zydus
Dedicated To Life

30TH ISAR 2026

20, 21, 22, FEBRUARY 2026

# Expert Consensus on the Optimal Use of Progesterone in Assisted Reproductive Technology, Early Pregnancy, and Gynecological Practice


Series Editor

**Dr. Ameet Patki**

President - ISAR

zydus
Dedicated To Life

# Comprehensive Natural Micronised progesterone range to nurture pregnancy

## For Maintenance of Pregnancy

# Naturogest SR 400/300/200

Natural Micronised Progesterone 400/300/200mg Smooth Release Tablets

## Also Available as

**Naturogest AQ 25/50**

Natural Micronised Progesterone 25/50 mg injection

**Naturogest 400/300/200/100**

Natural Micronised Progesterone 400/300/200/100mg Capsules

**Naturogest Gel**

Natural Micronised Progesterone Gel 8%

**Naturogest inj 100mg/1ml 200mg/2ml**

Natural Micronised Progesterone 100/200 mg injection

**Nurtures pregnancy, as Nature would**

zydus
Dedicated To Life

*In Threatened Miscarriage & Luteal Phase Support*

# Dydrogest

Dydrogesterone 10 mg Tablets

*Nest Assured, Rest Assured*

**6.4**
**Microns**
Particle Size[1]

MICRONIZED DYDROGESTERONE

Improved Surface Area → Higher Dissolution Rate → Better Solubility → Better Bioavailability

*In Recurrent Pregnancy Loss and Luteal Phase Support*

# Dydrogest ER 20

*Once daily*

Dydrogesterone Extended Release 20 mg Tablets

*Nest Assured, Rest Assured*

## REASSURE

Real-world Evidence And Scientific StUdy in REPL

*The world's first Evidence-backed, Real-world study of*
***Dydrogesterone ER 20 in RPL[2]***

**Studied in 828 RPL women**

**At 166 centers**

**Treated with Dydrogest ER 20**

***A breakthrough 92.3% pregnancies continued beyond 20 weeks[2]***

**ER:** Extended Release, **REPL:** Recurrent Early Pregnancy Loss

**Reference: 1.** Data on file. **2.** Purandare et al. Indian Journal of Obstetrics and Gynecology Research 2025;12(3):475–479.

# Consensus Development Expert Group - Faculty Members

zydus
Dedicated To Life

## Dr. Ameet Patki

Dr. Manish Banker

Dr. Umesh Jindal

Dr. Atul Munshi

Dr. Rohit Gutgutia

Dr. R.G. Patel

Dr. Monu Charan Pattanayak

Dr. Ekika Singh

Dr. Saurav Prakash Maity

Dr. Uday Thanawala

Dr. Meena Vishwakarma

Dr. Mehul Damani

Dr. Geeta Bharat

Dr. Shakti Kumar Tripathy

Dr. Basab Mukherjee

Dr. Uma Shankar

Dr. Gautam Khastgir

Dr. Padmaja Veeramachaneni

Dr. Nozer Sheriar

Dr. Sainath Bairagi

Dr. Ashish Parulekar

Dr. Priyankur Roy

Dr. Niharika Tyagi

Dr. Shradha Patil

Dr. Prashanth K. Adiga

Dr. Sonali Tawde

Dr. Paresh Patel

*Thank you to all the experts*

# Delegates:

Dr. Ritu Arya
Dr. Sreeparna Mondal
Dr. Swapan Biswas
Dr. Fatima M Ghanchi
Dr. Gunjan Jain
Dr. Prakrutha S
Dr. Divya Venugopalan
Dr. Swetha Patil
Dr. Vinutha Patil
Dr. Chekuri Swapna
Dr. Reeta Agarwal
Dr. Tejaswini P
Dr. A Swapna
Dr. Preethi Dayal
Dr. Hitesh Patel
Dr. Ankur R Patel
Dr. Prince Parikh

Dr. Nalini Bagul
Dr. Hitha Kashi
Dr. Hethyshi Ranganna
Dr. Avirupa Roy
Dr. Sisir Kumar Maity
Dr. Sanjoy Mukherjee
Dr. Ruhi Yasmin
Dr. Nilu Prasad
Dr. Deepika Taneja
Dr. Priyanka Aarya
Dr. R Rajini
Dr. Puvitha Suthagar
Dr. Suriya K
Dr. M Lavanya
Dr. Deepthi Kode
Dr. Koluri Radha
Dr. Priyadatt Patel

Dr. Shreya Iyengar Patel
Dr. Pankit Patel
Dr. Neeta Patel
Dr. Jigar Patel
Dr. Aditi Tandon
Dr. Suryakant Pophale
Dr. Premraj Khainar
Dr. Ramit Kamate
Dr. Snehlata Dubey
Dr. Anuja Choudhry
Dr. Nidhi Jain
Dr. Vandana Mishra
Dr. Henish Radadia
Dr. Sumina Reddy
Dr. Sadhvi Reddy
Dr. Nidhi Bajaj

*Thank you to all the experts*

# Expert Consensus on the Optimal Use of Progesterone in Assisted Reproductive Technology, Early Pregnancy, and Gynecological Practice


## Background

Progesterone plays a central role in reproductive physiology, implantation, and early pregnancy maintenance. Despite widespread clinical use, variability persists regarding the optimal route, dose, and duration of progesterone administration across assisted reproductive technology (ART) and gynecological settings.

## Objective

This expert consensus aimed to review current evidence and clinical practices to establish harmonized, evidence-based recommendations for the optimal use of progesterone in ART, early pregnancy, and abnormal uterine bleeding (AUB).

