

RESEARCH MONOGRAPH . COMPOUND PROFILE

Leuprolide

A synthetic GnRH agonist; the most prescribed GnRH analog worldwide; approved for prostate cancer, endometriosis, fibroids, and precocious puberty.

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AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Synthetic GnRH agonist (nonapeptide)

RESEARCH USE ONLY

ABSTRACT

Leuprolide (5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide; CAS 53714-56-0; molecular formula C₅₉H₈₄N₁₆O₁₂; molecular weight 1209.41) is a synthetic GnRH agonist nonapeptide developed at Abbott and approved by the FDA in 1985 under the trade name Lupron. Mechanism is identical to triptorelin: chronic exposure desensitizes pituitary GnRH receptors and suppresses LH/FSH after an initial 1-to-2-week flare. Plasma half-life is approximately 3 hours for the parent peptide; depot formulations release over 1, 3, 4, or 6 months. Leuprolide is the most prescribed GnRH analog globally and is the workhorse of clinical GnRH suppression. Approved indications: prostate cancer, endometriosis, uterine leiomyomata (fibroids), central precocious puberty, IVF protocols, and (recently) delayed puberty in transgender adolescents in some markets. Used as the canonical GnRH agonist in academic endocrine pharmacology and as a pharmacological tool for HPG axis manipulation.

1. Compound Identification

Leuprolide is described as synthetic gnrh agonist (nonapeptide). A synthetic GnRH agonist; the most prescribed GnRH analog worldwide; approved for prostate cancer, endometriosis, fibroids, and precocious puberty.

1.1 Class summary

Synthetic GnRH agonist (nonapeptide)

1.2 Subtitle

A synthetic GnRH agonist; the most prescribed GnRH analog worldwide; approved for prostate cancer, endometriosis, fibroids, and precocious puberty.

2. Abstract

Leuprolide (5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide; CAS 53714-56-0; molecular formula C₅₉H₈₄N₁₆O₁₂; molecular weight 1209.41) is a synthetic GnRH agonist nonapeptide developed at Abbott and approved by the FDA in 1985 under the trade name Lupron. Mechanism is identical to triptorelin: chronic exposure desensitizes pituitary GnRH receptors and suppresses LH/FSH after an initial 1-to-2-week flare. Plasma half-life is approximately 3 hours for the parent peptide; depot formulations release over 1, 3, 4, or 6 months. Leuprolide is the most prescribed GnRH analog globally and is the workhorse of clinical GnRH suppression. Approved indications: prostate cancer, endometriosis, uterine leiomyomata (fibroids), central precocious puberty, IVF protocols, and (recently) delayed puberty in transgender adolescents in some markets. Used as the canonical GnRH agonist in academic endocrine pharmacology and as a pharmacological tool for HPG axis manipulation.

3. Mechanism of Action

GnRH agonist nonapeptide; chronic exposure desensitizes pituitary GnRH receptors and suppresses LH/FSH. Mechanism identical to triptorelin.

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 depot 7.5 mg monthly, 22.5 mg three-monthly, or 30 mg four-monthly intramuscular or subcutaneous. Rodent studies 0.1 to 1 mg/kg.

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. Crawford ED, et al. A randomized phase III trial of long-acting leuprolide for advanced prostate cancer. Urology 2007.
2. Plosker GL, Brogden RN. Leuprorelin. Drugs Aging 1994.
3. Olshan AF, et al. Long-term effects of GnRH analog treatment for central precocious puberty. Hum Reprod Update 2006.

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