5.20 PROGESTERONE, Capsule 300 mg, Utrogestan®, BESINS HEALTHCARE AUSTRALIA PTY LTD

1 Purpose of Submission

1.1 The Category 4 submission requested a section 100 (In Vitro Fertilisation (IVF) Program) Authority Required (STREAMLINED) listing of an additional strength of progesterone capsule (Utrogestan®) on the Pharmaceutical Benefits Scheme (PBS), 300 mg twice daily (BID) for luteal phase support (LPS) as part of an assisted reproductive technology (ART) treatment cycle.

1.2 Listing was requested on a cost minimisation basis to progesterone capsule 200 mg (Utrogestan) three times daily (TID).

2 Background

2.1 Progesterone capsule 200 mg is currently listed on the PBS as Authority Required (STREAMLINED) listings for the:

- prevention of preterm birth on the General Schedule; and
- ART on the section 100 IVF Program.

Registration status

2.2 Progesterone capsule 300 mg was approved for registration by the Therapeutic Goods Administration (TGA) on 11 January 2024 for LPS and support during pregnancy. The product is not yet registered on the Australian Register of Therapeutic Goods (ARTG).

2.3 The TGA approved Product Information (PI) states that in luteal phase supplementation during ART, treatment should be started from the evening of the transfer at the latest, as 600 mg of progesterone in three divided doses of 200 mg capsules or in two divided doses of 300 mg capsules morning and evening.

Previous PBAC consideration

2.4 Progesterone capsule 300 mg has not been considered by the PBAC for LPS previously.

3 Requested listing

3.1 The submission requested the following new listing (in italics).

MEDICINAL PRODUCT medicinal product pack		**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
PROGESTERONE						
progesterone 200 mg pessary, 42		10930G	1	42	0	Utrogestan
progesterone 300 mg pessary, 15		*NEW*	*2*	*30*	*0*	*Utrogestan*
Restriction Summary 4997 / Treatment of Concept: 4997						
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – IVF Program					
	Prescriber type: ☒Medical Practitioners					
	Restriction type: ☒Authority Required (Streamlined)					
Prescribing rule level	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.					
	Indication: Assisted Reproductive Technology					
	Clinical criteria:					
	The treatment must be for luteal phase support as part of an assisted reproductive technology (ART) treatment cycle for infertile women					
	AND					
	Clinical criteria:					
	Patient must be receiving medical services as described in items 13200 or 13201 of the Medicare Benefits Schedule					
	Prescribing Instructions: The luteal phase is defined as the time span from embryo transfer until implantation confirmed by positive B-hCG measurement.					

3.2 The submission requested restriction criteria identical to the current listing for progesterone capsule 200 mg.

3.3 The current listing for 200 mg capsules has a pack size of 42 with a maximum pack quantity of 1. This provides 14 days of treatment with a TID dosing schedule. The proposed 300 mg capsule product has a pack size of 15 and the proposed listing is for a maximum pack quantity of 2 (30 units) with nil repeats. This would provide 15 days of treatment with the proposed BID dosing schedule, which is consistent with the average duration of the luteal phase and the maximum quantities of other PBS-listed progesterone products for LPS.

4 Comparator

4.1 The submission nominated progesterone capsule 200 mg TID as the main comparator. This was appropriate.

4.2 The submission did not nominate any secondary comparators. In its July 2016 consideration of progesterone capsule 200 mg, the PBAC considered that any form of progesterone currently listed on the PBS for ART could be an appropriate comparator (para 5.1, progesterone – Utrogestan, Public Summary Document (PSD), July 2016). At that time, progesterone 100 mg pessary (Oripro®; Endometrin®), progesterone 200 mg pessary (Oripro), and progesterone 8% vaginal gel (Crinone®) were listed. These brands are all currently listed.

4.3 The PBAC considered all other PBS-listed forms of progesterone indicated for LPS as appropriate comparators.

5 Consideration of the evidence

Sponsor hearing

5.6 There was no hearing for this item.

Consumer comments

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

Comparative effectiveness

5.8 The submission's request was based on the acceptance of the alternate dosing method by the TGA, which evaluated the comparative composition, a pharmacokinetic (PK) modelling report, and comparative dissolution tests.

