7.11 LANREOTIDE
Injection 120 mg (as acetate) in single dose pre-filled syringe
Somatuline® Autogel®, Ipsen Pty Ltd

1 Purpose of Application

1.1 The minor resubmission requested a Section 100 (Highly Specialised Drugs Program) listing of lanreotide for the treatment of non-functional gastroenteropancreatic neuroendocrine tumours (GEP-NETs) in adults with unresectable locally advanced or metastatic disease. Major submissions for this listing were considered and rejected by the PBAC at their November 2015, November 2016 and July 2017 PBAC meetings. The key differences from the July 2017 resubmission are:

- A further price reduction for lanreotide ([redacted]% rebate on the current AEMP compared with a [redacted]% rebate on the DPMQ in the July 2017 resubmission). The rebate is to be reduced to [redacted]% following the introduction of the statutory reductions proposed as part of the 2017 budget. Reducing the rebate as proposed will result in no change in the lanreotide price as a result of the proposed statutory reductions.
- Revised caps for the proposed RSA to account for the reduced price.
- Proposal to prospectively collect data on treatments used post-progression and to use these data to revise the price of lanreotide.

2 Requested listing

2.1 The resubmission requested the following listing. The requested listing is the same restriction that was proposed in the July 2017 PBAC submission. Additions proposed by the Secretariat to the requested listing are added in italics.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
LANREOTIDE 120 mg/0.5 mL injection, 0.5 mL syringe	2	5	$4,256.00 (Public) ([redacted])* $4,302.93 (Private) ([redacted])*[a]	Somatuline® Autogel® Ipsen

*Effective DPMQ

[a]Corrected from the DPMQ (private) of $[redacted] in the submission

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
PBS Indication:	Non-functional gastroenteropancreatic neuroendocrine tumour
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒Streamlined
Clinical criteria:	The condition must be World Health Organisation (WHO) grade 1 or 2 unresectable locally advanced disease; OR The condition must be World Health Organisation (WHO) grade 1 or 2 metastatic disease. *AND* *The treatment must be as monotherapy*
Population criteria:	Patient must be aged 18 years or older
Prescriber Instructions	Grade 1 GEP-NETs are defined by WHO as the following: (1) Mitotic count (10HPF) of less than 2; and (2) Ki-67 index (%) of less than or equal to 2 Grade 2 GEP-NETs are defined by WHO as the following: (1) Mitotic count (10HPF) of 2-20; and (2) Ki-67 index (%) of 3-20 The treatment must not be in combination with PBS-subsidised everolimus or sunitinib for this condition.

3 Background

3.1 Lanreotide is TGA registered for the treatment of GEP-NETs in adult patients with unresectable locally advanced or metastatic disease; acromegaly; and symptoms of carcinoid syndrome associated with carcinoid tumours.

3.2 Lanreotide is currently PBS listed for the treatment of acromegaly and functional carcinoid tumour.

3.3 The PBAC has previously considered three major submissions requesting listing for the treatment of GEP-NETs in November 2015, November 2016 and July 2017.

3.4 The November 2015 major submission requested a broad listing for the treatment of GEP-NETs. The PBAC rejected the request on the basis of uncertain clinical significance of the progression free survival (PFS) results from the CLARINET study and fundamental issues with the economic model structure. The PBAC considered that the proposed restriction for GEP-NETs should be tightened to better distinguish from carcinoid tumours.

3.5 The PBAC did not recommend the requested listing for the treatment of non-functional GEP-NETs at its November 2016 meeting based on uncertain and unacceptable cost-effectiveness at the price proposed. The PBAC recalled that it previously considered the requested restriction should be tightened to identify patients more likely to benefit from active treatment (i.e. unsuitable for watchful waiting) however the PBAC noted that it was not possible to identify patients most suitable for treatment based on any biomarkers of symptoms. Accordingly, the PBAC considered it may be more appropriate to leave the judgement of suitability for active treatment to clinicians.

