

## 5.15 LUTROPIN ALFA 75 IU, Powder for injection; Luveris®; Merck Serono Australia Pty Ltd

### 1 Purpose of Application

- 1.1 Section 100 (IVF/GIFT program) listing for lutropin alfa for treatment of severe luteinising hormone deficiency.

### 2 Requested listing

- 2.1 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
LUTROPIN ALFA Powder for injection 75IU. Vial of solvent, 1mL water for injections	1	1	\$ [REDACTED]	Luveris® Merck Serono Australia Pty Ltd
Category / Program	Section 100 (IVF/GIFT Treatment)			
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
Condition:	Stimulation of follicular development			
PBS Indication:	Stimulation of follicular development			
Treatment phase:				
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit (criteria for availability) <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined			
Clinical criteria:	<i>Patient must have severe LH deficiency</i>  <i>AND</i>  <i>Patient must be receiving medical treatment as described in items 13200, 13201, 13202 or 13203 of the Medicare Benefits Schedule</i>			
Administrative Advice	<i>Supply of these items is through an accredited IVF/GIFT clinic.</i> <i>For enquiries relating to the IVF/GIFT program, medical practitioners should contact Medicare Australia on 1800 700 270</i>			

- 2.2 The submission presented a cost-effectiveness of lutropin alfa supplementation of recombinant follicle stimulating hormone (rFSH) treatment, compared to rFSH alone.

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

### **3 Background**

- 3.1 TGA status: Luveris<sup>®</sup> was TGA registered on 24 March 2003 for use, in association with a rFSH preparation, for the stimulation of follicular development in women with severe luteinising hormone (LH) and FSH deficiency. In clinical trials, these patients were defined by an endogenous serum LH of less than 1.2 IU/L.
- 3.2 Lutropin alfa has not been considered previously for listing by the PBAC.
- 3.3 At the March 2014 meeting, the PBAC considered a submission for Section 100 listing (IVF/GIFT program) of a fixed dose combination (FDC) of rFSH 150IU and lutropin alfa 75IU (Pergoveris<sup>®</sup>). The submission was rejected as it had not established the comparative effectiveness and safety of the FDC to either rFSH given alone or the components – rFSH and lutropin alfa – given separately or other products containing human menopausal gonadotropin. The PBAC considered that the absence of lutropin alfa as a single-component product was a concern, noting that it would complicate dose titration in clinical practice.
- 3.4 A minor submission for the FDC Pergoveris<sup>®</sup> was submitted for consideration by the PBAC at the March 2015 meeting.

#### **4 Clinical place for the proposed therapy**

4.1 Lutropin alfa is used in assisted reproductive technology, as supplementation to rFSH in controlled ovarian stimulation for women with severe LH deficiency.

4.2 In the majority of women for whom rFSH therapy is indicated as part of a controlled ovarian stimulation regimen, no lutropin alfa is required. However, there are three subgroups of women who may not have sufficient endogenous LH to achieve optimal follicular development:

- women with hypogonadotropic hypogonadism (a rare condition);
- patients who experience profound pituitary down-regulation brought on by other assisted reproductive technology therapies; and
- women of advanced reproductive age.

Lutropin alfa is intended for use in women who demonstrate a poor response to rFSH-only treatment. The submission suggests that lutropin alfa should be administered at the discretion of the treating clinician based on the patient's individual clinical presentation and their response to ovarian stimulation, and states that there is little incentive to treat patients unnecessarily as excess LH levels may be detrimental to the achievement of a pregnancy.

#### **5 Comparator**

5.1 rFSH alone (no supplementation with lutropin alfa). ESC considered this to be the appropriate comparator.

#### **6 Consideration of the evidence**

##### **Sponsor hearing**

6.1 There was no hearing for this item.

##### **Consumer comments**

6.2 The PBAC noted and welcomed the input from health care professionals (12) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with lutropin alfa including affordable access to more options in IVF treatment.

6.3 The PBAC noted the advice received from ACCESS Australia's National Infertility Network Ltd clarifying the likely use of lutropin alfa in clinical practice. The PBAC specifically noted the advice that the use of lutropin alfa may provide for a small group of women who have inadequate levels of LH the possibility of achieving a pregnancy. The PBAC noted that this advice was consistent with the evidence provided in the submission.

