6.15 PEGVISOMANT

Injection set containing powder for injection 10 mg, 30 and diluent, 30,
Injection set containing powder for injection 15 mg, 30 and diluent, 30,
Injection set containing powder for injection 20 mg, 30 and diluent, 30,
Injection set containing powder for injection 20 mg, 1 and diluent, 1,
Somavert®, Pfizer Australia Pty Ltd

1 Purpose of Application

1.1 The minor submission requested the following changes to the definition of failure to achieve biochemical control in the current initial PBS restriction for pegvisomant:

- A reduction to the level of growth hormone (GH) from 2.5 mcg/L to 1 mcg/L;
- A reduction to the level of insulin-like growth factor 1 (IGF-1) from greater than 1.3 times the age- and sex-adjusted upper limit of normal (ULN) to greater than the age- and sex-adjusted ULN;
- A change from using both the GH and IGF-1 criteria to define failure to using either of these criteria; and
- To include GH levels in both mcg/L and mIU/L.

2 Requested listing

2.1 The sponsor's proposed changes to the pegvisomant listing are presented below with additions in *italics* and ~~strikethrough~~ for deletions.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
PEGVISOMANT			Somavert® Pfizer
10 mg, powder for injection, 30	1	5	
15 mg, powder for injection, 30	1	5	
20 mg, powder for injection, 30	1	5	
20 mg, powder for injection, 1	4	0	

Category / Program	Section 100 – Highly Specialised Drugs Program

Prescriber type:	☒Medical Practitioners
PBS Indication:	Acromegaly
Treatment phase:	Initial treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must have an age- and sex-adjusted insulin-like growth factor 1 (IGF-1) concentration greater than ~~1.3 times~~ *the* upper limit of normal (ULN), AND The treatment must be after failure to achieve biochemical control with a maximum indicated dose of either 30 mg octreotide LAR or 120 mg lanreotide ATG every 28 days for 24 weeks; unless contraindicated or not tolerated according to the TGA approved Product Information, AND The treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue.
Prescriber Instructions	Somatostatin analogues include octreotide, lanreotide and pasireotide Failure to achieve biochemical control is defined as: 1) Growth hormone level is greater than ~~2.5~~ *1* mcg/L; ~~and~~ *OR* 2) IGF-1 level is greater than ~~1.3 times~~ the age- and sex-adjusted ULN If treatment with octreotide or lanreotide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of contraindication. If intolerance to either octreotide or lanreotide treatment developed during the relevant period of use which is of a severity to necessitate withdrawal of the treatment, the application must provide details of the nature and severity of this intolerance. In a patient treated with radiotherapy, pegvisomant should be withdrawn every 2 years in the 10 years after completion of radiotherapy for assessment of remission. Pegvisomant should be withdrawn at least 8 weeks prior to the assessment of remission. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1). Two completed authority prescriptions should be submitted with the initial application for this drug. One prescription should be for the loading dose of 80 mg for a quantity of 4 vials of 20 mg with no repeats. The second prescription should be for subsequent doses, starting from 10 mg daily, and allowing dose adjustments in increments of 5 mg based on serum IGF-1 levels measured every 4 to 6 weeks in order to maintain the serum IGF-1 level within the age-adjusted normal range based on the dosage recommendations in the TGA-approved Product Information. The authority application must be made in writing and must include: a) two completed authority prescription forms ; and b) a completed Acromegaly Pegvisomant initial PBS Authority Application - Supporting Information Form; and c) in a patient who has been previously treated with radiotherapy for this condition, the date of completion of radiotherapy, the date and result of IGF-1 levels taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy; and d) a recent result of the IGF-1 level and the date of assessment; and

	e) demonstration of failure to achieve biochemical control after completion of a prior therapy with either octreotide or lanreotide
Administrative advice	No increase in the maximum quantity or number of units may be authorised for the loading dose.

