

WIKIPEDIA

# Raloxifene

**Raloxifene**, sold under the brand name **Evista** among others, is a medication used to prevent and treat osteoporosis in postmenopausal women and those on glucocorticoids.<sup>[4]</sup> For osteoporosis it is less preferred than bisphosphonates.<sup>[4]</sup> It is also used to reduce the risk of breast cancer in those at high risk.<sup>[4]</sup> It is taken by mouth.<sup>[4]</sup>

Common side effects include hot flashes, leg cramps, swelling, and joint pain.<sup>[4]</sup> Severe side effects may include blood clots and stroke.<sup>[4]</sup> Use during pregnancy may harm the baby.<sup>[4]</sup> The medication may worsen menstrual symptoms.<sup>[5]</sup> Raloxifene is a selective estrogen receptor modulator (SERM) and therefore a mixed agonist–antagonist of the estrogen receptor (ER).<sup>[4]</sup> It has estrogenic effects in bone and antiestrogenic effects in the breasts and uterus.<sup>[4]</sup>

Raloxifene was approved for medical use in the United States in 1997.<sup>[4]</sup> It is available as a generic medication.<sup>[4][6]</sup> In 2017, it was the 330th most commonly prescribed medication in the United States, with more than 900 thousand prescriptions.<sup>[7]</sup>

## Contents

### Medical uses

### Contraindications

### Side effects

### Overdose

### Pharmacology

Pharmacodynamics

Pharmacokinetics

### Chemistry

### History

### Society and culture

Names

Availability

Controversy

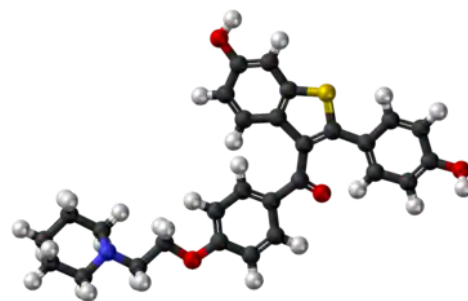
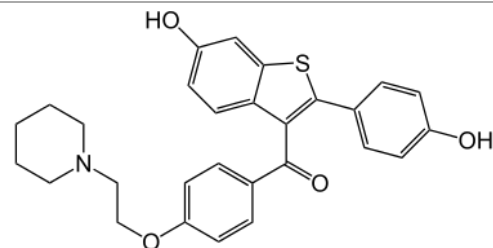
### Research

### References

### Further reading

### External links

## Raloxifene



## Clinical data

<b>Trade names</b>	Evista, Optruma, others
<b>Other names</b>	Keoxifene; Pharoxifene; LY-139481; LY-156758; CCRIS-7129
<b>AHFS/Drugs.com</b>	Monograph ( <a href="https://www.drugs.com/monograph/raloxifene-hydrochloride.html">https://www.drugs.com/monograph/raloxifene-hydrochloride.html</a> )
<b>MedlinePlus</b>	a698007 ( <a href="https://medlineplus.gov/druginfo/meds/a698007.html">https://medlineplus.gov/druginfo/meds/a698007.html</a> )
<b>License data</b>	<span><span><span></span></span><span> </span></span> EU EMA: by INN ( <a href="http://www.ema.europa.eu/ema/index.jsp?curl=%2Fpages%2Fmedicines%2Findexing%2Fepar_search.jsp&amp;mid=&amp;searchTab=searchByKey&amp;alreadyLoaded=true&amp;isNewQuery=true&amp;status=Authorised&amp;status=Withdrawn&amp;status=Suspended&amp;status=Refused&amp;keywordSearch=Submit&amp;searchType">http://www.ema.europa.eu/ema/index.jsp?curl=%2Fpages%2Fmedicines%2Findexing%2Fepar_search.jsp&amp;mid=&amp;searchTab=searchByKey&amp;alreadyLoaded=true&amp;isNewQuery=true&amp;status=Authorised&amp;status=Withdrawn&amp;status=Suspended&amp;status=Refused&amp;keywordSearch=Submit&amp;searchType</a> )

## Medical uses

Raloxifene is used for the treatment and prevention of osteoporosis in postmenopausal women.<sup>[8]</sup> It is used at a dosage of 60 mg/day for both the prevention and treatment of osteoporosis.<sup>[9]</sup> In the case of either osteoporosis prevention or treatment, supplemental calcium and vitamin D should be added to the diet if daily intake is inadequate.<sup>[10]</sup>

Raloxifene is used to reduce the risk of breast cancer in postmenopausal women. It is used at a dosage of 60 mg/day for this indication.<sup>[9]</sup> In the Multiple Outcomes of Raloxifene (MORE) clinical trial, raloxifene decreased the risk of all types of breast cancer by 62%, of invasive breast cancer by 72%, and of invasive estrogen receptor-positive breast cancer by 84%.<sup>[11]</sup> Conversely, it does not reduce the risk of estrogen receptor-negative breast cancer.<sup>[11]</sup> There were no obvious differences in effectiveness of raloxifene in the MORE trial for prevention of breast cancer at a dosage of 60 mg/m<sup>2</sup>/day relative to 120 mg/m<sup>2</sup>/day.<sup>[11]</sup> In the Study of Tamoxifen and Raloxifene (STAR) trial, 60 mg/day raloxifene was 78% as effective as 20 mg/day tamoxifen in preventing non-invasive breast cancer.<sup>[12]</sup> Women with undetectable levels of estradiol (<2.7 pg/mL) have a naturally low risk of breast cancer and, in contrast to women with detectable levels of estradiol, do not experience significant benefit from raloxifene in terms of reduction of breast cancer risk.<sup>[11]</sup>

## Contraindications

Raloxifene is contraindicated in lactating women or women who are or who may become pregnant.<sup>[13]</sup> It also may be of concern to women with active or past history of venous thromboembolic events, including deep vein thrombosis, pulmonary embolism, and retinal vein thrombosis.<sup>[14]</sup>

## Side effects

Common side effects of raloxifene include hot flashes (25–28% vs. 18–21% for placebo),<sup>[11]</sup> vaginal dryness, and leg cramps (generally mild; 5.5% vs. 1.9% for placebo).<sup>[13][1][15]</sup> Raloxifene does *not* cause breast tenderness, endometrial hyperplasia, menstrual bleeding, or endometrial cancer.<sup>[16]</sup> It does not appear to affect cognition or memory.<sup>[14][11]</sup> Raloxifene is a teratogen; i.e., it can cause developmental abnormalities such as birth defects.