5.9 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

5.10 The submission provided a comparison of the composition of the 300 mg capsule versus the 200 mg capsule.

Table 1: Composition of 300 mg and 200 mg dosage forms

Ingredient	Quantity per Capsule (mg)		Function	Reference to Standard
	200	300		
Capsule contents				
Micronised progesterone	200.0	300.0	Drug substance	Ph Eur
Sunflower oil refined	298.0	447.0	Suspension Medium	Ph Eur
Soybean lecithin	2.0	3.0	Surfactant	In-house 1
Capsule shell				
Gelatin	146.8	266.9	Gelling agent	Ph Eur
Glycerol	60.0	109.1	Maintenance of the flexibility of the soft gel (Plasticiser)	Ph Eur
Titanium dioxide	3.2	5.8	Opacifying agent	Ph Eur
Purified water	10.0	18.2	Solvent	Ph Eur

Source: Submission main body p17

5.11 The submission stated that the dosage form of the 300 mg strength remains a soft vaginal capsule, and its formulation contains the same excipients, the amounts of which are adjusted to accommodate the same ratio of the micronised progesterone content.

5.12 The submission referenced a report outlining the in-silico PK modelling of two different regimens of oral progesterone administration: 200 mg TID and 300 mg BID. The TGA Clinical Evaluation Report (CER) evaluator stated that the in-silico PK modelling report was based on PK parameters for oral progesterone dosing rather than intravaginal administration. Therefore, the modelling does not take into consideration key factors such as the impact of the uterine first-pass effect, nor the lack of first-pass metabolism.

5.13 The submission stated that to assess the in-vitro comparability of the current 200 mg capsules and the 300 mg capsules, the following dissolution studies were performed:

- Two dissolution tests were carried out for both dosage strengths with one capsule per cell.
- One dissolution test was carried out for both dosage strengths with:
  - Three capsules per cell for the 200 mg dosage strength
  - Two capsules per cell for the 300 mg dosage strength

5.14 The submission concluded that the dissolution studies showed a comparable release profile of the 300 mg capsules compared to the 200 mg capsules.

5.15 The submission further stated that patient compliance is likely to be significantly improved given the 300 mg soft capsules allow a simpler dosing regimen with a minimised intravaginal capsule burden.

5.16 The TGA evaluation stated that although there are marginal variations between the strengths (200 mg vs 300 mg), the mean dissolution at each time point was matching. Additionally, the TGA evaluator confirmed that three capsules of the 200 mg strength are equivalent to two capsules of the 300 mg strength, and the similarity factor was calculated as 70.2 (Utrogestan TGA Milestone 3 report, September 2023).

5.17 The Module 3 Evaluator concluded that the 300 mg soft capsule BID can be considered bioequivalent to the 200 mg soft capsule TID (Utrogestan TGA Clinical Evaluation Report, November 2023).

Comparative harms

5.18 The submission stated that the 300 mg strength is not anticipated to change the safety profile of Utrogestan. Both the 300 mg and 200 mg forms contain the same active ingredient and excipients and are delivered via the same route of administration within the current approved indications and dosing range. This was supported by the UK Drug Analysis Profile (DAP) and 2022 Periodic Safety Update Report (PSUR) which showed no change in the safety profile.

Clinical claim

5.19 The submission claimed the non-inferior comparative effectiveness and non-inferior comparative safety of progesterone capsule 300 mg BID compared with progesterone capsule 200 mg TID.

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

Economic analysis

5.21 As a Category 4 submission, the economic analysis has not been independently evaluated.

5.22 The submission presented a cost-minimisation approach (CMA) of progesterone capsule 300 mg BID compared with progesterone capsule 200 mg TID.

5.23 The equi-effective doses were estimated as progesterone capsule 300 mg BID over 15 days and progesterone capsule 200 mg TID over 14 days for LPS as part of an ART treatment cycle.

5.24 The equi-effective dose is derived from the PI which states that the usual dosage is 600 mg/day, in two or three divided doses, from the day of embryo transfer until at least the 7th week of pregnancy and not later than the 12th week of pregnancy.

5.25 Table 2 presents the previously recommended equi-effective doses for PBS-listed progesterone forms indicated for LPS.

