

RESEARCH MONOGRAPH . COMPOUND PROFILE

Enclomiphene

The (E)-isomer of clomiphene; a pure ER antagonist without the estrogenic zuclophene component, investigated for male hypogonadism.

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COMPOUND CLASS	Selective estrogen receptor antagonist ((E)-isomer of clomiphene)

RESEARCH USE ONLY

ABSTRACT

Enclomiphene ((E)-2-[4-(2-chloro-1,2-diphenylvinyl)phenoxy]-N,N-diethylethanamine; CAS 7599-79-3; molecular formula C₂₆H₂₈ClNO; molecular weight 405.96) is the (E)-isomer of clomiphene, a pure ER antagonist developed by Repros Therapeutics for male hypogonadism with the trade name Androxal. The compound antagonizes hypothalamic ER, releasing negative feedback on GnRH; consequent FSH and LH elevation drives endogenous testosterone production by Leydig cells. Distinct from exogenous testosterone replacement, enclomiphene preserves spermatogenesis and testicular volume because the elevated FSH supports continued Sertoli cell function. Phase 3 trials in obese men with secondary hypogonadism demonstrated efficacy in restoring eugonadal testosterone and improving spermatogenic parameters; the FDA declined approval (twice, 2015 and 2016) citing CMC and clinical pharmacology concerns rather than efficacy. The compound has been licensed and is in development at Cosette Pharmaceuticals. Plasma half-life is approximately 30 hours, much shorter than the 30-day zuclophene half-life. Used as the canonical pure SERM antagonist for male hypogonadism research and as PCT.

1. Compound Identification

Enclomiphene is described as selective estrogen receptor antagonist ((e)-isomer of clomiphene). The (E)-isomer of clomiphene; a pure ER antagonist without the estrogenic zuclomiphene component, investigated for male hypogonadism.

1.1 Class summary

Selective estrogen receptor antagonist ((E)-isomer of clomiphene)

1.2 Subtitle

The (E)-isomer of clomiphene; a pure ER antagonist without the estrogenic zuclomiphene component, investigated for male hypogonadism.

2. Abstract

Enclomiphene ((E)-2-[4-(2-chloro-1,2-diphenylvinyl)phenoxy]-N,N-diethylethanamine; CAS 7599-79-3; molecular formula C₂₆H₂₈ClNO; molecular weight 405.96) is the (E)-isomer of clomiphene, a pure ER antagonist developed by Repros Therapeutics for male hypogonadism with the trade name Androxal. The compound antagonizes hypothalamic ER, releasing negative feedback on GnRH; consequent FSH and LH elevation drives endogenous testosterone production by Leydig cells. Distinct from exogenous testosterone replacement, enclomiphene preserves spermatogenesis and testicular volume because the elevated FSH supports continued Sertoli cell function. Phase 3 trials in obese men with secondary hypogonadism demonstrated efficacy in restoring eugonadal testosterone and improving spermatogenic parameters; the FDA declined approval (twice, 2015 and 2016) citing CMC and clinical pharmacology concerns rather than efficacy. The compound has been licensed and is in development at Cosette Pharmaceuticals. Plasma half-life is approximately 30 hours, much shorter than the 30-day zuclophene half-life. Used as the canonical pure SERM antagonist for male hypogonadism research and as PCT.

3. Mechanism of Action

Pure ER antagonist ((E)-isomer of clomiphene); hypothalamic ER blockade increases FSH/LH and consequent endogenous testosterone with preserved spermatogenesis.

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

Trial doses 12.5 to 25 mg per oral administration daily; off-label PCT 12.5 to 25 mg daily. Rodent studies 1 to 10 mg/kg/day.

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. Wiehle RD, et al. Enclomiphene citrate stimulates testosterone production while preventing oligospermia. Fertil Steril 2014.
2. Kaminetsky J, et al. Oral enclomiphene citrate stimulates the endogenous production of testosterone and sperm counts in men with low testosterone. J Sex Med 2013.
3. Wiehle RD, et al. Pharmacology of enclomiphene citrate in male hypogonadism. Endocr Rev 2014.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.