5.12 PEGVISOMANT, Powder for injection 10 mg, powder for injection 15 mg, powder for injection 20 mg, Somavert®, Pfizer Australia Pty Ltd.

1 Purpose of Application

1.1 Section 100 (Highly Specialised Drugs) Authority Required listing of pegvisomant for the treatment of active acromegaly in patients who have failed to achieve biochemical control with somatostatin analogues (SSAs).

2 Requested listing

2.1 An abbreviated version of the requested listing is below. Suggestions and additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough to the following abbreviated version of the requested listing.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer	
PEGVISOMANT 20 mg, powder for injection	4	0	Public $[redacted] Private $[redacted]	Somavert®	Pfizer

Category / Program	*Section 100 – Highly Specialised Drugs Program*
Prescriber type:	☒ *Medical Practitioners*
PBS Indication:	*Acromegaly*
Treatment phase:	*Loading dose*
Restriction Level / Method:	☒ *Authority Required - In Writing*
Clinical criteria:	~~*Patient must have active acromegaly*~~ ~~*AND*~~ ~~*Patient must have had surgery OR patient is unfit or unwilling to undergo surgery*~~ ~~*AND*~~ ~~*Radiotherapy is contraindicated or patient is unfit or unwilling to undergo radiotherapy OR patient is receiving this drug as interim treatment while waiting the effects of radiotherapy*~~ ~~*AND*~~ ~~*Patient must have failed dopamine agonists*~~ *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 ≥ 1.3 times *upper limit of normal (*ULN). ~~*AND*~~ ~~*Treatment must cease if IGF-1 is not lower after 3 months of pegvisomant at 30 mg daily.*~~ ~~*AND*~~ ~~*Patient must have failed treatment with either octreotide LAR 30 mg or lanreotide ATG*~~

	~~*120 mg OR patient is intolerant or contraindicated to octreotide LAR 30 mg or lanreotide ATG 120 mg*~~ *AND* *The treatment must be after failure to achieve biochemical control with a maximum indicated dose of either 30 mg octreotide or 120 mg lanreotide every 28 days for 24 weeks, unless contraindicated or not tolerated according to the TGA approved Product Information* ~~*AND*~~ ~~*Patient must have failed treatment with pasireotide LAR OR patient must have been intolerant or contraindicated to pasireotide LAR or it is considered inappropriate*~~ *AND* *The treatment must be after failure to achieve biochemical control with a maximum indicated dose of pasireotide, unless contraindicated or not tolerated according to the TGA approved Product Information* *AND* *This treatment must be the sole PBS-subsidised therapy for this condition*
Population criteria:	*Patient must be 18 years or older*
Prescriber Instruction	*If treatment with octreotide, lanreotide or pasireotide is contraindicated according to the relevant TGA-approved Product Information, the application must provide details of contraindication.* *If intolerance to either octreotide, lanreotide or pasireotide treatment develops 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.* *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 IGF-1 level taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided at the time of approval.* *Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1)* *Treatment must cease if IGF-1 is not normalised after 3 months of pegvisomant treatment at a dose of 30 mg daily.*

Name, Restriction, Manner of administration and form	**Max. Qty**	**№.of Rpts**	**Dispensed Price for Max. Qty**	**Proprietary Name and Manufacturer**
PEGVISOMANT 10 mg, powder for injection	30	5	Public $[redacted] Private $[redacted]	Somavert® Pfizer

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒ Medical Practitioners
Condition:	Acromegaly
PBS Indication:	Acromegaly

Treatment phase:	*Initial treatment*
Restriction Level / Method:	☒ Authority Required - In Writing ☒ Authority Required - Telephone
Clinical criteria:	Patient must have received a PBS-subsidised loading dose with this drug for this condition *AND* *The 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 or 120 mg lanreotide every 28 days for 24 weeks, unless contraindicated or not tolerated according to the TGA approved Product Information* *AND* *The treatment must be after failure to achieve biochemical control with a maximum indicated dose of pasireotide, unless contraindicated or not tolerated according to the TGA approved Product Information* AND This treatment must be the sole PBS-subsidised therapy for this condition
Population criteria:	Patient must be over 18 years of age
Prescriber Instructions	*<contraindication instructions as per loading dose restriction>* *<withdrawal every 2 years after radiotherapy, definition of biochemical remission, and stopping rule as per loading dose restriction>* *Two completed authority prescriptions must be submitted with every initial application for this drug. The first authority prescription is for loading dose, and the second authority prescription is for initial treatment.*

Name, Restriction, Manner of administration and form	**Max. Qty**	**№.of Rpts**	**Dispensed Price for Max. Qty**	**Proprietary Name and Manufacturer**
PEGVISOMANT				Somavert® Pfizer
10 mg, powder for injection	30	5	Public $[redacted] Private $[redacted]	
15 mg, powder for injection	30	5	Public $[redacted] Private $[redacted]	
20 mg, powder for injection	30	5	Public $[redacted] Private $[redacted]	

Category / Program	*Section 100 – Highly Specialised Drugs Program*
Prescriber type:	☐ *Dental* ☒ *Medical Practitioners* ☐ *Nurse practitioners* ☐ *Optometrists* ☐ *Midwives*
PBS Indication:	*Acromegaly*
Treatment phase:	*Continuing treatment*
Restriction Level / Method:	☒ *Authority Required - Telephone*

Clinical criteria:	*Patient must have previously received PBS-subsidised treatment with this drug for this condition* *AND* *Patient must have a normalised age- and sex-adjusted insulin-like growth factor 1 (IGF-1) after 3 months of therapy of pegvisomant at 30 mg daily* *AND* *This treatment must be the sole PBS-subsidised therapy for this condition*
Population criteria:	*Patient must be 18 years or older*
Prescriber Instruction	*<withdrawal every 2 years after radiotherapy, definition of biochemical remission, and stopping rule as per loading dose restriction>*

2.2 The PSCR (p2) and pre-PBAC responses confirmed the submission was not seeking reimbursement for combination therapy with pasireotide, octreotide or lanreotide.

2.3 The submission also indicated that some patients were receiving pegvisomant under a special access scheme, and requested that they be grandfathered on to the PBS. No further details or a proposed grandfather restriction were provided.

2.4 The submission presented a cost-utility analysis of pegvisomant (10-30mg) compared with pasireotide (40mg or 60mg) and octreotide long-acting release (30mg) /lanreotide autogel (120mg).

2.5 The pre-PBAC response changed the basis on which listing for pegvisomant was being sought to a cost-minimisation to pasireotide (excluding cost offsets for diabetes). In conjunction with this change, the pre-PBAC response requested a PBS restriction consistent with pasireotide (with the exception of the restriction to patients aged 18 years or older).

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

3 Background

3.1 Pegvisomant was registered by the TGA on 7 December 2005 for the treatment of acromegaly in patients who have had inadequate response to surgery and/or radiation and/or other medical therapies or for whom these therapies are not appropriate.

3.2 Pegvisomant had not been considered previously by the PBAC.

4 Clinical place for the proposed therapy

4.1 Acromegaly is a rare condition characterised by a consistently high level of circulating growth hormone, primarily caused by benign tumours in the pituitary gland. As a result of increased growth hormone, there is also increased secretion of insulin-like growth factor-1 (IGF-1). Excess growth hormone and IGF-1 results in enlargement of the jaw and extremities, and over a prolonged period may lead to multiple significant comorbidities including cardiovascular complications, cerebrovascular events, gonadal dysfunction, impaired glucose tolerance and

diabetes, sleep apnoea, impaired respiratory function, colonic neoplasms, and bone and joint diseases.

4.2 The submission positioned pegvisomant as either second-line therapy in patients for whom long-acting octreotide or lanreotide was unsuccessful or contraindicated, and for whom pasireotide therapy was considered inappropriate; or third-line therapy in patients for whom both octreotide/lanreotide and pasireotide were unsuccessful. The submission also suggested that patients failing to achieve IGF-1 control with pasireotide or pegvisomant monotherapy would revert to treatment with a first generation SSA (long-acting octreotide or lanreotide). The pre-PBAC response (pg 2) revised the proposed clinical place in therapy, positioning it as a second-line therapy following failure with or contraindication to octreotide/lanreotide, as an alternative to pasireotide.

