5.12 PROGESTERONE, Pessary 400 mg, Utrogestan®, Besins Healthcare Australia Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested a General Schedule, Authority Required (STREAMLINED) listing for micronised progesterone 400 mg soft capsule/pessary (administered intravaginally) for the treatment of unexplained threatened miscarriage (uTM) in the first trimester, with vaginal bleeding in the current pregnancy and a history of previous miscarriage.

1.2 Listing was requested on the basis of a clinical claim of superior efficacy and non-inferior safety versus standard of care supported by a cost effectiveness analysis.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Women with unexplained threatened miscarriage in the first trimester, with vaginal bleeding in the current pregnancy and a history of previous miscarriage
Intervention	Progesterone 400 mg soft capsule/pessary twice a day (vaginal administration)
Comparator	Watch and wait, represented by placebo
Outcomes	Primary efficacy outcome: Birth of a live-born baby after at least 34 weeks of gestation Safety: Serious adverse events; antenatal, intrapartum, postpartum and neonatal complications
Clinical claim	In women with unexplained threatened miscarriage in the first trimester, with vaginal bleeding in the current pregnancy and a history of previous miscarriage, progesterone 400 mg pessary twice daily is superior in terms of the birth rate of a live born baby after at least 34 weeks of gestation and non-inferior in terms of safety, compared to placebo.

Source: Table 1-1, p13 of the submission.

2 Background

Registration status

2.1 Progesterone 400 mg pessary was TGA registered on 17 February 2022 for the treatment of uTM. The approved TGA indication is:

- Treatment of unexplained threatened miscarriage in women with bleeding in the current pregnancy and a history of at least 3 or more previous miscarriages.

  Use in women with less than 3 miscarriages may be warranted in those with reduced chances of future pregnancy such as those undergoing IVF treatment with limited viable egg and/or embryo availability or advanced fertility age. However, the benefit of treatment in clinical trials was limited to women with 3 or more miscarriages.

Previous PBAC consideration

2.2 The PBAC had not previously considered progesterone 400 mg for the treatment of uTM.

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

- prevention of preterm birth on the General Schedule. Use in this setting is limited to a singleton pregnancy, the patient must have a short cervix and/or a history of spontaneous preterm birth, and treatment must be administered no earlier than 16 weeks gestation; and
- luteal phase support as part of an assisted reproductive technology (ART) cycle on the Section 100 (IVF Program).

3 Requested listing

3.1 The Secretariat's suggested additions to the restriction are in italics, deletions in strikethrough.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
PROGESTERONE					
progesterone 400 mg pessary, 28	$[redacted]	2	56	1	Utrogestan

Category / Program: General Schedule
Prescriber type: ☒Medical Practitioners ☒Nurse practitioners ☒Midwife
Restriction type: ☒Authority Required (STREAMLINED)
Administrative Advice: *No increase in the maximum quantity or number of units may be authorised.*
Administrative Advice: *No increase in the maximum number of repeats may be authorised.*
Administrative Advice: *Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.*
Indication: Unexplained threatened miscarriage
Clinical criteria:
Patient must be pregnant
AND
Clinical criteria:
Patient must have vaginal bleeding ~~in the current pregnancy~~
AND
Clinical criteria:
Patient must have a history of previous miscarriage
AND
Clinical criteria:
~~The treatment must be commenced prior to 12 weeks gestation~~ *The treatment must be initiated no later than 12 weeks gestation*
AND
Clinical criteria:
~~The treatment should be continued to the 16th week of gestation and then ceased~~ *The treatment must cease after 16 weeks gestation*
Caution: Other known causes of threatened miscarriage should be ruled out before initiating treatment.
Caution: ~~Progesterone~~ *This drug* should not be used in women with undiagnosed vaginal bleeding, known missed abortion or ectopic pregnancy.

3.2 The submission requested an ex-manufacturer price (EMP) of $[redacted] (for 56 pessaries), resulting in a dispensed price for maximum quantity (DPMQ) of $[redacted]. This was derived from the corresponding cost per mg ($[redacted]) of the currently PBS-listed progesterone 200 mg pessary.

3.3 The TGA-approved Product Information (PI) recommends a progesterone dose of 400 mg twice daily, administered intravaginally, initiated at the first sign of vaginal bleeding in the first trimester and continued until at least 16 weeks' gestation. The Sub-Committees expected that patients may want to complete the full course of treatment, including the repeat prescription, rather than cease treatment at 16

weeks. It was noted that counselling of patients in the use of progesterone and cessation at 16 weeks would be required.

3.4 The requested restriction was broader than the approved TGA indication. Specifically, the restriction allows treatment of women with any history of previous miscarriage, whereas the TGA indication is limited to women with a history of 3 or more previous miscarriages. Although the TGA notes potential use in women with fewer than 3 previous miscarriages may be warranted in certain circumstances (e.g., reduced chances of future pregnancy due to IVF treatment, limited viable egg or embryo availability, or advanced maternal age), it states that the benefit of treatment in clinical trials was limited to women with 3 or more miscarriages. The 2021 National Institute for Health and Care Excellence (NICE; NG126) guidance recommends progesterone use in the broader population of women with a history of previous miscarriage[1]; however, the TGA considered the evidence provided to be insufficient to support the broader indication. The PSCR highlighted the portion of the Product Information which stated: "the dual risk factors of early pregnancy bleeding and a history of one or more previous miscarriage(s) identified high-risk women in whom progesterone may be of benefit" and noted that there is precedent for PBS listings to not strictly align with the TGA indication, such as unrestricted PBS listings for some oncology listings. The Sub-Committees noted the precedent of unrestricted PBS listings for some oncology drugs was not analogous to this requested listing for which broader use than the TGA indication was not robustly supported by the evidence (see paragraph 6.29) or consistently applied in clinical guidelines (see Table 2).

3.5 The PSCR reiterated that previous miscarriage is a major determinant of miscarriage risk and stated that the proposed PBS population of patients with a history of previous miscarriage ensures that progesterone 400 mg will be utilised in those patients who will derive the most clinical benefit from treatment. The Sub-Committees advised that although prior miscarriage is a risk marker for future miscarriage, one prior miscarriage is not a determinant of insufficient progesterone for future pregnancies.

3.6 Progesterone 200 mg pessary is PBS-listed for use after Week 16 of gestation for prevention of preterm birth in patients with a short cervix and/or a history of spontaneous preterm birth. No information was provided in the submission on the sequential use of progesterone 400 mg and 200 mg pessaries.

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

4 Population and disease

4.1 A threatened miscarriage refers to vaginal bleeding and uterine cramping in an otherwise viable pregnancy before 20 weeks' gestation, though more commonly

[1] National Institute for Health and Care Excellence (NICE), (2019), 'Ectopic pregnancy and miscarriage: diagnosis and initial management', Available at: www.nice.org.uk/guidance/ng126

occurring in the first trimester[2]. In the absence of a potential cause (e.g., genetic abnormality, ectopic pregnancy, or infection), this may be classified as uTM. In Australia, approximately one in four pregnancies experience vaginal bleeding in early pregnancy, and around one-third to one-half of these cases results in miscarriage[3].

4.2 In addition to maternal age, the number of previous miscarriages is a major determinant of miscarriage risk. Quenby et al. (2021) reported an estimated pooled miscarriage risk of 15.3% (95% confidence interval [CI]: 12.5, 18.7%) among recognised pregnancies[4]. Population prevalence estimates indicated that 10.8% of women had experienced one miscarriage, 1.9% had experienced two miscarriages, and 0.7% had experienced 3 or more miscarriages. When recurrent miscarriage was defined as two or more miscarriages, the population prevalence was 2.6%[4]. Based on Australian data[5], the proportion of women who had a history of miscarriage was potentially higher at approximately 28-30% (see paragraph 6.47).

4.3 The submission stated that progesterone is the only pharmacological intervention with evidence in uTM to increase the likelihood of live birth. Progesterone plays a critical role in maintaining pregnancy from conception through delivery; therefore, there is strong biological plausibility for the use of exogenous progesterone in the treatment of uTM.

4.4 While national and international guidelines generally support progesterone use in uTM, they differ in the number of prior miscarriages required to initiate treatment, as summarised in Table 2.