Raloxifene may infrequently cause serious blood clots to form in the legs, lungs, or eyes.<sup>[1]</sup> Other reactions experienced include leg swelling/pain, trouble breathing, chest pain, and

=inn&taxonomyPath=&tr eeNumber=&searchGenericType=generics&keyword=Raloxifene)

US DailyMed: Raloxifene (<https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=Raloxifene>)

US FDA: Evista (<https://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchTerm=Evista&SearchType=BasicSearch>)

### Pregnancy category

AU: X (High risk)

### Routes of administration

By mouth

### Drug class

Selective estrogen receptor modulator

### ATC code

G03XC01 (WHO ([https://www.whocc.no/atc\\_dd\\_index/?code=G03XC01](https://www.whocc.no/atc_dd_index/?code=G03XC01)))

### Legal status

#### Legal status

US: R-only

EU: Rx-only

In general:

R (Prescription only)

### Pharmacokinetic data

#### Bioavailability

2%<sup>[1][2]</sup>

#### Protein binding

>95%<sup>[1][2]</sup>

#### Metabolism

Liver, intestines (glucuronidation);<sup>[1][2][3]</sup> CYP450 system not involved<sup>[1][2]</sup>

#### Elimination half-life

Single-dose: 28 hours<sup>[1][2]</sup>

Multi-dose: 33 hours<sup>[1]</sup>

#### Excretion

Feces<sup>[2]</sup>

### Identifiers

#### IUPAC name

vision changes. Black box warnings were added to the label of raloxifene in 2007 warning of increased risk of death due to stroke for postmenopausal women with documented coronary heart disease or at increased risk for major coronary events, as well as increased risk for deep vein thrombosis and pulmonary embolism.<sup>[13]</sup> The risk of venous thromboembolism with raloxifene is increased by several-fold in postmenopausal women (RR = 3.1).<sup>[17][11]</sup> Raloxifene has a lower risk of thromboembolism than tamoxifen.<sup>[12]</sup> In the MORE trial, raloxifene caused a 40% decrease in risk of cardiovascular events in women who were at increased risk for coronary artery disease, although there was no decrease in cardiovascular events for the group as a whole.<sup>[11]</sup>

A report in September 2009 from Health and Human Services' Agency for Healthcare Research and Quality suggests that tamoxifen and raloxifene used to treat breast cancer, significantly reduce invasive breast cancer in midlife and older women, but also increase the risk of adverse side effects.<sup>[18]</sup>

A recent human case report in July 2016 suggests that raloxifene may in fact, at some point, also stimulate breast cancer growth leading to a reduction of advanced breast cancer disease upon the withdrawal of the drug.<sup>[19]</sup>

Unlike other SERMs, such as tamoxifen, raloxifene has no risk of uterine hyperplasia or endometrial cancer (RR = 0.8).<sup>[1][17][12]</sup>

Raloxifene does not increase the incidence of breast pain or tenderness in postmenopausal women.<sup>[15][20]</sup>

## Overdose

Raloxifene has been studied in clinical trials across a dosage range of 30 to 600 mg/day, and was well-tolerated at all dosages.<sup>[15]</sup>

## Pharmacology

### Pharmacodynamics

#### Mechanism of action

Raloxifene is a selective estrogen receptor modulator (SERM) and hence is a mixed agonist and antagonist of the estrogen receptor (ER) in different tissues.<sup>[4]</sup> It has estrogenic activity in some tissues, such as bone and the liver, and antiestrogenic activity in other tissues, such as the breasts and uterus.<sup>[4]</sup> Its

[6-hydroxy-2-(4-hydroxyphenyl)-benzothiope  
n-3-yl]-[4-[2-(1-piperidyl)ethoxy]phenyl]-me  
thanone

<b>CAS Number</b>	84449-90-1 ( <a href="https://commonchemistry.cas.org/detail?cas_rn=84449-90-1">https://commonchemistry.cas.org/detail?cas_rn=84449-90-1</a> ) ✓ as HCl: 82640-04-8 ( <a href="https://commonchemistry.cas.org/detail?cas_rn=82640-04-8">https://commonchemistry.cas.org/detail?cas_rn=82640-04-8</a> )
<b>PubChem CID</b>	5035 ( <a href="https://pubchem.ncbi.nlm.nih.gov/compound/5035">https://pubchem.ncbi.nlm.nih.gov/compound/5035</a> )
<b>IUPHAR/BPS</b>	2820 ( <a href="http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=2820">http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=2820</a> )
<b>DrugBank</b>	DB00481 ( <a href="https://www.drugbank.ca/drugs/DB00481">https://www.drugbank.ca/drugs/DB00481</a> ) ✓
<b>ChemSpider</b>	4859 ( <a href="https://www.chemspider.com/Chemical-Structure.4859.html">https://www.chemspider.com/Chemical-Structure.4859.html</a> ) ✓
<b>UNII</b>	YX9162EO3I ( <a href="https://precision.fda.gov/uniisearch/srs/unii/YX9162EO3I">https://precision.fda.gov/uniisearch/srs/unii/YX9162EO3I</a> ) as HCl: 4F86W47BR6 ( <a href="https://precision.fda.gov/uniisearch/srs/unii/4F86W47BR6">https://precision.fda.gov/uniisearch/srs/unii/4F86W47BR6</a> )
<b>KEGG</b>	D08465 ( <a href="https://www.kegg.jp/entry/D08465">https://www.kegg.jp/entry/D08465</a> ) as HCl: D02217 ( <a href="https://www.kegg.jp/entry/D02217">https://www.kegg.jp/entry/D02217</a> )
<b>ChEBI</b>	CHEBI:8772 ( <a href="https://www.ebi.ac.uk/chebi/searchId.do?chebiId=CHEBI:8772">https://www.ebi.ac.uk/chebi/searchId.do?chebiId=CHEBI:8772</a> ) ✓
<b>ChEMBL</b>	ChEMBL81 ( <a href="https://www.ebi.ac.uk/chembl/in">https://www.ebi.ac.uk/chembl/in</a> )

affinity ( $K_d$ ) for the ER $\alpha$  is approximately 50 pM, which is similar to that of estradiol.<sup>[15]</sup> Relative to estradiol, raloxifene has been reported to possess about 8 to 34% of the affinity for the ER $\alpha$  and 0.5 to 76% of the affinity for the ER $\beta$ .<sup>[21][22]</sup> Raloxifene acts as a partial agonist of the ER $\alpha$  and as a pure antagonist of the ER $\beta$ .<sup>[23][24]</sup> In contrast to the classical ERs, raloxifene is an agonist of the G protein-coupled estrogen receptor (GPER) ( $EC_{50}$  = 10–100 nM), a membrane estrogen receptor.<sup>[25][26]</sup>