## Methods

A multidisciplinary panel of reproductive endocrinologists and gynecologists reviewed contemporary literature and clinical data. Consensus statements were developed through evidence synthesis and expert deliberation, followed by live polling among IVF specialists. Agreement levels were categorized as “strongly agree,” “agree,” “disagree,” or “strongly disagree.”

## Results

The panel affirmed that vaginal progesterone remains the preferred base for luteal phase support (LPS) in IVF/ICSI, while oral dydrogesterone is an effective and well-tolerated alternative or adjunct in frozen embryo transfer (FET) cycles. Individualized LPS guided by serum progesterone levels improves implantation and live birth outcomes. Progestin-primed ovarian stimulation (PPOS) offers comparable efficacy to GnRH antagonist protocols with a lower risk of OHSS, particularly benefiting poor responders, women with PCOS, and oocyte donors. In early pregnancy, progesterone supplementation enhances live birth rates without increasing adverse outcomes, especially in women with recurrent miscarriage or bleeding. Oral progestins are effective in controlling AUB episodes.

## Conclusion

Progesterone therapy remains a cornerstone of reproductive medicine. Individualized, evidence-driven regimens optimize reproductive outcomes and ensure maternal–fetal safety across ART, early pregnancy, and gynecological care.

## Introduction

Progesterone is a key physiological component of the menstrual cycle and a critical regulator of pregnancy. It serves as a steroidogenic precursor for other gonadal and non-gonadal hormones and is therefore essential for both reproductive and non-reproductive processes [1]. Rising progesterone concentrations in the early luteal phase trigger the histological and functional transformation of the endometrium from a proliferative to a secretory state, preparing it for implantation [2]. During the luteal phase, the amplitude and duration of luteinizing hormone (LH)-driven progesterone pulses increase progressively thereby maintaining optimal endometrial receptivity [3,4].

When progesterone or estrogen concentrations decline prematurely, as may occur in stimulated or artificial cycles without adequate hormonal support, the luteal phase becomes shortened or defective, rendering implantation unlikely or impossible [5]. This forms the physiological basis for exogenous progesterone supplementation during the luteal phase in assisted reproduction technology (ART) cycles, including intrauterine insemination (IUI) and in vitro fertilization (IVF) [6,7].

Despite its established role in reproductive physiology and ART, several clinical challenges and controversies remain regarding the use of progesterone in clinical practice. These include uncertainty over the optimal route of administration (vaginal, oral, intramuscular, or subcutaneous), dose and duration of supplementation, and the need for rescue protocols in women with low mid-luteal progesterone levels [7,8]. Vaginal progesterone is generally considered the reference standard, though emerging evidence suggests that oral dydrogesterone provides comparable pregnancy and live birth rates in frozen embryo transfer (FET) cycles [9]. However, variability in trial design, formulations, and patient populations has limited the strength of conclusions. Additionally, there is no uniform agreement on when to discontinue luteal support, whether at biochemical pregnancy, fetal cardiac activity, or through the first trimester [10,11].

Given the heterogeneity of clinical practice and evolving new data, there is a strong need for harmonized, evidence-based recommendations to optimize progesterone use in reproductive medicine. Consensus-driven guidance can help standardize luteal support protocols, reduce variability between centers, and improve patient outcomes [12].

The present consensus aims to review and integrate current evidence and expert experience to formulate clear, graded recommendations on the optimal use of progesterone in reproductive medicine. The objectives include identifying best practices for route, dose, and timing of luteal support; defining monitoring and rescue strategies for suboptimal progesterone levels; and highlighting gaps for future research.

## Methods

A multidisciplinary panel of experts in gynecology was convened to evaluate specific statements regarding the role of progesterone in gynecological practice. The audience, comprising IVF specialists, participated in live polling, and their responses were recorded. Evidence summaries were drafted by dedicated subgroups, and voting was conducted in person. The level of agreement was categorized as strongly agree, agree, disagree, or strongly disagree. Manuscript preparation was based on the integration of consensus statements, supporting evidence, and relevant references.

## Recommendations

### 1. Luteal Phase Support in assisted reproductive technology (ART)

#### a. Combined vaginal progesterone base in IVF/ICSI

**Consensus Statement**

- There was strong agreement among experts that vaginal progesterone–based combination therapy improves the outcomes of clinical pregnancy and live birth rates in IVF/ICSI cycles.

**Supporting Evidence**

- A recent network meta-analysis by Kastora et al. (2024) evaluated 76 randomized controlled trials encompassing 26,536 participants to determine the most effective LPS strategy across key ART outcomes, including clinical pregnancy, live birth, biochemical pregnancy, miscarriage, multiple pregnancy, and ovarian hyperstimulation syndrome (OHSS). The analysis indicated that the combination of intramuscular and vaginal progesterone was associated with a higher incidence of multiple pregnancies, whereas combined regimens incorporating subcutaneous GnRH agonist (SC GnRH-a) on a vaginal progesterone base significantly improved both clinical pregnancy and live birth rates across GnRH agonist and antagonist stimulation protocols [13].

**Panel Recommendation**

- For luteal phase support in IVF/ICSI cycles, clinicians should use vaginal progesterone as the base therapy, with the option to combine it with other agents (such as GnRH agonists or estrogen) in selected patients to enhance clinical pregnancy and live birth rates.

#### b. Oral dydrogesterone vs vaginal progesterone (FET)

**Consensus Statement**

- The experts strongly agreed that oral dydrogesterone, when used for LPS, can give comparable results to vaginal progesterone in frozen-thawed embryo transfer cycles.