[2] Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) (2025), 'Miscarriage, Recurrent Miscarriage and Ectopic Pregnancy (C-Gyn 38) Clinical Guideline, Available at: https://ranzcog.edu.au/wp-content/uploads/Miscarriage-Ectopic-Pregnancy.pdf

[3] Department of Health, Victoria State Government, (2022), 'Pregnancy-bleeding problems', Available at: https://www.betterhealth.vic.gov.au/health/healthyliving/pregnancy-bleeding-problems#bhc-content

[4] Quenby, S., Gallos, I., Dhillon-Smith, R., et al. (2021), 'Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss,' Lancet 397(10285):1658-1667

[5] Preventive Health South Australia, (2025), 'Pregnancy Outcome in South Australia 2023', Adelaide: Pregnancy Outcome Unit, Epidemiology and Research Division, Preventive Health SA, Government of South Australia, Available at: https://www.preventivehealth.sa.gov.au/assets/downloads/Pregnancy-outcomes/Pregnancy-Outcome-in-South-Australia-2023_FINAL.pdf

Table 2: Key recommendations for progesterone treatment of uTM in current national and international guidelines

Guidelines	Recommendations	Evidence base
Australia and New Zealand guidelines		
RANZCOG 2025[2]	Progesterone (by any route) probably improves the live birth rate for women with early pregnancy bleeding and **≥2 previous miscarriages** (RR: 1.14; 95% CI: 1.04,1.24).	PRISM trial McLindon et al. (2023)
Queensland Health, 2022[6]	Progesterone may improve live birth outcome in women with **one or more previous miscarriages** and early pregnancy bleeding (ARR: 5.72%; 95% CI: 1.65, 9.8). For women with unexplained recurrent miscarriages (**≥3**), supplementation with progestogen therapy may reduce the rate of miscarriage in subsequent pregnancies.	Not specified Hass et al. (2019)
ACCEPT 2024[7]	Progesterone supplementation is recommended in women with **≥2 pregnancy losses** especially in the setting of a threatened miscarriage	Expert consensus based on PRISM trial
International guidelines		
NICE 2019[1]	400 mg twice daily of micronised **vaginal** progesterone increases the number of live births in women with early pregnancy bleeding and **a previous miscarriage** (RR:1.08; 95% CI: 1.02,1.15)	Cochrane review by Devall et al. (2021), which included pooled subgroup analyses of participants with ≥1 prior miscarriage, based on data from the PRISM trial and Gerhard et al. (1987)
UK RCOG 2023[8]	Progestogen supplementation should be considered in women with recurrent miscarriage (**≥3**) with bleeding in early pregnancy (RR: 1.28; 95% CI: 1.08, 1.51)	PRISM trial
ESHRE 2022[9]	Vaginal progesterone may improve live birth rate in women **with ≥3 pregnancy losses** and vaginal blood losses in a subsequent pregnancy (RR: 1.28; 95% CI: 1.08, 1.51)	PRISM trial

Source: Section 1.2.1, pp 23-29 of the submission

ACCEPT = Australasian Certificate of Reproductive Endocrinology and Infertility Consensus Expert Panel; ARR = absolute risk reduction; CI = confidence interval; ESHRE = European Society of Human Reproduction and Embryology; NICE = National Institute for Health and Care Excellence; RANZCOG = Royal Australian and New Zealand College of Obstetricians and Gynaecologists; RR = risk ratio; UK RCOG = United Kingdom Royal College of Obstetricians and Gynaecologists; uTM = unexplained threatened miscarriage;.

Bold indicates key differences in the guidelines.

4.5 The submission target population comprises women with uTM who present with vaginal bleeding in the first trimester of the current pregnancy and have a history of previous miscarriage.

4.6 Although the submission and the PSCR attributed differences in the number of prior miscarriages required across guidelines to variations in study populations and evidence bases, including differences in progesterone formulation, dose, route, and duration of therapy, the Sub-Committees noted that most guidelines are primarily informed by the PRISM trial.

[6] Queensland Health, (2025), Queensland Clinical Guidelines Early Pregnancy Loss Guideline No MN22.29-V8-R27, Available at: https://www.health.qld.gov.au/__data/assets/pdf_file/0033/139947/g-epl.pdf

[7] Suker A., Li Y., Robson D., et al., (2024), 'Australasian Recurrent Pregnancy Loss Clinical Management Guideline 2024 Part I', Aust N Z J Obstet Gynaecol, 64:432–44

[8] Regan L., Rai R., Saravelos S., et al. (2023), 'Recurrent Miscarriage: Green-top Guideline No. 17', BJOG, 130:e9–e39.

[9] The ESHRE Guideline Group on RPL, Atik R.B., Christiansen O.B., et al. (2023), 'ESHRE guideline: recurrent pregnancy loss: an update in 2022', Hum Reprod Open., 2023(1):hoad002.

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

5 Comparator

5.1 The submission nominated standard of care (SOC), representing 'watch and wait' approach, as the main comparator. The main argument provided in support of this nomination was the absence of a PBS-listed pharmacological treatment for uTM in patients prior to 16 weeks' gestation. The Sub-Committees considered that this was reasonable.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician highlighted the impact of miscarriage on patients and their partners and families. It was noted that there are no treatments currently available on the PBS for uTM with vaginal bleeding. The clinician highlighted the results of the PRISM trial stating that progesterone results in a clear benefit for patients who have experienced at least 3 prior miscarriages and probably demonstrated a benefit in those who have experienced 1 or 2 prior miscarriages. The clinician supported the proposed PBS indication of at least 1 prior miscarriage with vaginal bleeding, noting that progesterone was currently being prescribed for these patients, based on available evidence. The clinician also noted that progesterone should not be prescribed in patients with multiple prior miscarriages, but who do not have vaginal bleeding. Progesterone was described as being safe, with no known adverse events and it was noted that PBS listing would improve equity of access.

Consumer inputs

6.2 The PBAC noted and welcomed the input from individuals (12), health care professionals (5) and organisations (7) via the Office of Health Technology Assessment Consultation Hub. Individuals shared personal experiences noting that progesterone supports uTM and, although some pregnancies supported by progesterone still resulted in miscarriage, stated that it provides psychological reassurance. Individuals noted the high out-of-pocket costs currently associated with progesterone and expressed hope for equitable access through a PBS listing. Individuals also described the emotional toll of multiple miscarriages.

6.3 Health professionals emphasised the high prevalence and emotional impact of miscarriage. Evidence from large randomised controlled trials, including the PRISM trial and Cochrane meta-analyses, were cited to support the efficacy of progesterone and demonstrating an increased benefit with a greater number of prior miscarriages. The clinicians noted international and Australian clinical guidelines, including those from National Institute for Health and Care Excellence (NICE) and Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), which have

incorporated this evidence into recommendations, supporting the use of progesterone for uTM with vaginal bleeding. It was also noted that PBS listing would improve access and remove cost barriers.

6.4 The PBAC noted support for the listing from consumer groups, the Pink Elephants Support Network (PESN) and the Early Pregnancy Loss Coalition (EPLC). The PESN strongly endorsed the listing of progesterone for uTM, noting that it would move Australian clinical practice from a 'watch and wait' situation to evidence-based action and allow women presenting with uTM and vaginal bleeding to leave the hospital or their general practitioner with a plan of care. They also highlighted that the listing would remove financial barriers and provide equitable care. The EPLC noted that listing of progesterone would support more equitable, timely and compassionate care for patients experiencing uTM. They also noted that the NICE guidelines (UK) and the RANZCOG guidelines, on the basis of the PRISM and PROMISE trials, consider that progesterone is best clinical practice in cases of uTM.

6.5 Advice was also received from the following specialist medical organisations: RANZCOG, Australian and New Zealand Society of Reproductive Endocrinology and Infertility (ANZSREI), Australian College of Midwives (ACM), Australian College of Nurse Practitioners, and Evoca Women's Health. All organisations strongly supported the submission, noting that since the publication of the PRISM and PROMISE trials, progesterone has become routine clinical practice for women with uTM and prior pregnancy loss. All organisation cited equity of access issues and highlighted the need for PBS-funded treatment options. ANZSREI supported the TGA indication for progesterone (i.e. for use in women with at least 3 prior miscarriages) but noted that women with fewer previous miscarriages may still derive a clinically meaningful benefit, particularly in women of an advanced reproductive age, undergoing IVF treatment, limited embryo availability and reduced ovarian reserve or limited remaining fertility potential. RANZCOG noted that their clinical guideline supported use of progesterone in women with two or more previous miscarriages and stated that listing of progesterone for this population would offer several benefits including improving equity of access, enhancing clinical confidence and facilitating earlier intervention. The ACM noted the TGA indication and that the PRISM trial demonstrated an increasing benefit with greater miscarriage history. Evoca Women's Health stated that restricting access to women with 3 or more prior miscarriages would fail to reflect the real-world clinical burden of pregnancy loss, the established safety profile of this medication or the psychological harm inflicted on women and families who are denied an accessible, low-cost, low-risk treatment. It was also noted by a number of the organisations that further placebo-controlled trials would not be ethically feasible in this population as the PRISM and PROMISE trials have provided evidence that a safe, plausible and guideline-endorsed therapy exists.

Clinical studies

6.6 The submission was based on one head-to-head randomised controlled trial, PRISM, which compared the efficacy and safety of progesterone with placebo in women with

uTM and vaginal bleeding in early pregnancy. As the trial included women with and without previous miscarriages, the submission identified those with one or more previous miscarriages as the subgroup most closely aligned with the proposed PBS population. As noted above, the trial and proposed PBS populations were broader than the TGA indication. The subgroup of women with 3 or more prior miscarriages most closely aligned with the TGA indication.