3.6 At its July 2017 meeting, the PBAC again did not recommend the listing of lanreotide for the treatment of non-functional GEP-NETs. In making its decision, the PBAC reiterated that the clinical significance in the gain in PFS was unclear and that the economic model provided in the submission and previous submissions was fundamentally unreliable for estimating the cost-effectiveness of lanreotide for the requested listing.

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Comparator

4.1 The previous major submissions nominated 'watchful waiting' as the main comparator. This was unchanged in the current resubmission.

4.2 The PBAC previously accepted watchful waiting as the appropriate comparator for establishing the clinical and cost-effectiveness of lanreotide for the first-line treatment of non-functional GEP-NETs.

4.3 The resubmission did not nominate a comparator in the second-line/post-progression setting. The ESC has previously noted that potentially relevant comparators in the post-progression setting include octreotide, sunitinib, everolimus, interferon alfa-2b, cytotoxic chemotherapy, peptide receptor radionuclide therapy and various palliative surgeries (paragraph 5.3, July 2017 lanreotide Public Summary Document, (PSD)).

5 Consideration of the evidence

Sponsor hearing

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

Consumer comments

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

Clinical trials

5.3 As a minor submission, no new clinical trials were presented in the resubmission.

5.4 The previous submissions were based on one head-to-head trial (CLARINET, n=204) comparing lanreotide to placebo in patients with non-functional GEP-NETs with additional long-term data from an open-label extension study (Study 729, n=88).

Comparative effectiveness

5.5 The trial results remain unchanged from the previous submissions.

5.6 Treatment with lanreotide was associated with a statistically significant increase in PFS compared with placebo (HR 0.47, 95% CI 0.30, 0.73). Median PFS was 72 weeks for the placebo group and not reached for the lanreotide group.

5.7 There was no statistically significant difference in OS between treatment arms during the pivotal trial or during additional post-trial monitoring (HR 1.05; 95% CI: 0.55, 2.03), with four deaths observed during the CLARINET trial (two in each of the lanreotide and placebo arms).

Clinical claim

5.8 The July 2017 resubmission described lanreotide as superior in efficacy with respect to PFS, and inferior with respect to overall adverse-events, compared to placebo for treatment of GEP-NETs. The PBAC previously considered the claim of superior efficacy with respect to PFS and inferior safety to be appropriate.

5.9 The clinical claim remains unchanged from the July 2017 resubmission.

Special Pricing Arrangement

5.10 The July 2017 resubmission proposed a Special Pricing Arrangement (SPA) consisting of a [redacted]% rebate on the published DPMQ for the current PBS listing (resulting in effective DPMQs of $[redacted] for S100 Public and $[redacted] for S100 Private). The PBAC considered the proposed price reduction of [redacted]% to be modest and it did not provide greater confidence in the cost-effectiveness of lanreotide, particularly given the fundamental issues with the economic model and the likelihood that some patients better served by watchful waiting may receive active treatment through a broad PBS-listing for non-functional GEP-NETs.

5.11 The current resubmission proposed a SPA whereby the sponsor will provide a [redacted]% rebate on the current AEMP resulting in an effective AEMP of $[redacted] for 1 x 120 mg injection. The corresponding effective DPMQs for 2 x 120 mg injections are $[redacted] (S100 Public) and $[redacted] (S100 Private).

5.12 The resubmission noted that the Government's proposed statutory price reductions for medicines in the F1 formulary of 5% and 10% on the 5th and 10th anniversary of the date of first listing respectively would result in a 14.5% (10% followed by a further 5%) price reduction to lanreotide on 1 June 2018 if legislated. The resubmission requested that the SPA rebate amount be adjusted to [redacted]% of the published AEMP following the 14.5% price reduction. This would maintain the effective AEMP at $[redacted] following the 14.5% statutory price reduction.