**Clinical trial**

- 6.4 The submission was based on a published meta-analysis of 40 studies comparing lutropin alfa + rFSH to rFSH alone (n=6,443), with a pre-specified sub-group analysis of 'poor responders' (14 studies; n=1,179), used in the submission to represent the eligible PBS population. The submission also included an appendix summarising studies of patients with hypogonadotropic hypogonadism. Two of the trials, Study 21008 (RCT, n=39) and Study 6253 (dose ranging study, n=38), included relevant comparisons of lutropin alfa + rFSH and rFSH alone and were previously considered in the submission for the fixed dose combination of lutropin alfa + rFSH at the March 2014 PBAC meeting.
- 6.5 Details of the meta-analysis and trials presented in the submission are provided in the table below.

Public Summary Document – March 2015 PBAC Meeting

**Trials and associated reports presented in the submission**

Trial ID/First Author	Protocol title/ Publication title	Publication citation
<b>Meta-analyses of randomised trials</b>		
Lehert 2014	<p>Lehert P et al. Recombinant human follicle-stimulating hormone (r-hFSH) plus recombinant luteinizing hormone versus r-hFSH alone for ovarian stimulation during assisted reproductive technology: Systematic review and meta-analysis.</p> <p>r-hFSH Alone versus r-hFSH plus r-hLH in ART: A Meta-Analysis.</p>	<p>Reproductive Biology and Endocrinology 2014; 12(1): Article 17.</p> <p>Internal Sponsor's report of meta-analysis, 2012.</p>
Study 6253	<p>An open, randomised, dose-finding, multicentre, pivotal study to determine the minimal effective dose and assess the safety of recombinant human Luteinising Hormone (r-hLH) to support recombinant human Follicle Stimulating Hormone (r-hFSH)-induced follicular development in LH and FSH deficient anovulatory women (WHO Group I).</p> <p>The European Recombinant Human LH Study Group. Recombinant human Luteinizing Hormone (LH) to support recombinant human Follicle-Stimulating Hormone (FSH)-induced follicular development in LH- and FSH-deficient anovulatory women: A dose-finding study.</p>	<p>Clinical Study Report (Synopsis only), 1997</p> <p>Journal of Clinical Endocrinology and Metabolism 1998; 83(5): 1507-1514.</p>
Study 21008	<p>A phase III, prospective, randomized, controlled, double-blind, multicenter study to confirm the efficacy and safety of recombinant human Luteinizing Hormone (r hLH), 75 IU, administered subcutaneously, to support recombinant human Follicle Stimulating Hormone (r hFSH)-induced follicular development in women with hypogonadotropic hypogonadism and severe LH deficiency who desire pregnancy.</p> <p>Shoham Z, Smith H, Yeko T, et al. Recombinant LH (lutropin alfa) for the treatment of hypogonadotrophic women with profound LH deficiency: a randomized, double-blind, placebo-controlled, proof-of-efficacy study.</p> <p>Kaufmann R, Dunn R, Vaughn T, et al. Recombinant human luteinizing hormone, lutropin alfa, for the induction of follicular development and pregnancy in profoundly gonadotrophin-deficient women.</p>	<p>Clinical Study Report (Synopsis only), 2001</p> <p>Clinical Endocrinology 2008; 69:471-478.</p> <p>Clinical Endocrinology 2007; 67:563-569.</p>

Source: Table B.2-2, p32 of the submission

- 6.6 The key features of the evidence in the submission are summarised in the table below.

Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
<b>Lutropin alfa + rFSH vs rFSH alone</b>						
Lehert 2014	6,443	Included 40 studies (see Table in Attachment 1 below), 5 of which were divided into separate sub-groups and considered as separate studies (total 45 'studies'); sub-group analysis of 14 'poor responder' studies; assessed clinical pregnancy, live births and OHSS rate (safety). All trials were one cycle duration.			Clinical pregnancy	
Study 21008	39	R, DB, PG, placebo controlled 1 cycle	Low	Patients with hypogonadotropic hypogonadism	Clinical pregnancy, OHSS	Not used
Study 6253	38	R, OL, PG, dose finding 1 cycle + up to 2 additional optional cycles	High			

Abbreviations: DB, double blind; OHSS, ovarian hyperstimulation syndrome; OL, open label; PG, parallel group; R, randomised.

Source: compiled during the evaluation

- 6.7 The studies included in the meta-analysis, which was commissioned by the sponsor, are at unclear or high risk of bias. Thus, the effect size for clinical pregnancy and live birth may be overestimated.