## Clinical effects

Raloxifene has antiestrogenic effects in the mammary glands in preclinical studies.<sup>[15]</sup> In accordance, raloxifene reduces breast density in postmenopausal women, a known risk factor for breast cancer.<sup>[27]</sup> It does not stimulate the uterus in postmenopausal women, and results in no increase in risk of endometrial thickening, vaginal bleeding, endometrial hyperplasia, or endometrial cancer.<sup>[28][15][20]</sup> At the same time, raloxifene has minimal antiestrogenic effect in the uterus in premenopausal women.<sup>[28]</sup> This may possibly be due to inadequate tissue exposure of the uterus to raloxifene in these estrogen-rich individuals.<sup>[28]</sup>

In premenopausal women, raloxifene increases levels of follicle-stimulating hormone (FSH) and estradiol.<sup>[11]</sup> Conversely, in postmenopausal women, raloxifene has been found to reduce levels of the gonadotropins, luteinizing hormone (LH) and FSH, while not affecting levels of estradiol.<sup>[11][28]</sup> Raloxifene also decreases prolactin levels in postmenopausal women.<sup>[28]</sup> In men, raloxifene has been found to disinhibit the hypothalamic–pituitary–gonadal axis (HPG axis) and thereby increase total testosterone levels.<sup>[29][30][31][32]</sup> Due to the simultaneous increase in sex hormone-binding globulin (SHBG) levels however, free testosterone levels often remain unchanged in men during therapy with raloxifene.<sup>[29]</sup>

Raloxifene has estrogenic effects on liver protein synthesis.<sup>[11]</sup> It increases SHBG levels in both pre- and postmenopausal women as well as in men.<sup>[11][29]</sup> The medication decreases levels of total and low-density lipoprotein (LDL) cholesterol, C-reactive protein, apolipoprotein B, and homocysteine.<sup>[11][28]</sup>

Conversely, it has little effect on levels of triglycerides and high-density lipoprotein (HDL).<sup>[11]</sup> Raloxifene has been shown to inhibit the oxidation of LDL cholesterol *in vitro*.<sup>[15]</sup> The medication has been found to decrease insulin-like growth factor 1 (IGF-1) levels in pre- and postmenopausal women as well as in men.<sup>[30]</sup> It has also been found to increase insulin-like growth factor binding protein 3 (IGFBP-3) levels in pre- and postmenopausal women.<sup>[11]</sup> Due to activation of estrogen receptors in the liver, raloxifene has procoagulatory effects, such as decreasing levels of fibrinogen and influencing levels of other coagulation factors.<sup>[11][28][15]</sup> For these reasons, raloxifene increases the risk of thrombosis.<sup>[11][28]</sup>

	<a href="https://pubchem.ncbi.nlm.nih.gov/compound/inspact/ChEMBL81">dex.php/compound/inspact/ChEMBL81</a> ) ✓
<b>PDB ligand</b>	RAL (PDBe ( <a href="https://www.ebi.ac.uk/pdbe-srv/PDBeXplore/ligand/?ligand=RAL">https://www.ebi.ac.uk/pdbe-srv/PDBeXplore/ligand/?ligand=RAL</a> ), RCSB PDB ( <a href="https://www.rcsb.org/ligand/RAL">https://www.rcsb.org/ligand/RAL</a> ))
<b>CompTox Dashboard</b> (EPA)	DTXSID3023550 ( <a href="https://comptox.epa.gov/dashboard/chemical/details/DTXSID3023550">https://comptox.epa.gov/dashboard/chemical/details/DTXSID3023550</a> )
<b>ECHA InfoCard</b>	100.212.655 ( <a href="https://echa.europa.eu/substance-information/-/substanceinfo/100.212.655">https://echa.europa.eu/substance-information/-/substanceinfo/100.212.655</a> )
<b>Chemical and physical data</b>	
<b>Formula</b>	C <sub>28</sub> H <sub>27</sub> NO <sub>4</sub> S
<b>Molar mass</b>	473.59 g·mol <sup>−1</sup>
<b>3D model (JSmol)</b>	Interactive image ( <a href="http://chemapps.stolaf.edu/jmol/jmol.php?model=O%3DC%28c1c3ccc%28O%29cc3sc1c2ccc%28O%29cc2%29c5ccc%28OCCN4CCCC4%29cc5">http://chemapps.stolaf.edu/jmol/jmol.php?model=O%3DC%28c1c3ccc%28O%29cc3sc1c2ccc%28O%29cc2%29c5ccc%28OCCN4CCCC4%29cc5</a> )
<b>SMILES</b>	<chem>O=C(c1c3ccc(O)cc3sc1c2ccc(O)cc2)c5ccc(OCCN4CCCC4)cc5</chem>
<b>InChI</b>	InChI=1S/C28H27NO4S/c30-21-8-4-20(5-9-21)28-26(24-13-10-22(31)18-25(24)34-28)27(32)19-6-11-23(12-7-19)33-17-16-29-14-2-1-3-15-29/h4-13,18,30-31H,1-3,14-17H2 ✓
	Key:GZUITABIAKMVPG-UHFFFAOYSA-N ✓
	(verify)

Raloxifene increases bone mineral density in postmenopausal women but decreases it in premenopausal women.<sup>[11]</sup> In the MORE trial, the risk of vertebral fractures was decreased by 30%, and bone mineral density was increased in the spine (by 2.1% at 60 mg, 2.4% at 120 mg) and femoral neck (2.6% at 60 mg, 2.7% at 120 mg).<sup>[17]</sup> It has been found to possess estrogenic effects in adipose tissue in postmenopausal women, promoting a shift from an android fat distribution to a gynoid fat distribution.<sup>[33][34]</sup> The medication has been found to increase levels of leptin, an adipokine.<sup>[11]</sup>

Tissue-specific estrogenic and antiestrogenic activity of SERMs

Medication	Breast	Bone	Liver				Uterus	Vagina	Brain	
			Lipids	Coagulation	SHBG	IGF-1			Hot flashes	Gonadotropins
Estradiol	+	+	+	+	+	+	+	+	+	
"Ideal SERM"	-	+	+	±	±	±	-	+	±	
Bazedoxifene	-	+	+	+	+	?	-	±	?	
Clomifene	-	+	+	?	+	+	-	?	±	
Lasofoxifene	-	+	+	+	?	?	±	±	?	
Ospemifene	-	+	+	+	+	+	±	±	±	
Raloxifene	-	+	+	+	+	+	±	-	±	
Tamoxifen	-	+	+	+	+	+	+	-	±	
Toremifene	-	+	+	+	+	+	+	-	±	

**Effect:** + = Estrogenic / agonistic. ± = Mixed or neutral. - = Antiestrogenic / antagonistic. **Note:** SERMs generally increase gonadotropin levels in hypogonadal and eugonadal men as well as premenopausal women (antiestrogenic) but decrease gonadotropin levels in postmenopausal women (estrogenic). **Sources:** See template.