6.7 The submission also presented results from two systematic reviews and/or meta-analyses of progestogens for preventing miscarriage as supportive evidence (Devall et al., 2021 and Zhao et al., 2024). Both publications included subgroup analyses for women with one or more previous miscarriages, aligning with the proposed population. The Sub-Committees noted that the results of the systematic reviews appeared driven by Coomarasamy et al. 2019 (PRISM).

6.8 Although another trial, PROMISE, was also conducted to assess the role of progesterone in uTM, participants were not required to have vaginal bleeding in early pregnancy, and no subgroup analyses by bleeding status were undertaken. The submission therefore considered the PROMISE trial to be misaligned with the proposed PBS population and excluded it from the main evaluation. While this exclusion was reasonable given the population differences, it was noted that the PROMISE trial was included as key evidence, alongside with PRISM trial, in the TGA submission.

6.9 Details of the included trial and meta-analyses presented in the submission are provided in Table 3.

Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
PRISM trial EUCTR2014-002348-42 ISRCTN14163439	Effectiveness of progesterone to prevent miscarriage in women with early pregnancy bleeding: A randomised placebo-controlled trial (PRISM Trial: PRogesterone In Spontaneous Miscarriage Trial) PRISM: progesterone in spontaneous miscarriage Coomarasamy A, Devall A, et al. A Randomised Trial of Progesterone in Women with Bleeding in Early Pregnancy Coomarasamy A, Harb H, et al. Progesterone to prevent miscarriage in women with early pregnancy bleeding: the PRISM RCT Coomarasamy A, Devall A et al. Micronised vaginal progesterone to prevent miscarriage: a critical evaluation of randomised evidence	CSR *N Engl J Med.,* 2019; 380(19):1815-1824. *Health Technol Assess.,* 2020; 24(33):1-70 *Am J Obstet Gynecol.,* 2020; 223(2):167-176
Devall et al., 2021	Devall A, Papadopoulou A, et al. Progestogens for preventing miscarriage: a network meta-analysis	*Cochrane Database Syst Rev.,* 2021
Zhao et al., 2024	Zhao Y, D'Souza R, et al. Progestogens in women with threatened miscarriage or recurrent miscarriage: A meta-analysis.	*Acta Obstet Gynecol Scand.,* 2024; 103(9):1689-1701

Source: Table 2-3, p40 and Section 2.2.3.2, pp40-41 of the submission.
CSR = clinical study report; RCT = randomised controlled trial.

6.10 The key features of the included evidence are summarised in Table 4.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Primary outcome	Use in economic analysis
PRISM	N=4,153 Progesterone=2,079 Placebo=2,074	R, DB, MC	Low	Women aged 16-39 years with vaginal bleeding in early pregnancy (<12 weeks), with pre-specified and *post hoc* subgroup analyses based on number of previous miscarriages	Birth of a live-born baby ≥34 weeks of gestation	Yes; subgroup of women who have had ≥1 previous miscarriage
Devall et al., 2021	Progesterone=928 Placebo=901 from two trials: Coomarasamy et al., 2019 and Gerhard et al., 1987	Meta-analysis	Low	Subgroup analysis is presented for women who have had ≥1 previous miscarriage and early pregnancy bleeding	Live birth, miscarriage (<24 weeks) and preterm birth (<37 weeks).	No
Zhao et al., 2024	Progesterone=995 Placebo=978 from 3 trials: Coomarasamy et al., 2019; McLindon et al., 2023; and Gerhard et al., 1987	Meta-analysis	Low	Subgroup analysis is presented for women who have had ≥1 previous miscarriage and early pregnancy bleeding	Live birth	No

Source: Table 2-6, p45; Table 2-10, p49; Table 2-17, p60; Figure 2.5, p62 and Figure 2.6, p64 of the submission.
DB = double blind; MC = multi-centre; N = total participants in group; R = randomised.

6.11 The PRISM trial did not directly evaluate the efficacy of the progesterone 400 mg vaginal pessary for which listing is sought in the current submission. Instead, progesterone was administered as two 200 mg pessaries until 16 weeks of gestation in the PRISM trial. This evidence was accepted by the TGA to support the registration of the 400 mg pessary.

Comparative effectiveness

PRISM trial

6.12 Table 5 summarises the key results from the PRISM trial for the primary outcome of live birth at least after 34 weeks' gestation. Table 5 also reports results from sensitivity analyses, as well as pre-specified and *post hoc* subgroup analyses stratified by the number of previous miscarriages.

Table 5: Results for the primary outcome of live birth after at least 34 weeks

	Progesterone n/N (%)	Placebo n/N (%)	Relative Rate (95% CI)	P-value / interaction p-value
Primary outcome (live birth at ≥34 week)	1,513/2,025 (75)	1,459/2,013 (72)	1.03 (1.00, 1.07)	0.08
Sensitivity analysis[a]	1,513/2,079 (73)	1,459/2,074 (70)	1.04 (1.00, 1.08)	0.04
Subgroup analyses				
Prespecified subgroup analysis 1: number of prior miscarriages (0, 1 or 2, ≥3)				
0	824/1,111 (74)	840/1,127 (75)	0.99 (0.95, 1.04)	0.007
1 or 2	591/777 (76)	534/738 (72)	1.05 (1.00, 1.12)	
≥3	98/137 (72)	85/148 (57)	1.28 (1.08, 1.51)	
***Post hoc* subgroup analysis 2: number of prior miscarriages (0, ≥1)**				
0	824/1,111 (74)	840/1,127 (75)	0.99 (0.95, 1.04)	0.01
≥1	689/914 (75)	619/886 (70)	1.09 (1.03, 1.15)	
***Post hoc* subgroup analysis 3: number of prior miscarriages (0, 1, 2, ≥3)**				
0	824/1,111 (74)	840/1,127 (75)	0.99 (0.95, 1.04)	0.02
1	413/547 (76)	367/502 (73)	1.04 (0.97, 1.12)	
2	178/230 (77)	167/236 (71)	1.08 (0.97, 1.19)	
≥3	98/137 (72)	85/148 (57)	1.28 (1.08, 1.51)	

Source: Table 2-11, p51; Table 2-12, p51; Figure 2.3, p57; and Figure 2.4, p59 of the submission.
CI = confidence interval; n = number of participants with event; N = total participants in group.
[a] Sensitivity analysis was performed on the primary outcome to test the impact of any missing data.

6.13 In the intention-to-treat population, the proportion of participants achieving the primary outcome of live birth after at least 34 weeks of gestation was numerically higher in the progesterone group (75%) compared with the placebo group (72%). This corresponded to a relative rate (RR) of 1.03 (95% CI: 1.00, 1.07); however, the difference between treatment groups was not statistically significant.

6.14 Sensitivity analysis was performed on the primary outcome to test the impact of any missing data. When assuming that all missing outcomes were treatment failures (2.6% in the progesterone group and 3.0% in the placebo group), the difference between the progesterone and placebo groups was statistically significant (RR = 1.04; 95% CI: 1.00, 1.08; $p < 0.05$). In contrast, when missing outcomes were handled using multiple imputation, the difference between treatment groups did not reach statistical significance.

6.15 Among the pre-specified subgroup analyses, no evidence of a treatment effect was observed in women with no previous miscarriages (RR = 0.99; 95% CI: 0.95, 1.04). A small treatment effect was observed in women with one or two previous miscarriages (RR = 1.05; 95% CI: 1.00, 1.12), whereas a larger effect was observed in women with 3 or more previous miscarriages (RR = 1.28; 95% CI: 1.08, 1.51). These results should be interpreted with caution, as only 7–8% of the study population (142 and 159 women in the progesterone and placebo groups, respectively) had a history of 3 or more prior miscarriages.

6.16 The submission also presented *post hoc* subgroup analyses comparing participants with no prior miscarriages and those with one or more previous miscarriages, with further stratification by one, 2, or 3 or more prior miscarriages. In the proposed PBS population, i.e. patients with a least one previous miscarriage, treatment with progesterone was associated with a higher number of live births after at least 34

weeks of gestation (RR = 1.09; 95% CI: 1.03, 1.15). The largest treatment effect was demonstrated in women with 3 or more previous miscarriages (RR = 1.28; 95% CI: 1.08, 1.51). While the results were consistent with the pre-specified subgroup analyses, the *post hoc* nature limits interpretability for decision making.

6.17 The results for the key secondary outcomes in PRISM trial are presented in Table 6. The secondary outcomes were reported for the overall population and not stratified by number of previous miscarriages.