### Comparative effectiveness

- 6.8 The meta-analysis compared rates of clinical pregnancy and live births for all studies, and for separate sub-groups of normal responders and poor responders. Poor responders were used in the submission to represent the eligible PBS population. Missing data for clinical pregnancy and live births were imputed where possible.

Results of comparative efficacy for clinical pregnancies and live births

Trial ID	rFSH + Lutropin alfa n/N (%)	rFSH n/N (%)	RR [95% CI]	OR [95% CI]
<b>Clinical pregnancy</b>				
Lehert 2014 - Overall	891/3139 (28.4%)	818/3254 (25.1%)	1.09 [1.01, 1.18]	1.18 [1.05, 1.32]
Cochran Q test for heterogeneity (for RR): Q(df=42)=42.8, p=0.4370				
Lehert 2014 - Normal responders	741/2547 (29.1%)	704/2667 (26.4%)	1.09 [0.95, 1.24]	NR
Lehert 2014 - Poor responders	150/592 (25.3%)	114/587 (19.4%)	1.30 [1.01, 1.67]	NR
Study 21008	1/26 (3.8%)	1/13 (7.7%)	NR	NR
Study 6253	3/18 (16.6%) <sup>a</sup>	0/8 (0.0%)	Not calculable	NR
<b>Live births</b>				
Lehert 2014 - Overall	732/3065 (23.9%)	671/3172 (21.2%)	1.11 [1.01, 1.21]	1.18 [1.04, 1.34]
Cochran Q test for heterogeneity (for RR): Q(df=38)=35.8, p=0.5679				
Lehert 2014 - Normal	622/2540 (24.5%)	588/2654 (22.2%)	1.10	NR

Trial ID	rFSH + lutropin alfa n/N (%)	rFSH n/N (%)	RR [95% CI]	OR [95% CI]
responders			[0.94, 1.29]	
Lehert 2014 - Poor responders	110/525 (21.0%)	83/518 (16.0%)	1.30 [0.95, 1.78]	NR
Study 21008	1/26 (3.8%)	1/13 (7.7%)	NR	NR
Study 6253	NR	NR	NR	NR

<sup>a</sup> Lutropin alfa 75IU and 225IU arms only. Lutropin alfa 25IU arm not included.  
Source: Table B.6-1, p69 of the submission; compiled during the evaluation.

- 6.9 For the poor responder population in the Lehert 2014 meta-analysis, there were statistically significantly greater numbers of clinical pregnancies in the lutropin alfa + rFSH treatment arm compared to the rFSH only treatment arm. The point estimate showed a higher number of live births in the lutropin alfa + rFSH treatment arm than in rFSH only arm, but this difference was not statistically significant. There was substantial imputation of data for the live birth outcome. In the poor responder subgroup, █ of the █ studies (██████) included in the live birth outcome measure used imputed data.
- 6.10 Results from the hypogonadotropic hypogonadism Studies 21008 and 6253 were not informative due to low patient numbers and limited reporting of patient-relevant outcome measures of clinical pregnancy and live births.

### Comparative harms

- 6.11 The key safety concern for treatments during controlled ovarian stimulation is ovarian hyperstimulation syndrome (OHSS). OHSS rates were only reported in 11 of the meta-analysed trials; all 11 trials were from the 'normal responder' subgroup.

#### Results of comparative efficacy for clinical pregnancies and live births

Trial ID	rFSH + lutropin alfa n/N (%)	rFSH n/N (%)	RR [95% CI]	OR [95% CI]
<b>OHSS rates</b>				
Lehert 2014 (Overall population, n=11 trials)	15/1297 (1.2%)	29/1224 (2.4%)	0.61 [0.32, 1.13]	0.59 [0.31, 1.12]
Study 21008	0/27 (0.0%)	1/12 (8.3%)	NR	NR
Study 6253	2/53 (3.8%)	0/11 (0.0%)	NR	NR

Source: Table B.6-1, p69 of the submission; compiled during the evaluation.

### Benefits/harms

- 6.12 A summary of the comparative benefits and harms for lutropin alfa + rFSH versus rFSH alone is presented in the table below.