## Pharmacokinetics

### Absorption

The absorption of raloxifene is approximately 60%.<sup>[1][2]</sup> However, due to extensive first-pass metabolism, the absolute bioavailability of raloxifene is only 2.0%.<sup>[1][2]</sup> Raloxifene is rapidly absorbed from the intestines upon oral administration.<sup>[1]</sup> Peak plasma levels of raloxifene occur 0.5 to 6 hours after an oral dose.<sup>[1][2]</sup> In healthy postmenopausal women treated with 60 mg/day raloxifene, peak circulating raloxifene levels normalized by dose and body weight were (i.e., divided by (mg/kg)), 0.50 ng/mL (500 pg/mL) after a single dose and 1.36 ng/mL (1,360 pg/mL after multiple doses).<sup>[13]</sup>

### Distribution

Raloxifene is widely distributed throughout the body.<sup>[1]</sup> There is extensive distribution of raloxifene into the liver, serum, lungs, and kidneys.<sup>[1]</sup> The volume of distribution of raloxifene with a single 30 to 150 mg oral dose is approximately 2348 L/kg, which corresponds to ~170,000 L for a 72 kg person.<sup>[1][35]</sup> Both raloxifene and its glucuronide metabolites show high plasma protein binding (>95%), including to both albumin and α<sub>1</sub> acid glycoprotein, but not to sex hormone-binding globulin.<sup>[1][2]</sup> More specifically, raloxifene is 98.2 ± 0.4% bound to plasma proteins.<sup>[36]</sup>

### Metabolism



Raloxifene is metabolized in the liver and undergoes enterohepatic recycling.<sup>[2]</sup> It is metabolized exclusively by glucuronidation and is not metabolized by the cytochrome P450 system.<sup>[1][2]</sup> Less than 1% of radiolabeled material in plasma comprises unconjugated raloxifene.<sup>[2]</sup> The metabolites of raloxifene include several glucuronides.<sup>[1]</sup> The elimination half-life of raloxifene after a single dose is 27.7 hours (1.2 days), whereas its half-life at steady state at a dosage of 60 mg/day is 15.8 to 86.6 hours (0.7–3.6 days), with an average of 32.5 hours (1.4 days).<sup>[1][2][13]</sup> The extended half-life of raloxifene is attributed to enterohepatic recirculation and its high plasma protein binding.<sup>[1]</sup> Raloxifene and its glucuronide conjugates are interconverted by reversible metabolism and enterohepatic recycling, which prolongs the elimination half-life of raloxifene with oral administration.<sup>[2]</sup> The medication is deconjugated into its active form in a variety of tissues, including liver, lungs, spleen, bone, uterus, and kidneys.<sup>[1]</sup>

## Elimination

Raloxifene is mainly excreted in bile and is eliminated in feces.<sup>[1][2]</sup> Less than 0.2% of a dose is excreted unchanged in urine and less than 6% of a dose is excreted in urine as glucuronide conjugates.<sup>[2]</sup>

## Chemistry

---

Raloxifene hydrochloride has the empirical formula  $C_{28}H_{27}NO_4S \cdot HCl$ , which corresponds to a molecular weight of 510.05 g/mol. Raloxifene hydrochloride is an off-white to pale-yellow solid that is slightly soluble in water.<sup>[13]</sup>

Raloxifene is a benzothiophene derivative and is structurally distinct from the triphenylethylene SERMs like tamoxifen, clomifene, and toremifene.<sup>[37]</sup> It is the only benzothiophene SERM to have been marketed.<sup>[37]</sup> A benzothiophene SERM that was not marketed is arzoifene (LY-353381).<sup>[38]</sup> Bazedoxifene (Duavee, Viviant) and pipendoxifene (ERA-923) are structurally related to raloxifene but are technically not benzothiophenes and instead are indoles.<sup>[38]</sup>

## History

---

Raloxifene was approved in the United States for the prevention of postmenopausal osteoporosis in 1997, the treatment of postmenopausal osteoporosis in 1999, and to prevent or reduce the risk of breast cancer in certain postmenopausal women in 2007.<sup>[39][40][41][42]</sup> It received orphan designation in 2005.<sup>[39]</sup>

## Society and culture

---

### Names

*Raloxifene* is the generic name of the drug and its INN and BAN, while *raloxifène* is its DCF and *raloxifene hydrochloride* is its USAN, BANM, and JAN.<sup>[43][44][45][46]</sup> It has also been known by the name *keoxifene*.<sup>[43][44][46]</sup>

Raloxifene is sold mainly under the brand name Evista and to a lesser extent the brand name Optruma.<sup>[46][44]</sup> It is also sold under a variety of other brand names in various countries.<sup>[46]</sup>

### Availability

Raloxifene is available widely throughout the world, including in the United States, Canada, the United Kingdom, Ireland, elsewhere throughout Europe, Australia, New Zealand, South Africa, Latin America, Southern, Eastern, and Southeastern Asia, and elsewhere in the world such as in Israel and Egypt.<sup>[46][44]</sup>

Raloxifene is provided in the form of 60 mg oral tablets.<sup>[9]</sup>

## Controversy

An editorial in Lancet Oncology criticized the way that research about the medication for breast cancer prevention was released.<sup>[47]</sup>

## Research

Clinical studies of raloxifene for metastatic breast cancer in women have been conducted but found little effectiveness at 60 mg/day in those previously treated with tamoxifen, though modest effectiveness has been observed at higher doses.<sup>[11][48]</sup> In contrast to tamoxifen, raloxifene is not approved for the treatment of breast cancer.<sup>[49]</sup>