4.3 The ESC noted the difference in the mechanism of action for pegvisomant and SSAs; pegvisomant blocks the growth hormone receptor, reducing the effects of excess growth hormone and decreasing secretion of IGF-1, while SSAs reduce secretion of growth hormone. The ESC noted that international guidelines[1] suggest that for patients who partially respond to SSA therapy, combination therapy with pegvisomant and a SSA should be considered, and noted that clinical trials investigating combination therapy are currently underway[2]. The pre-PBAC response stated that a restriction for combination therapy with pegvisomant and a SSA is not requested.

4.4 The PBAC noted that the loading dose of 80 mg of pegvisomant is administered by subcutaneous injection under medical supervision, followed by daily subcutaneous injections of pegvisomant 10 mg. Serum IGF-1 levels should be obtained every 4-6 weeks and appropriate dose adjustments made in increments of 5 mg/day to maintain serum IGF-1 levels within age-adjusted normal ranges and to alleviate signs and symptoms of acromegaly. The maximum daily maintenance dose should not exceed 30mg/day. Treatment is ongoing while the patient shows a response to treatment.

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

5 Comparator

5.1 The submission nominated the long-acting SSAs, pasireotide, octreotide and lanreotide as the main comparators. The main argument provided in support of this nomination was that these therapies were the most likely to be replaced in practice, and in the absence of alternative treatments, octreotide and lanreotide would be continued even if responses to these treatments are inadequate. The PBAC accepted this argument in its consideration of pasireotide (PSD, November 2015), while noting the uncertain cost-effectiveness of the continued use of lanreotide and

[1] Katznelson et al. Acromegaly: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2014; 99 (11):3933-3951, page 3943; and Giustina et al. A consensus on the medical treatment of acromegaly. Nat Rev Endocrinol 2014; 10:243-248, page 245.

[2] A search of clinicaltrials.gov for "pegvisomant" AND "acromegaly" AND "somatostatin" resulted in 6 trials including the following (with the clincialtrials.gov identifier): NCT02668172 (pasireotide vs pasireotide + pegvisomant); NCT00595140 (pegvisomant vs pegvisomant + octreotide vs pegvisomant + carbergoline); and NCT01538966 (high dose monthly SSA + weekly pegvisomant vs low dose monthly SSA + daily pegvisomant vs low dose monthly SSA + weekly pegvisomant).

octreotide as comparators for pasireotide despite suboptimal biochemical control. Accordingly, the ESC considered that pasireotide, octreotide and lanreotide were appropriate comparators for pegvisomant with a similar caveat regarding the cost-effectiveness of their continued use despite suboptimal biochemical control.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician discussed the place in therapy and clinical need for the drug, particularly in children (who are not included in the TGA registered indication and are excluded from the PBS listing for pasireotide), the impact of high IGF-1 levels on mortality, and addressed matters in response to the Committee's questions. The clinician also advised that most clinicians would prefer to prescribe combination therapy with pegvisomant and a SSA to a significant proportion of their patients, but advised that clinicians would prefer to have pegvisomant subsidised for use only as monotherapy rather than not at all. The PBAC considered that the hearing was informative as it provided a clinical perspective on the clinical place of pegvisomant in treating this disease.

Consumer comments

6.2 The PBAC noted and welcomed the input from individuals (3), health care professionals (1) and organisations (2) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with pegvisomant including reduction in growth velocity, reduced pain and improved quality of life.

6.3 The PBAC noted the advice received from the Endocrine Society of Australia supporting the use of pegvisomant. The Endocrine Society of Australia indicated that some tumour types do not respond well to SSAs, and that pegvisomant is a good treatment option in these cases. The advice also stated that biochemical control with pegvisomant is greater when it is used in combination with long-acting SSAs and combination therapy allows for pegvisomant to be prescribed at a lower weekly dose. The PBAC also noted the advice received from the Australian Pituitary Foundation supporting the use of pegvisomant, and providing additional comments from patients (included with the summary of patient comments above). The PBAC noted that this advice was supportive of the evidence provided in the submission.

Clinical trials

6.4 The submission was based on a naïve indirect comparison of a post hoc sub-group from one placebo-controlled pegvisomant trial (Trial 3614) and one trial of pasireotide versus an active control arm of either long-acting octreotide or lanreotide (Gadelha 2014). Additional efficacy and safety data were included from one supplementary trial of pegvisomant monotherapy versus octreotide + pegvisomant versus octreotide monotherapy (Trial 1006); and 14 non-randomised studies assessing long-term

efficacy and safety of pegvisomant, including ACROSTUDY, a multicentre long-term post-marketing surveillance study of pegvisomant.

6.5 Details of the trials presented in the submission are provided in Table 1.

Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Randomised trials		
3614	A randomized, multicenter, double-blind, placebo-controlled study of B2036-PEG in the treatment of acromegaly. Trainer PJ, Drake WM, Katznelson L, et al. Treatment of acromegaly with the growth hormone-receptor antagonist pegvisomant.	Clinical Study Report, December 31, 1999. *New England Journal of Medicine* 2000; 342(16):1171-1177.
Gadelha 2014	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.
Supplementary randomised trial		
1006	Protocol number: A6291006. A randomized, parallel group, three-arm study to evaluate treatment with a combination of pegvisomant plus Sandostatin LAR®, pegvisomant (alone), and Sandostatin LAR® (alone) in patients with acromegaly. Trainer PJ, Ezzat S, D'Souza GA, et al. A randomized, controlled, multicentre trial comparing pegvisomant alone with combination therapy of pegvisomant and long-acting octreotide in patients with acromegaly.	Clinical Study Report, 25 October 2006. *Clinical Endocrinology* 2009; 71, 549–557.
Non-randomised studies		
1002	Protocol number: A6291002 (467-MET-9119-008). Investigation of the effects of pegvisomant on cardiac mass and cardiac function and on cardiovascular risk factors in patients with active acromegaly.	Clinical Study Report, 2 March 2007.
1007/1008	Protocol number: A6291007 (SOMAV-9119-010). A multi-center, open-label compassionate use program to provide pegvisomant to acromegaly patients refractory to conventional therapy. Protocol number: A6291008 (SOMAV-9119-011). A multi-center, open-label clinical study to provide pegvisomant to acromegaly in patients refractory to conventional therapy.	Clinical Study Report, 27 March 2006. Clinical Study Report, 27 March 2006.
1017	Protocol number: A6291017. A multi-centre, open-label study for the compassionate use of pegvisomant in acromegalic patients refractory to conventional therapy and for patients who received the product during the clinical development program. Ezzat S, Gaspo R, Serri O, et al. A Canadian multi-centre, open-label long-term study of pegvisomant treatment in refractory acromegaly.	Clinical Study Report, 20 January 2008. *Clin Invest Med* 2009; 32(6):E265-E277.
3613A	Protocol number: SEN-3613A. An open-label extension study of pegvisomant in the treatment of acromegaly (amendment).	Clinical Study Report, 13 December 2002.
3615	Protocol number: SEN-3615. An open-label extension study of pegvisomant in the treatment of acromegaly.	Clinical Study Report, 17 December 2002.