Table 2: PBAC previously recommended equi-effective doses

Medicine (form)	Item code	Strength (mg)	Pack Size	Max Qty (packs)	Max Qty (units)	Dose/ day (mg)	Treatment cycle duration
Crinone 8% (pre-filled gel applicator)	6366C	90	15	2	30	90	15
Endometrin (pessary)	10116K	100	21	2	42	200	14
						300	14
Oripro (pessary)	9608Q	100	15	3	45	200	22.5
						800	5.625
	9609R	200	15	3	45	200	45
						800	11.25
Utrogestan (capsule)	10930G	200	42	1	42	600	14
Cyclogest (Pessary)	Not-listed	400	15	2	3	800	15

Source: Compiled by Evaluation

5.26 Table 3 summarises the essential features of the CMA presented in the submission.

Table 3: Key assumptions and components of the CMA

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented in Section 2 of the submission, progesterone 300 mg BID is non-inferior in terms of efficacy, compared to progesterone 200 mg TID.
Therapeutic claim: safety	Based on evidence presented in Section 2 of the submission, progesterone 300 mg BID is non-inferior in terms of safety, compared to progesterone 200 mg TID.
Evidence base	In-silico PK modelling, dissolution studies and previously evaluated clinical data for Utrogestan 200 mg TID.
Equi-effective doses (from the PI)	200 mg TID – PBS 10930G The recommended dosage is 600 mg/day, in three divided doses, from the day of embryo transfer until at least the 7th week of pregnancy and not later than the 12th week of pregnancy. The PBS listing for 200 mg TID has no repeats which is a shorter duration of treatment than recommended in the PI. 300 mg BID – proposed The recommended dosage is 600 mg/day, in two divided doses, from the day of embryo transfer until at least the 7th week of pregnancy and not later than the 12th week of pregnancy. **The EED is 200 mg TID = 300 mg BID**
Direct medicine costs	The cost-minimisation of 300 mg BID and 200 mg TID is based on the dosage recommendations in the PI per day of treatment. 200 mg TID – PBS 10930G The pack size is 42 soft capsules (pessary) with a maximum quantity of 1. At three doses per day, the duration of each PBS service is 14 days. The PBS restriction for 200 mg TID has zero repeats which means one supply aligns with the length of the luteal phase of approximately 14 days. 300 mg BID - proposed The pack size is 15 soft capsules (pessary) with a maximum quantity of 2. At two doses per day, the duration of each PBS supply is 15 days. The proposed PBS restriction for 300 mg BID also has zero repeats which means one supply aligns with the length of the luteal phase of approximately 14 days. As such, for both the 300 mg and 200 mg doses, one PBS service is required for the course of treatment. 200 mg TID – PBS 10930G The February 2024 AEMP is $75.53 (DPMQ $87.90). 14 days of treatment equals a daily cost of $5.40 300 mg BID - proposed A daily cost of $5.40 over 15 days leads to an AEMP of $80.93 (DPMQ $93.30)
Other costs or cost offsets	No other costs or cost offsets are included in the analysis.

Source: Submission main body

Abbreviations: AEMP = approved ex-manufacturer price, BID = two times a day, CMA = cost-minimisation approach, DPMQ = dispensed price for maximum quantity, EED = equi-effective dose, PBS = Pharmaceutical Benefits scheme, PI = product information, TID = three times a day

5.27 Table 4 presents the results of the CMA. The CMA was calculated at an equivalent price per day of treatment, as opposed to an equivalent price based on the treatment course.

Table 4: Results of the cost minimisation approach

Listing	Dose (mg) per capsule	Frequency (times per day)	Capsules per pack	Max Qty	Number of capsules per PBS service	Duration of PBS service (days)	AEMP /pack	AEMP per day	DPMQ
Current (10930G)	200	3	42	1	42	14	$75.53	$5.40	$87.90
Proposed	300	2	15	2	30	15	$40.465	$5.40	$93.30

Source: Submission main body
Abbreviations: AEMP = approved ex-manufacturer price, DPMQ = dispensed price for maximum quantity, LPS = luteal phase support, Max Qty = maximum quantity, mg = milligram, PBS = Pharmaceutical Benefits Scheme
Please note that progesterone for LPS is listed under the S100 IVF program meaning a $4.00 markup plus a $8.37 pharmacist dispensing fee is applied to calculate the dispensed price for maximum quantity.