**Supporting Evidence**

- A recent systematic review and meta-analysis by Stavridis et al. (2025), including five randomized controlled trials (n = 636), demonstrated that oral dydrogesterone and vaginal progesterone yield comparable reproductive outcomes for luteal-phase support in frozen–thawed embryo transfer (FET) cycles, with no significant differences in clinical pregnancy, live birth, or miscarriage rates (OR for live birth = 1.08; 95% CI 0.67–1.75) [14]. Similarly, the Phase III LOTUS trial by Tournaye et al. (2017) found oral dydrogesterone 30 mg/day to be non-inferior to vaginal progesterone 600 mg/day for IVF luteal support, reporting comparable pregnancy (37.6% vs 33.1%) and live-birth rates (34.6% vs 29.8%), confirming dydrogesterone's efficacy and tolerability [15].

**Panel Recommendation**

- For luteal phase support (LPS) in frozen–thawed embryo transfer (FET) cycles, clinicians may use oral dydrogesterone as an effective alternative to vaginal progesterone, as both have demonstrated comparable clinical pregnancy and live birth rates.

### c. Combination therapy: dydrogesterone + vaginal progesterone

**Consensus Statement**

- The experts strongly agreed that adding dydrogesterone to vaginal progesterone for luteal phase support in FET cycles may help reduce miscarriage rates and improve live birth rates.

**Supporting Evidence**

- In a large prospective cohort study by Vuong et al. (2021), 1,364 women undergoing FET were administered either vaginal micronized progesterone alone or in combination with oral dydrogesterone for luteal phase support. The combination regimen yielded a higher live birth rate (46.3% vs. 41.3%; adjusted RR 1.30, 95% CI 1.01–1.68; P = 0.042) and a significantly lower miscarriage rate (<12 weeks: 3.4% vs. 6.6%; RR 0.51, P = 0.009). These findings demonstrate that adjunctive dydrogesterone enhances reproductive outcomes, likely by overcoming variability in vaginal progesterone absorption, thereby improving endometrial receptivity and implantation stability in FET cycles [16].

**Panel Recommendation**

- In FET cycles, clinicians may consider using a combination of oral dydrogesterone and vaginal progesterone for luteal phase support to reduce miscarriage rates and improve live birth outcomes.

### d. Individualized LPS based on serum P4 levels

**Consensus Statement**

- The experts strongly agreed that individualized LPS based on serum progesterone levels on the day of embryo transfer (ET) in FET cycles using hormone replacement therapy (HRT) can help enhance pregnancy outcomes.

**Supporting Evidence**

- In a large retrospective cohort study of 1,257 HRT-FET cycles, Arik Alpcetin et al. (2025) demonstrated that individualizing LPS based on serum progesterone levels on the day of embryo transfer significantly optimized outcomes. Patients with low P4 (<10 ng/mL) who received "rescue" therapy either by doubling the vaginal progesterone dose or adding subcutaneous progesterone achieved pregnancy rates comparable to those with adequate P4 levels, indicating successful compensation for luteal deficiency. These findings highlight the clinical value of P4-guided individualized LPS in improving implantation and live birth outcomes in HRT-FET cycles [17].

**Panel Recommendation**

- In HRT-FET cycles, clinicians should measure serum progesterone (P4) levels on the day of embryo transfer and, if P4 is below the optimal threshold (<10–12 ng/mL or per laboratory standards), adjust luteal support by increasing vaginal progesterone or adding subcutaneous/intramuscular progesterone to improve implantation and live birth rates.

### e. Early discontinuation of progesterone after hCG positivity

**Consensus Statement**

- The experts agreed that in fresh IVF cycles, progesterone supplementation can be stopped as early as the first positive hCG test, with minimal impact on ongoing pregnancy rate, miscarriage, and live birth rate.

**Supporting Evidence**

- A systematic review and meta-analysis by Watters et al. (2020) evaluated the optimal duration of luteal phase support (LPS) in fresh IVF/ICSI cycles, including randomized controlled trials comparing early versus extended progesterone supplementation. The

pooled analysis demonstrated no significant difference in ongoing pregnancy, miscarriage, or live birth rates between women who discontinued progesterone after a positive serum hCG and those who continued until 8–12 weeks of gestation. These findings indicate that prolonged progesterone administration offers no additional clinical benefit, supporting early discontinuation of LPS once pregnancy is biochemically confirmed [18].

**Panel Recommendation**

- In fresh IVF cycles, clinicians may consider discontinuing progesterone supplementation after the first positive hCG test, as early cessation has minimal impact on ongoing pregnancy, miscarriage, and live birth rates.

### f. Role of 17-OHPC in FET

**Consensus Statement**

- The experts disagreed that 17-OHPC provides effective luteal phase support in women undergoing FET cycles; the correct recommendation is that luteal phase support should be continued for up to 10–12 weeks of gestation.

**Supporting Evidence**

- A retrospective comparative study by Seshadri et al. (2022) involving 896 frozen embryo transfer (FET) cycles compared intramuscular (IM) natural progesterone (Prontogest) with 17-α-hydroxyprogesterone caproate (17-OHPC; Lentogest) for luteal phase support. The 17-OHPC group demonstrated higher live birth rates (50.9% vs. 41.8%; OR 0.63, 95% CI 0.31–0.91; $p < 0.05$) and lower miscarriage rates (14.5% vs. 19.2%; $p = 0.028$) compared with natural IM progesterone, with similar gestational age and neonatal outcomes. Although these findings suggest potential efficacy of 17-OHPC, evidence remains limited and heterogeneous, and current guidelines continue to recommend maintaining progesterone supplementation up to 10–12 weeks of gestation for optimal early pregnancy support [19].