Trial ID	Protocol title/ Publication title	Publication citation
Basavilbaso 2010	Basavilbaso NG, Guitelman N, Nagelberg A, et al. Experience from the Argentine pegvisomant observational study: preliminary data.	In Arzt E, Bronstein M, Guitelman M (eds). *Pituitary Today II: New Molecular, Physiological and Clinical Aspects. Frontiers of Hormone Research* 2010; 38:42-49,
Colao 2006	Colao A, Pivonello R, Auriemma RS, et al. Efficacy of 12-month treatment with the GH receptor antagonist pegvisomant in patients with acromegaly resistant to long-term, high-dose somatostatin analog treatment: effect on IGF-1 levels, tumor mass, hypertension and glucose tolerance.	*European Journal of Endocrinology* 2006; 154:467–477.
De Marinis 2007	De Marinis L, Bianchi A, Fusco A, et al. Long-term effects of the combination of pegvisomant with somatostatin analogs (SSA) on glucose homeostasis in non-diabetic patients with active acromegaly partially resistant to SSA.	*Pituitary* 2007; 10:227–232.
Filopanti 2012	Filopanti M, Olgiati L, Mantovani G, et al. Growth hormone receptor variants and response to pegvisomant in monotherapy or in combination with somatostatin analogs in acromegalic patients: a multicenter study.	*J Clin Endocrinol Metab* 2012; 97:E165–E172.
Jorgensen 2005	Jørgensen JO, Feldt-Rasmussen U, Frystyk J, et al. Cotreatment of acromegaly with a somatostatin analog and a growth hormone receptor antagonist.	*J Clin Endocrinol Metab* 2005; 90(10):5627–5631.
Marazuela 2011	Marazuela M. Paniagua AE, Gahete MD et al. Somatotroph tumor progression during pegvisomant therapy: a clinical and molecular study.	*J Clin Endocrinol Metab* 2011; 96:E251–E259.
Ramos-Levi 2016	Ramos-Levi A, Bernabeu I, Álvarez-Escolá C, et al. Long-term treatment with pegvisomant for acromegaly: a 10-year experience.	*Clinical Endocrinology* 2016; 84(4):540.
Schreiber 2007	Schreiber I, Buchfelder M, Droste M, et al. Treatment of acromegaly with the GH receptor antagonist pegvisomant in clinical practice: Safety and efficacy evaluation from the German pegvisomant observational study.	*European Journal of Endocrinology* 2007; 156:75–82.
ACROSTUDY / Trial 1010	Protocol: A6291010. ACROSTUDY – A multicenter, post marketing surveillance study of Somavert therapy in patients with acromegaly. van der Lely AJ, Biller BMK, Brue T, et al. Long-term safety of pegvisomant in patients with acromegaly: comprehensive review of 1288 subjects in ACROSTUDY.	Clinical Study Report, 25 January 2011. *J Clin Endocrinol Metab* 2012, 97(5):1589–1597.
Bernabeu 2016	Bernabeu I, Pico A, Venegas E, et al, Spanish ACROSTUDY Group. Safety of long-term treatment with pegvisomant: analysis of Spanish patients included in global ACROSTUDY.	*Pituitary* 2016; 19(2):127-37.
Brue 2009	Brue T. ACROSTUDY: Status update on 469 patients.	*Hormone Research* 2009; (Suppl 1):34-38).
Buchfelder 2009	Buchfelder M, Schlaffer S, Droste M, et al., on behalf of the investigators of the German Pegvisomant Observational Study. The German ACROSTUDY: past and present.	*European Journal of Endocrinology* 2009; 161:S3–S10.
Chanson 2015	Chanson P, Brue T, Delemer B, et al., for the Médecins de l'Étude ACROSTUDY Pegvisomant treatment in patients with acromegaly in clinical practice: the French ACROSTUDY.	*Annales of Endocrinology* 2015; 76:664–670.
Freda 2015	Freda PU, Gordon MB, Kelepouris N, et al. Long-term treatment with pegvisomant: as monotherapy in patients with acromegaly: experience from ACROSTUDY.	*Endocrine Practice* 2015; 21(3):264-274.
Grottoli 2015	Grottoli S, Maffei P, Bogazzi F, et al. ACROSTUDY: the Italian experience.	*Endocrine* 2015; 48:334-341.

Trial ID	Protocol title/ Publication title	Publication citation
Trainer 2009b	Trainer PJ. ACROSTUDY: the first 5 years.	*European Journal of Endocrinology* 2009; 161:S19–S24.

Source: Table B.2.3, pp 56-58; Table B.2.2(iv), p192 of the submission

6.6 The key features of the randomised trials are summarised in Table 2. The submission conducted a post hoc subgroup analysis of individual patient data from Trial 3614 in order to assess efficacy in a sample of patients chosen to be representative of the proposed PBS population (i.e. patients inadequately controlled on previous treatments). The population in the subgroup appeared to be less treatment-experienced than patients in the proposed PBS restriction, as no patients were treated with a long-acting SSA in the three months prior to study entry. The PSCR (p1) indicated that although long acting SSAs were not allowed prior to study entry, short-acting SSAs were, and the PSCR argued that the efficacy of short- and long-acting SSAs are equivalent and therefore the selected subgroup could be considered representative. However, it is uncertain whether short- and long- acting SSAs would be used in the same disease stage, and hence population. The proportion of patients in this subgroup with prior use of SSAs was unclear. In the PSCR (p1) the sponsor indicated that 72.3% of the total population and 66.7% of the 'PBS subgroup' had been treated with SSAs, however it was unclear when the SSA treatment occurred. Further, no information was available on the proportion of patients in the PBS subgroup who had uncontrolled IGF-1 levels whilst taking a SSA. The pre-PBAC response stated that 40% of the PBS subgroup were uncontrolled on SSAs. The ESC considered that the representativeness of the PBS subgroup to the requested PBS population remained unclear. The patient population in the comparator trial (Gadelha 2014) was more consistent with the requested PBS restriction.

Table 2: Key features of the included randomised trials

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Pegvisomant vs placebo						
Trial 3614	112	MC, R, DB, placebo controlled 12 weeks	Low	Uncontrolled acromegaly	% change from baseline in IGF-1	% normalised IGF-1
Pegvisomant vs octreotide LAR						
Trial 1006	84	R, OL, active control 3 months	Unclear	Acromegaly inadequately controlled on octreotide LAR (adequately controlled = active control arm)	Adverse events	No
Pasireotide vs octreotide LAR/lanreotide ATG						
Gadelha 2014	198	R, MC, partially blinded, three-arm, active control 24 weeks	Low	Acromegaly inadequately controlled on octreotide LAR or lanreotide ATG	Biochemical control (IGF-1 and GH)	% normalised IGF-1

Abbreviations: ATG, autogel; DB, double blind; GH, growth hormone; IGF-1, insulin-like growth factor-1; MC, multi-centre; LAR, long acting release; OL, open label; R, randomised.
Source: compiled during the evaluation

6.7 The ESC noted that the primary outcome for the pegvisomant trial, Trial 3614, did not include biochemical control in terms of growth hormone levels because pegvisomant does not reduce the secretion of growth hormone (unlike the SSAs).

6.8 IGF-1 normalisation was used as a surrogate for mortality and morbidity associated with acromegaly. The evaluation considered that the causal relationship between IGF-1 and mortality was weakly supported by the available evidence. The PSCR (p3) did not agree that the relationship was weakly supported and referred to the list of observational studies included in the submission to support a positive correlation between IGF-1 and mortality. The ESC considered that while it was plausible that a reduction in IGF-1 levels may translate to a reduction in mortality risk, the use of IGF-1 normalisation as the outcome did not consider reductions in IGF-1 that do not reach normal but may still confer some clinical benefit. The ESC further considered that the relationship established between IGF-1 response and mortality with SSAs may not be directly applicable to that for pegvisomant, which has a different mechanism of action.

6.9 The PBAC agreed with the ESC that it is plausible that normalised IGF-1 may translate to a reduction in mortality risk.

Comparative effectiveness

6.10 Table 3 presents the proportion of patients who achieved normalisation of IGF-1 concentrations in the overall population and PBS subgroup of the key pegvisomant trial, Trial 3614. The submission and the ESC noted the uncertainty around the estimates given the small sample sizes and consequently wide confidence intervals for the PBS subgroup comparisons.

Table 3: 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
Source: Table B.6.5 (i), p82; Table B.6.6 (i), p83 of the submission

6.11 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 only statistically significant for the overall population and not the PBS subgroup.

6.12 The key efficacy outcome used in the indirect comparison of pegvisomant, pasireotide and octreotide/lanreotide was mean IGF-1 times the upper limit of normal. However, the key efficacy outcome used in the submission's economic model was the proportion of patients with normalised IGF-1. A naïve indirect comparison of the proportion of patients achieving normalised IGF-1 in the

pegvisomant Trial 3614 PBS subgroup and pasireotide trial Gadelha 2014 is presented in Table 4.