5.28 The submission's approach to the CMA was not consistent with previous PBAC recommendations. At its July 2022 meeting, the PBAC recommended the listing of progesterone 400 mg pessary based on, among other matters, its assessment, that the cost-effectiveness of Cyclogest® would be acceptable if it were cost-minimised against the least costly progesterone treatment for LPS currently listed on the PBS (para 7.1, progesterone – Cyclogest, PSD, July 2022). In its CMA versus progesterone 200 mg capsule (Utrogestan), the July 2022 submission calculated the approved ex-manufacturer price (AEMP) at an equivalent price per treatment course (Table 11, progesterone – Cyclogest, PSD, July 2022).

5.29 The Evaluation provided an updated CMA with an equivalent price per treatment course in Table 5.

Table 5: Amended results of the cost minimisation approach (Evaluation)

	Dose (mg) per capsule	Frequency (times per day)	Capsules per pack	Max Qty	Number of capsules per PBS service	Duration of PBS service i.e., one course (days)	AEMP/ pack	AEMP per day	DPMQ
Current 10930G	200	3	42	1	42	14	$75.53	$5.40	$87.90
Proposed	300	2	15	2	30	15	$37.77	$5.04	$87.90

Source: Compiled by Evaluation
Abbreviations: AEMP = approved ex-manufacturer price, DPMQ = dispensed price for maximum quantity, LPS = luteal phase support, Max Qty = maximum quantity, mg = milligram, PBS = Pharmaceutical Benefits Scheme

5.30 In its pre-PBAC response, the sponsor accepted the CMA with an equivalent price per treatment course.

5.31 The PBAC could only recommend listing progesterone 300 mg at a higher price than the alternative therapy or therapies if it was satisfied that it provides, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies *(National Health Act 1953, Section 101(3B))*. The alternative therapies in this case should include other PBS-listed forms of progesterone indicated for LPS.

5.32 A comparison of the currently PBS-listed progesterone forms indicated for LPS is shown in Table 6.

Table 6: AEMP comparison of PBS-listed progesterone forms indicated for LPS

Medicine (form)	Item code	Strength (mg)	Pack Size	Max Qty (packs)	Max Qty (units)	Dose/ day (mg)	Treatment cycle duration	AEMP/ pack	AEMP Total cost/ cycle
Crinone 8% (pre-filled gel applicator)	6366C	90	15	2	30	90	15	$93.82*	$93.82*
						180	15		$187.64*
Endometrin (pessary)	10116K	100	21	2	42	200	14	$31.21	$62.42
						300	14		$62.42
Oripro (pessary)	9608Q	100	15	3	45	200	22.5	$47.88	$143.64
						800	5.625		$143.64
	9609R	200	15	3	45	200	45	$35.40	$106.20
						800	11.25		$106.20
Utrogestan (capsule)	10930G	200	42	1	42	600	14	$75.53	$75.53
	[NEW]	300	15	2	30	600	15	-	-

Source: PBS website, April 2024 Ex-manufacturer spreadsheet. Compiled by Evaluation
Abbreviations: AEMP = approved ex-manufacturer price; LPS = luteal phase support
*Subject to special pricing arrangements

Committee-In-Confidence information

5.33 [redacted]

- [redacted]
- [redacted]

End Committee-In-Confidence information

Drug cost/patient/course: $88.20

5.34 Using the pre-PBAC response CMA with an equivalent price per treatment course, the estimated drug cost/patient per course would be $88.20, based on a 15-day course.

5.35 The current AEMP for progesterone capsule 200 mg is $75.53 for 14 days of treatment ($5.40 per day). The pre-PBAC response proposed a daily treatment cost of progesterone capsule 300 mg of $5.04 with a 15-day course. This led to an equivalent AEMP of $75.53 for the requested listing. As listing is requested for the section 100 IVF program, a $4.00 markup and an $8.67 (as of 1 July 2024) pharmacist dispensing fee is applied when calculating the dispensed price for maximum quantity (DPMQ).

