cm
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[16142] The maximum duration of each recommencement treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks worth of treatment (with up to 1 repeat allowed). [amend 16148] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for recommencement of treatment; AND, 3. Recent growth data (height and weight, not older than three months); AND, 4. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less); AND, 5. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy
Administrative Advice	[16513] If recommencement of treatment is sought under a different indication than that under which the patient was previously receiving treatment an application for recommencement of treatment as a reclassified patient should be submitted. [NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	50438
Restriction Number	11656
Treatment of Code (ToC)	8494
Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth
Treatment phase	Recommencement of treatment as a reclassified patient
Restriction Level / Method	Authority required
Treatment criteria	[16426]

	[16422] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in paediatric endocrinology; or [16425] Must be treated by a medical practitioner in consultation with a nominated specialist or consultant physician in general paediatrics AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[23446] [23445] Patient must have previously received treatment under the PBS S100 Growth Hormone Program (treatment) under a category other than short stature and slow growth AND [23398] [23400] Patient must have had a lapse in treatment AND [17237] [[NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies); or [[NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by a significant medical illness; or [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by major surgery (e.g. renal transplant); or [[NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by an adverse reaction to growth hormone; or [NEW] The treatment must not have lapsed due to failure to respond to growth hormone for the most recent treatment period (32 weeks for an initial or recommencement treatment period and 26 weeks for a continuing treatment period, whichever applies), unless response was affected by non-compliance due to social/family problems AND [23447] [17279] Patient must have previously received treatment under the indication short stature associated with chronic renal insufficiency, have undergone a renal transplant and a 12 month period of observation following the transplant, and have an estimated glomerular filtration rate of greater than or equal to 30mL/minute/1.73m2 measured by creatinine clearance, excretion of radionuclides such as DTPA, or by the height/creatinine formula; or [23448] Patient must have had a height at or below the 1st percentile for age and sex immediately prior to commencing treatment and a growth velocity below the 25th percentile for bone age and sex measured over the 12 month interval immediately prior to commencement of treatment (or the 6 month interval immediately prior to commencement of treatment if the patient was an older child at commencement of treatment) AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND

	[15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16071] [16069] Patient must be male and must not have a height greater than or equal to 167.7 cm; or [16070] Patient must be female and must not have a height greater than or equal to 155.0 cm AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more
Population criteria	
Foreword	
Definitions	
Prescriber Instructions	[23357] An older child is defined as a male with a chronological age of at least 12 years or a bone age of at least 10 years, or a female with a chronological age of at least 10 years or a bone age of at least 8 years. [16142] The maximum duration of each recommencement treatment phase is 32 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23488] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for recommencement of treatment as a reclassified patient; AND, 3. (a) A minimum of 12 months of growth data (height and weight measurements) from immediately prior to commencement of treatment, or a minimum of 6 months of growth data from immediately prior to commencement of treatment if the patient was an older child at commencement of treatment; and the result of a bone age assessment performed within the 12 months immediately prior to commencement of treatment; OR, (b) Confirmation that the patient has previously received treatment under the indication short stature associated with chronic renal insufficiency, has undergone a renal transplant and a 12 month period of observation following the transplant, and has an estimated glomerular filtration rate of greater than or equal to 30mL/minute/1.73m2 measured by creatinine clearance, excretion of radionuclides such as DTPA, or by the height/creatinine formula; AND, 4. Recent growth data (height and weight, not older than three months); AND, 5. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less)AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 16 weeks' worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	
Benefit Type	NEW
Restriction Number	NEW
Treatment of Code (ToC)	NEW