Table 4: Naïve indirect comparison of proportion of patients with normalised IGF-1

Outcome	Trial 3614 (PBS subgroup), Week 12				Gadelha 2014, Week 24		
	Placebo N=19	PEG 10mg N=11	PEG 15mg N=12	PEG 20mg N=18	PAS 40mg N=65	PAS 60mg N=65	OCT/LAN N=68
% normal IGF-1	2 (10.5%)	2 (18.2%)	7 (61.5%)	14 (77.8%)	16 (25%)	17 (26%)	0 (0%)

Abbreviations: LAN, lanreotide; OCT, octreotide; PAS, pasireotide; PEG, pegvisomant
Source: Table B.6.6(i), pp83-84; Section B.6.1(iv), p187 of the submission

6.13 The naïve indirect comparison of pegvisomant, pasireotide and octreotide/lanreotide presented in Section B of the submission used mean IGF-1 times the upper limit of normal (Table 5).

Table 5: Naïve indirect comparison of mean IGF-1 times the upper limit of normal

Outcome	Trial 3614 (PBS subgroup), Week 12				Gadelha 2014, Week 12		
	Placebo N=19	PEG 10mg N=11	PEG 15mg N=12	PEG 20mg N=18	PAS 40mg N=65	PAS 60mg N=65	OCT/LAN N=68
Mean x ULN (95% CI)	1.69 (1.34, 2.14)	1.33 (0.96, 1.85)	0.73 (0.48, 1.11)	0.69 (0.54, 0.88)	1.5 (1.3, 1.8)	1.4 (1.2, 1.7)	2.4 (2.2, 2.7)

Abbreviations: IGF-1, insulin-like growth hormone factor-1; LAN, lanreotide; OCT, octreotide; PAS, pasireotide; PEG, pegvisomant; ULN, upper limit of normal
Mean = geometric mean (GM), ie, exponentiation of arithmetic mean of log-transformed values;
95% CI for GM = exponentiation of 95% CI for arithemetic mean of log-transformed values
Source: Table B.6.1 (v), p192 of the submission.

6.14 The ESC noted that differences in use of prior therapies and patient characteristics between the trials, small patient numbers in the pegvisomant PBS subgroup, and the lack of a common comparator means that any comparison between the trials should be interpreted with caution. The clinical importance of any differences between treatments was unclear.

6.15 Results from supportive pegvisomant trial, Trial 1006, showed no significant difference in the proportion of patients achieving IGF-1 normalisation at Week 40 with pegvisomant monotherapy (14/25, 56%) versus pegvisomant/octreotide combination therapy (16/26, 62%). However, the median dose of pegvisomant at Week 40 was significantly greater in the pegvisomant monotherapy group (20 mg/day) than in the combination therapy group (15 mg/day).

6.16 IGF-1 results from the non-randomised pegvisomant studies included in the submission were generally consistent with those reported in key pegvisomant trial, Trial 3614.

6.17 Growth hormone levels increased, as expected, with pegvisomant use in Trial 3614, but the increase in growth hormone was less when pegvisomant was combined with long acting octreotide in Trial 1006, compared with the pegvisomant monotherapy group. Growth hormone levels reduced with the use of pasireotide in Gadelha (2014)

6.18 In the overall population of the key pegvisomant trial (Trial 3614) at Week 12, scores for individual signs and symptoms of acromegaly decreased from baseline in all pegvisomant groups, with the largest decreases observed in the pegvisomant

20 mg/day group. There were statistically significant decreases noted in the 15 mg and 20 mg pegvisomant groups for soft tissue swelling, excessive perspiration and fatigue, and all pegvisomant groups had statistically significantly improved total signs and symptoms scores compared with the placebo group. No results were presented for acromegaly signs and symptoms in the comparator trial (Gadelha 2014), however the authors noted there were more improvements in acromegaly symptom scores in patients given pasireotide than in patients given octreotide or lanreotide.

6.19 There was no significant change in pituitary tumour volume noted in the included pegvisomant trials, although there is a risk of increasing tumour size, with possible local effects on the optic chiasm. However, pasireotide (and to a lesser extent octreotide/lanreotide) treatment was associated with a reduction in tumour volume. The reduction in tumour volume is an expected effect associated with the SSAs, and can be beneficial for some patients. The ESC considered that this was a key reason why clinicians may wish to use pegvisomant in combination with an SSA (paragraph 4.3 also refers). A lack of comparative evidence with pegvisomant means that the extent of this potential benefit to patients resulting from a reduction in tumour volume is uncertain. However, the PBAC also noted that patients receiving pegvisomant did not experience a difference in the occurrence of headaches compared with placebo, which may be related to a lack of change in tumour volume.

Comparative harms

6.20 The comparative safety of pegvisomant and pasireotide was based on a naïve indirect comparison of the overall (safety) populations from Trial 3614 and Gadelha 2014, using treatment-emergent adverse events occurring in 5% or more of any treatment group (Table 6). The submission stated that many of the adverse events reported for both treatments were attributable to the disease rather than the treatments.

6.21 The submission noted the adverse events of interest for pegvisomant were injection site reactions and abnormal liver function; and for pasireotide were hyperglycaemic-related adverse events (increased blood glucose, diabetes, hyperglycaemia) and cholelithiasis. Cholelithiasis events were also noted in the octreotide/lanreotide group. Differences in the types of adverse events reported and differences in the trial populations mean any attempt to compare the safety profiles of these two treatments is highly uncertain. The PSCR (p2) argued that there was clear evidence that pegvisomant is safer than pasireotide based on a comparison of adverse events occurring in more than 15% of patients (particularly referring to rates of diabetes and hyperglycaemia). The ESC noted that the safety profiles of pegvisomant and pasireotide were different, and were established in separate, small clinical trial populations. The ESC therefore considered that it was difficult to make a direct comparison between the safety profiles. The PBAC noted that due to the occurrence of abnormal liver function associated with pegvisomant, the American Association of Clinical Endocrinologists (AACE) recommends liver function testing at monthly intervals for the first 6 months, quarterly for the following 6 months, and then biannually[3].

[3] American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. Endocrine practice, vol17 (suppl 4), July/August 2011.

6.22 Differences in the types of adverse events reported for the different drug classes means any attempt to compare the safety profiles of pegvisomant, pasireotide and octreotide/lanreotide is highly uncertain.

Table 6: Comparison of treatment-emergent adverse events in Trial 3614 and Gadelha 2014

Characteristic	Trial 3614 – Pegvisomant (12 weeks)			Gadelha 2014 (24 weeks)		
	10mg/day (N = 26)	15mg/day (N = 26)	20mg/day (N = 28)	Pasireotide 40mg (N=63)	Pasireotide 60mg (N=62)	Octreotide/ lanreotide (N=66)
Abdominal pain	-	-	-	5 (8%)	5 (8%)	2 (3%)
Alopecia	-	-	-	1 (2%)	4 (6%)	0 (0%)
Anaemia	-	-	-	4 (6%)	2 (3%)	2 (3%)
Asthenia	2 (7.7%)	2 (7.7%)	2 (7.1%)	-	-	-
Atrioventricular block first degree	-	-	-	4 (6%)	0 (0%)	0 (0%)
Blood glucose increased	-	-	-	3 (5%)	4 (6%)	0 (0%)
Cholelithiasis	-	-	-	6 (10%)	8 (13%)	9 (14%)
Diabetes	-	-	-	13 (21%)	16 (26%)	5 (8%)
Diarrhoea	1 (3.8%)	0	4 (14.3%)	10 (16%)	12 (19%)	3 (5%)
Dizziness	2 (7.7%)	1 (3.8%)	1 (3.6%)	5 (8%)	1 (2%)	2 (3%)
Flatulence	0	1 (3.8%)	3 (10.7%)	-	-	-
Flu syndrome	1 (3.8%)	3 (11.5%)	2 (7.1%)	-	-	-
Glucose tolerance impaired	-	-	-	2 (3%)	3 (5%)	4 (6%)
Headache	3 (11.5%)	2 (7.7%)	3 (10.7%)	9 (14%)	2 (13%)	3 (5%)
Hypoglycaemia	-	-	-	2 (3%)	4 (6%)	0 (0%)
Hyperglycaemia	-	-	-	21 (33%)	19 (31%)	9 (14%)
Hypertension	0	2 (7.7%)	0	-	-	-
Infection	6 (23.1%)	0	0	-	-	-
Injection site reaction	2 (7.7%)	1 (3.8%)	3 (10.7%)	-	-	-
Injury accidental	2 (7.7%)	1 (3.8%)	0	-	-	-
Liver function abnormal	3 (11.5%)	1 (3.8%)	1 (3.6%)	-	-	-
Nausea	0	2 (7.7%)	4 (14.3%)	2 (3%)	4 (6%)	2 (3%)
Nasopharyngitis	-	-	-	4 (6%)	7 (11%)	2 (3%)
Oedema peripheral	2 (7.7%)	0	1 (3.6%)	-	-	-
Pain	2 (7.7%)	1 (3.8%)	4 (14.3%)	-	-	-
Pain back	2 (7.7%)	0	1 (3.6%)	-	-	-
Pain chest	1 (3.8%)	2 (7.7%)	0	-	-	-
Paraesthesia	0	0	2 (7.1%)	-	-	-
Sinusitis	2 (7.7%)	0	1 (3.6%)	-	-	-
Somnolence	0	2 (7.7%)	2 (7.1%)	-	-	-
Sweat	3 (11.5%)	1 (3.8%)	0	-	-	-