**Panel Recommendation**

- In frozen embryo transfer (FET) cycles, clinicians should continue luteal phase support for up to 10–12 weeks of gestation rather than using 17-OHPC, as extended progesterone supplementation ensures optimal support of early pregnancy.

## 2. Progestin-Primed Ovarian Stimulation (PPOS)

### a. Comparable developmental potential of oocytes

**Consensus Statement**

- The experts agreed that not all frozen–thawed embryo transfer (FET) cycles require progestin-primed ovarian stimulation (PPOS). Oocytes collected in PPOS cycles have similar developmental potential, including comparable blastocyst euploidy rates. Frozen embryo transfer outcomes of PPOS and GnRH analogue cycles are similar in terms of ongoing pregnancy, live birth, obstetric, and perinatal outcomes; therefore, PPOS can be preferred for ovarian stimulation in ART.

**Supporting Evidence**

- Recent evidence consolidates the role of Progestin-Primed Ovarian Stimulation (PPOS) as a viable alternative to GnRH analogue cycles. A comprehensive review by Baris Ata (2024) found that oocytes retrieved in PPOS cycles exhibit comparable developmental potential—including blastocyst euploidy rates—to those from GnRH analogue protocols, and first FET outcomes (ongoing pregnancy/live births, obstetric and neonatal measures)

remain similar. Moreover, meta-analysis data show no significant difference in euploid blastocyst number or live birth rates between PPOS and GnRH-antagonist cycles [20].

**Panel Recommendation**

- PPOS can be considered a suitable ovarian stimulation protocol in ART, as it provides comparable embryological, pregnancy, and perinatal outcomes to GnRH analogue cycles, though it is not required for all FET cases.

### b. PPOS across patient types

**Consensus Statement**

- The experts agreed that PPOS can be used in all patient types except those with progesterone receptor–positive breast cancer with consistent results, and it appears to be a patient-friendly and cost-effective option when a fresh embryo transfer is not intended.

**Supporting Evidence**

- An open-label randomized controlled trial by Ye et al. (2024) compared progestin-primed ovarian stimulation (PPOS) with the GnRH antagonist protocol in 348 women with normal ovarian reserve undergoing IVF. The study found comparable cumulative live-birth rates (55.8% vs 52.9%), implantation, and miscarriage rates between groups, with no cases of premature LH surge or OHSS in PPOS cycles. Both protocols yielded similar numbers of retrieved and mature oocytes and viable embryos. These findings demonstrate that PPOS is an effective, safe, patient-friendly, and cost-efficient alternative to GnRH analog regimens, suitable for freeze-all strategies in ART practice [21].

**Panel Recommendation**

- PPOS may be used safely and effectively across most patient groups, except in those with progesterone receptor–positive breast cancer, as it offers consistent outcomes and is a convenient, cost-effective choice when a freeze-all strategy is planned.

### c. Clinical outcomes and OHSS prevention

**Consensus Statement**

- The experts remained neutral regarding the long-term safety and the reported higher number of oocytes obtained with PPOS, as current evidence is insufficient to draw definitive conclusions. Although PPOS in IVF/ICSI cycles is associated with a higher number of embryos, lower incidence of OHSS, and similar stimulation duration and oocyte maturity rates, the long-term safety in offspring requires further research.

**Supporting Evidence**

- A recent systematic review by Lokshin et al. (2024) evaluated randomized controlled trials comparing progestin-primed ovarian stimulation (PPOS) with conventional GnRH agonist and antagonist protocols in IVF/ICSI cycles. The analysis demonstrated that PPOS achieves comparable numbers of retrieved oocytes, MII oocytes, and embryos, while being associated with a lower incidence of ovarian hyperstimulation syndrome (OHSS) and similar pregnancy and live birth outcomes. The review also indicated no significant differences in neonatal outcomes or congenital malformations, suggesting that PPOS is a clinically effective and safe approach for ovarian stimulation. However, the authors emphasized that long-term safety data in offspring remain limited, and further studies are warranted to establish the minimal effective dose and confirm long-term safety [22].

**Panel Recommendation**

- PPOS may be considered an effective and safe option for ovarian stimulation in ART, but clinicians should interpret data on oocyte yield and long-term child safety with caution until more robust evidence becomes available.

### d. Patient subgroups benefiting most

**Consensus Statement**

- The experts agreed that poor ovarian responders, patients with PCOS, women of advanced maternal age, and oocyte donors are the patient populations that benefit most from using PPOS.

**Supporting Evidence**

- A large multicenter retrospective study by Murria et al. (2025) compared progestin-primed ovarian stimulation (PPOS) using medroxyprogesterone acetate (MPA) with the GnRH antagonist protocol across 17,000+ donor oocyte cycles. PPOS yielded comparable implantation (57.7% vs 55.8%), ongoing pregnancy (49.4% vs 48.2%), and cumulative live birth rates (65.6% vs 65.5%), with slightly higher oocyte survival and blastocyst formation rates. PPOS showed no adverse effect on embryo quality or neonatal outcomes and offers reduced OHSS risk and improved patient convenience. These findings support the use of PPOS, particularly in oocyte donors, poor responders, PCOS, and older women, as a safe and effective ART strategy [23].