Economic analysis

5.13 As a minor submission, the submission did not provide a new economic model. At its July 2017 meeting, the PBAC considered that any future major resubmission would require a new economic model to provide a reliable estimate of cost-effectiveness.

5.14 The resubmission did not provide a revised incremental cost-effectiveness ratio based on the model included in the July 2017 resubmission incorporating the proposed effective AEMP. This is appropriate given the PBAC considered the economic model provided in the July 2017 resubmission (as well as the previous submissions) to be fundamentally unreliable for estimating the cost-effectiveness of lanreotide for the requested listing.

Post-progression treatments

5.15 At its July 2017 meeting, the PBAC noted the economic model was highly sensitive to assumptions relating to post-progression treatments, and the differential post-progression use of lanreotide between treatment arms in particular with the results ranging from lanreotide being dominant to costs per QALY gained at more than $200,000/QALY. The PBAC also noted that compared with the November 2016 submission, there were substantial changes to post-progression treatments and associated costs and this was based on a survey of three clinicians. Overall, the PBAC considered the post-progression treatment costs, as well as the duration of these treatments applied in the model, to be overestimated in favour of lanreotide.

5.16 The minor resubmission claimed that it was not possible to provide more accurate estimates of post-progression treatments with the current evidence. The resubmission stated that the sponsor is establishing a national registry of patients with NETs (including patients with GEP-NETs) to capture treatment patterns post-progression. The resubmission proposed that the post-progression treatment data captured in the registry could be used as part of an annual update to the economic model over the five-year term of the risk share arrangement and that the price of lanreotide could be adjusted accordingly.

Drug cost/patient/year: $[redacted].

5.17 The resubmission did not present a revised average cost per patient. The Department estimated the average cost for lanreotide per patient per year was $[redacted] based on 13 injections per year (i.e. 6.5 scripts of the maximum quantity of 2x120 mg injection) at $[redacted] for public hospital and $[redacted] for private hospital and the assumption of 64% of use through public hospitals. The estimated average cost was lower than in the July 2017 submission ($[redacted]) due to the application of a [redacted]% discount to the current weighted Public/Private published DPMQ compared with a [redacted]% discount in the July 2017 submission.

Estimated PBS usage & financial implications

5.18 The submission used an epidemiological approach to estimate the utilisation and financial implications associated with the first five years of listing lanreotide for the treatment of GEP-NETs (see Table 1). The submission used the same sources of data as the July 2017 submission. The PBAC considered the estimated utilisation and financial implications presented in the July 2017 submission to be uncertain due to:

- Limited available Australian data to inform Australian utilisation estimates. The underlying incidence/prevalence rates used were based on the Yao study (2004 US SEER data) rather than the Van der Swan (2013) study used in the November 2016 submission.
- The assumption that 23% of the eligible PBS population would be managed with a watchful waiting approach based on the proportion of patients from the CLARINET trial with WHO Grade 1 tumour, a primary location in the mid-gut, and a hepatic tumour burden ≤25%). However, application of this proportion to the prevalent PBS GEP-NET population was likely to overestimate the number of patients suitable for watchful waiting.
- The prevalence-based approach used to estimate the budget impacts did not distinguish between first-line and post-progression use, and therefore, the proportion of lanreotide use in the post-progression setting was unclear.
- The resubmission did not account for the potential use of lanreotide at a higher dose (or higher dose frequency) in patients who experience disease progression whilst on lanreotide.

- Substitution of lanreotide currently being used in the prevalent GEP-NET population outside of current PBS restrictions (i.e. leakage) may represent a cost-offset that was not quantified in the submission.

5.19 The impact of the potential cost-offsets due to decreased utilisation of other therapies including everolimus, sunitinib and lanreotide on the financial forecasts were estimated in this minor resubmission.