Summary of comparative benefits and harms for lutropin alfa + rFSH and rFSH alone

Trial	Lutropin alfa + rFSH	rFSH alone	RR (95% CI)	Event rate/100 patients*		OR (95% CI)
				Lutropin alfa + rFSH	rFSH alone	
<b>Benefits</b>						
<b>Clinical pregnancy</b>						
Overall	891/3139	818/3254	1.09 [1.01, 1.18]	28.4	25.1	1.18 [1.05, 1.32]
Normal responders	741/2547	704/2667	1.09 [0.95, 1.24]	29.1	26.4	NR
Poor responders	150/592	114/587	1.30 [1.01, 1.67]	25.3	19.4	NR
<b>Live births</b>						
Overall	732/3065	671/3172	1.11 [1.01, 1.21]	23.9	21.2	1.18 [1.04, 1.34]
Normal responders	622/2540	588/2654	1.10 [0.94, 1.29]	24.5	22.2	NR
Poor responders	110/525	83/518	1.30 [0.95, 1.78]	21.0	16.0	NR
<b>Harms</b>						
	Lutropin alfa + rFSH	rFSH alone	RR (95% CI)	Event rate/100 patients*		OR (95% CI)
				Lutropin alfa + rFSH	rFSH alone	
<b>Ovarian Hyperstimulation Syndrome</b>						
ITT population (N=11 studies)	15/1297	29/1224	0.61 [0.32, 1.13]	1.2	2.4	0.59 [0.31, 1.12]

\* Duration of exposure: one cycle

Abbreviations: rFSH, recombinant follicle stimulating hormone; ITT, intention to treat; OR, odds ratio; RR, risk ratio

Source: Compiled during the evaluation

6.13 On the basis of meta-analysis evidence of poor responders (the relevant PBS population) presented in the submission, for every 100 patients treated with lutropin alfa + rFSH in comparison to rFSH alone;

- Approximately 5.9 additional patients would achieve clinical pregnancy over a duration of exposure of one treatment cycle.
- There was no significant difference in the number of live births.
- There was no significant difference in the frequency of ovarian hyperstimulation syndrome over one treatment cycle (these adverse event data were for 'normal responders' only).

**Clinical claim**

6.14 The submission described lutropin alfa (supplementary to rFSH therapy) as superior in terms of comparative effectiveness and superior in terms of comparative safety over rFSH alone, in poor responders. This may be reasonable for clinical pregnancy, but not for live births, given the non-statistically significant difference between treatment arms for live births, and the imputation of the data in the majority of the trials for poor responders. The treatment effect size may be overestimated due to the risk of bias in the studies included in the meta-analysis. The ESC noted the Pre-Sub-Committee Response (PSCR, p1) explanation that in poor responders, it is not unexpected that the improvement in live birth rate did not quite reach statistical significance due to the additional sample size required for this outcome. Since the

improvement in live birth rate reached statistical significance in the overall population, and since clinical and ongoing pregnancy rates were higher in the poor responder population than in the overall population, it is likely that the 30% difference in live birth rate observed in the poor responder population did not reach statistical significance because it was underpowered. The claim of superior safety was also based on a non-statistically significant difference between treatment arms, and no data from the poor responder population.

- 6.15 The PBAC considered that the claim of superior comparative effectiveness was reasonable for clinical pregnancy but less certain for live birth.
- 6.16 The PBAC considered that the claim of superior comparative safety was not adequately supported by the data but that there was no increase in OHSS in the overall population.

For more detail on PBAC’s view, see section 7 “PBAC outcome”.

### Economic analysis

- 6.17 A stepped economic evaluation was presented in the submission. This was based on the Leher 2014 meta-analysis, with a modelled evaluation of cost-effectiveness using clinical pregnancy as the outcome, and live births as a supplementary outcome. The ESC agreed that a cost-effectiveness analysis rather than a cost utility analysis was appropriate but considered live births to be the most relevant outcome.

#### Summary of model structure and rationale

Component	Summary
Time horizon	Up to [redacted] treatment cycles in the model base case versus one cycle in meta-analysis
Outcomes	Clinical pregnancies, live births
Methods used to generate results	Markov cohort expected value analysis
Health states	Start fresh cycle, live birth, discontinue IVF
Cycle length	Unspecified and variable
Transition probabilities	Probability of OHSS, clinical pregnancy, live birth, miscarriage, discontinuation of IVF for non-medical reasons

Source: compiled during the evaluation

- 6.18 The model was most sensitive to the duration of lutropin alfa treatment in each cycle.