Abbreviations: AE, adverse event
Source: Table B.6.2 (v), pp193-194 of the submission

Benefits/harms

6.23 The naïve indirect comparison presented in the submission did not allow for a comparison of the benefits and harms of pegvisomant and pasireotide or octreotide/lanreotide. Accordingly, a benefits/harms table has not been presented.

Clinical claim

6.24 The submission described pegvisomant as superior in terms of comparative efficacy and superior in terms of comparative safety over pasireotide and over ongoing treatment with octreotide or lanreotide.

6.25 The claim of superior efficacy was based on a naïve indirect comparison of mean IGF-1 levels times the upper limit of normal. The ESC considered the claim was inadequately supported for the following reasons:

- Poor exchangeability between the pegvisomant trial subgroup and the comparator trial
- Lack of a common comparator between trials
- Use of a post-hoc subgroup from Trial 3614 with small patient numbers and uncertainty around estimates (wide confidence intervals)
- Unclear clinical importance of any difference in IGF-1 levels between treatments (and unclear reliability as a surrogate outcome).

The PSCR (p1) argued that "the superiority of pegvisomant relative to the somatostatin analogues (SSAs) for IGF-1 normalisation was confirmed by three Australian endocrinologists". However, the ESC considered that expert opinion alone is not acceptable evidence of superiority.

6.26 The safety data presented in the submission was limited to a naïve comparison of treatment-emergent adverse events. The ESC considered that the different safety profiles for pegvisomant, pasireotide and octreotide/lanreotide mean that any attempt to compare the safety profiles of these treatments is highly uncertain.

6.27 The pre-PBAC response (p1) acknowledged that it was difficult to demonstrate superiority of pegvisomant compared with pasireotide with a high degree of certainty. The pre-PBAC response stated that "14.23 mg per day of pegvisomant can be expected to provide IGF-1 normalisation in 55% of patients relative to 25% of patients receiving pasireotide 40 mg or 60 mg per month. Therefore a larger number of patients will achieve control of their acromegaly with pegvisomant than pasireotide."

6.28 The PBAC agreed with the ESC that the clinical claim of superior efficacy was inadequately supported by the evidence, particularly with regards to the use of a *post hoc* naïve indirect comparison and the unclear clinical importance of a difference in IGF-1 levels and reliability as a surrogate outcome. Accordingly, the PBAC agreed that a cost minimisation approach was more appropriate, while also noting the difficulty of establishing non-inferiority on the basis of a naïve indirect comparison. However, the PBAC agreed that pegvisomant is at least non-inferior to pasireotide in terms of an increase in the proportion of patients achieving normalisation of IGF-1.

Economic analysis

6.29 The submission presented a cost-utility analysis using a decision analytic, Markov model. A summary of the model structure and rationale is presented in Table 7. The model was configured as a decision tree, with two treatment alternatives:

- comparator group, which represented the current treatment options for second-line treatment of acromegaly (pasireotide, octreotide or lanreotide);
- pegvisomant group, which represented the proposed situation of pegvisomant being PBS-listed for second-line treatment of acromegaly.

Table 7: Summary of model structure and rationale

Component	Summary
Time horizon	45 years in the model base case versus 12 weeks in Trial 3614
Outcomes	Life-years, QALYs
Methods used to generate results	Markov cohort expected-value analysis (1000 patients).
Health states	Normalised IGF-1, diabetes Normalised IGF-1, no diabetes High IGF-1, diabetes High IGF-1, no diabetes Remission (normalised IGF-1) due to previous radiotherapy Dead
Cycle length	One year. Half-cycle corrections were applied.
Transition probabilities	Rates of IGF-1 normalisation due to drug treatment and pasireotide-related diabetes risk were applied in the first cycle of the model only. Ongoing transition probabilities for diabetes; treatment discontinuation; normalisation of IGF-1 due to delayed effect of radiation therapy; and mortality.

Source: compiled during the evaluation

6.30 Key drivers of the economic model are presented in Table 8.

Table 8: Key drivers of the model

Description	Method/Value	Impact
Scenario analysis	The model compared two scenarios with multiple treatment options (pegvisomant available scenario versus comparator scenario) rather than pegvisomant versus pasireotide or octreotide/lanreotide.	High, favours pegvisomant
IGF-1 normalisation as surrogate for mortality outcomes	IGF-1 normalisation was used as a surrogate for mortality, utilities and costs in the model. The relationship between IGF-1 and mortality is weakly supported by the available evidence.	Unclear impact
Treatment algorithm	The model assumed limited treatment switching options beyond the first cycle. The model did not include any option for combination therapy with a somatostatin analogue and pegvisomant.	Unclear impact
Health state utilities	In a sensitivity analysis, an arbitrary utility decrement of 0.05 was applied to pegvisomant treatment to account for adverse events. Alternative utilities for patients with high IGF-1 (±0.05) were also tested in sensitivity analyses.	Moderate impact
Disease costs	Costs of managing acromegaly were based on US costs converted to Australian dollars which are unlikely to be relevant to the Australian setting. This conversion did not adequately account for differences in treatment patterns and unit costs between these two very different health care systems and the ESC considered it was likely to overstate the costs of managing acromegaly.	Unclear impact but the ESC considered this was likely to favour pegvisomant
Pegvisomant dosing and rates of IGF-1 normalisation	IGF-1 normalisation rates were obtained from a fixed dose trial in which patients did not have doses titrated to effect, and in which patients were not representative of the requested PBS population. The calculations used to determine the average dose and level of IGF-1 normalisation used in the model underestimated the dose required to achieve the expected effectiveness of pegvisomant, which impacts on costs and outcomes.	Unclear impact but the ESC considered this was likely to favour pegvisomant

Source: compiled during the evaluation

6.31 The ESC noted that patients who fail pegvisomant or pasireotide are assumed to switch to treatment with octreotide or lanreotide which has associated costs but zero utility gain. This does not reflect the possible clinical benefit associated with a reduction, but not normalisation, of IGF-1. This assumption favoured pegvisomant.

6.32 The model may not accurately reflect the treatment algorithm for acromegaly. The model assumed limited treatment switching options beyond the first cycle and did not include any option for combination therapy with a SSA and pegvisomant (while noting that such a listing was not sought).

6.33 The ESC considered that the average dose required to achieve the rate of IGF-1 normalisation, and therefore the costs of treatment, may have been underestimated because:

- The dose at the beginning of ACROSTUDY (before dose titration could occur) was compared with IGF-1 normalisation at 12 weeks in Trial 3614 where doses were not titrated and the representativeness of the study population to the PBS population was uncertain. In clinical practice, doses will be titrated to effect, and this method did not account for any dose titration, thereby underestimating the dose. The model also assumed that the average dose remained constant for the duration of the model.
- The conversion of dose ranges in the ACROSTUDY to specific dosing causes uncertainty and is likely to cause a higher assumed dose (and hence response) than was actually observed.
- The submission assumed a linear relationship between dose and proportion with normalised IGF-1 between the 10 mg and 15 mg dose strengths, where no such relationship has been established.
- As discussed in paragraph 6.6, the population in the PBS subgroup appears to be less treatment experienced than patients in the proposed PBS restriction. Given patients in a third-line setting will have failed two prior therapies versus one prior therapy in a second-line setting they could be more difficult to treat and may be less likely to achieve IGF-1 normalisation than the trial population.