5.20 The estimated use and financial implications are presented in Table 1.

Table 1: Estimated use and financial implications

	Year 1 (2018)	Year 2 (2019)	Year 3 (2019)	Year 4 (2021)	Year 5 (2022)
Adult Australian population (Population ≥18 years of age)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Prevalence of NETs (35/100,000 population)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of NETs that are GEP-NETs (60.52%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion who have metastatic or locally advanced disease (65%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion who have non-functional disease (68.19%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion who have a WHO Grade 1 or Grade 2 tumour (68.79%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion not suitable for watchful waiting /Eligible patients (77%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lanreotide uptake rate	65%	70%	75%	*80%*[a]	*80%*[a]
Total number of patients per year (same as estimated in July 2017 resubmission)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of packs dispensed per year[b]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of packs dispensed per year, July 2017 resubmission	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cost of lanreotide (effective price)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Total co-payment	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Net cost of listing to the PBS/RPBS (effective price)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Net cost of listing to the PBS/RPBS (effective price), July 2017	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Displaced medicines	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Net cost to the PBS/RPBS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Table 6 p.14; Table 7 p.17; Table 8, p.18 of the submission, Table 11 lanreotide July 2017 PSD.
Abbreviations: GEP-NETs, gastroenteropancreatic neuroendocrine tumours; WHO, World Health Organization.
[a] Uptake rate is cited as 85% in Table 6 of resubmission; however the resubmission text refers to 80% and calculated patient numbers are consistent with 80% uptake.
[b] Based on 13.04 packs per patient per year and 100% compliance. The July 2017 submission assumed 13 packs per patient per year and 90% compliance.

The redacted table shows that at year 5, the estimated number of patients was less than 10,000 per year.

5.21 The estimated number of packs dispensed per year is higher in the current resubmission versus the July 2017 resubmission despite no change to the estimated number of patients treated (Table 1). This is because the current resubmission assumed 100% compliance (despite stating that 90% compliance has been assumed

in the financial implications) compared with 90% previously, and 13.04 packs per patient per year compared with 13 previously. The pre-PBAC response provided revised net PBS/RPBS costs (excluding cost offsets for displaced medicines) adjusting for 90% compliance and 13 packs per patient per year. The revised net PBS/RPBS costs excluding and including cost offsets for displace medicines have been incorporated into Table 3 below.

5.22 The resubmission estimated a net cost to the PBS/RPBS (excluding any cost-offsets due to displaced medicines) of $10 - $20 million in year one increasing to $10 - $20 million in year five. The July 2017 submission estimated a net cost of $10 - $20 million in year one increasing to $10 - $20 million in year five.

5.23 The resubmission estimated net savings associated with reduced use of post-progression lanreotide, everolimus and sunitinib of [redacted] in year one reducing to [redacted] in year five.

5.24 The submission estimated the MBS costs associated with an increase in specialist visits to be approximately [redacted] to [redacted] per year over the five years.

5.25 The sensitivity analysis presented in the resubmission assessing the uptake rates and proportion of well differentiated GEP-NET cases treated with watchful waiting are summarised in Table 2. The resubmission only assessed scenarios where the net PBS/RPBS costs were increased.

Table 2: Sensitivity analyses for estimated net PBS/RPBS costs (including cost offsets for displaced medicines)

	Year 1 (2018)	Year 2 (2019)	Year 3 (2019)	Year 4 (2021)	Year 5 (2022)
Base case	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proportion of well differentiated GEP-NET cases treated with watchful waiting (base case = 23%)					
Lower bound: 18%	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Extreme: 0%	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Uptake rate of lanreotide (base case = 65% in year 1, 70% in year 2, 75% in year 3 and 80% in years 4 and 5)					
78% in year 1, 84% in year 2, 90% in year 3, 96% in years 4 and 5	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
80% in year 1 and 100% in years 2 to 5	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Multivariate sensitivity analysis					
Uptake of 80% in year 1 and 100% in years 2-5; Watchful waiting: 18%	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Uptake of 80% in year 1 and 100% in years 2-5; Watchful waiting: 0%	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Table 11 p.20 of the submission.