2.2 The PBAC noted that changing the definition of failure to achieve biochemical control to require meeting one of the GH or IGF-1 criteria may be inconsistent with the clinical criteria for pegvisomant which only specifies that IGF-1 should be higher than the upper limit of normal.

2.3 The submission noted that many laboratories reflect GH level as mIU/mL and, as such, endocrinologists have requested that the definition of biochemical control include GH levels in both mcg/L and mIU/L. The pre-PBAC response proposed a GH level of 1mcg/L or 3mIU/L as appropriate.

2.4 The submission did not state if the requested change should also apply to pasireotide, the other second-line agent currently listed for the treatment of acromegaly. The PBAC considered it would be appropriate for the pegvisomant and pasireotide restriction criteria to be consistent

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Background

Clinical data previously considered by the PBAC

3.1 At the November 2016 PBAC meeting, the PBAC recommended the Authority Required (Section 100) listing of pegvisomant as a second-line therapy for the treatment of patients with acromegaly, on a cost-minimisation basis to pasireotide. The PBAC accepted the requested clinical place of therapy as a second-line treatment for patients who had not achieved biochemical control using octreotide long acting repeatable (LAR) or lanreotide autogel (ATG) (Pegvisomant Public Summary Document, November 2016 PBAC Meeting).

3.2 The submission considered in November 2016 was based on a naïve indirect comparison of a post hoc subgroup from one placebo-controlled pegvisomant trial (Trial 3614, Trainer 2000)[1] and one active-controlled pasireotide trial (Gadelha 2014)[2]. Trial 3614 was a 12 week, randomised, double blind, placebo-controlled study of three different doses of pegvisomant in patients with uncontrolled acromegaly. The PBAC considered that the representativeness of the subgroup in Trial 3614 to the requested

[1] Trainer PJ, Drake WM, Katznelson L, Freda PU, Herman BV, van der Lely MD, Dimaraki EV, Stewart PM, Friend KE, Lee V, Besser GM and Scarlett JA. Treatment of acromegaly with the growth hormone-receptor antagonist pegvisomant. New England Journal of Medicine, 2000; 342(16):1171-1177.

[2] Gadelha MR, Bronstein MD, Brue T, et al, on behalf of the Pasireotide C2402 Study Group. Pasireotide versus continued treatment with octreotide or lanreotide in patients with inadequately controlled acromegaly (PAOLA): a randomised, phase 3 trial. Lancet Diabetes Endocrinol 2014; 2:875–884.

PBS population was unclear. Gadelha was a randomised, partially blinded, active controlled study in acromegaly patients inadequately controlled on octreotide LAR or lanreotide ATG. The PBAC considered the patient population in the pasireotide study was more consistent with the requested PBS restriction and the inclusion criteria of this study forms the basis of the current criteria for pegvisomant and pasireotide.

3.3 Table 1 presents the proportion of patients who achieved normalisation of IGF-1 concentrations in the overall population and PBS subgroup of Trial 3614 considered at the November 2016 PBAC meeting. There were statistically significant differences between the placebo and pegvisomant 15 mg and 20 mg groups for both the overall population and the PBS subgroup in the number of patients with normalised IGF-1 levels at week 12. The difference between the placebo and pegvisomant 10 mg group was found to be statistically significant for the overall population but not the PBS subgroup.

Table 1: Patients with IGF-1 normalisation at Week 12, Trial 3614 overall subjects and PBS subgroup

IGF-1 normalisation	Placebo	Pegvisomant		
		10 mg/day	15 mg/day	20 mg/day
Overall population (ITT)				
At week 12, n/N (%)	3/31 (9.7)	10/26 (38.5)	18/26 (75.0)	23/28 (82.1)
P-value vs placebo	-	p=0.0157	p=0.0001	p=0.0001
PBS subgroup				
At week 12, n/N (%)	2/19 (10.5)	2/11 (18.2)	7/12 (58.3)	14/18 (77.8)
Adjusted odds ratio (95% CI) vs placebo	-	2.09 (0.1, 34.7)	11.64 (1.5, 164.2)	28.04 (3.8, 376.1)