Estimated PBS usage and financial implications

5.36 The submission used a market-share approach to estimate the PBS usage and financial implications.

Table 7: Key inputs for financial estimates

Data	Value	Source	Comment
Predicted prescriptions			
Predicted prescriptions for all progesterone medicines on the PBS for LPS	Yr 1: [redacted][1] Yr 2: [redacted][1] Yr 3: [redacted][1] Yr 4: [redacted][1] Yr 5: [redacted][1] Yr 6: [redacted][2]	Mi Portal IQVIA PBS Services, accessed February 2024	Submission based Year 1 on 2025 forecasted services.
Treatment utilisation			
Uptake rate – Utrogestan 200 mg	Yr 1: 5% Yr 2: 13% Yr 3: 20% Yr 4: 26% Yr 5: 31% Yr 6: 35%	Assumption by the Sponsor	No justification for the uptake rates. Sponsor stated uptake rates based on long-term experience in the market.
Scripts (quantity / packs) dispensed	Yr 1: [redacted][3] Yr 2: [redacted][3] Yr 3: [redacted][3] Yr 4: [redacted][4] Yr 5: [redacted][4] Yr 6: [redacted][4]	Based on the assumed uptake rates and a script equivalence of 1:1 for progesterone 300 mg capsule to progesterone 200 mg capsule (Utrogestan)	High uncertainty due to: • Uptake rate (assumed) • Annual growth rate (estimated) The submission did not account for possibly market share of other PBS-listed progesterone forms indicated for LPS. There is a risk that the magnitude of the net impact on the PBS may be underestimated
Costs			
Utrogestan 300 mg x 15 capsules	AEMP: $80.93	Requested price. CMA to cost per day of progesterone 200 mg capsule.	This approach to the CMA is not consistent with the PBAC's previous consideration of new progesterone forms.
Alternative progesterone brands: • Crinone • Utrogestan • Endometrin • Oripro 100 • Oripro 200	• Crinone 8% vaginal gel, 90 mg = $93.82 (per pack) • Endometrin 100 mg x 21 pessaries = $31.21 • Utrogestan 200 mg x 42 capsules = $75.53 • Oripro 100 mg x 15 pessaries = $47.88 • Oripro 200 mg x 15 pessaries = $35.40	Schedule of Pharmaceutical Benefits • 6366C (Crinone), • 10116K (Endometrin) • 10930G (Utrogestan) • 9608Q (Oripro 100) • 9609R (Oripro 200)	Some current PBS-listed progesterone medications have SPAs that may result in lower costs to the government than the proposed listing price for Utrogestan 300 mg. As such, the net impact on PBS budget might be underestimated.
Patient co-payment	General ordinary: $31.60 General safety net: $7.70 Concessional ordinary: $7.70 RPBS ordinary: $7.70	PBS website	Verified

Source: Submission main body – compiled during the evaluation.
Abbreviations: LPS = luteal phase support, PBS = pharmaceutical benefits scheme, PBAC = pharmaceutical benefits advisory committee, SPA = special pricing arrangement

The redacted values correspond to the following ranges
1 50,000 to < 60,000
2 60,000 to < 70,000
3 5,000 to < 10,000
4 10,000 to < 20,000

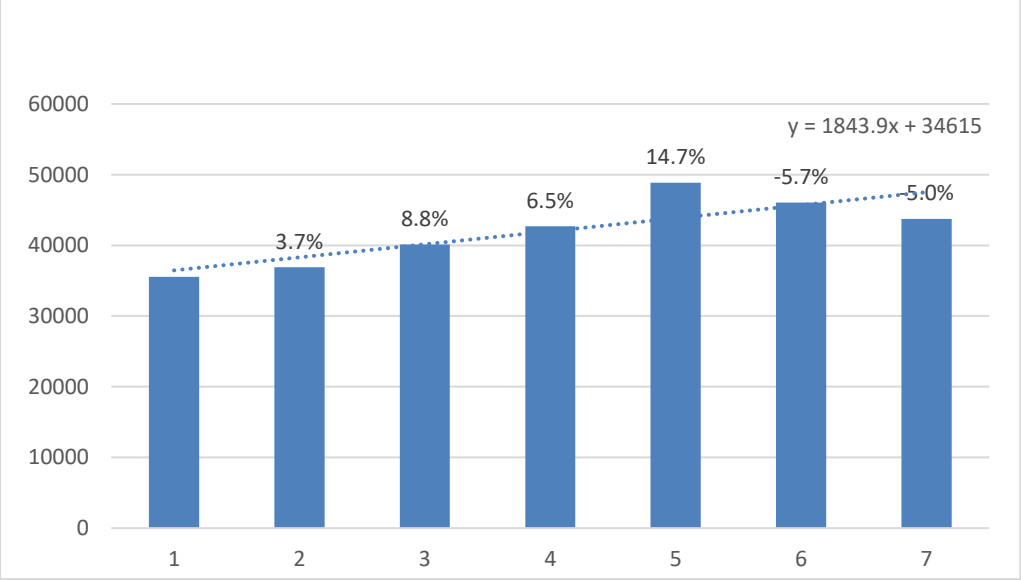
5.37 The submission estimated the growth rate in the LPS market at 3% over the forward estimates to align with the expected rate of growth in fresh cycle ART. The submission considered this estimate more appropriate than extrapolating the PBS item statistics which show a surge in 2021 and 2022 due to COVID.