The redacted table shows that at year 5, the estimated the net cost to the PBS would be $10 - $30 million per year.

Financial Management – Risk Sharing Arrangements

5.26 The resubmission proposed a risk sharing arrangement (RSA) where an annual cap is applied, with a rebate for expenditure above that amount. The resubmission

reiterated that the purpose of the RSA is to mitigate against a higher than expected rate of conversion of patients who are eligible for watchful waiting to active treatment with lanreotide and to account for the uncertain rates of utilisation of lanreotide in post-progressive disease in practice. The proposed financial caps and rebates in the current resubmission and July 2017 resubmission are presented in Table 3.

5.27 The pre-PBAC response provided revised annual caps which adjusted for 90% compliance with lanreotide and the use of 13 packs per patient per year consistent with the July 2017 resubmission. The pre-PBAC response also proposed new annual caps and rebates. The revised annual caps and new annual caps and rebates are presented in Table 3 below. The financial estimates provided in the Pre-PBAC response have not been verified.

Table 3: Proposed financial cap through an RSA

	Year 1	Year 2	Year 3	Year 4	Year 5
Net PBS/RPBS cost (excluding cost offsets for displaced medicines)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Net PBS/RPBS cost (excluding cost offsets for displaced medicines) – adjusted for 90% compliance and 13 packs per patient per year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proposed annual caps and rebates – current submission	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proposed annual caps – adjusted for 90% compliance and 13 packs per patient per year	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proposed annual caps and rebates – July 2017 submission	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Proposed annual caps and rebates – pre-PBAC response	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Table 12 p.20 of the submission, Table 12 lanreotide July 2017 PSD.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

6.1 The PBAC deferred its decision on listing lanreotide on the PBS for the treatment of non-functional gastroenteropancreatic neuroendocrine tumours (GEP-NETs) on the basis that the cost-effectiveness of the proposed listing was uncertain. The PBAC advised that further negotiations between the Department and sponsor would be required to establish a price of lanreotide and financial caps which would adequately offset the uncertainty around cost-effectiveness.

6.2 The PBAC recalled the many comments received from patients with non-functional GEP-NETs prior to its July 2017 consideration of lanreotide and its previous meeting between representatives of the PBAC and the Unicorn Foundation. The PBAC acknowledged there is strong support from consumers for subsidised access to

lanreotide for this condition.

6.3 The PBAC recalled that the clinical data from the CLARINET trial did not support a difference in OS between treatment arms (HR 1.05, 95% CI 0.55, 2.03; favouring placebo). However, lanreotide was associated with a statistically significant increase in progression-free survival (PFS) compared with placebo (HR 0.47, 95% CI 0.30, 0.73). The PBAC recalled that the clinical significance of the gain in PFS was unclear as radiologic progression assessed in the trial may not necessarily be directly associated with a change in clinical symptoms. The PBAC reiterated this was a source of uncertainty noting that no new data were presented in the submission to address this issue.

6.4 The PBAC maintained there is likely to be a clinically meaningful benefit with treatment with lanreotide, which would outweigh the potential adverse events, for a small, well selected group of patients. However, given the variable and sometimes indolent nature of the disease, not all patients within the broad population of patients with non-functional GEP-NETs would benefit from active treatment with lanreotide.

6.5 The PBAC recalled it considered the economic model provided in the previous submissions to be fundamentally unreliable for estimating the cost-effectiveness of lanreotide for the requested listing, largely on the basis of uncertainties around the applied post-progression treatment sequences, durations and costs. The PBAC noted the proposal to use post-progression treatment data captured by the sponsor's national registry of NETs patients to update the economic model and adjust the price of lanreotide following listing. However, the PBAC considered that in the absence of a new economic model, additional data would not provide more certainty of the cost-effectiveness of lanreotide in this setting. The PBAC considered that while a revised economic model had not been provided in the submission, a significant price reduction in conjunction with a risk share agreement would be sufficient to offset the uncertainty around cost-effectiveness.