6.34 The submission nominated a time horizon of 45 years for the economic model, arguing that the average age of diagnosis of acromegaly patients is approximately 45 years, and that life expectancy can be expected to be restored to that of the general population when IGF-1 values are restored. The ESC noted that the time horizon was considerably longer than the available evidence and assuming that life expectancy is restored to that of the general population was optimistic. However, the ESC noted the cost per QALY gained increased with a longer time horizon and therefore that the longer time horizon was a conservative assumption in this instance.

6.35 Table 9 summarises the results of the economic evaluation presented in the submission.

Table 9: Results of the modelled economic evaluation

Component	Pegvisomant group	Comparator group	Increment
Costs per person	$[redacted]	$716,024	$[redacted]
Life years per person	15.936	15.557	0.379
QALYs per person	12.088	11.296	0.792
Incremental cost/additional life year gained			**$[redacted]**
Incremental cost/additional QALY gained			**$[redacted]**

Abbreviations: QALYs, quality adjusted life years
Source: Table D.5.1, D.5.2, p287 of the submission

6.36 The pegvisomant treatment scenario was associated with an incremental cost effectiveness ratio (ICER) of $15,000 - $45,000 per QALY gained. The ESC noted that pasireotide has a Special Pricing Arrangement and this ICER was underestimated as it was based on the published price of pasireotide.

6.37 The ESC noted that the incremental cost per QALY gained with the availability of pegvisomant was independent of the efficacy of pegvisomant (although incremental costs and incremental QALYs changed; the overall ICER was unchanged). This is because the efficacy of pegvisomant effectively determined the size of the population in the economic analysis – in the 'pegvisomant available arm' of the model, any

patients not controlled on pegvisomant receive the comparator treatments which 'cancel out' with patients in the comparator arm. The PSCR (p2) claimed it was not true that the model was independent of the effectiveness of pegvisomant; however the ESC agreed with the evaluation that changing the effectiveness in the model does not change the ICER.

6.38 The PSCR (p2) argued that the comparison of treatment algorithms rather than individual products was appropriate, as it reflected how pegvisomant would be used in clinical practice, and noted that this approach has previously been accepted by the PBAC for pregabalin for neuropathic pain. In March 2011, the PBAC considered that the model comparing prescribing patterns with pregabalin, to prescribing patterns without pregabalin, was not unreasonable when substantial uptake not associated with switching between drug therapies was expected (pregabalin March 2011 PSD). The ESC considered that 'treatment pathway' approaches that model 'the world with' and 'the world without' a new treatment are likely to be appropriate when a new treatment changes the treatment pathway and there are cost and outcome consequences of this change (as well as any differences in costs and outcomes of the drug versus its comparator). In this case, pegvisomant is another treatment option following pasireotide and therefore the treatment pathway will not otherwise change and substantial uptake beyond switching is unlikely to occur. As such, the ESC considered that the current model had limited usefulness for informing PBAC decision making given the outcome of the economic evaluation was independent of the efficacy of pegvisomant and a direct comparison would have been more appropriate.

6.39 During the evaluation, an alternative modelled evaluation was conducted which compared pegvisomant treatment alone with pasireotide treatment alone in patients uncontrolled on octreotide/lanreotide (Table 10). The ESC considered that the alternative modelled evaluation was a more appropriate basis for decision making than the model presented in the submission.

Table 10: Alternative cost utility analysis conducted during the evaluation comparing pasireotide with pegvisomant

Component	Pegvisomant group	Comparator group	Increment
Costs	$ [redacted]	$716,169	$ [redacted]
Life Years	15.856	15.557	0.299
QALYs	11.899	11.296	0.603
Incremental cost/ life year gained			**$** [redacted]
Incremental cost/ QALY gained			**$** [redacted]

Abbreviations: QALYs, quality adjusted life years

Source: Constructed during the evaluation using 'Pegvisomant economic model – Section D' spreadsheet

6.40 In the alternative analysis, pegvisomant was associated with an incremental cost per QALY gained of $45,000 - $75,000. The ESC noted that this ICER was underestimated as it was based on the published price of pasireotide. In this alternative model, patients did not switch between pegvisomant and pasireotide, but reverted to octreotide/lanreotide if IGF-1 remained uncontrolled. Patients reverting to octreotide/lanreotide continued to have high IGF-1 levels as the treatment was considered to have zero effectiveness in the model.

6.41 The ESC noted that both the submission base case model and alternative model assumed that patients who are uncontrolled on pegvisomant and pasireotide will

switch back to lanreotide/octreotide and remain uncontrolled (with zero utility gain) on these treatments. Accordingly, a large proportion of patients are accruing costs but not receiving any benefit. The ESC considered that it may not be appropriate to assume no utility gain for these patients as there may be some benefit from reducing (but not normalising) IGF-1 and growth hormone (as was argued by the sponsor as a justification for not including a stopping rule for pegvisomant). A sensitivity analysis was conducted to determine the effect of applying a small utility gain to patients who revert to octreotide/lanreotide. Assuming a utility gain of 25% of the difference between the utility values for high and normalised IGF-1 resulted in an increase in the submission base case ICER to $15,000 - $45,000 per QALY (from $15,000 - $45,000 per QALY) and to $75,000 - $105,000 per QALY (from $45,000 - $75,000 per QALY) in the evaluation's revised model directly comparing pegvisomant and pasireotide.

6.42 The pre-PBAC response, in noting the difficulty in demonstrating superiority of pegvisomant compared with pasireotide with a high degree of certainty, offered an effective price for pegvisomant equivalent to that of pasireotide (excluding cost offsets for diabetes). The pre-PBAC response proposed an equi-effective dose of 14.23 mg pegvisomant to 40 mg and 60 mg pasireotide, and requested that the cost-offsets applied to pasireotide for additional diabetes management not be applied to pegvisomant. The pre-PBAC response stated that the proposed price does not take the following monitoring costs (which were included in the economic model) into account:

- $35.40 for pegvisomant (liver function tests);
- $276.85 for pasireotide (ECG, ultrasound of the gall bladder, thyroid function, ACTH and free cortisol); and
- $146.10 for octreotide/lanreotide (thyroid function tests and ultrasound of the gall bladder).

6.43 The PBAC considered that the uncertainties associated with the average dose, as described by the ESC (see paragraph 6.33) remained, and therefore it was likely that some patients would require a higher dose of pegvisomant to achieve IGF-1 normalisation, which would result in higher costs. As such, the PBAC considered that for treatment with pegvisomant (regardless of one, or a combination of the 10 mg, 15 mg and 20 mg strengths) an equivalent cost per day against pasireotide, consistent with dosing as outlined in the respective Product Information documents and on a flat pricing basis, is appropriate. The PBAC also noted that pasireotide has a Special Pricing Arrangement, and that the cost of pegvisomant should be calculated on the effective price of pasireotide.

6.44 The PBAC considered that it was reasonable for the cost-offsets for diabetes that are applied to pasireotide to not be applied to pegvisomant, as pegvisomant use is not associated with a higher occurrence of diabetes. However, the PBAC considered that due to the risk of abnormal liver function, cost offsets for liver function testing, based on 8 sets of tests over a 2 year period (see paragraph 6.21) using MBS item number 66512 should be included in the calculation of the pegvisomant price to ensure that there is no additional cost to the Commonwealth.

Drug cost/patient/year: $[redacted] for 10mg/day dose, up to $[redacted] for 30mg/day dose

6.45 The effective cost of pegvisomant and comparators per patient per year were based on the weighted average public/private hospital costs (49.02%/50.98%) for each dose. Treatment is ongoing for this chronic condition. Cost per patient per year by pegvisomant dose and for comparators is presented in Table 12.

6.46 The PBAC noted that as the pre-PBAC response proposed a cost-minimisation to pasireotide, the drug cost per patient per year would need to be recalculated based on the recommended equi-effective dose, cost-offsets and the effective price of pasireotide.