Note: Odds Ratios for PBS subgroup were estimated by exact logistic regression with treatment as factor, region (Europe/US) and baseline IGF-1 as covariates.
Abbreviations: CI, confidence intervals; IGF-1, insulin-like growth factor 1; ITT, intention to treat; PBS, Pharmaceutical Benefits Scheme;
Source: Pegvisomant November 2016 Public Summary Document

3.4 The PBAC noted that on the basis of the naïve indirect comparison of a post hoc PBS subgroup that pegvisomant was associated with IGF-1 normalisation in 55% of patients (23/31 patients), compared with 25% (33/130 patients) of patients receiving pasireotide 40 mg or 60 mg. Overall, the PBAC considered that the evidence supported the listing of pegvisomant on the basis of a cost-minimisation comparison to pasireotide. The PBAC considered that pegvisomant did not have the same risk of hyperglycaemia or diabetes as pasireotide.

Treatment algorithm for acromegaly

3.5 The submission stated current literature supports the proposed revised definition of failure to achieve biochemical control (Colao 2012[3], Diaz-Thomas 2017[4], Granada

[3] Colao A. Are we achieving pharmacological disease control in acromegaly? European endocrinologist, 2012; 8(2):105–11.
[4] Diaz-Thomas A. Gigantism and acromegaly guidelines. Accessed on 13 December 2018: https://emedicine.medscape.com/article/925446-guidelines

2018[5], Katznelson 2014[6], Melmed 2018[7]). The treatment goal is considered normalisation of IGF-1 levels as this reflects disease control and decreases the risk of developing complications from comorbidities and may reduce mortality (Melmed 2018). Guidelines also report that discordant GH and IGF-1 results can occur in 9-39% of patients receiving medical therapy for acromegaly. For this reason, the sponsor proposed that the definition of biochemical control be based on GH or IGF-1, instead of GH and IGF-1.

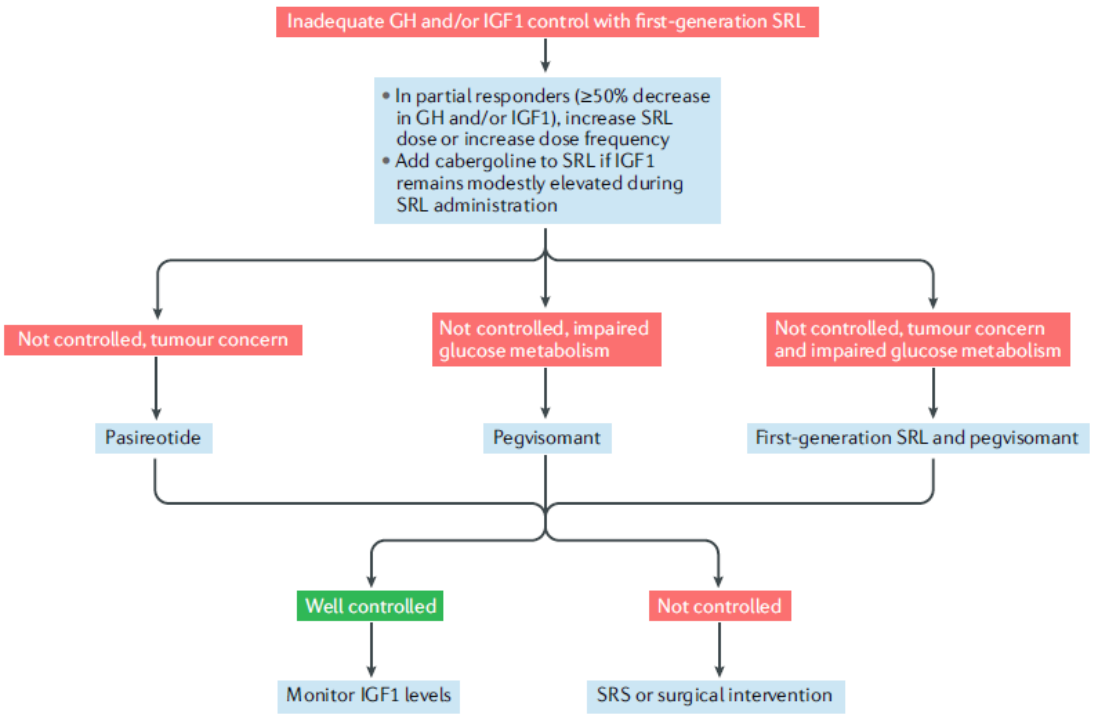
3.6 The Acromegaly Consensus Group, consisting of 37 experts in acromegaly management, has recently published an algorithm for the treatment of acromegaly in patients inadequately controlled with first-line somatostatin analogues (SSAs, octreotide and lanreotide) (Melmed 2018). The algorithm proposes a patient not controlled on first-line SSAs should be either changed to a second-line agent or be treated with a combination of first-line SSAs and pegvisomant, depending on the presence of clinically relevant residual tumour and/or impaired glucose tolerance (Figure 1). Disease control is defined as normalisation of IGF-1.