**Panel Recommendation**

- Consider PPOS as the preferred ovarian stimulation protocol for poor responders, patients with PCOS, women of advanced age, and oocyte donors, as it offers favourable outcomes and reduces the risk of OHSS in these groups.

### e. PPOS with dydrogesterone in donor cycles

**Consensus Statement**

- The experts agreed that initiating PPOS earlier in the cycle (from day 2 or day 5 rather than day 7) may be more appropriate, although evidence shows that PPOS with dydrogesterone starting from day 7 yields outcomes comparable to a GnRH antagonist protocol in oocyte donor cycles.

**Supporting Evidence**

- A retrospective cohort study by Hendrickx et al. (2024) compared PPOS with dydrogesterone (10 mg BID) initiated on cycle day 2, 5, or 7 versus the GnRH antagonist protocol in 1,124 oocyte donor cycles. The results showed no significant difference in the number of retrieved oocytes, mature (MII) oocytes, fertilization, or blastocyst formation rates among groups. Clinical pregnancy and live birth outcomes following FET were also equivalent. Early initiation (day 2–5) demonstrated slightly improved follicular synchronization without compromising oocyte quality. These findings support flexible dydrogesterone start days in PPOS, ensuring efficacy and safety comparable to GnRH antagonist protocols [24].

**Panel Recommendation**

- In oocyte donor cycles, clinicians may initiate PPOS with dydrogesterone from day 2 or day 5 of stimulation, as starting earlier may optimize follicular synchronization while maintaining outcomes comparable to GnRH antagonist protocols.

## 3. Progesterone in Early Pregnancy and Recurrent Loss

### a. Low P4 levels linked with BMI and prior loss

**Consensus statement**

- High BMI & higher number of pregnancy loss is associated with low progesterone levels in early pregnancy.

**Supporting Evidence**

- A prospective cohort study by Dahlberg et al. (2025) investigated 1,199 pregnancies in women with recurrent pregnancy loss (RPL) to assess factors associated with low early pregnancy progesterone levels. The study found that higher BMI and a greater number of prior miscarriages were independently associated with low serum progesterone (<35 nmol/L) in early gestation (adjusted OR for BMI 1.06, 95% CI 1.02–1.10; OR for prior losses 1.24, 95% CI 1.04–1.49). These findings indicate that metabolic and reproductive history factors can adversely influence luteal function and progesterone production, potentially contributing to early pregnancy loss [25].

**Panel Recommendation**

- In women with elevated BMI or a history of recurrent pregnancy loss, clinicians should consider monitoring early pregnancy progesterone levels, as low P4 may indicate the need for supplementation to support implantation and early gestation.

### b. Progesterone improves live births without added risk

**Consensus statement**

- The experts agreed that progesterone treatment for recurrent pregnancy loss (RPL) can increase live birth rates without increasing adverse maternal or neonatal outcomes in women at risk of pregnancy loss.

**Supporting evidence**

- A 2024 systematic review and meta-analysis by Zhao et al. evaluated 15 randomized controlled trials including 6,616 pregnancies to determine the efficacy and safety of progesterone supplementation in women with threatened or recurrent miscarriage. The pooled analysis demonstrated that progestogen therapy probably increases live birth rates compared with placebo (RR 1.07; 95% CI 1.01–1.13; moderate certainty) without increasing the risk of maternal or neonatal adverse events. The benefit was most pronounced among women with one or more prior miscarriages, whereas women without previous losses showed uncertain benefit. No significant differences were observed in congenital anomalies (RR 1.06; 95% CI 0.76–1.48) or serious adverse maternal outcomes (RR 1.07; 95% CI 0.83–1.40). These findings confirm that progesterone supplementation is effective and safe in improving live birth outcomes among women at increased risk of pregnancy loss [26].

**Panel recommendation**

- Clinicians should consider progesterone supplementation in women with a history of recurrent pregnancy loss, as it has been shown to improve live birth rates without elevating maternal or neonatal risks.

### c. Use in women with recurrent miscarriage and bleeding

**Consensus statement**

- The experts agreed that progestogen supplementation should be considered in women with recurrent miscarriage who present with bleeding in early pregnancy. The recommended regimen is 40 mg stat, followed by 10 mg three times daily for up to seven days after the bleeding stops.

**Supporting evidence**

- The 2023 RCOG Green-top Guideline No. 17 on Recurrent Miscarriage recommends that progestogen supplementation should be considered in women with recurrent miscarriage who present with bleeding in early pregnancy. The guideline specifically advises a regimen of 400 mg micronized vaginal progesterone twice daily, initiated at the onset of bleeding and continued until 16 weeks of gestation. This recommendation (Grade B) is supported by randomized controlled data demonstrating that progesterone therapy in this population can reduce miscarriage risk and improve live birth outcomes without significant maternal or neonatal adverse effects [27].

**Panel recommendation**

- In women with recurrent miscarriage presenting with early pregnancy bleeding, initiate progestogen therapy with 40 mg stat, then continue 10 mg three times daily for seven days after bleeding ceases to support pregnancy continuation.

### d. Progesterone in Abnormal Uterine Bleeding (AUB)

**Consensus statement**

- The experts agreed that norethisterone or medroxyprogesterone acetate, when used alone, can help stop bleeding in cases of abnormal uterine bleeding (AUB).