Table 12: Cost per patient per year for pegvisomant and for comparators, weighted by public/private hospital use

Drug	DPMQ		Calculation	Weighted average cost per patient per year
	Public hospital	Private hospital		
Pegvisomant 10mg	$[redacted]	$[redacted]	Weighted public/private DPMQ × 365.25 days per year/30 days' treatment per max qty	$[redacted]
Pegvisomant 15mg	$[redacted]	$[redacted]		$[redacted]
Pegvisomant 20mg	$[redacted]	$[redacted]		$[redacted]
Pegvisomant 25mg	-	-	Annual cost of 10mg + 15mg doses	$[redacted]
Pegvisomant 30mg	-	-	Annual cost of 10mg + 20mg doses	$[redacted]
Pasireotide 20mg, 40mg, 60mg	$7,800	$7847.02	Weighted public/private DPMQ × 365.25 days per year/56 days' treatment per max qty	$51,030
Octreotide LAR 30mg	$4,354.94	$4,401.94		$28,561
Lanreotide ATG 120mg	$4,256	$4,303.02		$27,915

Abbreviations: ATG, autogel; DPMQ, dispensed price for maximum quantity; LAR, long-acting release
Note: Pasireotide has a flat pricing structure across all dose strengths

Estimated PBS usage & financial implications

6.47 This submission was not considered by DUSC. The submission used an epidemiological approach to estimate the extent of use and financial implications to government associated with the PBS listing of pegvisomant (Table 13).These estimates were based on the cost-effectiveness proposal in the submission, and have not been updated based on the cost-minimisation proposal in the pre-PBAC response.

Table 13: 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]
Cost to the PBS/RPBS	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost saving from substitution of other treatments					
Reduction in cost to the PBS/RPBS of octreotide/ lanreotide and pasireotide	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Net cost of listing pegvisomant on the PBS/RPBS					
Net cost to PBS (less co-payments)	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Medicare costs associated with pegvisomant listing					
Pegvisomant monitoring costs	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Reduction in octreotide/ lanreotide monitoring costs	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Reduction in pasireotide monitoring costs	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]	-$[redacted]
Total					
Net cost to government	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

Source: Compiled using the Somavert_Section E Excel spreadsheet.

[a] The submission assumed one loading dose pack and 11 maintenance packs of pegvisomant for each patient per year. During the evaluation this was corrected to one loading dose pack and 12.13 maintenance packs per year. Similarly for the comparators the submission assumed 12 packs (2 packs per dispensing) per year, which was corrected to 13.04 packs per year.

6.48 The redacted table above shows that at year 5, the estimated number of packs was less than 10,000 per year. After the evaluation corrected for the number of packs used per year, pegvisomant was estimated to cost the PBS less than $10 million per year by the fifth year of listing (total of $10 million - $20 million over the first five years). The cumulative cost to government was $10 million - $20 million over the first five years. The reduced cost to government compared with the PBS estimate of less than $10 million was due to lower monitoring costs (pathology tests, medical imaging, and electrocardiograms) for pegvisomant compared with octreotide, lanreotide and pasireotide.

6.49 The ESC noted that the financial estimates of listing pegvisomant on the PBS were uncertain due to the following issues:

- The average daily dose of pegvisomant was based on the weighted average dose from the start of the post-marketing surveillance ACROSTUDY, and did not reflect titration of doses to achieve IGF-1 normalisation.
- The likely underestimate of use with only [redacted]% uptake assumed from patients who would otherwise be treated with pasireotide, given that all patients with acromegaly have a relatively high risk of developing diabetes, and prescribers may wish to avoid the potential hyperglycaemic events associated with pasireotide.
- Patients who were uncontrolled after a trial of pegvisomant and pasireotide monotherapy were assumed to switch back to octreotide/lanreotide, whereas in clinical practice they would likely continue on the treatment that provided the most effective IGF-1 control, or be considered for combination therapy.
- The treatment compliance and discontinuation rates used in the analysis were not adequately justified.

- The true prevalence and incidence of acromegaly in Australia is unknown.
- The time spent on treatments that failed to control IGF-1 (including dose titration phases), and on pasireotide prior to diabetes development was not accounted for in the analysis.
- The use of pegvisomant in combination with an SSA could lead to additional costs, and was not considered in the analysis; while noting that such a listing was not sought.
- It was unclear whether IGF-1 control would be maintained indefinitely, or if higher doses of pegvisomant would be required subsequently.
- The financial estimates were dependent on the IGF-1 normalisation rates specified for each treatment option, which were largely based on assumptions.

Quality Use of Medicines

6.50 The submission described educational materials that the sponsor will provide to relevant healthcare professionals, with information on requirements for managing and monitoring pegvisomant treatment.

6.51 The PBAC considered that octreotide, lanreotide and pasireotide might have some compliance advantages to pegvisomant, in that pegvisomant is a daily subcutaneous injection whilst the comparators are intramuscular injections administered once every 28 days. The impact, if any, on effectiveness is unknown.

Financial Management – Risk Sharing Arrangements

6.52 The submission acknowledged the probability of a volume-based Risk Sharing Arrangement being required with a positive recommendation for listing on the PBS, but did not provide specific details of such an arrangement. The sponsor stated its willingness to consider an outcomes-based Risk Sharing Arrangement, based on the measurement of patients achieving IGF-1 normalisation with pegvisomant in clinical practice.

6.53 The submission presented a proposed special pricing arrangement for pegvisomant in the form of a confidential rebate of [redacted]% of the PBS-listed DPMQ.

6.54 The PBAC considered that in light of the recommendation, the financial estimates, and therefore the basis for a Risk Sharing Arrangement Subsidisation Cap will need to be updated to account for the potential of prescribing multiple strengths and to further ensure that there is no additional cost to the Commonwealth.

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

7 PBAC Outcome

7.1 The PBAC recommended the Authority Required listing of pegvisomant as a second-line therapy for the treatment of patients with acromegaly, on the basis that it should be available only under special arrangements under Section 100 (Highly Specialised Drugs Program) on a cost minimisation basis to pasireotide whereby an

equivalent cost per day of treatment is established consistent with the respective TGA-approved Product Information.

7.2 The PBAC noted that the submission requested listing for the treatment of acromegaly in patients who failed to achieve biochemical control with SSAs (pasireotide and long-acting octreotide/lanreotide) on the basis of a cost-utility analysis compared with continued use (with inadequate response) of SSAs. The pre-PBAC response changed the requested listing to be following failure with long-acting octreotide/lanreotide (in the same line of therapy as pasireotide) on the basis of a cost-minimisation analysis to pasireotide (excluding the cost offsets for diabetes for pasireotide). The PBAC considered that the nominated comparators, pasireotide and long-acting octreotide/lanreotide, were appropriate.

7.3 The PBAC considered there was a clinical need for pegvisomant as an alternative therapy for patients who have uncontrolled IGF-1 despite treatment with an SSA. The PBAC also noted the advice received through the sponsor hearing and consumer comments that there is a particular clinical need in children, as pasireotide is only TGA registered for use in patients aged 18 years or older. The PBAC accepted the requested clinical place of therapy as second-line for patients who had not achieved biochemical control using long-acting octreotide/lanreotide.

7.4 The PBAC considered that some clinicians may wish to prescribe combination therapy with pegvisomant and an SSA. In this regard, the PBAC noted the differences in the mechanism of action for pegvisomant and SSAs and that international treatment guidelines suggest that combination therapy with pegvisomant and an SSA be considered for patients who partially respond to SSA therapy (see paragraph 4.3). The PBAC also noted that the advice from the clinician at the sponsor hearing confirmed this view. As PBS-subsidised combination therapy was not requested in the current submission, the clinical effectiveness, safety and cost-effectiveness of combination therapy has not been considered by the PBAC.