Category / Program	S100 - Section 100 (Growth Hormone) (Code GH)
Prescriber Type(s)	Medical Practitioners
PBS Indication	[15683] Short stature and slow growth
Treatment phase	Changing drug treatment of this PBS-indication
Restriction Level / Method	Authority required
Treatment criteria	[15885] [15685] Must be treated by a specialist or consultant physician in paediatric endocrinology; or [15884] Must be treated by a specialist or consultant physician in general paediatrics in consultation with a nominated specialist or consultant physician in paediatric endocrinology AND [NEW TC3] Patient must be undergoing PBS-subsidised treatment of this indication where each of the following applies: (i) the drug is changing, (ii) a Continuing treatment authority application for growth hormone has not been rejected in the past AND [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone
Clinical criteria	[17597] [17596] Patient must have previously received treatment under the PBS S100 Growth Hormone Program under the short stature and slow growth category AND [NEW CC3] Patient must have been treated with PBS-subsidised growth hormone for less than 32 weeks; or [NEW CC4] Patient must have been treated with PBS-subsidised growth hormone for the most recent treatment period (either: (i) 32 weeks for an initial/recommencement treatment period, (ii) 26 weeks for a continuing treatment period) where each of the following applies: (i) has been treated for at least 32 weeks, (ii) has been assessed for growth for the most recent treatment period where either: (a) the assessment demonstrates adequate growth irrespective of dose, (b) the assessment demonstrates an inadequate response to treatment dosed less than the upper dose limit of the previous growth hormone AND [15708] [15707] Patient must not have a condition with a known risk of malignancy including chromosomal abnormalities such as Down and Bloom syndromes AND [15711] [15710] Patient must not have an active tumour or evidence of tumour growth or activity AND [16068] [16066] Patient must be male and must not have a bone age of 15.5 years or more; or [16067] Patient must be female and must not have a bone age of 13.5 years or more AND [16136] [16134] Patient must be male and must not have a height greater than or equal to 167.7cm; or [16135] Patient must be female and must not have a height greater than or equal to 155.0cm
Population criteria	

Foreword	
Definitions	
Prescriber Instructions	[NEW PI1] Definition of an adequate response to treatment: Patient must have either: (i) achieved the 50th percentile growth velocity for bone age and sex, (ii) achieved an increase in height standard deviation score for chronological age and sex, (iii) achieved a minimum growth velocity of 4cm/year, (iv) achieved and maintained mid parental height standard deviation score. Prescribers must assess if there is an adequate response to growth hormone treatment. [16059] The maximum duration of each continuing treatment phase is 26 weeks. Prescribers must determine an appropriate weekly dose in accordance with the dosing arrangements detailed in the National Health (Growth Hormone Program) Special Arrangement 2015 and request the appropriate number of vials/cartridges required to provide sufficient drug for 13 weeks' worth of treatment (with up to 1 repeat allowed). [amend 23360] The authority application must be in writing and must include:, 1. A completed authority prescription form; AND, 2. A completed Growth Hormone Authority Application Supporting Information Form for continuing treatment; AND, 3. Growth data (height and weight) for the most recent 6 month treatment period, including data at both the start and end of the treatment period. The most recent data must not be older than three months; AND, 4. A bone age result performed within the last 12 months (except for a patient whose chronological age is 2.5 years or less); AND, 5. The final adult height (in cm) of the patient's mother and father (where available); AND, 6. The proprietary name (brand), form and strength of the growth hormone requested, and the number of vials/cartridges required to provide sufficient drug for 13 weeks worth of treatment (with up to 1 repeat allowed). [16016] Prescribers must keep a copy of any clinical records relating to the prescription, including such records required to demonstrate that the prescription was written in compliance with any relevant circumstances and/or purposes. These records must be kept for 2 years after the date the prescription to which the records relate is written. [28759] In children with diabetes mellitus prescribers must ascertain that a growth failure is not due to poor diabetes control, diabetes control is adequate, and regular screening occurs for diabetes complications, particularly retinopathy.
Administrative Advice	[NEW AA1] The upper dose limit of somatrogon is 20.73 mg/m2/week. The upper dose limit of somatropin is 7.5 mg/m2/week
Cautions	

8.2 Flow-on changes to all PBS restrictions of somatropin indicated for SSABGHD and SSSG:

- Remove population criteria "Patient must be aged 3 years old".
- Replace concept code 23434 with 23443 where applicable.
- Replace existing somatropin continuing treatment phase restriction with the continuing treatment phase restriction outlined above for the respective indications.
- Amend concept code 23443 to read "the growth hormone" instead of "somatropin".
- Add changing drug treatment phase.
- Add this treatment criterion to all treatment phases: [NEW TC1] Patient must be undergoing treatment for the stated indication with only one growth hormone.

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

Pfizer is pleased that the PBAC has recommended somatrogon for children with biochemical growth hormone deficiency, and short stature and slow growth. PBS reimbursement of this weekly treatment option will reduce the burden associated with daily injections for Australian children and their caregivers.