[5] Granada ML. Biochemical follow-up of treated acromegaly. Limitations of the current determinations of IGF-1 and perspective. Minerva Medica, 2018.

[6] Katznelson L, Laws ER, Melmed S, Molitch ME, Murad MH, Utz A and Wass JAH. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2014, 99(11):3933–3951.

[7] Melmed S, Bronstein MD, Chanson P, Klibanski A, Casanueva FF, Wass JAH, Stasburger CJ, Luger A, Clemmons DR and Giustina A. A consensus statement on acromegaly therapeutic outcomes. Nature Reviews: Endocrinology, 2018; 14:552-561.

Figure 1 A proposed algorithm for the treatment of acromegaly in patients inadequately controlled with first-generation SSAs (octreotide, lanreotide).



GH, growth hormone; IGF-1, insulin-like growth factor 1; SRL, somatatostatin receptor ligand; SRS, stereotactic radiosurgery
Source: Figure 1, page 557, Melmed 2018

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item.

Requested Change

4.3 To support the changes to the definition of biochemical control, the minor submission presented a subgroup analysis of the pivotal clinical study (Trial 3614) from the November 2016 submission. Of the 111 intention to treat (ITT) patients in Trial 3614, 91 (82%) qualified for the PBS relevant subgroup for this minor submission. Outcomes included change from baseline in IGF-1 concentrations (primary outcome) and normalisation of IGF-1 (secondary outcome). As this was a minor submission, the clinical data provided was not fully evaluated.

Table 2: Differences between Trial 3614 ITT population, the subgroup for the current restriction and the subgroup for the proposed restriction

	Trial 3614 ITT population	Trial 3614 subgroup (current restriction)	Trial 3614 subgroup (proposed restriction)
Number of patients	111	61	91
Diagnosis	Diagnosis of acromegaly based on accepted criteria made or confirmed at one of the participating study sites		
Previous treatment		At least one of: • Previous surgery • Previous radiotherapy • Previous radiosurgery • Previous SSA treatment	At least one of: • Previous surgery • Previous radiotherapy • Previous radiosurgery • Previous SSA treatment
IGF-1	Visit 2 IGF-1 value ≥ 30% above ULN*	> 1.3 x ULN	> ULN
GH	Not specified	Not specified	> 1 µg/L

GH, growth hormone; IGF-1, insulin-like growth factor 1; ULN, upper limit of normal

*Note patients were untreated. Exclusion criteria were prior treatment with any long-acting somatostatin analogue within 3 months of Visit 1 or prior treatment with any somatostatin analogue within 2 weeks of Visit 2

Source: Table 1, page 6 of the minor submission

4.4 The mean percentage reduction in IGF-1 and proportion of patients achieving normalisation of IGF-1 at Week 12 in the subgroup compared to the ITT population is presented in Table 3.