6.6 The PBAC recalled that at its November 2016 meeting, it considered a significant reduction in the requested price would be required to provide greater confidence in the cost-effectiveness of lanreotide. The PBAC also recalled that it considered the 15% price reduction proposed in the July 2017 submission to be modest and did not provide greater confidence in the cost-effectiveness of lanreotide. The PBAC noted that the proposed rebate of [redacted]% in the submission would equate to a [redacted]% price reduction (i.e. a further [redacted]% reduction from the price proposed in the July 2017 submission) if the Government's proposed statutory price reductions is legislated. The PBAC considered that a rebate of [redacted]% excluding the proposed statutory price reduction (i.e. the rebate should remain at [redacted]% of the published price even if the published price is reduced) would be appropriate to address the uncertainty regarding the cost-effectiveness of lanreotide.

6.7 The PBAC recalled that it considered the estimated utilisation and financial implications presented in the July 2017 submission to be uncertain due to the issues

raised in paragraph 5.18. The PBAC considered that the estimated utilisation and financial implications remain uncertain, noting the same data sources and assumptions from the previous submission were used. Considering the possibility that some patients suitable for watchful waiting may receive treatment for lanreotide if listed for this condition and the uncertainties around the utilisation and financial estimates, the PBAC advised that a Risk Sharing Arrangement with 100% rebate above the financial caps would be required to manage the risk of any use above what is expected. The PBAC further advised that the annual caps should not exceed $[redacted] million in each year covered by the Risk Sharing Arrangement.

6.8 The PBAC noted that this submission is not eligible for an Independent Review, as the submission was not rejected.

Outcome:

Deferred

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

The sponsor had no comment.

Addendum to the November 2017 PBAC Minutes:

12.10 LANREOTIDE
Injection 120 mg (as acetate) in single dose pre-filled syringe
Somatuline® Autogel®, Ipsen Pty Ltd

9 Purpose of Reconsideration

9.1 Subsequent to its deferral at the November 2017 PBAC meeting, the Sponsor, Ipsen Pty Ltd, requested the PBAC consider a revised pricing offer for the listing of lanreotide for the treatment of non-functional gastroenteropancreatic neuroendocrine tumours (GEP-NETs) in adults with unresectable locally advanced or metastatic disease.

10 Sponsor Proposal

10.1 In its proposal, the Sponsor was agreeable to a Risk Sharing Arrangement (RSA) consisting of annual caps set to $[redacted] million and 100% rebate for Commonwealth expenditure above the financial estimates in each year as previously advised by the PBAC (paragraph 6.7, November 2017 Public Summary Document (PSD)). However, the sponsor argued that a price reduction of [redacted]% excluding any statutory price reductions, which the PBAC previously considered would be appropriate to address the uncertainty regarding the cost-effectiveness of lanreotide (paragraph 6.6, November 2016 PSD) would result in a loss to the sponsor of $[redacted] per script for this indication. The sponsor stated that this would equate to providing the drug at a cost.

10.2 The sponsor highlighted that on 1 June 2018, a 5% and 10% statutory anniversary price reduction was applied to the approved ex-manufacturer price of lanreotide for 10 and 15 years of listing on the PBS.

10.3 The sponsor stated that it had made a consistent cost of goods case for the product of $[redacted] since the first major submission for this indication in November 2015 and indicated that the proposed ex-manufacturer price of $[redacted] in its November 2017 minor resubmission represented a $[redacted] profit per injection.

10.4 Based on the cost of goods for lanreotide, the sponsor indicated it could only provide an additional [redacted]% price reduction to the [redacted]% price reduction to the ex-manufacturer price as proposed at the November 2017 submission.

