

RESEARCH MONOGRAPH . COMPOUND PROFILE

Progesterone (Research)

The principal endogenous progestogen; a progesterone receptor agonist with luteal phase, gestational, and neurosteroid functions.

DOCUMENT	KDC-MN-388
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	Endogenous progestogen / PR agonist

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ABSTRACT

Progesterone (pregn-4-ene-3,20-dione; CAS 57-83-0; molecular formula $C_{21}H_{30}O_2$; molecular weight 314.46) is the principal endogenous progestogen, biosynthesized from cholesterol via pregnenolone in the corpus luteum, adrenal cortex, and (during pregnancy) placenta. The compound is a high-affinity progesterone receptor (PR) agonist with secondary effects at the glucocorticoid receptor (mineralocorticoid antagonism contributing to natriuretic effects) and at GABA-A receptors (the pregnanolone metabolite is a positive allosteric modulator producing sedation). Approved indications: menopausal hormone therapy (combined with estrogen for endometrial protection in women with intact uterus), assisted reproductive technology luteal support, secondary amenorrhea, and prevention of preterm birth (intramuscular formulation). Oral micronized progesterone (Prometrium) is highly subject to first-pass metabolism producing the sedating allopregnanolone metabolite; vaginal and transdermal forms produce more direct PR effects with less sedation. Plasma half-life is short (5 to 20 minutes for parent; metabolites variable). Used as the canonical PR agonist in research.

1. Compound Identification

Progesterone (Research) is described as endogenous progestogen / pr agonist. The principal endogenous progestogen; a progesterone receptor agonist with luteal phase, gestational, and neurosteroid functions.

1.1 Class summary

Endogenous progestogen / PR agonist

1.2 Subtitle

The principal endogenous progestogen; a progesterone receptor agonist with luteal phase, gestational, and neurosteroid functions.

2. Abstract

Progesterone (pregn-4-ene-3,20-dione; CAS 57-83-0; molecular formula C₂₁H₃₀O₂; molecular weight 314.46) is the principal endogenous progestogen, biosynthesized from cholesterol via pregnenolone in the corpus luteum, adrenal cortex, and (during pregnancy) placenta. The compound is a high-affinity progesterone receptor (PR) agonist with secondary effects at the glucocorticoid receptor (mineralocorticoid antagonism contributing to natriuretic effects) and at GABA-A receptors (the pregnanolone metabolite is a positive allosteric modulator producing sedation). Approved indications: menopausal hormone therapy (combined with estrogen for endometrial protection in women with intact uterus), assisted reproductive technology luteal support, secondary amenorrhea, and prevention of preterm birth (intramuscular formulation). Oral micronized progesterone (Prometrium) is highly subject to first-pass metabolism producing the sedating allopregnanolone metabolite; vaginal and transdermal forms produce more direct PR effects with less sedation. Plasma half-life is short (5 to 20 minutes for parent; metabolites variable). Used as the canonical PR agonist in research.

3. Mechanism of Action

Progesterone receptor agonist; secondary glucocorticoid receptor activity (mineralocorticoid antagonism) and GABA-A potentiation via allopregnanolone metabolite.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Clinical 100 to 200 mg PO nightly (HRT) or 8 percent vaginal gel; preterm prevention 250 mg IM weekly.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Stanczyk FZ, et al. Progestogens used in postmenopausal hormone therapy: differences in their pharmacological properties, intracellular actions, and clinical effects. Endocr Rev 2013.
2. Fischer Walker CL, et al. Progesterone and 17-OH progesterone caproate for prevention of preterm birth. Obstet Gynecol 2017.
3. Belelli D, Lambert JJ. Neurosteroids: endogenous regulators of the GABA(A) receptor. Nat Rev Neurosci 2005.

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