Table 3: Primary outcome results for the minor submission

	Group	Trial 3614 subgroup (proposed restriction)	Trial 3614 ITT population
Mean reduction in IGF-1 at Week 12	**Placebo**	4%	4%
	Pegvisomant 10 mg/day	31%	27%
	Pegvisomant 15 mg/day	47%	50%
	Pegvisomant 20 mg/day	61%	63%
Proportion of patients achieving normalised IGF-1 at Week 12	**Placebo**	10.7%	9.7%
	Pegvisomant 10 mg/day	45.0%	38.5%
	Pegvisomant 15 mg/day	68.4%	75.0%
	Pegvisomant 20 mg/day	77.3%	82.1%

IGF-1, insulin-like growth factor-1; ITT intention to treat

Source: Information on pages 17-18 of the minor submission

4.5 The submission stated that, for mean reduction in IGF-1, the results in the subgroup are in line with those seen in the ITT population. With respect to normalised status, the submission states that pegvisomant treatment was associated with a dose-dependent increase in the incidence of IGF-1 normalisation, which correlates with the conclusion from the analysis of the ITT population.

Estimated PBS usage & financial implications

4.6 Pasireotide was listed on the PBS on 1 September 2016 and pegvisomant was listed on 1 September 2017. The number of items processed from September 2016 to December 2018 is summarised in Table 4.

Table 4: PBS and RPBS items processed

Items processed	Sept 16 to Aug 17	Sept 17 to Aug 18	Sept 18 to Dec 18
Pegvisomant	-	107	69
Pasireotide	106	133	49

Source: http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

4.7 The November 2016 submission estimated that pegvisomant use would be 4,000 packs by Year 5 (see Table 5 below). While not clear in the minor submission, one pack is assumed to be equivalent to one item (or prescription).

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Estimated pegvisomant use					
Total packs (including loading dose)[a]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[a] These numbers differ from the numbers presented in the November 2016 PBAC Public Summary Document which were [redacted] in Year 1 to [redacted] in Year 5.

Source: Table 9, pg 20 of the minor submission

4.8 No estimate of the financial impact of the proposed restriction change was provided. However, the minor submission claimed the low uptake of pegvisomant to date is due in part to the fact that patients who have not responded to long-acting octreotide and lanreotide do not meet the criteria for failure of biochemical control in the current PBS restriction.

4.9 The sponsor claimed that the proposed restriction would not result in increased usage beyond the estimate in the original PBAC submission. Table 6 includes the assumptions used to determine how many patients might be eligible for treatment in the November 2016 submission. The PBAC noted that low uptake could also be attributed to a lower than estimated prevalence of acromegaly and/or fewer patients being uncontrolled with surgery or SSAs rather than not meeting the criteria for failure of biochemical control.

Table 6: Estimated number of patients eligible for treatment with pegvisomant

Eligible patients	Current Year (2016)	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Acromegaly population in Australia	2,000	2,035	2,069	2,103	2,138	2,172	2,206
First line medical therapy							
Number of patients uncontrolled with surgery/radiotherapy/dopamine agonist and treated with SSA (octreotide/lanreotide) (**[redacted]%**)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of patients uncontrolled with SSA (octreotide/lanreotide) (**[redacted]%**)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
*Second line medical therapy**							
Number of patients treated with pegvisomant (**[redacted]%**)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

SSA, somatostatin analogue

*a small number of patients were expected to receive treatment with pegvisomant in subsequent lines of therapy

Abbreviations: SSA, somatostatin analogue

Source: November 2016 submission, page 300

The redacted table shows that at Year 6, the estimated number of patients was less than 10,000.