Table 8: PBS item statistics 10930G - Progesterone Utrogestan Capsule 200 mg

Calendar Year	PBS Services				RPBS Services		Total	Growth	
	General - Ordinary	General - Safety Net	Concessional - Ordinary	Concessional - Free Safety Net	RPBS - Ordinary	RPBS - Safety Net		Services	%
2016	58	1	0	0	0	0	59	-	-
2017	3,496	0	87	0	0	0	3,583	3,524	5973
2018	7,085	2	300	0	0	0	7,387	3,804	106
2019	10,031	2	497	8	2	0	10,540	3,153	43
2020	12,664	10	712	9	0	0	13,395	2,855	27
2021	16,964	24	1,000	10	8	0	18,006	4,611	34
2022	15,572	18	743	19	5	0	16,357	-1,649	-9
2023	16,422	3	633	22	11	0	17,091	734	4
Total	82,292	60	3,972	68	26	0	86,418	-	-

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Reparation Pharmaceutical Benefits Scheme
Source: Medicare statistics website; Utilisation and Cost Model Workbook sheet 3a.

Figure 1: Total PBS Services for progesterone LPS market – Historical + Year-on-Year Growth



Source: Updated Utilisation and Cost Model workbook 2e. Scripts Market; Mi Portal IQCIA PBS Services accessed February 2024
Abbreviations: LPS = luteal phase support; PBS = pharmaceutical benefits scheme

Table 9: Forecasted growth of PBS-listed LPS market

Year	Services	Growth
2017	35562	-
2018	36889	3.7%
2019	40117	8.8%
2020	42706	6.5%
2021	48857	14.4%
2022	46064	-5.7%
2023	43742	-5.0%
2024	49366	12.9%
2025	51210	3.7%
2026	53054	3.6%
2027	54898	3.5%
2028	56742	3.4%
2029	58586	3.2%
2030	60430	3.1%
2031	62274	3.1%

Source: Updated Utilisation and Cost Model workbook 2e. Scripts Market; Mi Portal IQCIA PBS Services accessed February 2024
Scripts were forecasted using the line of best fit of PBS Services from 2017 to 2023 (Figure 1)
Abbreviations: LPS = luteal phase support; PBS = pharmaceutical benefits scheme
The shaded cells represent forecasted services and growth.

5.38 The submission based the 3% estimate on an extrapolation of the PBS data for progesterone capsule 200 mg in Table 8 and the total LPS PBS market in Table 9. The submission stated that the 2024 growth rate value of 12.4% is overestimated but noted 3.7% to 3.1% growth in 2025 to 2030.

5.39 The submission's estimated services in 2024 for progesterone 200 mg capsule is presented in Table 10.

Table 10: Estimated progesterone services by beneficiary type for LPS on the PBS/RPBS for 2024

Medicine	Form	Item code	General - Ordinary Services	General - Safety Net Services	Concessional - Ordinary Services	Concessional - Free Services	RPBS - Ordinary Services	RPBS - Safety Net Services
Progesterone Utrogestan	Capsule 200 mg	10930G	16,915	3	652	23	11	0

Abbreviations: LPS = luteal phase support, PBS = pharmaceutical benefits scheme; RPBS = reparation pharmaceutical benefits scheme
Source: Sheet 2e – Scripts – market, rows 49-50. To estimate 2024 services for use in the workbook, the 2023 data was increased by 3%.

5.40 The submission estimated the progesterone 200 mg growth is not expected to change as a result of the proposed listing. Table 11 presents the submission's expected uptake from progesterone 200 mg.

Table 11: Market growth and uptake with progesterone 300 mg

	2024	2025	2026	2027	2028	2029	2030
Estimated annual rate of growth	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	-
Proportion applicable to indication	100%	100%	100%	100%	100%	100%	100%
Proportion affected by the proposed medicine							
10930G Utrogestan 200	0.0%	30.0%	40.0%	50.0%	55.0%	60.0%	65.0%

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Reparation Pharmaceutical Benefits Scheme
Source: Sheet 2e. Scripts – market, rows 101-110. Substitution rates are Sponsor estimates

5.41 Further correspondence from the sponsor in relation to corrections to the financial estimates stated that the uptake rates were estimated by the sponsor based on its experience in women's health and its insight into LPS market dynamics.