Table 6: Results of key secondary outcomes

Outcome	Progesterone n/N (%)	Placebo n/N (%)	RR[a] or mean difference[b] 95% CI
Secondary maternal outcomes – pregnancy outcomes[c]			
Ongoing pregnancy at 12 weeks	1,672/2,025 (83%)	1,602/2,013 (80%)	**1.04 (1.01, 1.07)**
Miscarriage at < 24 weeks[d]	410/2,025 (20%)	451/2,013 (22%)	0.91 (0.81, 1.01)
Live birth at < 34 weeks	68/2,025 (3%)	64/2,013 (3%)	1.06 (0.76, 1.49)
Ectopic pregnancy	0/2,025	2/2,013 (< 1%)	–
Stillbirth (intrauterine death at ≥ 24 weeks)	5/2,025 (< 1%)	6/2,013 (< 1%)	0.82 (0.25, 2.66)
Termination[e]	34/2,025 (2%)	36/2,013 (2%)	0.94 (0.59, 1.50)
Secondary maternal outcomes – other outcomes (in live births at ≥ 24 weeks)			
Twins[f]	29/1,581 (2%)	22/1,523 (1%)	1.28 (0.74, 2.22)
Mode of delivery			
Unassisted vaginal	845/1,577 (53%)	794/1,515 (52%)	1.02 (0.96, 1.10)
Instrumental vaginal	224/1,577 (14%)	199/1,515 (13%)	1.08 (0.91, 1.29)
Vaginal breech delivery	4/1,577 (< 1%)	7/1,515 (< 1%)	0.55 (0.16, 1.88)
Elective C-section	257/1,577 (16%)	224/1,515 (15%)	1.10 (0.93, 1.29)
Emergency C-section	241/1,577 (15%)	286/1,515 (19%)	**0.80 (0.69, 0.94)**
Other	6/1,577 (< 1%)	5/1,515 (< 1%)	–
Missing	4 (–)	8 (–)	–
Secondary neonatal outcomes (in live births at ≥ 24 weeks)			
Birthweight adjusted for gestational age and sex (using intergrowth[g] standards), centiles [mean (SD), n]	61.6 (28.2), 1,599	61.6 (28.2), 1,537	-0.21 (-2.16, 1.74)

Source: Table 2-13, p52 of the submission.

CI = confidence interval; C-section = caesarean section; n = number of participants reporting data; N = total participants in group; RR = relative rate; SD = standard deviation.

[a] For binary outcomes, RR<1 favours the progesterone group apart from live birth at ≥ 34 weeks and ongoing pregnancy at 12 weeks where RR>1 would favour progesterone.

[b] For continuous outcomes, mean difference < 0 favours the progesterone group.

[c] A total of 5 women on progesterone and 3 women on placebo had both a live birth ≥ 34 weeks and a miscarriage; one woman on placebo had both a termination and a miscarriage; and one woman on placebo had both a live birth < 34 weeks and a stillbirth.

[d] Median gestational age (IQR) in progesterone group, 8 (7–10) weeks; median gestational age (IQR) in placebo group, 8 (7–10) weeks.

[e] Reasons in progesterone group: social, n = 13; medical, n = 21. Reasons in placebo group: social, n = 12; medical, n = 24. Median gestational age (IQR) in progesterone group, 14 (12–19) weeks; median gestational age (IQR) in placebo group, 15 (11–18) weeks.

[f] Total number of babies, N = 3155: progesterone group, n = 1610; placebo group, n = 1545.

[g] Chatfield et al., 2013

Bold indicates statistical significance.

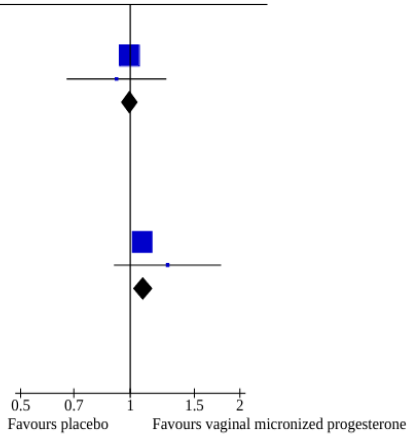
6.18 Progesterone treatment was associated with a statistically significant increase in the rate of ongoing pregnancy at 12 weeks' gestation (RR = 1.04; 95% CI: 1.01, 1.07) and a statistically significant reduction in the rate of emergency caesarean section (RR = 0.80; 95% CI: 0.69, 0.94). No statistically significant differences were observed between treatment groups for the remaining outcomes.

Devall et al., 2021

6.19 To inform the efficacy of progestogens in the subgroup of women with one or more prior miscarriage, the results of the meta-analysis by Devall et al. (2021), which was based on two trials: PRISM trial and Gerhard et al. (1987), were presented. The key results are presented in the forest plot below.

Figure 1: Threatened miscarriage: vaginal micronised progesterone versus placebo, live birth (sub-grouped by no previous miscarriages and one or more previous miscarriages)

Study or Subgroup	Vaginal micronised progesterone Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.8.1 No previous miscarriages and early pregnancy bleeding						
Coomarasamy 2019	824	1111	840	1127	98.8%	1.00 [0.95 , 1.04]
Gerhard 1987	10	12	10	11	1.2%	0.92 [0.67 , 1.26]
Subtotal (95% CI)		**1123**		**1138**	**100.0%**	**0.99 [0.95 , 1.04]**
Total events:	834		850			
Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
1.8.2 One or more previous miscarriages and early pregnancy bleeding						
Coomarasamy 2019	689	914	619	886	98.3%	1.08 [1.02 , 1.14]
Gerhard 1987	13	14	11	15	1.7%	1.27 [0.90 , 1.78]
Subtotal (95% CI)		**928**		**901**	**100.0%**	**1.08 [1.02 , 1.14]**
Total events:	702		630			
Heterogeneity: Chi² = 0.84, df = 1 (P = 0.36); I² = 0%						
Test for overall effect: Z = 2.75 (P = 0.006)						
Test for subgroup differences: Chi² = 5.03, df = 1 (P = 0.02), I² = 80.1%						



Source: Figure 2-5, p62 of the submission.
CI = confidence interval; M-H = Mantel-Haenszel test.

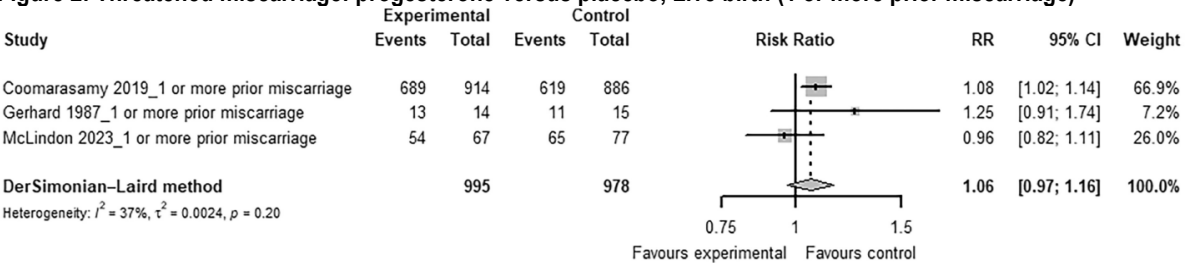
6.20 In women with no previous miscarriages and early pregnancy bleeding, there was no significant improvement in the live birth rate (RR = 0.99, 95% CI: 0.95, 1.04) when treated with progesterone compared to placebo. However, for women with one or more previous miscarriages and early pregnancy bleeding, progesterone statistically significantly increased the live birth rate compared to placebo (RR = 1.08, 95% CI: 1.02, 1.14).

6.21 Notably, the meta-analysis had limitations. The overall findings were predominantly driven by the PRISM trial, which contributed 99.8% of the statistical weight. In contrast, Gerhard et al. (1987) included a small number of participants (N=52) with only 29 women having one or more previous miscarriages. Furthermore, the vaginal progesterone dose used in the Gerhard et al. (1987) (25 mg twice daily) was substantially lower than that evaluated in PRISM (400 mg twice daily). Consequently, Gerhard et al. (1987) was not included in the main analysis due to misalignment with the proposed intervention for PBS listing.

Zhao et al. (2024)

6.22 The recent meta-analysis by Zhao et al. (2024) incorporated data from McLindon et al. (2023), in addition to PRISM trial and Gerhard et al. (1987), to assess the efficacy of progestogens in subgroup of women with one or more prior miscarriages. The key results are presented in the forest plot below.

Figure 2: Threatened miscarriage: progesterone versus placebo, Live birth (1 or more prior miscarriage)



Source: Figure 2.6, p64 of the submission.
CI = confidence interval; RR = risk ratio.

6.23 The analysis showed progesterone numerically, but not statistically, improved live birth rates for patients with threatened miscarriage with one or more previous miscarriages (RR = 1.06, 95% CI: 0.97, 1.16).

6.24 Similar to Devall et al. (2021), results from Zhao et al. (2024) were largely driven by the PRISM trial (67% of the statistical weight). McLindon et al. (2023) used a different progesterone dosing regimen (400 mg once nightly) compared with PRISM (400 mg twice daily) and was excluded from the main analysis due to misalignment with the proposed intervention for PBS listing.

Comparative harms

6.25 The submission presented data on serious adverse events, and antenatal, intrapartum, postpartum and neonatal complications from the PRISM trial; however, these were reported for the overall population and not stratified by number of previous miscarriages.