**Supporting evidence**

- Multiple clinical studies and reviews support the efficacy of oral progestins for acute abnormal uterine bleeding (AUB). A recent narrative review summarized favourable safety, tolerability, and haemostatic effects of norethisterone/NETA in AUB management, reporting consistent reductions in menstrual blood loss and good patient acceptability [28]. Randomized studies and guideline reviews also demonstrate that medroxyprogesterone acetate (MPA) is effective for AUB due to ovulatory dysfunction, and that oral progestins are an accepted medical option alongside tranexamic acid and hormonal therapies in acute AUB algorithms [29].

**Panel recommendation**

- For the management of abnormal uterine bleeding, clinicians may use norethisterone or medroxyprogesterone acetate as monotherapy to effectively control and stop bleeding episodes.

## Summary of Recommendations

The following table summarizes the panel's key evidence-based recommendations across major clinical contexts involving progesterone use. These statements reflect consensus interpretations of current literature and expert experience, emphasizing individualized care, optimal therapeutic timing, and clinical safety in reproductive endocrinology and gynecologic practice.

Table 1: Summary of recommendations

| Topic | Summary of Panel Recommendations |
|---|---|
| Luteal Phase Support in ART | • Vaginal progesterone is the base for LPS<br>• Oral dydrogesterone is an effective alternative or adjunct in FET<br>• Individualize LPS using serum P4 levels<br>• Progesterone can be stopped after positive hCG in fresh cycles<br>• Continue LPS up to 10–12 weeks in FET; avoid 17-OHPC |
| PPOS | • PPOS provides outcomes comparable to GnRH-ant protocols, reduces OHSS, and is cost-effective<br>• It benefits poor responders, PCOS, older women, and donors; avoid in PR-positive breast cancer<br>• Start PPOS early (Day 2–5) for optimal results |
| Progesterone in Early Pregnancy & Recurrent Loss | • Low early-pregnancy P4 is linked with high BMI and recurrent loss.<br>• Progesterone therapy improves live birth rates without added risk and should be initiated in RPL with bleeding (40 mg stat + 10 mg TID × 7 days). |
| AUB | • Norethisterone or medroxyprogesterone acetate alone is effective for stopping bleeding episodes. |

## Research Gaps and Future Directions

Although progesterone therapy is central to ART and early pregnancy support, several evidence gaps remain. One of the aspects being progesterone thresholds for luteal sufficiency; optimal serum P4 cut-offs for predicting implantation success remain undefined across formulations and assays [30]. The literature regarding duration of luteal support also remains scarce; the minimal effective duration of progesterone post-implantation is uncertain, with limited RCT data supporting early discontinuation [31]. In addition to this, the long-term child outcomes should also be assessed. Data on neurodevelopmental safety after in-utero progesterone exposure are sparse and heterogeneous [32]. Addressing these gaps through standardized, multicentre trials will refine progesterone use, optimize efficacy, and ensure maternal–fetal safety.

### Limitations

Although this consensus integrates a broad body of evidence and expert clinical experience, several limitations should be acknowledged. First, a significant proportion of the supporting data is derived from meta-analyses and systematic reviews of heterogeneous randomized trials. While such studies provide comprehensive synthesis, they may inherit methodological biases, variable patient populations, inconsistent LPS protocols, and differing progesterone formulations and assay thresholds. These factors can limit the precision and generalizability of pooled outcomes.

## Conclusion

Progesterone remains integral to reproductive medicine, supporting luteal function, implantation, and early pregnancy. Expert consensus affirms that vaginal progesterone is

the preferred base for luteal phase support in IVF/ICSI, with oral dydrogesterone serving as an effective and well-tolerated alternative in FET cycles. Individualizing progesterone therapy based on serum P4 levels enhances clinical outcomes, while early discontinuation after hCG positivity is safe in fresh cycles. PPOS offers comparable efficacy to GnRH analog protocols with lower OHSS risk, particularly benefiting poor responders, PCOS, older women, and donors. In early pregnancy and recurrent miscarriage, progesterone supplementation improves live birth rates without increasing adverse outcomes and is recommended for women with bleeding or prior losses. Additionally, oral progestins effectively manage abnormal uterine bleeding. Overall, progesterone therapy should be individualized and evidence-driven to optimize reproductive success and ensure maternal–fetal safety in ART and early pregnancy care.

Conflict of Interest: There was no conflict of interest.