#### Results of the stepped economic evaluation

Step and component	Lutropin alfa + rFSH	rFSH	Increment
<b>Step 1: trial-based costs and outcomes (1 cycle)</b>			
Costs	\$ [redacted]	\$ [redacted]	\$ [redacted]
Clinical pregnancy	0.253	0.193	0.060
Incremental cost/extra clinical pregnancy gained after 1 cycle			\$ [redacted]
<b>Step 2: base-case modelled evaluation (maximum of [redacted] cycles)</b>			
Costs	\$ [redacted]	\$ [redacted]	\$ [redacted]
Clinical pregnancy	0.501	0.413	0.089
Incremental cost/extra clinical pregnancy gained after maximum of [redacted] cycles*			Dominates
<b>Step 3: supplementary modelled evaluation (live births, maximum of [redacted] cycles)</b>			
Costs	\$ [redacted]	\$ [redacted]	\$ [redacted]

Step and component	Lutropin alfa + rFSH	rFSH	Increment
Live births**	0.413	0.336	0.078
Incremental cost/extra live birth gained after maximum of [redacted] cycles*			\$ [redacted]

Source: Table D.5.1, p93; Table D.5.2, Table D.5.3, Table D.5.4, p94 of the submission

\* The modelled evaluation of clinical pregnancies and live births uses a maximum of [redacted] IVF cycles, but with patient dropouts the number of cycles averages 2.32 for the lutropin alfa + rFSH group and 2.53 for the rFSH only group in the base case modelled evaluation (clinical pregnancy outcome). The Australian average number of cycles is 2.55 per patient, from the UNSW ART in ANZ 2011 report.

\*\* The model assumes that the probability of converting from clinical pregnancy to live birth is the same in both treatment arms ([redacted]%). This may be a conservative assumption given the (non-statistically significant) 30% increase in live birth rate reported for rLH. (PSCR, p3).

- 6.19 The ESC noted the additional estimates for the ICERs provided in the Pre Sub-Committee Response were not materially different to those in the submission.

**Drug cost/patient/cycle:** approximately \$ [redacted] (75IU/day x [redacted] days)

- 6.20 The dose and duration of treatment with lutropin alfa is individualised. The treatment duration in the Leheret 2014 meta-analysis averaged [redacted] days. The daily dose may also vary for each patient; the recommended starting dose is 75IU per day. The range of doses in the studies submitted is from 75 units to 600 units. The range of rFSH and lutropin alfa doses used in the trials is consistent with the heterogeneity of treatment practice for assisted reproductive technology.

- 6.21 The number of treatment cycles also varies for each patient. The Australian average number of cycles is 2.55 per patient, from the UNSW ART in ANZ 2011 report.

### Estimated PBS usage & financial implications

- 6.22 This submission was not considered by DUSC. The submission used a mixed market share and epidemiological approach to estimate use and financial implications of listing lutropin alfa. The submission used the University of NSW ART in ANZ 2011 report to estimate the number of Australian patients undergoing ovarian stimulation treatment, and European market data for the number of these patients likely to require treatment with lutropin alfa. Uptake rates of lutropin alfa from the eligible population were assumed in the submission.

#### Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Estimated extent of use</b>					
Total ART cycles (8.3% annual growth)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ovarian stimulated autologous fresh cycles (98.8% x 61.3% of total ART cycles)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Number of cycles eligible for lutropin alfa (severe LH deficiency, 20%)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Uptake rate of lutropin alfa	[redacted] %	[redacted] %	[redacted] %	[redacted] %	[redacted] %
Estimated cycles of lutropin alfa	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Year 1	Year 2	Year 3	Year 4	Year 5
Total packs per year (7 packs per cycle)	■	■	■	■	■
Estimated total net cost					
Net cost to PBS	\$ ■	\$ ■	\$ ■	\$ ■	\$ ■

Source: Table E.2-1, p98; Table E.2-2, p99; Table E.2-3, p99; Table E.2-4, p100; Table E.2-5, p100; Table E.3-2, p101 of the submission

- 6.23 The redacted table above shows that the listing of lutropin alfa on the PBS will result in a cost to the PBS of <\$10 million in each year up to Year 5.

### Financial Management – Risk Sharing Arrangements

- 6.24 The Sponsor proposed a risk share arrangement, with a per vial price reduction of ■% (\$■ per vial) for each vial sold above the annual projections in any one year.