6.26 There were no significant between-group differences in maternal or neonatal serious adverse events (5% [105/2025] in the progesterone group and 5% [98/2013] in the placebo group). Similarly, no significant between-group differences were observed for antenatal, intrapartum, postpartum and neonatal complications, with neonatal congenital abnormalities occurring in 3.4% of babies in both groups.

6.27 Devall et al. (2021) found no statistically significant difference in the outcomes of congenital abnormalities (RR = 1.00; 95% CI: 0.68, 1.46) or adverse events (RR =1.07; 95% CI: 0.81, 1.39), based on the results from the PRISM trial. While Zhao et al. (2024) reported no statistically significant differences for the outcomes of congenital abnormalities (RR = 1.06; 95% CI: 0.76, 1.48) or serious adverse events (RR = 1.07; 95% CI: 0.83, 1.40), it also included studies for recurrent miscarriage and dydrogesterone, limiting its relevance to this submission.

Benefits/harms

6.28 On the basis of direct comparative evidence presented by the submission, for every 100 patients with uTM and vaginal bleeding, with or without prior miscarriage, treated with progesterone pessary in comparison with placebo for a mean treatment period of approximately seven weeks:

- There would be approximately 5 additional live births after at least 34 weeks gestation among women with a history of at least one previous miscarriage (which was the PBS proposed population).
- There would be approximately 14 additional live births after at least 34 weeks gestation among women who have experienced 3 or more prior miscarriages.
- There would be approximately 3 additional ongoing pregnancies at 12 weeks gestation in the overall population.
- There would be approximately 2 fewer miscarriages at less than 24 weeks gestation in the overall population.
- There would be no difference in live birth rates at less than 34 weeks gestation, ectopic pregnancy, stillbirth, or termination of pregnancy in the overall population.
- There would be no difference in adverse events between those treated with progesterone and those treated with placebo in the overall population.

Clinical claim

6.29 The submission described progesterone as superior in terms of effectiveness compared to SOC in women with uTM and a history of prior miscarriage. The evidence from the PRISM trial demonstrated that the difference in live birth rate was statistically significantly in favour of progesterone for patients with at least one previous miscarriage, i.e. the proposed PBS population (RR = 1.09; 95% CI: 1.03, 1.15). The PSCR stated that this result was clinically meaningful in the context of miscarriage prevention, particularly given the absence of PBS-subsidised alternatives, the substantial physical and psychological burden associated with pregnancy loss, and the favourable safety profile of progesterone. However, the evaluation considered the result in patients with at least one prior miscarriage should be interpreted with caution as it was based on *post hoc* analyses which limit the interpretability for decision making, and the results were primarily driven by the subgroup of women who had experienced at least 3 prior miscarriages (RR = 1.28; 95% CI: 1.08, 1.51). The PSCR acknowledged that the magnitude of benefit was greatest in women with 3 or more prior miscarriages, but it argued that statistically significant and clinically meaningful improvements in live birth rates were observed in women with one or more previous miscarriages, supporting a continuum of risk, rather than a threshold effect. Noting that the post-hoc evidence used to support this claim was less robust, the Sub-Committees considered that while a biological gradient makes sense clinically, a balance needed to be achieved in terms of offering patients appropriate treatment and over treating. As such, the Sub-Committees advised that the evidence base supported the narrower TGA indication for treatment of uTM in patients with bleeding in the current pregnancy and a history of 3 or more miscarriages.

6.30 The Sub-Committees considered that the claim of non-inferior safety compared to placebo appeared to be reasonable.

6.31 The PBAC considered that the claim of superior comparative effectiveness was not adequately supported for the proposed population, i.e. patients who have had at least 1 prior miscarriage. The PBAC considered that progesterone was superior compared to placebo in patients who have experienced at least 3 prior miscarriages.

6.32 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

6.33 The submission presented a cost-effectiveness analysis using incremental cost per live birth framework, comparing live birth and miscarriage rates and the associated costs between patients treated with progesterone and those receiving placebo. This was based on the submission's claim that progesterone had superior efficacy and non-inferior safety compared to placebo for the treatment of women with uTM and a history of previous miscarriage.

6.34 The submission assumed that each uTM would result in either a live birth or a miscarriage. The live birth rates, and consequently miscarriage rates, were based on *post hoc* subgroup analysis of women with uTM and one or more previous miscarriage in the PRISM trial. In the trial, the risk difference between progesterone and placebo for this subgroup was 5.5% (95% CI: 1.4%, 9.6%), corresponding to a number needed to treat of 18.12. Notably, the absolute risk difference was greater in women with ≥3 prior miscarriages than in those with ≥1 prior miscarriage (14% vs. 5.5%). While the submission conducted sensitivity analyses using the 95% CI for the difference in live birth rates, additional sensitivity analysis conducted during evaluation explored the impact of applying the live birth difference for women with ≥3 prior miscarriages (refer to Table 8).

6.35 The cost of progesterone for an 8-week course was $[redacted] (DPMQ = $[redacted] x 2). The average cost per patient was calculated by applying a relative dose intensity (RDI) of 85%. This value was assumed based on the compliance in the PRISM trial, where >80% adherence was reported in approximately 70% of patients at 12 weeks and by 55% of patients at 16 weeks in the progesterone arm. This resulted in an estimated dispensed cost per patient of progesterone of $[redacted]. This assumption was uncertain and explored in sensitivity analyses (refer to Table 8). The cost of SOC, or 'watch and wait', was assumed to be $0.

6.36 The RANZCOG guidelines for management of miscarriage describe two options: surgical termination and expectant management. The submission assumed that 70% of patients would undergo surgical termination of pregnancy (STOP), while 30% would undergo expectant management. Of those initially managed with expectant management, it was further assumed that 30% would subsequently require surgical management. The cost of expectant management incurred no direct procedural costs. The cost of surgical management was derived from mifepristone and misoprostol PBAC submission (Table 14, Public Summary Document [PSD], July 2014 PBAC meeting), and inflated to 2025 prices, resulting in an estimated cost of $2,006.41 per procedure and a weighted average cost of $1,585.07 ([0.7 x $2,006.41] + [0.3 x 0.3 X

$2,006.41]). The cost of surgical management of miscarriage presented in the submission was based on outdated data.

6.37 Secondary analyses included the cost of a live birth, which was estimated using AR-DRG for births in public hospitals, based on cost weights for AR-DRG codes O01, O02 and O60 from version 11.0 of the NHCDC Public Sector Report 2020–21. These costs were inflated to 2025 prices using the Consumer Price Index (CPI) published by the Australian Bureau of Statistics (ABS). The estimated cost of full-term live birth was $10,795.52. Using updated cost data from the NHCDC Public Sector Report 2022-23, resulted in an estimated cost of full-term live birth of $11,947.68 (inflated to 2025 prices).

6.38 The Sub-Committees noted that the submission did not conduct a literature review to inform the costs included in the analysis. The Sub-Committees identified a cost-effectiveness study (Okeke Ogwulu et al, 2020[10]) that was based on the results of the PRISM trial and which included the costs of (i) pregnancy (e.g. hospital, day unit and emergency visits and hospitalisation costs) during the antenatal and postnatal periods, (ii) the delivery mode (vaginal, caesarean section, complications), (iii) primary care services and (iv) management of miscarriage (spontaneous resolution and surgical and medical management). The Sub-Committees also identified a recent Australian study (Callander et al, 2026[11]) that compared the costs of private and public obstetric care. Based on these studies, the Sub-Committees considered that costs applied in the submission were uncertain and outdated. The pre-PBAC response provided sensitivity analyses which included costs associated with pregnancy, but no workings or information relating to the additional costs was provided. There also appeared to be an error in these sensitivity analyses, as the incremental costs did not account for the difference in miscarriage costs, thus they are not presented below in Table 8.

6.39 Table 7 summarises the results of the economic evaluation.

[10] Okeke Ogwulu CB, at al. The cost-effectiveness of progesterone in preventing miscarriages in women with early pregnancy bleeding: an economic evaluation based on the PRISM trial. BJOG. 2020. doi:10.1111/141-0528.16068

[11] Callander EJ, et al. Maternal and neonatal outcomes and health system costs in standard public maternity care compared to private obstetric-led care: A population-level matched cohort study. BJOG. 2026;133:72-82.