Raloxifene has been studied in men for a variety of uses, such as for treatment of schizophrenia, prostate cancer, and osteoporosis.<sup>[50][51][52][53][54][32][31][55][56][57][58]</sup> It has been studied in combination with castration and bicalutamide, a nonsteroidal antiandrogen, for the treatment of prostate cancer.<sup>[58][55]</sup>

Raloxifene has been studied as an adjunct in the treatment of schizophrenia in postmenopausal women.<sup>[59]</sup> A 2017 meta-analysis concluded that it was safe and effective for this indication, although further studies with larger sample sizes are needed for confirmation.<sup>[59]</sup> It may be effective in women with less severe symptoms.<sup>[59]</sup>

A tissue-selective estrogen-receptor complex (TSEC) of estradiol and raloxifene has been studied in postmenopausal women.<sup>[60]</sup>

Raloxifene (60 mg/day) was reported to be effective in the treatment of pubertal gynecomastia in adolescent boys in a small retrospective chart review.<sup>[61][62][63]</sup> Other SERMs are also known to be effective in the treatment of gynecomastia.<sup>[64]</sup>

Raloxifene has been reported to augment the antidepressant effects of selective serotonin reuptake inhibitors (SSRIs).<sup>[65]</sup>

June 18th 2020, Exscalate4CoV (<https://www.exscalate4cov.eu>), the private-public consortium supported by the EU's Horizon 2020 programme for research and innovation, led by Dompé farmaceutici (<https://www.dompe.com>) and currently representing 18 partners (including Fraunhofer Institute (<http://www.ime.fraunhofer.de>), CINECA (<https://www.cineca.it>), Chelonia Applied Science (<https://www.chelonia.swiss>), Swiss Institute of Bioinformatics (<https://www.sib.swiss>) and others) has requested access to clinical trials for the use of Raloxifene in Covid 19 patients. Raloxifene, already proven effective against Mers and Sars in preclinical tests, has been indicated as effective against Sars-Cov2 by the "in-silico" research conducted by the consortium which has shown efficacy in countering the replication of the virus in cells. The IP for its use against Sars-Cov2 has already been protected on May 6 2020 in the name Dompé farmaceutici, Fraunhofer Institute and KU Leuven, to facilitate the largest possible access. Raloxifene would be used in mildly symptomatic Covid19 patients to halt the spread of infection. This result emerged from the first virtual (in silico) screening conducted on the Consortium's supercomputers



A bottle of raloxifene.

of more than 400.000 molecules (safe-in-man drugs and natural products) made available by Dompé farmaceutici and the partner Fraunhofer (IME) to the Consortium. The molecules were prioritized if in clinical stage or already on the market. 7.000 molecules with certain promising characteristics were tested.

## References

---

1. Morello, Karla C.; Wurz, Gregory T.; DeGregorio, Michael W. (2003). "Pharmacokinetics of Selective Estrogen Receptor Modulators". *Clinical Pharmacokinetics*. **42** (4): 361–372. doi:10.2165/00003088-200342040-00004 (<https://doi.org/10.2165%2F00003088-200342040-00004>). ISSN 0312-5963 (<http://www.worldcat.org/issn/0312-5963>). PMID 12648026 (<https://pubmed.ncbi.nlm.nih.gov/12648026>). S2CID 13003168 (<https://api.semanticscholar.org/CorpusID:13003168>).
2. Hochner-Celnikier D (1999). "Pharmacokinetics of raloxifene and its clinical application". *Eur. J. Obstet. Gynecol. Reprod. Biol.* **85** (1): 23–9. doi:10.1016/s0301-2115(98)00278-4 (<https://doi.org/10.1016%2Fs0301-2115%2898%2900278-4>). PMID 10428318 (<https://pubmed.ncbi.nlm.nih.gov/10428318>).
3. Jeong, Eun Ju; Liu, Yong; Lin, Huimin; Hu, Ming (2005-03-15). "Species- and Disposition Model-Dependent Metabolism of Raloxifene in Gut and Liver: Role of UGT1A10". *Drug Metabolism and Disposition*. ASPET. **33** (6): 785–794. doi:10.1124/dmd.104.001883 (<https://doi.org/10.1124%2Fdmd.104.001883>). PMID 15769887 (<https://pubmed.ncbi.nlm.nih.gov/15769887>). S2CID 24273998 (<https://api.semanticscholar.org/CorpusID:24273998>).
4. "Raloxifene Hydrochloride Monograph for Professionals" (<https://www.drugs.com/monograph/raloxifene-hydrochloride.html>). *Drugs.com*. American Society of Health-System Pharmacists. Retrieved 22 March 2019.
5. Yang, Z. D.; Yu, J.; Zhang, Q. (August 2013). "Effects of raloxifene on cognition, mental health, sleep and sexual function in menopausal women: a systematic review of randomized controlled trials". *Maturitas*. **75** (4): 341–348. doi:10.1016/j.maturitas.2013.05.010 (<https://doi.org/10.1016%2Fj.maturitas.2013.05.010>). ISSN 1873-4111 (<https://www.worldcat.org/issn/1873-4111>). PMID 23764354 (<https://pubmed.ncbi.nlm.nih.gov/23764354>).
6. *British national formulary : BNF 76* (76 ed.). Pharmaceutical Press. 2018. pp. 736–737. ISBN 9780857113382.
7. "Raloxifene Hydrochloride - Drug Usage Statistics" (<https://clincalc.com/DrugStats/Drugs/RaloxifeneHydrochloride>). *ClinCalc*. Retrieved 11 April 2020.
8. "Raloxifene: MedlinePlus Drug Information" (<https://medlineplus.gov/druginfo/meds/a698007.html>). *medlineplus.gov*. Retrieved 2018-11-07.
9. Mosby (5 March 2013). *Mosby's Drug Reference for Health Professions - E-Book* (<https://books.google.com/books?id=41z07XtCfa0C&pg=PA1379>). Elsevier Health Sciences. pp. 1379–. ISBN 978-0-323-18760-2.
10. Ohta, Hiroaki; Hamaya, Etsuro; Taketsuna, Masanori; Sowa, Hideaki (January 2015). "Quality of life in Japanese women with postmenopausal osteoporosis treated with raloxifene and vitamin D: post hoc analysis of a postmarketing study". *Current Medical Research and Opinion*. **31** (1): 85–94. doi:10.1185/03007995.2014.975339 (<https://doi.org/10.1185%2F03007995.2014.975339>). ISSN 1473-4877 (<https://www.worldcat.org/issn/1473-4877>). PMID 25299349 (<https://pubmed.ncbi.nlm.nih.gov/25299349>). S2CID 24671531 (<https://api.semanticscholar.org/CorpusID:24671531>).
11. Fabian CJ, Kimler BF (March 2005). "Selective estrogen-receptor modulators for primary prevention of breast cancer". *J. Clin. Oncol.* **23** (8): 1644–55. doi:10.1200/JCO.2005.11.005 (<https://doi.org/10.1200%2FJCO.2005.11.005>). PMID 15755972 (<https://pubmed.ncbi.nlm.nih.gov/15755972>).
12. Kirby I. Bland; Edward M. Copeland; V. Suzanne Klimberg; William J Gradishar (29 June 2017). *The Breast E-Book: Comprehensive Management of Benign and Malignant Diseases* (<https://books.google.com/books?id=hJwqDwAAQBAJ&pg=PA231>). Elsevier Health Sciences. pp. 231–. ISBN 978-0-323-51187-2.