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

5.1 The PBAC recommended the following changes to the definition of failure to achieve biochemical control in the current initial PBS restriction for pegvisomant:

- A reduction to the level of growth hormone (GH) from 2.5 mcg/L to 1 mcg/L;
- A reduction to the level of insulin-like growth factor 1 (IGF-1) from greater than 1.3 times the age- and sex-adjusted upper limit of normal (ULN) to greater than the age- and sex-adjusted ULN;

5.2 The PBAC recommended changing the definition to using either GH or IGF-1 in the definition of failure to achieve biochemical control. The PBAC noted the initial restriction criteria for pegvisomant did not include a clinical criteria related to GH levels but only for IGF-1 levels. The PBAC noted that discordance of GH and IGF-1 results can occur in up to 30% of patients and the reasons for discordance can be complex. The PBAC considered the impact of changing the definition of failure to achieve biochemical control to using either GH or IGF-1 levels was uncertain.

5.3 The PBAC noted the Katznelson (2014)[8] treatment guidelines discussed in the submission, as well as an international consensus[9] on acromegaly treatment, and considered these provided clinical support for the restriction changes. The PBAC noted the clinical data provided in the minor submission, and considered the subgroup analysis to be informative but of limited value in its decision-making. The PBAC recalled it has previously considered the representativeness of subgroups in the study to the PBS population unclear.

5.4 The PBAC noted standardisation issues for GH and IGF-1 assays, particularly with respect to laboratories reflecting GH levels in mIU/mL as well as mcg/L, with the latter being used in the PBS restrictions for the acromegaly agents. In accordance with the pre-PBAC response, the PBAC advised that the current pegvisomant restriction should be amended to reflect GH levels in both units, with 1 mcg/L being equal to 3 mIU/L.

5.5 The PBAC considered it would be appropriate for the changes made to the pegvisomant restriction criteria to also be made to the pasireotide restriction criteria to ensure both second line agents have consistent criteria. The PBAC also recommended the change to GH and IGF-1 levels be reflected in the clinical criteria for the initial restriction for pegvisomant and pasireotide. The PBAC noted the restriction criteria for the first line agents include reference to GH and IGF-1 levels and would welcome a submission from the sponsors of these agents proposing changes to better align the criteria with treatment guidelines.

5.6 The PBAC considered that while the low uptake of pegvisomant could be attributed to a number of factors, the recommended changes to the criteria may improve access for this small patient population. The PBAC considered the change in restriction was unlikely to increase usage beyond what was included in the original PBAC submission for pegvisomant

5.7 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Amend existing listing as follows:

[8] Katznelson L, Laws ER, Melmed S, Molitch ME, Murad MH, Utz A and Wass JAH. Acromegaly: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2014, 99(11):3933–3951.

[9] Giustina A, Chanson P, Bronstein MD, Klibanski A, Lambert S, Casanueva FF, Trainer P, Ghigo E, Ho K, Melmed S. A Consensus on Criteria for Cure of Acromegaly. J Clin Endocrinol Metab 2010, 95:3131-3148.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
PEGVISOMANT			Somavert® Pfizer
10 mg injection [30 vials] (&) inert substance diluent [30 syringes], 1 pack	1	5	
15 mg injection [30 vials] (&) inert substance diluent [30 syringes], 1 pack	1	5	
20 mg injection [30 vials] (&) inert substance diluent [30 syringes], 1 pack	1	5	
20 mg injection [1 vial] (&) inert substance diluent [1 syringe], 1 pack	4	0	

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒Medical Practitioners
PBS Indication:	Acromegaly
Treatment phase:	Initial treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must have an age- and sex-adjusted insulin-like growth factor 1 (IGF-1) concentration greater than ~~1.3 times~~ *the* upper limit of normal (ULN), AND The treatment must be after failure to achieve biochemical control with a maximum indicated dose of either 30 mg octreotide LAR or 120 mg lanreotide ATG every 28 days for 24 weeks; unless contraindicated or not tolerated according to the TGA approved Product Information, AND The treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue.
Prescriber Instructions	Somatostatin analogues include octreotide, lanreotide and pasireotide Failure to achieve biochemical control is defined as: 1) Growth hormone level is greater than ~~2.5~~ *1* mcg/L or *3mIU/L*; ~~and~~ *OR* 2) IGF-1 level is greater than ~~1.3 times~~ *the* age- and sex-adjusted ULN If treatment with octreotide or lanreotide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of contraindication. If intolerance to either octreotide or lanreotide treatment developed during the relevant period of use which is of a severity to necessitate withdrawal of the treatment, the application must provide details of the nature and severity of this intolerance.