Table 7: Results of the economic evaluation

	Cost	Progesterone arm		SOC		Increment
		RDI	Weighted cost per patient	RDI	Weighted cost per patient	
Base case (excluding hospitalisation cost of live birth)						
Progesterone treatment [A]	$[redacted][a]	85%	$[redacted]	NA	NA	-
Miscarriage management [B]	$1,585.07	24.6%[b]	$390.20	30.1%[b]	$477.67	-
Total cost [C = A+B]		$[redacted]		$477.67		$[redacted]
Live birth rates based on PRISM trial [D]		75.4%		69.9%		5.5%
Incremental cost per additional live birth (no hospitalisation cost) [C/D]						$[redacted][1]
Secondary analysis (including hospitalisation cost of live birth)						
Progesterone treatment [A]	$[redacted]	85%	$[redacted]	0.00%	$0.00	-
Miscarriage management [B]	$1,585.07	24.6%[b]	$390.20	30.1%	$477.67	-
Cost of live birth[c] [E]	$10,795.52	75.4%	$8,137.98	69.9%	$7,542.24	-
Total cost [F = A+B+E]		$[redacted]		$8,019.91		$[redacted]
Live birth rates based on PRISM trial [D]		75.4%		69.9%		5.5%
Incremental cost per additional live birth (includes hospitalisation cost) [F/D]						$[redacted][2]

Source: Table 3-3, p83 of the submission.
NA = not applicable; RDI = relative dose intensity; SOC = standard of care
[a] Based on 8 weeks treatment with progesterone 400 mg twice daily and a DPMQ of $[redacted] for 56 pessaries.
[b] In the progesterone arm, 75.4% of the women successfully prevented miscarriage and resulted in live birth, based on PRISM trial, resulting in 24.6% of them requiring miscarriage management. In the placebo arm, 69.9% of the women did not experience miscarriage which resulted in live birth, based on PRISM trial, resulting in 30.1% of them requiring miscarriage management.
[c] Estimated in the submission (0.7 x $2,006.41] + [0.3 x 0.3 x $2,006.41], based on National Hospital Cost Data Collection Public Sector Report 2020–21 cost data, inflated to 2025 price.
The redacted values correspond to the following ranges:
[1] *$5,000 to < $15,000*
[2] *$15,000 to < $25,000*

6.40 Using the live birth rates from the PRISM trial in women with one or more previous miscarriage, the incremental cost of treatment was estimated to be $[redacted], resulting in a cost per additional live birth of $[redacted] (excluding hospitalisation costs of live birth). When hospitalisation costs were included, the incremental cost of treatment increased to $[redacted], resulting in a cost per additional live birth of $15,000 to < $25,000.

6.41 To provide context for willingness to pay for an additional live birth, the submission compared the estimated cost associated with ART and surrogacy. The average healthcare cost of live-birth babies conceived following non-donor ART treatment in Australia was estimated at $32,903 in 2006 (not adjusted for inflation)[12]. In addition, Surrogacy Australia has estimated the average cost of surrogacy at approximately $55,000 to $60,000 over a two-year period[13]. On this basis, the submission considered the cost of $15,000 to < $25,000 per additional live birth (including hospitalisation costs) to be reasonable. The PBAC noted that, in November 2009, ganirelix was recommended on the IVF/GIFT program on the basis of an incremental cost per clinical pregnancy versus nafarelin of less than $15,000.

[12] Chambers GM, Ho MT, Sullivan EA, (2006), 'Assisted reproductive technology treatment costs of a live birth: an age-stratified cost-outcome study of treatment in Australia', Med J Aust. 184(4):155-8.
[13] Surrogacy Australia (2026), 'Frequently asked questions', Available at: https://www.surrogacyaustralia.org/faq/

6.42 Table 8 presents the sensitivity analyses presented in the submission and conducted during the evaluation.

Table 8: Sensitivity analyses presented by the submission and conducted during the evaluation

	Excluding hospitalisation			Including hospitalisation		
	Incremental cost	Cost per additional live birth	% change from base case	Incremental cost	Incremental Cost per additional live birth	% change from base case
Base case	$[redacted]	$[redacted][1]	-	$[redacted]	$[redacted][2]	-
Live birth rate based on subgroup analysis of women with prior miscarriage (base case: RD = 5.52% for ≥ 1 prior miscarriage)						
RD = 14% for ≥ 3 prior miscarriage	$[redacted]	$[redacted][3]	-78%	$[redacted]	$[redacted][1]	-[redacted]%
Treatment duration (base case: 8 Weeks)						
7 weeks	$[redacted]	$[redacted][3]	-16%	$[redacted]	$[redacted][2]	-[redacted]%
9 weeks	$[redacted]	$[redacted][1]	16%	$[redacted]	$[redacted][2]	[redacted]%
Relative Dose Intensity (base case: 85%)						
90%	$[redacted]	$[redacted][1]	8%	$[redacted]	$[redacted][2]	[redacted]%
100%	$[redacted]	$[redacted][1]	23%	$[redacted]	$[redacted][2]	[redacted]%
Unit cost of miscarriage management (base case: $1,585.07)						
$3,456.14[a]	$210.78	$3,819.59	-33%	$806.52	$14,615.11	-[redacted]%
Unit cost of a live birth, i.e. hospitalisation costs (base case: $10,795.52)						
$11,947.68	$[redacted]	$[redacted]	-	$[redacted]	$[redacted]	+[redacted]%

Source: Conducted during evaluation using the Attachment 4.1 Workbook.
RD = risk difference.
[a] Estimated during the evaluation (0.7 x $4,375] + [0.3 x 0.3 x $4,375], based on the National Hospital Cost Data Collection Public Sector Report 2022–23 cost data for abortion [$4,375[inflated to 2025 price
The redacted values correspond to the following ranges:
[1] *$5,000 to < $15,000*
[2] *$15,000 to < $25,000*
[3] *$0 to < $5,000*

6.43 The PSCR noted that when the population is narrowed, e.g. to those who have experienced at least 3 prior miscarriages, at the current proposed price, the cost per additional live birth decreased and the cost effectiveness improved. The PSCR stated that, in such a scenario, a higher price for progesterone may be justified.

Drug cost/patient/course

6.44 At the proposed DPMQ of $[redacted], the cost per course per patient, assuming an average treatment course of eight weeks and 85% compliance, is $[redacted]. The estimated drug costs based on the trial dose and duration, and the sponsor's economic model and financials are presented in Table 9.

Table 9: Drug cost per patient for progesterone pessary

	Trial dose and duration	Model	Financial estimates
Mean dose	400 mg twice daily	400 mg twice daily	400 mg twice daily
Relative dose intensity	Compliance in the progesterone group was >80% for 70% of the patients at 12 weeks, and >80% adherence for 55% of patients at 16 weeks.	85%	85%
Mean duration	50 days (~7 weeks)	8 weeks	8 weeks
Cost/patient/course	NE	$[redacted]	$[redacted]

Source: Section 3.3, p80; Table 4-4, p88 of the submission.
NE = not estimable.

Estimated PBS usage & financial implications

6.45 This submission was considered jointly by DUSC and ESC.

6.46 The submission applied an epidemiological approach to estimate the financial impact of listing progesterone for women with uTM and a history of previous miscarriage. Table 10 summarises the key inputs and data sources to estimate the utilisation of progesterone.

Table 10: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Eligible population: Clinically recognised pregnancies		
Number of women aged 15–44	5,683,390 in 2027; based on ABS population sheet	Based on South Australian data 99.7% of women who gave birth were ≤ 44 years of age.
Number of live births	292,318 registered births; based on ABS 2024 data	A slight variation from AIHW estimates of 285,305 births in 2023 and a declining trend since 2007 was noted.
Number of miscarriages	147,000; based on COPE 2026	This was uncertain due to the absence of a national miscarriage registry in Australia; other sources suggested lower estimates of approximately 110,000[a,b].
Number of still births	2,479; based on AIHW 2023 data	-
Number of abortions	73,884; calculated using the incidence of abortion (1.3%) from the South Australia abortion report 2023 and the total number of women aged 15-44	As individuals seeking abortion are unlikely to require treatment to prevent miscarriage, the Sub-Committees considered that abortions should be excluded from the total number of clinically recognised pregnancies. The pre-PBAC response agreed that these patients should be removed from the analysis.
Total clinically recognised pregnancies	515,681; sum of live births, miscarriages, still births and abortions.	The Sub-Committees considered that this estimate was uncertain due to assumptions underlying miscarriage estimates, the use of predominantly 2024 data as a basis for the 2027 population and the inclusion of abortions.
Population growth rate	1.6%; based on ABS 2025 data	The evaluation considered that it may be inappropriate to assume pregnancy growth would be the same as overall population growth, as the 1.6% growth was mainly driven by net overseas migration. The Sub-Committees agreed with the evaluation, noting that the live birth growth rate was 1.9% in 2025 (ABS, 2025). The pre-PBAC response stated that use of a 1.9% live birth rate was reasonable.
Women with prior miscarriage	13.4%; based on Quenby et al., 2021	The estimate used is for women with a history of previous miscarriage; however, this was broader than the TGA indication, which limits the use of progesterone in women with ≥3 previous miscarriages. The Sub-Committees noted that the rate of 13.4% from Quenby, 2021 was lower than the rate reported in Sount Australian data (27.7%) and in an Australian prospective cohort study (30.3%; see paragraph 6.47) The Sub-Committees also noted that this input was highly variable depending on the number of previous miscarriages. Based on Quenby, 2021, it would be reduced to 0.7% if restricted to women with ≥ 3 previous miscarriages. The pre-PBAC response stated that Australia lacked current population-level data on the rate of miscarriage.
Adjustment for ectopic pregnancy	97.7%; based on the ectopic rate of 2.3% reported in the South Australia Pregnancy Outcome report 2023	The RANZCOG Clinical Guideline reported that ectopic pregnancies occur in 1.25%, resulting an adjustment of 98.75%. The Sub-Committees noted that this input was uncertain, but the estimates were not highly sensitive to changes in this parameter.