13. [Raloxifene label \(http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2007/022042lbl.pdf\)](http://www.accessdata.fda.gov/drugsatfda_docs/label/2007/022042lbl.pdf) Last updated 09/2007]
14. Gizzo S, Saccardi C, Patrelli TS, Berretta R, Capobianco G, Di Gangi S, Vacilotto A, Bertocco A, Noventa M, Ancona E, D'Antona D, Nardelli GB (2013). "Update on raloxifene: mechanism of action, clinical efficacy, adverse effects, and contraindications". *Obstet Gynecol Surv.* **68** (6): 467–81. doi:10.1097/OGX.0b013e31828baef9 (<https://doi.org/10.1097%2FOGX.0b013e31828baef9>). PMID 23942473 (<https://pubmed.ncbi.nlm.nih.gov/23942473>). S2CID 9003157 (<https://api.semanticscholar.org/CorpusID:9003157>).
15. Goldstein, S. R. (2000). "A pharmacological review of selective oestrogen receptor modulators" (<https://doi.org/10.1093%2Fhumupd%2F6.3.212>). *Human Reproduction Update.* **6** (3): 212–224. doi:10.1093/humupd/6.3.212 (<https://doi.org/10.1093%2Fhumupd%2F6.3.212>). ISSN 1355-4786 (<https://www.worldcat.org/issn/1355-4786>). PMID 10874566 (<https://pubmed.ncbi.nlm.nih.gov/10874566>).
16. Seeman E (2001). "Raloxifene". *J. Bone Miner. Metab.* **19** (2): 65–75. doi:10.1007/s007740170043 (<https://doi.org/10.1007%2Fs007740170043>). PMID 11281162 (<https://pubmed.ncbi.nlm.nih.gov/11281162>).
17. Park, W (2002). "Selective estrogen receptor modulators (SERMS) and their roles in breast cancer prevention". *Trends in Molecular Medicine.* **8** (2): 82–88. doi:10.1016/S1471-4914(02)02282-7 (<https://doi.org/10.1016%2FS1471-4914%2802%2902282-7>). ISSN 1471-4914 (<https://www.worldcat.org/issn/1471-4914>). PMID 11815274 (<https://pubmed.ncbi.nlm.nih.gov/11815274>).
18. Agency for Healthcare Research and Quality, Rockville, MD. (September 2009). "Medications Effective in Reducing Risk of Breast Cancer But Increase Risk of Adverse Effects" (<https://archive.ahrq.gov/news/newsroom/press-releases/2009/brcanmed.html>). Retrieved 2009-09-14.
19. Lemmo, W (2016). "Anti-Estrogen Withdrawal Effect With Raloxifene? A Case Report" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5739193>). *Integrative Cancer Therapies.* Published Online Before Print July 13 (3): 245–249. doi:10.1177/1534735416658954 (<https://doi.org/10.1177%2F1534735416658954>). PMC 5739193 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5739193>). PMID 27411856 (<https://pubmed.ncbi.nlm.nih.gov/27411856>).
20. Haskell, Sally G. (2003). "Selective Estrogen Receptor Modulators". *Southern Medical Journal.* **96** (5): 469–476. doi:10.1097/01.SMJ.0000051146.93190.4A (<https://doi.org/10.1097%2F01.SMJ.0000051146.93190.4A>). ISSN 0038-4348 (<https://www.worldcat.org/issn/0038-4348>). PMID 12911186 (<https://pubmed.ncbi.nlm.nih.gov/12911186>). S2CID 40607634 (<https://api.semanticscholar.org/CorpusID:40607634>).
21. Weatherman, Ross V; Clegg, Nicola J; Scanlan, Thomas S (2001). "Differential SERM activation of the estrogen receptors (ER $\alpha$  and ER $\beta$ ) at AP-1 sites" (<https://doi.org/10.1016%2FS1074-5521%2801%2900025-4>). *Chemistry & Biology.* **8** (5): 427–436. doi:10.1016/S1074-5521(01)00025-4 ([https://doi.org/10.1016%2FS1074-5521\(01\)00025-4](https://doi.org/10.1016%2FS1074-5521(01)00025-4)). ISSN 1074-5521 (<https://www.worldcat.org/issn/1074-5521>). PMID 11358690 (<https://pubmed.ncbi.nlm.nih.gov/11358690>).
22. Escande A, Pillon A, Servant N, Cravedi JP, Larrea F, Muhn P, Nicolas JC, Cavallès V, Balaguer P (May 2006). "Evaluation of ligand selectivity using reporter cell lines stably expressing estrogen receptor alpha or beta". *Biochem. Pharmacol.* **71** (10): 1459–69. doi:10.1016/j.bcp.2006.02.002 (<https://doi.org/10.1016%2Fj.bcp.2006.02.002>). PMID 16554039 (<https://pubmed.ncbi.nlm.nih.gov/16554039>).
23. Greene, G. L.; Shiau, A. K.; Nettles, K. W. (2004). "A Structural Explanation for ER $\alpha$ /ER $\beta$  SERM Discrimination". *New Molecular Mechanisms of Estrogen Action and Their Impact on Future Perspectives in Estrogen Therapy* (46): 33–45. doi:10.1007/978-3-662-05386-7\_3 ([https://doi.org/10.1007%2F978-3-662-05386-7\\_3](https://doi.org/10.1007%2F978-3-662-05386-7_3)). ISBN 978-3-662-05388-1. PMID 15248503 (<https://pubmed.ncbi.nlm.nih.gov/15248503>).