## 7 PBAC Outcome

- 7.1 The PBAC recommended the listing of lutropin alfa for treatment of severe LH deficiency, on the basis that it should be available only under special arrangements under Section 100 (IVF/GIFT program) listing.
- 7.2 The PBAC is satisfied that lutropin alfa provides, for a small group of women who have inadequate levels of LH, a significant improvement in clinical pregnancies and potentially live births.
- 7.3 The PBAC agreed with the proposed PBS restriction as amended by the Secretariat.
- 7.4 The PBAC agreed that the clinical place for lutropin alfa would be limited to three subgroups of women who may not have sufficient endogenous LH to achieve optimal follicular development:
- women with hypogonadotropic hypogonadism (a rare condition);
  - patients who experience profound pituitary down-regulation brought on by other assisted reproductive technology therapies; and
  - women of advanced reproductive age.
- 7.5 The PBAC did not share ESC's concerns about the dose of lutropin alfa, as it would be unusual for women to receive more than 150IU.
- 7.6 The PBAC accepted rFSH alone (no supplementation with lutropin alfa) as the appropriate comparator.
- 7.7 The key clinical trial evidence was the meta-analysis by Lehert 2014, with a subgroup of poor responder patients representing the eligible PBS population. The PBAC noted the ESC concern about the bias in the individual studies within the meta-analysis and the Pre-PBAC response discussion on how the biases were addressed. Overall, the PBAC considered the evidence to be less than ideal, but nonetheless informative.

- 7.8 The PBAC accepted, for the poor responder population in the Leher 2014 meta-analysis, that there were statistically significantly greater numbers of clinical pregnancies in the lutropin alfa + rFSH treatment arm compared to the rFSH only treatment arm. Despite the point estimate showing a higher number of live births in the lutropin alfa + rFSH treatment arm than in rFSH only arm, this difference was not statistically significant and the PBAC was not confident that the explanation provided in the Pre Sub-Committee response regarding the lack of statistical power in the sub group was sufficient to accept a claim of superiority with regard to live birth. However, PBAC did consider live birth to be the most relevant patient outcome and accepted this would be the most appropriate outcome for assessing cost effectiveness.
- 7.9 The PBAC did not accept the superior safety claim but considered that there is no increased risk of OHSS with this treatment.
- 7.10 The PBAC accepted the incremental cost/extra live birth of \$██████████, noting that the ICER would likely remain cost-effective even if the probability of live birth was reduced.
- 7.11 The PBAC did not consider this product would be used unnecessarily and that the proposed estimates of use were acceptable.
- 7.12 The PBAC noted the proposed risk share arrangement, with a per vial price reduction of ██████% (\$██████ per vial) for each vial sold above the annual projections in any one year. The PBAC considered any risk share arrangement should consider minimising Government financial risk for use above 150IU.
- 7.13 The PBAC advised that lutropin alfa is not suitable for prescribing by nurse practitioners.
- 7.14 The PBAC recommended that the Safety Net 20 Day Rule should not apply as this is a section 100 item.

**Outcome:**

Recommended

**8 Recommended listing**

- 8.1 Add new item:

Public Summary Document – March 2015 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
LUTROPIN ALFA Powder for injection 75IU. Vial of solvent, 1mL water for injections	1	1	TBD	Luveris® Merck Serono Australia Pty Ltd
Category / Program	Section 100 (IVF/GIFT Treatment)			
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
Condition:	Stimulation of follicular development			
PBS Indication:	Stimulation of follicular development			
Treatment phase:				
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit (criteria for availability) <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined			
Clinical criteria:	<i>Patient must have severe LH deficiency</i>  <i>AND</i>  <i>Patient must be receiving medical treatment as described in items 13200, 13201, 13202 or 13203 of the Medicare Benefits Schedule</i>			
Administrative Advice	<i>Supply of these items is through an accredited IVF/GIFT clinic.</i> <i>For enquiries relating to the IVF/GIFT program, medical practitioners should contact Medicare Australia on 1800 700 270</i>			

## 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

We note the Pre-Sub-Committee evaluation comments that:

- The criteria for availability is consistent with the TGA registered indication
- Treatment details are consistent with those in the TGA-approved Product Information
- This dose is consistent with the TGA-approved dose

We also note that the PBS supply arrangements for IVF medicines (and therefore Luperis) will change as of 1 July 2015 and thus the maximum quantity stated above is incorrect.

Reimbursement of Luperis provides an important medicine for some women who may otherwise not achieve a pregnancy.