	In a patient treated with radiotherapy, pegvisomant should be withdrawn every 2 years in the 10 years after completion of radiotherapy for assessment of remission. Pegvisomant should be withdrawn at least 8 weeks prior to the assessment of remission. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1). Two completed authority prescriptions should be submitted with the initial application for this drug. One prescription should be for the loading dose of 80 mg for a quantity of 4 vials of 20 mg with no repeats. The second prescription should be for subsequent doses, starting from 10 mg daily, and allowing dose adjustments in increments of 5 mg based on serum IGF-1 levels measured every 4 to 6 weeks in order to maintain the serum IGF-1 level within the age-adjusted normal range based on the dosage recommendations in the TGA-approved Product Information. The authority application must be made in writing and must include: a) two completed authority prescription forms ; and b) a completed Acromegaly Pegvisomant initial PBS Authority Application - Supporting Information Form; and c) in a patient who has been previously treated with radiotherapy for this condition, the date of completion of radiotherapy, the date and result of IGF-1 levels taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy; and d) a recent result of the IGF-1 level and the date of assessment; and e) demonstration of failure to achieve biochemical control after completion of a prior therapy with either octreotide or lanreotide
Administrative advice	No increase in the maximum quantity or number of units may be authorised for the loading dose.

Amend existing listing for Pasireotide as follows:

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒Medical Practitioners
PBS Indication:	Acromegaly
Treatment phase:	Initial treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must not have previously received PBS-subsidised treatment with this drug for this condition, AND Patient must have a mean growth hormone (GH) level greater than ~~2.5~~ *1* microgram per litre *or 3mIU*/L, ~~*AND*~~ *OR* Patient must have an age- and sex- adjusted insulin-like growth factor 1 (IGF-1) level greater than ~~1.3 times~~ *the* upper limit of normal (ULN), AND The treatment must be after failure to achieve biochemical control with a maximum indicated

	dose of either 30 mg octreotide LAR or 120 mg lanreotide ATG every 28 days for 24 weeks; unless contraindicated or not tolerated according to the TGA approved Product Information, AND The treatment must not be given concomitantly with PBS-subsidised pegvisomant.
Population criteria:	Patient must be aged 18 years or older.
Prescriber Instructions	Failure to achieve biochemical control is defined as: 1) Growth hormone level is greater than ~~2.5~~ *1* mcg/L *or 3mIU/L*; ~~and~~ *OR* 2) IGF-1 level is greater than ~~1.3 times~~ *the* age- and sex-adjusted ULN If treatment with octreotide or lanreotide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of contraindication. If intolerance to either octreotide or lanreotide treatment developed during the relevant period of use which is of a severity to necessitate withdrawal of the treatment, the application must provide details of the nature and severity of this intolerance. In a patient treated with radiotherapy, pasireotide should be withdrawn every 2 years in the 10 years after completion of radiotherapy for assessment of remission. Pasireotide should be withdrawn at least 8 weeks prior to the assessment of remission. Biochemical evidence of remission is defined as: 1) Growth hormone (GH) levels of less than ~~2.5~~ *1* mcg/L *or 3mIU/*L; ~~and~~ *OR* 2) normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1) The authority application must be made in writing and must include: a) a completed authority prescription form; and b) a completed Acromegaly PBS Authority Application - Supporting Information Form; and c) a signed patient acknowledgment; and d) in a patient who has been previously treated with radiotherapy for this condition, the date of completion of radiotherapy must be provided; and a copy of GH and IGF-1 levels taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided; and e) a recent copy of GH and IGF-1 levels must be provided.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

Pfizer is pleased that the PBAC has recommended the changes to the restriction for pegvisomant which will improve access to this treatment for acromegaly patients.