24. Barkhem, Tomas; Carlsson, Bo; Nilsson, Yvonne; Enmark, Eva; Gustafsson, Jan-Åke; Nilsson, Stefan (1998). "Differential Response of Estrogen Receptor  $\alpha$  and Estrogen Receptor  $\beta$  to Partial Estrogen Agonists/Antagonists". *Molecular Pharmacology*. **54** (1): 105–112. doi:10.1124/mol.54.1.105 (https://doi.org/10.1124%2Fmol.54.1.105). ISSN 0026-895X (https://www.worldcat.org/issn/0026-895X). PMID 9658195 (https://pubmed.ncbi.nlm.nih.gov/9658195).
25. Prossnitz ER, Arterburn JB (July 2015). "International Union of Basic and Clinical Pharmacology. XCVII. G Protein-Coupled Estrogen Receptor and Its Pharmacologic Modulators" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4485017). *Pharmacol. Rev.* **67** (3): 505–40. doi:10.1124/pr.114.009712 (https://doi.org/10.1124%2Fpr.114.009712). PMC 4485017 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4485017). PMID 26023144 (https://pubmed.ncbi.nlm.nih.gov/26023144).
26. Petrie WK, Dennis MK, Hu C, Dai D, Arterburn JB, Smith HO, Hathaway HJ, Prossnitz ER (2013). "G protein-coupled estrogen receptor-selective ligands modulate endometrial tumor growth" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3863501). *Obstet Gynecol Int.* **2013**: 472720. doi:10.1155/2013/472720 (https://doi.org/10.1155%2F2013%2F472720). PMC 3863501 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3863501). PMID 24379833 (https://pubmed.ncbi.nlm.nih.gov/24379833).
27. Jeon-Hor, Chen; et al. (September 15, 2003). "Reduction of Breast Density Following Tamoxifen Treatment Evaluated by 3-D MRI: Preliminary Study" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3005955). *Magn Reson Imaging*. **29** (1): 91–8. doi:10.1016/j.mri.2010.07.009 (https://doi.org/10.1016%2Fj.mri.2010.07.009). PMC 3005955 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3005955). PMID 20832226 (https://pubmed.ncbi.nlm.nih.gov/20832226).
28. Draper, Michael W.; Chin, William W. (2003). "Molecular and Clinical Evidence for the Unique Nature of Individual Selective Estrogen Receptor Modulators". *Clinical Obstetrics and Gynecology*. **46** (2): 265–297. doi:10.1097/00003081-200306000-00008 (https://doi.org/10.1097%2F00003081-200306000-00008). ISSN 0009-9201 (https://www.worldcat.org/issn/0009-9201). PMID 12808380 (https://pubmed.ncbi.nlm.nih.gov/12808380). S2CID 5132467 (https://api.semanticscholar.org/CorpusID:5132467).
29. Corona G, Rastrelli G, Rattelli G, Maggi M (February 2015). "The pharmacotherapy of male hypogonadism besides androgens". *Expert Opin Pharmacother.* **16** (3): 369–87. doi:10.1517/14656566.2015.993607 (https://doi.org/10.1517%2F14656566.2015.993607). PMID 25523084 (https://pubmed.ncbi.nlm.nih.gov/25523084). S2CID 8891640 (https://api.semanticscholar.org/CorpusID:8891640).
30. Duarte FH, Jallad RS, Bronstein MD (November 2016). "Estrogens and selective estrogen receptor modulators in acromegaly". *Endocrine*. **54** (2): 306–314. doi:10.1007/s12020-016-1118-z (https://doi.org/10.1007%2Fs12020-016-1118-z). PMID 27704479 (https://pubmed.ncbi.nlm.nih.gov/27704479). S2CID 10136018 (https://api.semanticscholar.org/CorpusID:10136018).
31. Birzniece V, Sutanto S, Ho KK (April 2012). "Gender difference in the neuroendocrine regulation of growth hormone axis by selective estrogen receptor modulators" (https://doi.org/10.1210%2Fjc.2011-3347). *J. Clin. Endocrinol. Metab.* **97** (4): E521–7. doi:10.1210/jc.2011-3347 (https://doi.org/10.1210%2Fjc.2011-3347). PMID 22319035 (https://pubmed.ncbi.nlm.nih.gov/22319035).
32. Uebelhart B, Herrmann F, Pavo I, Draper MW, Rizzoli R (September 2004). "Raloxifene treatment is associated with increased serum estradiol and decreased bone remodeling in healthy middle-aged men with low sex hormone levels". *J. Bone Miner. Res.* **19** (9): 1518–24. doi:10.1359/JBMR.040503 (https://doi.org/10.1359%2FJBMR.040503). PMID 15312253 (https://pubmed.ncbi.nlm.nih.gov/15312253). S2CID 36104038 (https://api.semanticscholar.org/CorpusID:36104038).
33. Xu, Beibei; Lovre, Dragana; Mauvais-Jarvis, Franck (2016). "Effect of selective estrogen receptor modulators on metabolic homeostasis". *Biochimie*. **124**: 92–97. doi:10.1016/j.biochi.2015.06.018 (https://doi.org/10.1016%2Fj.biochi.2015.06.018). ISSN 0300-9084 (https://www.worldcat.org/issn/0300-9084). PMID 26133657 (https://pubmed.ncbi.nlm.nih.gov/26133657). "In healthy postmenopausal women, raloxifene treatment for one year prevented body weight gain and abdominal adiposity by promoting a shift from an android to gynoid fat distribution [46]."

