

RESEARCH MONOGRAPH . COMPOUND PROFILE

Raloxifene

A benzothiophene SERM; an osteoporosis drug with breast cancer prevention activity but no uterine partial agonism, distinguishing it from tamoxifen.

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COMPOUND CLASS	Second-generation SERM (benzothiophene)

ABSTRACT

Raloxifene ([6-hydroxy-2-(4-hydroxyphenyl)benzothiophen-3-yl]-[4-(2-piperidin-1-ylethoxy)phenyl]methanone; CAS 84449-90-1; molecular formula C₂₈H₂₇NO₄S; molecular weight 473.58) is a benzothiophene second-generation SERM developed at Eli Lilly and approved by the FDA in 1997 under the trade name Evista. Distinct from tamoxifen by tissue selectivity profile: ER antagonism in breast and uterus, partial agonism in bone and liver. The absence of uterine partial agonism eliminates the endometrial cancer risk seen with tamoxifen and is the principal distinguishing clinical feature. Plasma half-life is approximately 27 hours; metabolism is via glucuronidation. Approved for postmenopausal osteoporosis treatment and prevention, and for breast cancer risk reduction in postmenopausal women at high risk. The MORE and STAR trials established the breast cancer prevention activity. Adverse events include thromboembolism (similar to tamoxifen), hot flashes, and leg cramps. Used as the canonical second-generation SERM with bone-selective profile.

1. Compound Identification

Raloxifene is described as second-generation serm (benzothiophene). A benzothiophene SERM; an osteoporosis drug with breast cancer prevention activity but no uterine partial agonism, distinguishing it from tamoxifen.

1.1 Class summary

Second-generation SERM (benzothiophene)

1.2 Subtitle

A benzothiophene SERM; an osteoporosis drug with breast cancer prevention activity but no uterine partial agonism, distinguishing it from tamoxifen.

2. Abstract

Raloxifene ([6-hydroxy-2-(4-hydroxyphenyl)benzothiophen-3-yl]-[4-(2-piperidin-1-ylethoxy)phenyl]methanone; CAS 84449-90-1; molecular formula C₂₈H₂₇NO₄S; molecular weight 473.58) is a benzothiophene second-generation SERM developed at Eli Lilly and approved by the FDA in 1997 under the trade name Evista. Distinct from tamoxifen by tissue selectivity profile: ER antagonism in breast and uterus, partial agonism in bone and liver. The absence of uterine partial agonism eliminates the endometrial cancer risk seen with tamoxifen and is the principal distinguishing clinical feature. Plasma half-life is approximately 27 hours; metabolism is via glucuronidation. Approved for postmenopausal osteoporosis treatment and prevention, and for breast cancer risk reduction in postmenopausal women at high risk. The MORE and STAR trials established the breast cancer prevention activity. Adverse events include thromboembolism (similar to tamoxifen), hot flashes, and leg cramps. Used as the canonical second-generation SERM with bone-selective profile.

3. Mechanism of Action

Benzothiophene SERM; ER antagonist in breast and uterus, partial agonist in bone and liver. No uterine partial agonism distinguishes it from tamoxifen.

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 60 mg per oral administration 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. Cummings SR, et al. The effect of raloxifene on risk of breast cancer in postmenopausal women: results from the MORE randomized trial. JAMA 1999.
2. Vogel VG, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer (STAR P-2). JAMA 2006.
3. Riggs BL, Hartmann LC. Selective estrogen-receptor modulators: mechanisms of action and application to clinical practice. N Engl J Med 2003.

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.