7.5 The PBAC recommended that the restriction for pegvisomant be managed as a Complex Authority Restriction by the Department of Human Services and be based on the current written authority restriction for pasireotide, with the following changes:

- A criterion preventing combination use of pegvisomant with a PBS-subsidised SSA should be added as the cost-effectiveness of combination treatment has not been assessed. A similar flow-on change should be made to the octreotide, lanreotide and pasireotide restrictions to specify that “treatment must not be in combination with PBS-subsidised pegvisomant”.
- The restriction to be silent on age, to allow for use in patients aged less than 18 years.
- A stopping rule, consistent with the listings for octreotide and lanreotide that “treatment must cease if IGF-1 is not lower after 3 months of treatment at the maximum tolerated dose”. In November 2015, the PBAC did not recommended a stopping rule for pasireotide because it was considered that clinicians are unlikely to continue ineffective treatment due to the substantial risk of harms. Pegvisomant is not associated with the same risk of hyperglycaemia and diabetes, and therefore a stopping rule was considered necessary.

- In addition, the PBAC noted that some patients are currently receiving pegvisomant through a special access scheme and that it would be reasonable for these patients to be grandfathered on to the PBS.

7.6 The PBAC noted that on the basis of the naïve indirect comparison of a *post hoc* PBS sub-group from one placebo-controlled pegvisomant trial (Trial 3614) and a trial of pasireotide versus an active control arm of either long-acting octreotide or lanreotide (Gadelha 2014), pegvisomant was associated with IGF-1 normalisation in 55% of patients (23/31 patients – see Table 4), compared with 25% (33/130 patients) of patients receiving pasireotide 40 mg or 60 mg per month. However, the PBAC noted that growth hormone levels increased with pegvisomant, as expected given the different mechanism of action, and that pituitary tumour volume did not change (with a risk of increasing tumour size). The PBAC noted that reduction in tumour volume is an expected effect associated with SSAs, and can be beneficial for some patients. The PBAC considered that the clinical importance of these differences was unclear. The PBAC further considered that although a causal relationship between IGF-1 and mortality had not been demonstrated, evidence suggests that there may be an association between GH and IGF-1 levels and mortality, and it was therefore a reasonable surrogate marker. Overall, the PBAC considered that the clinical claim of superior efficacy was inadequately supported by the evidence and that a listing on the basis of a cost-minimisation comparison to pasireotide was more appropriate.

7.7 The PBAC noted the issues raised by the ESC with regard to the economic model and financial estimates, but did not consider these further in view of the cost-minimisation proposal provided in the pre-PBAC response.

7.8 The PBAC noted that the sponsor proposed an equi-effective dose of 14.23 mg pegvisomant to 40 mg and 60 mg pasireotide. The PBAC recommended pegvisomant under the conditions discussed in paragraphs 6.34-6.44.

7.9 The PBAC considered that as pegvisomant does not carry the same risk of hyperglycaemia or diabetes as pasireotide, the cost offset applied to pasireotide for diabetes treatment should not be applied to pegvisomant. However, the PBAC noted that abnormal liver function has been observed with pegvisomant treatment, and that the AACE guidelines for the treatment of acromegaly recommend testing liver function for patients on pegvisomant (see paragraph 6.21). The PBAC therefore considered that a cost-offset for liver function testing should be included in the cost minimisation analysis for pegvisomant (see paragraph 6.44).

7.10 The PBAC noted that the financial estimates in the submission will require updating in line with the recommended second-line listing on the basis of cost minimisation to pasireotide. The PBAC recommended that the listing of pegvisomant should be cost neutral to the government (taking into account liver function tests and excluding the cost offsets applied to pasireotide for diabetes). The PBAC noted that the risk that patients may be prescribed pegvisomant in combination with an SSA is intended to be managed through the restriction.

7.11 The PBAC advised that under subsection 101(3BA) of the *National Health Act 1953*, that pegvisomant should not be treated as interchangeable on an individual patient basis with any other drug.

7.12 The PBAC advised that pegvisomant is not suitable for prescribing by nurse practitioners, in line with other treatments for acromegaly.

7.13 The PBAC noted that the Early Supply Rule does not currently apply to Section 100 (Highly Specialised Drugs Program) listings. The PBAC recommended that if the Early Supply Rule is applied to Section 100 listings in the future, it should not be applied to pegvisomant given the need for dose adjustments 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.

7.14 The PBAC noted that this submission is not eligible for an Independent Review, as it was a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new item:

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

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒Medical Practitioners
PBS Indication:	Acromegaly
Treatment phase:	Loading dose
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 ≥ 1.3 times 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 Treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue.
Prescriber Instruction	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 develops 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. Failure to achieve biochemical control is defined as: 1) Growth hormone level is greater than 2.5 mcg/L; and 2) IGF-1 level is greater than 1.3 times the age- and sex-adjusted ULN Somatostatin analogues include octreotide, lanreotide and pasireotide. 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. 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 IGF-1 level taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided at the time of approval. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1). Treatment must cease if IGF-1 is not lower after 3 months of pegvisomant treatment at the maximum tolerated dose. The authority application must be made in writing and must include: a) a completed authority prescription form for the loading dose; and b) a completed Acromegaly PBS Authority Application - Supporting Information Form; and c) a signed patient or parent/authorised guardian 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 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.
Administrative advice	No increase in the maximum quantity or number of units may be authorised 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 Complex Drugs Programs Reply Paid 9826 HOBART TAS 7001 Special Pricing Arrangements apply

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	

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒Medical Practitioners
Condition:	Acromegaly
PBS Indication:	Acromegaly
Treatment phase:	Initial treatment
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have been authorised a PBS-subsidised loading dose with this drug for this condition AND Treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue.
Prescriber Instructions	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. Somatostatin analogues include octreotide, lanreotide and pasireotide. 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 IGF-1 level taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided at the time of approval. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1). Treatment must cease if IGF-1 is not lower after 3 months of pegvisomant treatment at the maximum tolerated dose. Prescriptions for dose adjustments must provide sufficient quantity to allow appropriate dose adjustments made in increments of 5 mg per day 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 completed authority prescription forms sufficient for dose adjustments.

Administrative advice	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 Complex Drugs Programs Reply Paid 9826 HOBART TAS 7001 Special Pricing Arrangements apply

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	

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐ Dental ☒ Medical Practitioners ☐ Nurse practitioners ☐ Optometrists ☐ Midwives
PBS Indication:	Acromegaly
Treatment phase:	Continuing treatment
Restriction Level / Method:	☒ Authority Required - In Writing ☒ Authority Required - Telephone
Clinical criteria:	Patient must have previously received PBS-subsidised treatment with this drug under the Initial treatment restriction for this condition, AND Treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue, AND Treatment must cease if IGF-1 is not lower after 3 months of pegvisomant treatment at the maximum tolerated dose.
Prescriber Instruction	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. Somatostatin analogues include octreotide, lanreotide and pasireotide. 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 IGF-1 level taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided at the time of approval. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1).

Administrative advice	Applications for authorisation under this criterion may be made by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Special Pricing Arrangements apply

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

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☒Medical Practitioners
Condition:	Acromegaly
PBS Indication:	Acromegaly
Treatment phase:	Grandfathering
Restriction Level / Method:	☒Authority Required - In Writing
Clinical criteria:	Patient must have received non-PBS treatment with this drug for this condition prior to [listing date] AND Treatment must not be given concomitantly with a PBS-subsidised somatostatin analogue. AND Treatment must cease if IGF-1 is not lower after 3 months of pegvisomant treatment at the maximum tolerated dose.
Prescriber Instructions	Somatostatin analogues include octreotide, lanreotide and pasireotide. 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. 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 IGF-1 level taken at the most recent two yearly assessment in the 10 years after completion of radiotherapy must be provided at the time of approval. Biochemical evidence of remission is defined as normalisation of sex- and age- adjusted insulin-like growth factor 1 (IGF-1). A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria. 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 or parent/authorised guardian 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 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 IGF-1 levels must be provided.
Administrative advice	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 Complex Drugs Programs Reply Paid 9826 HOBART TAS 7001 Special Pricing Arrangements apply

Flow on changes to PBS restrictions for octreotide, lanreotide and pasireotide
Add clinical criterion: "Treatment must not be given concomitantly with PBS-subsidised pegvisomant."

9 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.

10 Sponsor's Comment

Pfizer Australia welcomes the PBAC recommendation to list pegvisomant on the PBS for acromegaly. Pegvisomant provides an important treatment option, with an alternative mechanism of action, in acromegaly patients who have failed other treatments.