Parameter	Value applied and source	Comment
Adjustment for known causes of TM/other obstetric conditions	90.0%; based on the Repeated pregnancy loss guideline 2022, ESHRE Guideline Group	The Sub-Committees noted that this parameter was uncertain, as the estimate appeared to be based on a small, very-low-quality study reporting the cumulative live birth rates following preimplantation genetic testing and could not be identified in the cited source.
Bleeding in current pregnancy	25.0%; based on Miscarriage Australia Fact sheet	-
Uptake rate	[redacted]% in Year 1, increasing to [redacted]% in Year 4; based on sponsor's assumption	The Sub-Committees considered the uptake rates were overestimated for patients with 1–2 prior miscarriages but reasonable for patients with ≥ 3 prior miscarriages.
Proposed treatment: Progesterone 400 mg pessary twice a day		
Treatment duration	8 weeks; based on PRISM trial	Progesterone may be administered from Week 6–8 through to Week 16 in clinical practice, based on Coomarasamy et al. (2020). The Sub-Committees noted that a treatment duration of 8 weeks aligned with the economic analysis.
Compliance	85%; based on PRISM trial	This was based on adherence observed in the PRISM trial. The Sub-Committees noted that although this aligned with the economic analysis, it resulted in an average of 1.7 scripts per person. The Sub-Committee's noted that the number of scripts per person should be a whole number.
Progesterone 400 mg pessary, 28, 1 pack	$[redacted]; requested DPMQ	-

Source: Table 4-1, p86; Table 4-5, p88; Attachment 5.1 to the submission.
ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; COPE = Centre of Perinatal Excellence; DPMQ = Dispensed Price for Maximum Quantity; ESHRE = European Society of Human Reproduction and Embryology; RANZCOG = Royal Australian and New Zealand College of Obstetricians and Gynaecologists; TM = threatened miscarriage; TGA = Therapeutic Goods Administration.
[a] 'Breaking the silence on miscarriage', Commonwealth of Australia (available at: https://www.health.gov.au/ministers/the-hon-ged-kearney-mp/media/breaking-the-silence-on-miscarriage)
[b] 'What is miscarriage', Miscarriage Australia (available at: https://miscarriageaustralia.com.au/understanding-miscarriage/what-is-miscarriage/)

6.47 Overall, the number of patients eligible for treatment and the utilisation of progesterone was uncertain due to following reasons:

- The rate for prior miscarriage applied in the submission of 13.4% from Quenby et al. (2021) was lower than the rate reported in South Australian[14] data of 27.7% (68.8% of women had a previous pregnancy, of whom 40.3% experienced a miscarriage). This higher estimate was further supported by an Australian national prospective cohort study (Hure et al., 2012[15]), which reported a miscarriage rate of 30.3%. Variations in prior miscarriage rate were tested in sensitivity analyses (see Table 12). The Sub-Committees considered that the rate for prior miscarriage applied in the submission was likely underestimated. Further, the Sub-Committees noted that this parameter was highly variable depending on the number of prior miscarriages experienced and, according to Quenby, 2021, would be reduced to

[14] Preventive Health South Australia, (2025), 'Pregnancy Outcome in South Australia 2023', Adelaide: Pregnancy Outcome Unit, Epidemiology and Research Division, Preventive Health SA, Government of South Australia, Available at: https://www.preventivehealth.sa.gov.au/assets/downloads/Pregnancy-outcomes/Pregnancy-Outcome-in-South-Australia-2023_FINAL.pdf
[15] Hure AJ., Powers JR., Mishra GD., et al, (2012), 'Miscarriage, Preterm Delivery, and Stillbirth: Large Variations in Rates within a Cohort of Australian Women', PLoS ONE 7(5):e37109.

0.7% if progesterone was restricted to women with ≥ 3 previous miscarriages. The pre-PBAC response stated that Australia lacks recent population-level data required to estimate how common miscarriage is.

- The Sub-Committees considered that the inclusion of women who had had an abortion in the total number of clinically recognised pregnancies was not appropriate as these patients would not require treatment to prevent miscarriage. The Sub-Committees advised that these patients should be excluded from the total number of clinically recognised pregnancies. The pre-PBAC response agreed that removal of these patients was reasonable.
- The proportion of ectopic pregnancies may have been overestimated, thereby underestimating the adjustment applied, as the RANZCOG Guideline reported a lower rate (1.25%) compared with the assumed (2.3%). Furthermore, the adjustment for known causes of threatened miscarriage or obstetric condition was uncertain, as the proportion could not be traced to the cited source. The Sub-Committees considered that this assumption was uncertain but noted the estimates were not highly sensitive to this assumption.
- The evaluation considered that the assumed uptake rate of [redacted]% in Year 1, increasing to [redacted]% from Year 4, may be underestimated given the absence of PBS-listed treatment options for the target population. The Sub-Committees considered the uptake rates were overestimated for women with 1–2 prior miscarriages but reasonable for those who had experienced ≥ 3 prior miscarriages.
- The Sub-Committees noted that the average number of scripts per person (1.7) should be a whole number.

6.48 Table 11 presents the estimated financial implications of listing progesterone on the PBS/RPBS.

Table 11: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]
Number of scripts dispensed[a]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of progesterone pessary						
Cost to PBS less copayments ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Cost to RPBS less copayments ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to PBS/RPBS ($)	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]

Source: Table 4-2, p87; Table 4-6, p88 and Table 4-7, p88 of the submission.
PBS = Pharmaceutical Benefits Scheme; RPBS = Reparation Pharmaceutical Benefits Scheme
[a] Average prescriptions per patient were based on 1.7 packs of progesterone for an 8-week treatment duration, assuming 85% compliance.
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*

6.49 The total cost to the PBS/RPBS of listing progesterone for women with uTM and a previous history of one or miscarriage was estimated to be $0 to < $10 million in Year 6, and total $20 million to < $30 million over the first 6 years of listing.

6.50 The financial estimates were sensitive to assumptions regarding the uptake rates, prevalence of prior miscarriages, bleeding rates, compliance rate, and treatment duration, with higher values substantially increasing the estimated financial impact, as presented in Table 12.

Table 12: Results of the one-way sensitivity analyses presented by the submission and conducted during the evaluation

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	% Change
Base case	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-
Uptake rate (base case: [redacted]% in Y1 increasing to [redacted]% in Year 4)							
Increased to [redacted]% in Year 1 and [redacted]% in Year 4 (i.e. + 20%)	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	[redacted]%
Prior miscarriage rate (base case: 13.4% for ≥ 1 prior miscarriage)							
Increased to 16.1%	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Increased to 27.7%[a]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Changed to 2.6% for ≥2 prior miscarriages[b]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-[redacted]%
Changed to 0.7% for ≥3 prior miscarriages[b]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-[redacted]%
Bleeding rate (base case: 25%)							
Decreased to 20%	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-[redacted]%
Increased to 30%	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	[redacted]%
Obstetric adjustment (base case: include)							
Exclude	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Number of miscarriages (base case: 147,000)							
Decreased to 117,600[c]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	-[redacted]%
Increased to 176,400[c]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Compliance rate (base case: 85%)							
Increased to 100%[d]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Treatment duration (base case: 8 weeks)							
Increased to 9 weeks[e]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%
Increased to 10 weeks[e]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	$[redacted][1]	+[redacted]%

Source: Table 4-10, p92 of the submission.
RANZCOG = Royal Australian and New Zealand College of Obstetricians and Gynaecologists.
[a] Estimated in the evaluation based on the South Australia Pregnancy Outcome report 2023 that 68.8% of the women had previous pregnancy, and 40.3% of them experienced miscarriage in a prior pregnancy.
[b] Quenby et al. (2021) reported prevalence of 2.6% for ≥2 miscarriages and 0.7% for ≥3 miscarriages.
[c] Variation in the number of miscarriage by -/+20% given the uncertainties in the proposed estimate.
[d] Assuming 100% compliance with two prescriptions per treatment.
[e] Coomarasamy et al. (2020) indicated treatment could be provided from 6 to 8 weeks until 16 weeks in a real-life scenario.
The redacted values correspond to the following ranges:
[1] $0 to < $10 million

6.51 The Sub-Committees requested a series of additional scenario analyses:

Scenario 1: Increase the annual population growth rate to 1.9% to reflect the current ABS estimate.

Scenario 2: Excluded abortions from the eligible population, as the Sub-Committees considered that women seeking abortions are unlikely to require treatment.

Scenario 3: Reduced the proportion of women with a prior miscarriage to 0.7% by restricting the treatment to those women with ≥ 3 miscarriages.