## References


1. Nagy B, Szekeres-Barthó J, Kovács GL, Sulyok E, Farkas B, Várnagy Á, Vértes V, Kovács K, Bódis J. Key to Life: Physiological Role and Clinical Implications of Progesterone. Int J Mol Sci. 2021 Oct 13;22(20):11039. doi: 10.3390/ijms222011039. PMID: 34681696; PMCID: PMC8538505.
2. Reed BG, Carr BR. The Normal Menstrual Cycle and the Control of Ovulation. [Updated 2018 Aug 5]. In: Feingold KR, Ahmed SF, Anawalt B, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279054
3. Mesen TB, Young SL. Progesterone and the luteal phase: a requisite to reproduction. Obstet Gynecol Clin North Am. 2015 Mar;42(1):135-51. doi: 10.1016/j.ogc.2014.10.003. Epub 2015 Jan 5. PMID: 25681845; PMCID: PMC4436586.
4. Diagnosis and treatment of luteal phase deficiency: a committee opinion. Available from: https://www.asrm.org/practice-guidance/practice-committee-documents/diagnosis-and-treatment-of-luteal-phase-deciency-a-committee-opinion-2021/. Accessed on: 30th October 2025.
5. Tesarik et al. Luteal Phase in Assisted Reproductive Technology. Front. Reprod. Health, 07 December 2020 Sec. Assisted Reproduction. Volume 2 – 2020 https://doi.org/10.3389/frph.2020.595183
6. Garg A, Zielinska AP, Yeung AC, Abdelmalak R, Chen R, Hossain A, Israni A, Nelson SM, Babwah AV, Dhillo WS, Abbara A. Luteal phase support in assisted reproductive technology. Nat Rev Endocrinol. 2024 Mar;20(3):149-167. doi: 10.1038/s41574-023-00921-5. Epub 2023 Dec 18. PMID: 38110672.
7. Banerjee, K., et al. (2020). Luteal phase support in assisted reproductive technologies. F&S Reports, 1(2), 145-154. https://doi.org/10.1016/j.xfss.2020.07.020
8. Palomba, S., Santagni, S. & La Sala, G.B. Progesterone administration for luteal phase deficiency in human reproduction: an old or new issue?. J Ovarian Res 8, 77 (2015). https://doi.org/10.1186/s13048-015-0205-8
9. Barrenetxea G, Prego O, Celis R, Martínez E, De Las Heras M, Gómez O, Aguirre O, Samojluk S, Barrenetxea J. Effects of vaginal vs oral progesterone supplementation before embryo transfer on live birth rates and levels: a randomized trial. Reprod Fertil. 2025 Mar 20;6(1):e240094. doi: 10.1530/RAF-24-0094. PMID: 40052716; PMCID: PMC11949523.
10. B. Alsbjerg, P. Humaidan. What to expect from a 'standard vaginal progesterone regimen' in hormone replacement therapy frozen embryo transfer (HRT-FET) – a PRISMA review and meta-analysis. Reproductive BioMedicine Online. Volume 50, Issue 5, May 2025, 104736

11. Xie, Yx., Jiang, Ll., Huang, J. et al. Comparison of oral dydrogesterone and vaginal progesterone for luteal phase support in natural and modified natural cycle frozen embryo transfers. J Ovarian Res 18, 183 (2025). https://doi.org/10.1186/s13048-025-01765-5

12. Balachandren N, Veeramani M, Suriyakumar S, Wiley S, Mavrelos D, Yasmin E, Kastora SL. Comparison of Luteal Support Protocols in Frozen IVF/ICSI Cycles: A Network Meta-Analysis. BJOG. 2025 Aug;132(9):1187-1201. doi: 10.1111/1471-0528.18172. Epub 2025 May 2. PMID: 40313195; PMCID: PMC12232591.

13. Kastora SL, Gkova G, Stavridis K, Balachandren N, Kastoras A, Karakatsanis A, Mavrelos D. Comparison of luteal support protocols in fresh IVF/ICSI cycles: a network meta-analysis. Sci Rep. 2024 Jun 24;14(1):14492. doi: 10.1038/s41598-024-64804-z. PMID: 38914570; PMCID: PMC11196689.

14. Stavridis K, Balafoutas D, Kalampokas T, Benetou V, Samoli E, Vlahos N, Kasdagli MI. Oral Dydrogesterone Versus Vaginal Progesterone for Luteal Phase Support in Frozen-Thawed Embryo Transfer Cycles: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Clin Med. 2025 May 7;14(9):3238. doi: 10.3390/jcm14093238. PMID: 40364269; PMCID: PMC12072605.

15. Tournaye, H., Sukhikh, G.T., Kahler, E., & Griesinger, G. (2017). A Phase III randomized controlled trial comparing the efficacy, safety and tolerability of oral dydrogesterone versus micronized vaginal progesterone for luteal support in in vitro fertilization. Human reproduction, 32 10, 2152 .

16. Vuong LN, Pham TD, Le KTQ, Ly TT, Le HL, Nguyen DTN, Ho VNA, Dang VQ, Phung TH, Norman RJ, Mol BW, Ho TM. Micronized progesterone plus dydrogesterone versus micronized progesterone alone for luteal phase support in frozen-thawed cycles (MIDRONE): a prospective cohort study. Hum Reprod. 2021 Jun 18;36(7):1821-1831. doi: 10.1093/humrep/deab093. PMID: 33930124.

17. Arik Alpcetin SI, Ince O, Akcay B, Cevher Akdulum MF, Demirdag E, Erdem A and Erdem M (2025) Comparison of Individualized Rescue Luteal Phase Support Strategies with Vaginal and Combined Vaginal & Subcutaneous Progesterone Administration in Artificial Frozen-Thawed Blastocyst Embryo Transfer Cycles Based on Serum Progesterone levels. Front. Endocrinol. 15:1503008. doi: 10.3389/fendo.2024.1503008

18. Watters M, Noble M, Child T, Nelson S. Short versus extended progesterone supplementation for luteal phase support in fresh IVF cycles: a systematic review and meta-analysis. Reprod Biomed Online. 2020 Jan;40(1):143-150. doi: 10.1016/j.rbmo.2019.10.009. Epub 2019 Oct 24. PMID: 31864902.

19. Seshadri S, Odia R, Ozturk O, Saab W, AlChami A, Gonzalez XV, Salim S, Saab W, Serha P. A Comparative Analysis of Outcomes Between Two Different Intramuscular Progesterone Preparations in Women Undergoing Frozen Embryo Transfer Cycles. J Reprod Infertil. 2022 Jan-Mar;23(1):46-53. doi: 10.18502/jri.v23i1.8452. PMID: 36045879; PMCID: PMC9361726.

20. Ata B, Kalafat E. Progestin-primed ovarian stimulation: for whom, when and how? Reprod Biomed Online. 2024 Feb;48(2):103639. doi: 10.1016/j.rbmo.2023.103639. Epub 2023 Oct 22. PMID: 38159467.