5.42 The estimated number of prescribed units of progesterone 300 mg is summarised in Table 12 and was derived by applying the utilisation data presented in Table 10 and Table 11.

Table 12: Utrogestan 300 prescriptions dispensed over six years

	2025	2026	2027	2028	2029	2030
PBS	1	1	1	2	2	2
RPBS	3	3	3	3	3	3
Estimated total volume	1	1	1	2	2	2

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Reparation Pharmaceutical Benefits Scheme
Source: Sheet 3a. Scripts – proposed, rows 14-39

The redacted values correspond to the following ranges
1 5,000 to < 10,000
2 10,000 to < 20,000
3 < 500

5.43 The submission considered that progesterone 300 mg capsule will only replace progesterone 200 mg capsule and no other PBS-listed form of progesterone indicated for LPS. Table 13 presents the number of prescriptions substituted over time.

Table 13: Change in the units dispensed of existing Utrogestan 200 mg for LPS

Medicine / molecule	2025	2026	2027	2028	2029	2030
PBS	1	1	1	2	2	2
RPBS		3	3	3	3	3
Estimated total volume	1	11		2	2	2

Abbreviations: LPS = Luteal Phase Support; PBS = Pharmaceutical Benefits Scheme; RPBS = Reparation Pharmaceutical Benefits Scheme
Source: Sheet 4a – Scripts -affected, rows 14 to 39

The redacted values correspond to the following ranges
1 5,000 to < 10,000
2 10,000 to < 20,000
3 < 500

5.44 The submission stated that each PBS-listed form of progesterone indicated for LPS has its own unique formulation, presentation, description and adverse effect profile. The submission provided a clinical letter in support of the listing, stating that Utrogestan is the most widely used progesterone preparation in IVF practice in Australia and that

300 mg BID dosing would largely replace the current regime and would significantly improve the patient experience during a very stressful part of the IVF cycle.

5.45 The submission did not consider that the rationale of replacement occurring due to the reduced number of daily pessaries required for Utrogestan 300 mg could apply to the other PBS-listed forms of progesterone. The submission therefore did not account for any uptake of any alternative therapies in its financial estimates except for Utrogestan 200 mg TID. As the requested AEMP is higher than that of other alternative therapies, the cost to Government may be underestimated should new patients initiate treatment with progesterone 300 mg over other, less costly, alternative therapies.

5.46 The estimated extent of use, cost of progesterone capsule 300 mg to the PBS/RPBS, and the net financial implications to the PBS/RPBS are presented in Table 14. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

5.47 The submission estimated that 50,000 to < 60,000 scripts of progesterone capsule 300 mg would be dispensed over the first six years of listing (5,000 to < 10,000 in Year 1 to 10,000 to < 20,000 in Year 6).

5.48 The submission stated that the estimated net financial impact to the PBS/RPBS for the listing of progesterone capsule 300 mg is $0 to < $10 million over six years (Year 1: $0 to < $10 million to Year 6: $0 to < $10 million).

Table 14: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	[redacted]1	[redacted]1	[redacted]1	[redacted]2	[redacted]2	[redacted]2
Estimated financial implications of progesterone capsule 300 mg						
Cost to PBS/RPBS less co-payment	[redacted]3	[redacted]3	[redacted]3	[redacted]3	[redacted]3	[redacted]3
Estimated financial implications of progesterone capsule 200 mg						
Cost to PBS/RPBS less co-payment	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4	[redacted]4
Net financial implications						
Net cost to PBS/RPBS	[redacted]3	[redacted]3	[redacted]3	[redacted]3	[redacted]3	[redacted]3

Source: Submission main body Table 4-5; 4-6; 4-8 and 4-9
Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

The redacted values correspond to the following ranges
1 5,000 to < 10,000
2 10,000 to < 20,000
3 $0 to < $10 million
4 net cost saving

5.49 The submission stated that the cost is due to the 300 mg capsule listing providing 15 days' supply compared to the current 200 mg capsule listing providing 14 days' supply. However, the cost impact is because the CMA was calculated with an equivalent price per day of treatment instead of price per treatment course.