11 PBAC Outcome

11.1 The PBAC recommended the listing of lanreotide on the PBS for the treatment of non-functional GEP-NETs in adults with unresectable locally advanced or metastatic

disease on the basis that it was now satisfied that the proposed listing would be sufficiently cost-effective at the proposed price.

11.2 The PBAC acknowledged there is strong support from consumers for subsidised access to lanreotide for this condition and recalled the many comments received from patients with non-functional GEP-NETs prior to its previous considerations of lanreotide and its previous meeting between representatives of the PBAC and the Unicorn Foundation. The PBAC noted there were currently no other treatment options for this patient population.

11.3 The PBAC recalled it previously considered that a price reduction of [redacted]% excluding the anniversary statutory price reductions (i.e. the total price reduction should remain at [redacted]% even if the price is reduced through statutory price reductions) would be appropriate to address the uncertainty regarding the cost-effectiveness of lanreotide (paragraph 6.6, November 2017 PSD). The PBAC also recalled that this uncertainty was due in part to uncertainty around the utilisation of lanreotide which that the PBAC considered was adequately addressed with the sponsor's proposed Risk Sharing Arrangement (RSA) of 100% rebate on Commonwealth expenditure above the annual financial caps set to $[redacted] million.

11.4 The PBAC noted that the sponsor's concerns regarding the cost of goods for lanreotide has not been raised directly in the previous submissions for lanreotide for this indication. However, the PBAC considered that given the high clinical need for treatment options for this condition, relatively small patient population and proposed RSA with 100% rebate above the annual estimated expenditure, lanreotide would be sufficiently cost-effective if listed for this indication at the proposed price.

11.5 The PBAC affirmed that the proposed price would equate to an additional [redacted]% price reduction on top of a total price reduction of [redacted]% to the current price of lanreotide.

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

11.7 The PBAC advised that lanreotide is not suitable for prescribing by nurse practitioners.

11.8 The PBAC advised that the Early Supply Rule should apply to lanreotide.

11.9 The PBAC noted that this submission would not meet the criteria for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

Recommended listing

11.10 Add new item:

Restriction wording to be finalised.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
LANREOTIDE 120 mg/0.5 mL injection, 0.5 mL syringe	2	5	Somatuline® Autogel® Ipsen

Category / Program	Section 100 – Highly Specialised Drugs Program
Prescriber type:	☐Dental ☒Medical Practitioners ☐Nurse practitioners ☐Optometrists ☐Midwives
PBS Indication:	Non-functional gastroenteropancreatic neuroendocrine tumour
Restriction Level / Method:	☐Restricted benefit ☐Authority Required - In Writing ☐Authority Required - Telephone ☐Authority Required – Emergency ☐Authority Required - Electronic ☒Streamlined
Clinical criteria:	The condition must be World Health Organisation (WHO) grade 1 or 2 unresectable locally advanced disease; OR The condition must be World Health Organisation (WHO) grade 1 or 2 metastatic disease. AND The treatment must be as monotherapy
Population criteria:	Patient must be aged 18 years or older
Prescriber Instructions	Grade 1 GEP-NETs are defined by WHO as the following: (1) Mitotic count (10HPF) of less than 2; and (2) Ki-67 index (%) of less than or equal to 2 Grade 2 GEP-NETs are defined by WHO as the following: (1) Mitotic count (10HPF) of 2-20; and (2) Ki-67 index (%) of 3-20 The treatment must not be in combination with PBS-subsidised everolimus or sunitinib for this condition.

12 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.

13 Sponsor's Comment

Ipsen thanks the PBAC for their consideration and hard work in reaching this decision. This positive recommendation for Somatuline® Autogel® in the treatment of patients with non-functional GEP-NETs, aligns PBS access for patients with international guidelines and best practices. Ipsen is working with the Department of Health to ensure that this PBAC recommendation is listed on the PBS as soon as possible.