21. Ye H, Shi L, Quan X, Hou M, Ma H, Xue S, Yu Z, Chen Q, Sun L. Cumulative live birth rate of in vitro fertilization cycle via progestin-primed ovarian stimulation versus gonadotropin-releasing hormone antagonist protocol in infertile women with normal ovarian reserve: an open-label, randomized controlled trial. Hum Fertil (Camb). 2024 Dec;27(1):2316005. doi: 10.1080/14647273.2024.2316005. Epub 2024 Feb 15. PMID: 38357937.

22. Lokshin et al. Progestin-primed ovarian stimulation outcomes in in-vitro fertilization (IVF) – A systematic review of the literature. Gynecological Endocrinology. October 202440(1) DOI:10.1080/09513590.2024.2414783

23. Murria L, Giles J, Bori L, Remohí J, Cobo A. Progestin prime ovarian stimulation provides comparable outcomes to GnRH antagonist in donor cycles with vitrified oocytes. Fertil Steril. 2025 Oct;124(4):701-710. doi: 10.1016/j.fertnstert.2025.05.154. Epub 2025 May 20. PMID: 40403912.

24. Hendrickx S, De Vos M, De Munck N, Mackens S, Ruttens S, Tournaye H, Blockeel C. Progestin primed ovarian stimulation using dydrogesterone from day 7 of the cycle onwards in oocyte donation cycles: a longitudinal study. Reprod Biomed Online. 2024 May;48(5):103732. doi: 10.1016/j.rbmo.2023.103732. Epub 2023 Nov 20. PMID: 38458058.

25. E S Dahlberg et al Association of pre-pregnancy characteristics with progesterone levels in early pregnancy: A prospective cohort study of women with RPL , Human Reproduction, June 2025.

26. Zhao Y, D'Souza R, Gao Y, et al.Progestogens in women with threatened miscarriage orrecurrent miscarriage: A meta-analysis. Acta Obstet GynecolScand. 2024;103:1689-1701. doi:10.1111/aogs.14829

27. Regan L, Rai R, Saravelos S, Li TC; Royal College of Obstetricians and Gynaecologists. Recurrent MiscarriageGreen-top Guideline No. 17. BJOG. 2023 Nov;130(12):e9-e39. doi: 10.1111/1471-0528.17515. Epub 2023 Jun 19. PMID: 37334488.

28. Boruah AM, Banerjee D, Bhardwaj F, Mallya S, Singal R, Sharma S, Gautam A. Effect of norethisterone dose and duration in the management of abnormal uterine bleeding: a narrative review and case report. Drugs Context. 2024 Jul 4;13:2024-4-1. doi: 10.7573/dic.2024-4-1. PMID: 38989130; PMCID: PMC11235183.

29. Bender RA. Medroxyprogesterone Acetate for Abnormal Uterine Bleeding Due to Ovulatory Dysfunction: The Effect of 2 Different-Duration Regimens. Med Sci Monit. 2022 Jun 24;28:e936727. doi: 10.12659/MSM.936727. PMID: 35746846; PMCID: PMC9248354.

30. Melo P, Chung Y, Pickering O, Price MJ, Fishel S, Khairy M, Kingsland C, Lowe P, Petsas G, Rajkhowa M, Sephton V, Tozer A, Wood S, Labarta E, Wilcox M, Devall A, Gallos I, Coomarasamy A. Serum luteal phase progesterone in women undergoing frozen embryo transfer in assisted conception: a systematic review and meta-analysis. Fertil Steril. 2021 Dec;116(6):1534-1556. doi: 10.1016/j.fertnstert.2021.07.002. Epub 2021 Aug 10. PMID: 34384594.

31. Watters M, Noble M, Child T, Nelson S. Short versus extended progesterone supplementation for luteal phase support in fresh IVF cycles: a systematic review and meta-analysis. Reprod Biomed Online. 2020 Jan;40(1):143-150. doi: 10.1016/j.rbmo.2019.10.009. Epub 2019 Oct 24. PMID: 31864902.

32. Simons NE, Leeuw M, Van't Hooft J, Limpens J, Roseboom TJ, Oudijk MA, Pajkrt E, Finken M, Painter RC. The long-term effect of prenatal progesterone treatment on child development, behaviour and health: a systematic review. BJOG. 2021 May;128(6):964-974. doi: 10.1111/1471-0528.16582. Epub 2020 Nov 28. PMID: 33112462; PMCID: PMC8246867.

# Notes

# Notes

# Notes

# Notes

zydus
Dedicated To Life

For Ovarian Stimulation

Rx

# Briogyn 300/900 IU

Follitropin Alfa with Preloaded Pen

**Precise • Consistent • Convenient**

## Follitropin Alfa same as innovator*


**Pre-filled** & **Pre-loaded** Pen

zydus
Dedicated To Life


**Indian Society For Assisted Reproduction (ISAR)**

Trade World, C-911, C Wing, 9th Floor, Kamala City,
Senapati Bapat Marg, Lower Parel West,
Mumbai-400013

+ 919987645906
+ 917304304104

isar.office@gmail.com

www.isarindia.net

https://www.facebook.com/profile.php?id=61558900400676#

https://www.youtube.com/@isar.official

https://www.instagram.com/isarsocialmedia24/

https://www.linkedin.com/in/isarsocialmedia24/

https://twitter.com/IsarSocialmedia


ZHL/Mass Cluster-Gynova/WHC/02-2026/00