5.50 The pre-PBAC accepted that the CMA be calculated at an equivalent price per treatment course and that the subsequent estimated net financial impact to the PBS/RPBS for the listing of progesterone capsule 300 mg would be nil.

5.51 The submission identified that the key sources of uncertainty are the growth rate of the LPS market in ART and the uptake rate. The submission presented a sensitivity analysis (Table 15) based on altered growth and uptake rates.

Table 15: Results of the sensitivity analysis

	2025	2026	2027	2028	2029	2030
Base case	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
LPS growth rate to 5%	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
LPS growth rate to 0%	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Uptake reduced by 20%	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Uptake increased by 20%	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]

Source: Submission main body
Abbreviations: LPS = luteal phase support

The redacted values correspond to the following ranges
1 $0 to < $10 million

6 PBAC Outcome

6.1 The PBAC recommended the Authority Required (STREAMLINED) listing of progesterone capsule 300 mg (Utrogestan) BID on the basis it should be available only under special arrangements covered under the PBS section 100 (IVF Program) for LPS as part of an ART treatment cycle. The PBAC's recommendation for listing was based on, among other matters, its assessment, that the cost-effectiveness of progesterone 300 mg capsule would be acceptable if it were cost-minimised at an equivalent price per treatment course against the least costly progesterone for luteal phase support currently listed on the PBS.

6.2 The PBAC did not consider it appropriate to cost-minimise based on an equivalent price per day of treatment. The PBAC advised that the CMA should be calculated at an equivalent price per treatment course and noted that the sponsor accepted this in its pre-PBAC response.

6.3 The PBAC accepted the main comparator as progesterone 200 mg TID. The PBAC also reaffirmed its July 2016 advice that it considered all other PBS-listed forms of progesterone indicated for LPS as appropriate comparators.

6.4 The PBAC considered the equi-effective doses as progesterone capsule 300 mg BID for 15 days equivalent to progesterone 200 mg capsule TID for 14 days. The PBAC reaffirmed its July 2016 advice that progesterone 200 mg capsule TID for 14 days was equivalent to progesterone 8% vaginal gel 90 mg (Crinone®) QD (once per day) for 15 days and progesterone tablet 100 mg (Endometrin®) BID or TID for 14 days.

6.5 The PBAC noted the TGA had considered progesterone 300 mg capsule BID and

progesterone 200 mg capsule TID bioequivalent and considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety was reasonable.

6.6 The PBAC advised that the proposed restrictions were appropriate, noting they were identical to the current progesterone 200 mg listing. The PBAC advised the requested maximum quantity of 30 units and nil repeats was appropriate and aligned with the TGA approved PI. The PBAC also noted that, consistent with the section 100 (IVF Program) listed medicines policy, repeats are not permissible for these medicines.

6.7 The PBAC advised that progesterone 300 mg capsule will likely only replace progesterone 200 mg capsule in practice. The PBAC advised that the estimated annual growth rate and the estimated uptake rates were appropriate.

6.8 The PBAC considered that the proposed listing should not result in any additional cost to Government.

6.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because progesterone 300 mg capsule is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over other PBS listings of progesterone for LPS, or not expected to address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

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

Outcome:
Recommended

7 Recommended listing

7.1 Add new medicinal product pack:

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
PROGESTERONE						
progesterone 200 mg pessary, 42		10930G	1	42	0	Utrogestan
progesterone 300 mg pessary, 15		NEW	2	30	0	Utrogestan
Restriction Summary 4997 / Treatment of Concept: 4997						
Concept ID (for internal Dept. use)	**Category / Program:** Section 100 – IVF Program					
	Prescriber type: ☒Medical Practitioners					
	Restriction type: ☒Authority Required (Streamlined)					
Prescribing rule level	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.					
	Indication: Assisted Reproductive Technology					
	Clinical criteria:					
	The treatment must be for luteal phase support as part of an assisted reproductive technology (ART) treatment cycle for infertile women					
	AND					
	Clinical criteria:					
	Patient must be receiving medical services as described in items 13200 or 13201 of the Medicare Benefits Schedule					
	Prescribing Instructions: The luteal phase is defined as the time span from embryo transfer until implantation confirmed by positive B-hCG measurement.					

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

8 Context for Decision

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

9 Sponsor's Comment

The sponsor had no comment.