Scenario 4: Combined scenario 1 – 3.

6.52 The results of these scenario analyses are summarised in Table 13 below.

Table 13: Sensitivity analysis based on advice provided by the Sub-Committees

Net cost PBS/RPBS*	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total	Δ% total
Baseline	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted]	$ [redacted][3]	-
Scenario 1	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][3]	+ [redacted]%
Scenario 2	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][2]	- [redacted]%
Scenario 3	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	- [redacted]%
Scenario 4	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	$ [redacted][1]	- [redacted]%

Source: Scenario analyses conducted by the Department based on Sub-Committees' advice.
PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme
* Scenario descriptions provided in 6.45.
The redacted values correspond to the following ranges:
[1] *$0 to < $10 million*
[2] *$10 million to < $20 million*
[3] *$20 million to < $30 million*

Quality Use of Medicines

6.53 The submission did not present any additional evidence regarding quality use of progesterone pessary. The Sub-Committees considered the sponsor should propose quality use of medicines (QUM) activities.

6.54 The pre-PBAC response stated that the sponsor will implement a targeted QUM program to support the appropriate use of progesterone which will include structured engagement with key opinion leaders in reproductive medicine and obstetrics, professional education and patient information materials.

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

7 PBAC Outcome

7.1 The PBAC recommended the listing of progesterone for the treatment of unexplained threatened miscarriage (uTM) in women during the first trimester, with vaginal bleeding in the current pregnancy and a history of 3 or more prior miscarriages. The PBAC was satisfied that progesterone provides, for some patients, a significant improvement in live birth rates over standard of care, which is a 'watch and wait' approach. The PBAC noted that the submission requested listing for the population who has a history of at least one prior miscarriage but that this indication did not align with the TGA approved indication and considered that the evidence provided was insufficient to support the broader indication. The PBAC considered that the requested price was cost effective based on the incremental cost per live birth approach. The PBAC noted that for the estimated financial implications the number of eligible patients would need to be adjusted down to reflect the narrower recommended population, and uptake rates increased.

7.2 The PBAC noted the strong support received for the submission from individuals, health professionals and medical organisations that was received via the Office of Health Technology Assessment Consultation Hub. The PBAC also noted the advice

received via the sponsor hearing process. The PBAC noted that the advice received emphasised the high prevalence and emotional impact of miscarriage and that the listing of progesterone on the PBS would reduce out of pocket costs for patients, improving equity of access.

7.3 The PBAC noted that the submission was based on the evidence from the PRISM trial, which compared progesterone to placebo in patients with uTM and vaginal bleeding in early pregnancy. The PBAC considered that the comparator of standard of care, which is a 'watch and wait' approach, represented by placebo, was reasonable.

7.4 The PBAC noted that the evidence from the PRISM trial included women with vaginal bleeding in early pregnancy with and without previous miscarriage. The proportion of participants achieving the primary outcome of live birth after at least 34 weeks of gestation was numerically higher in the progesterone group (75%) compared with the placebo group (72%) but was not statistically significant (RR = 1.03; 95% CI: 1.00, 1.07). The PBAC noted the difference in live birth rate for the proposed PBS population i.e. patients with at least one previous miscarriage was statistically significantly in favour of progesterone (RR = 1.09; 95% CI: 1.03, 1.15, based on a *post-hoc* subgroup analysis). However, the PBAC noted that subgroup analysis showed live birth outcomes with one and two prior miscarriages, was not statistically significant, and the difference in patients with at least one prior miscarriage was primarily driven by the subgroup of women who had experienced at least 3 prior miscarriages (RR = 1.28; 95% CI: 1.08, 1.51, based on the pre-specified subgroup analysis). The PBAC noted that the PSCR and pre-PBAC response acknowledged that the magnitude of benefit was greatest in patients who had experienced at least 3 miscarriages, but it was argued that the evidence supported a continuum of risk, rather than a threshold effect. The PBAC noted the Sub-Committees had considered that while a biological gradient made sense clinically, a balance needed to be achieved in terms of offering patients appropriate treatment and over treating where there is a paucity of evidence.

7.5 The PBAC noted the results of meta-analyses (Devall et al. (2021) and Zhao et al. (2024)) used to support the proposed PBS population were largely driven by the PRISM trial results. The PBAC also noted that although the TGA, the submission and national and international guidelines all supported the use of progesterone in uTM with vaginal bleeding, they differed on the number of prior miscarriages required to initiate treatment.

7.6 Overall, the PBAC noted that the evidence used to support the use of progesterone in patients with 1-2 prior miscarriage was not statistically significant. The PBAC agreed with the Sub-Committees that the evidence base supported the narrower TGA indication for the treatment of uTM with vaginal bleeding in the current pregnancy and a history of 3 or more miscarriages. For this population, the PBAC considered that progesterone was superior in terms of efficacy compared to placebo.

7.7 In terms of safety, the PBAC noted that there were no significant differences between the progesterone and placebo in the PRISM trial. The PBAC considered that the claim of non-inferior safety was reasonable.

7.8 The PBAC noted that the economic evaluation was presented as an incremental cost per additional live birth. The PBAC considered that this was an appropriate outcome in this circumstance. The PBAC noted that the evaluation included the cost of progesterone treatment, the cost of miscarriage management and the live birth rates from PRISM with a secondary analysis that included hospitalisation costs associated with a live birth.

7.9 The PBAC noted that the incremental cost per additional live birth in patients who have experienced at least 3 prior miscarriages was $[redacted] (no hospitalisation costs) and $[redacted] (including hospitalisation costs; see Table 8). The PBAC noted that some of the cost inputs were based on outdated data but, overall, considered that these outcomes were reasonably indicative of cost-effectiveness in this circumstance. In determining this, the PBAC took into consideration the precedent of the previous PBAC consideration for ganirelix for the IVF/GIFT program, noted in paragraph 6.41.18

7.10 The PBAC noted that a number of the inputs used to estimate the financial impact of listing progesterone were uncertain. The PBAC considered that the patients who had undergone an abortion should be removed from the total of clinically recognised pregnancies, that the population growth rate should be increased from 1.6% to 1.9% and proportion of women with prior miscarriage (13.4%) should be reduced to reflect the proportion of women who had experienced 3 or more prior miscarriages (0.7%). The PBAC noted that these changes corresponded to Scenario 4 in Table 13. The PBAC considered that the uptake rate would likely be higher in clinical practice and the scenario with 20% higher uptake was reasonable. The PBAC also advised that the number of scripts per patient should be a whole number to account for wastage.

7.11 The PBAC considered that the proposed restriction should be amended to restrict use to patients who have a history of at least 3 previous miscarriages. The PBAC considered it was a routine and crucial part of clinical practice to determine obstetric history and pregnancy risks and that confirming the history of prior miscarriages was manageable and appropriate. The PBAC considered that the other minor changes suggested by the Secretariat in Section 3 were reasonable. The PBAC advised that the prescriber type should include nurse practitioners and midwives.

7.12 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were met. Specifically, the PBAC found that in the circumstances of its recommendation for progesterone:

a) The treatment is expected to provide a substantial and clinically relevant improvement in the rate of live births over standard of care in patients with a history of three or more prior miscarriages;

b) The treatment is expected to address a high and urgent unmet clinical need due to no alternative treatments being listed on the PBS;

c) It would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A on the basis of the preceding findings

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

Outcome:

Recommended

8 Recommended listing

8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
PROGESTERONE					
Progesterone 400 mg pessary, 28	NEW	2	56	1	Utrogestan
Restriction Summary [new 1] / Treatment of Concept: [new 1A]					
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners ☒Midwife				
	Restriction type: ☒Authority Required (Streamlined) [new/existing code]				
Prescribing rule level	**Administrative Advice:** No increase in the maximum quantity or number of units may be authorised.				
Prescribing rule level	**Administrative Advice:** No increase in the maximum number of repeats may be authorised.				
	Indication: Unexplained threatened miscarriage				
	Clinical criteria:				
	Patient must be pregnant				
	Clinical criteria:				
	Patient must have vaginal bleeding				
	AND				
	Clinical criteria:				
	Patient must have a history of at least three previous miscarriages				
	AND				
	Clinical criteria:				
	The treatment must be initiated no later than 12 weeks gestation				
	AND				
	Clinical criteria:				
	The treatment must cease after 16 weeks gestation				
	Caution: Other known causes of threatened miscarriage should be ruled out before initiating treatment.				
	Caution: This drug should not be used in women with undiagnosed vaginal bleeding, known missed abortion or an ectopic pregnancy.				

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

9 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.

10 Sponsor's Comment

Besins Healthcare Australia welcomes the PBAC's recommendation to list Utrogestan 400 mg for women experiencing threatened miscarriage who have a history of previous miscarriages. If listed, eligible women will have access to a PBS-subsidised treatment option rather than the current "watch and wait" approach. We remain committed to working with the Australian Government to progress the listing and improve equitable access to evidence-based care.