34. Francucci, C. M.; Pantaleo, D.; Iori, N.; Camilletti, A.; Massi, F.; Boscaro, M. (2014). "Effects of raloxifene on body fat distribution and lipid profile in healthy post-menopausal women". *Journal of Endocrinological Investigation*. **28** (9): 623–631. doi:10.1007/BF03347261 (https://doi.org/10.1007%2FBF03347261). ISSN 0391-4097 (https://www.worldcat.org/issn/0391-4097). PMID 16218045 (https://pubmed.ncbi.nlm.nih.gov/16218045). S2CID 28467435 (https://api.semanticscholar.org/CorpusID:28467435). "These results [...] suggest, for the first time, that RLX promotes the shift from android to gynoid fat distribution, and prevents the uptrend of abdominal adiposity and body weight compared with untreated women."
35. Snyder KR, Sparano N, Malinowski JM (September 2000). "Raloxifene hydrochloride". *Am J Health Syst Pharm*. **57** (18): 1669–75, quiz 1676–8. doi:10.1093/ajhp/57.18.1669 (https://doi.org/10.1093%2Fajhp%2F57.18.1669). PMID 11006795 (https://pubmed.ncbi.nlm.nih.gov/11006795).
36. Miller JW, Skerjanec A, Knadler MP, Ghosh A, Allerheiligen SR (July 2001). "Divergent effects of raloxifene HCl on the pharmacokinetics and pharmacodynamics of warfarin". *Pharm Res*. **18** (7): 1024–8. doi:10.1023/a:1010904815275 (https://doi.org/10.1023%2Fa%3A1010904815275). PMID 11496940 (https://pubmed.ncbi.nlm.nih.gov/11496940). S2CID 1713984 (https://api.semanticscholar.org/CorpusID:1713984).
37. Eric S. Orwoll; Michael Bliziotes (2 August 2002). *Osteoporosis: Pathophysiology and Clinical Management* (https://books.google.com/books?id=iX31BwAAQBAJ&pg=PA320). Springer Science & Business Media. pp. 320–. ISBN 978-1-59259-278-4.
38. Stuart Silverman; Bo Abrahamsen (29 December 2015). *The Duration and Safety of Osteoporosis Treatment: Anabolic and Antiresorptive Therapy* (https://books.google.com/books?id=5bFPCwAAQBAJ&pg=PA24). Springer. pp. 24–. ISBN 978-3-319-23639-1.
39. Institute of Medicine; Board on Health Sciences Policy; Committee on Accelerating Rare Diseases Research and Orphan Product Development (3 April 2011). *Rare Diseases and Orphan Products: Accelerating Research and Development* (https://books.google.com/books?id=HnYyeNIY3WwC&pg=PT113). National Academies Press. pp. 113–. ISBN 978-0-309-15806-0. {{cite book}}: |author2= has generic name (help)
40. *Reducing Breast Cancer Risk with Drugs* (https://books.google.com/books?id=jpNsg\_Sx2wMC&pg=PA10). Am Cncl on Science, Health. pp. 10–. GGKEY:CBEALLAHP8W.
41. Sydney Lou Bonnicks (10 November 2007). *Bone Densitometry for Technologists* (https://books.google.com/books?id=0NGsgFaf\_9QC&pg=PA277). Springer Science & Business Media. pp. 277–. ISBN 978-1-59259-992-9.
42. Jie Jack Li; Douglas S. Johnson (27 March 2013). *Modern Drug Synthesis* (https://books.google.com/books?id=NtdT5maa\_pMC&pg=RA2-PA73). John Wiley & Sons. pp. 2–. ISBN 978-1-118-70124-9.
43. J. Elks (14 November 2014). *The Dictionary of Drugs: Chemical Data: Chemical Data, Structures and Bibliographies* (https://books.google.com/books?id=0vXTBwAAQBAJ&pg=PA1063). Springer. pp. 1063–. ISBN 978-1-4757-2085-3.
44. *Index Nominum 2000: International Drug Directory* (https://books.google.com/books?id=5GpcTQD\_L2oC&pg=PA909). Taylor & Francis. 2000. pp. 909–. ISBN 978-3-88763-075-1.
45. I.K. Morton; Judith M. Hall (31 October 1999). *Concise Dictionary of Pharmacological Agents: Properties and Synonyms* (https://books.google.com/books?id=mqaOMOt61IC&pg=PA245). Springer Science & Business Media. pp. 245–. ISBN 978-0-7514-0499-9.
46. "Raloxifene" (https://www.drugs.com/international/raloxifene.html).
47. Thelancetoncology (2006). "A STARring role for raloxifene?". *Lancet Oncol*. **7** (6): 443. doi:10.1016/S1470-2045(06)70701-X (https://doi.org/10.1016%2FS1470-2045%2806%2970701-X). PMID 16750489 (https://pubmed.ncbi.nlm.nih.gov/16750489).
48. Provinciali N, Suen C, Dunn BK, DeCensi A (October 2016). "Raloxifene hydrochloride for breast cancer risk reduction in postmenopausal women". *Expert Rev Clin Pharmacol*. **9** (10): 1263–1272. doi:10.1080/17512433.2016.1231575 (https://doi.org/10.1080%2F17512433.2016.1231575). PMID 27583816 (https://pubmed.ncbi.nlm.nih.gov/27583816). S2CID 26047863 (https://api.semanticscholar.org/CorpusID:26047863).

49. James F. Holland; Raphael E. Pollock (2010). *Holland-Frei Cancer Medicine 8* (<https://books.google.com/books?id=R0FbhLsWHBEC&pg=PA743>). PMPH-USA. pp. 743–. ISBN 978-1-60795-014-1.
50. Blum A, Hathaway L, Mincemoyer R, Schenke WH, Csako G, Waclawiw MA, Panza JA, Cannon RO (2000). "Hormonal, lipoprotein, and vascular effects of the selective estrogen receptor modulator raloxifene in hypercholesterolemic men". *Am. J. Cardiol.* **85** (12): 1491–4, A7. doi:10.1016/s0002-9149(00)00802-x (<https://doi.org/10.1016%2Fs0002-9149%2800%2900802-x>). PMID 10856400 (<https://pubmed.ncbi.nlm.nih.gov/10856400>).
51. Doran PM, Riggs BL, Atkinson EJ, Khosla S (2001). "Effects of raloxifene, a selective estrogen receptor modulator, on bone turnover markers and serum sex steroid and lipid levels in elderly men" (<https://doi.org/10.1359%2Fjbm.2001.16.11.2118>). *J. Bone Miner. Res.* **16** (11): 2118–25. doi:10.1359/jbm.2001.16.11.2118 (<https://doi.org/10.1359%2Fjbm.2001.16.11.2118>). PMID 11697809 (<https://pubmed.ncbi.nlm.nih.gov/11697809>). S2CID 28216610 (<https://api.semanticscholar.org/CorpusID:28216610>).
52. Dimaraki EV, Symons KV, Barkan AL (2004). "Raloxifene decreases serum IGF-I in male patients with active acromegaly" (<https://doi.org/10.1530%2Feje.0.1500481>). *Eur. J. Endocrinol.* **150** (4): 481–7. doi:10.1530/eje.0.1500481 (<https://doi.org/10.1530%2Feje.0.1500481>). PMID 15080777 (<https://pubmed.ncbi.nlm.nih.gov/15080777>).
53. Duschek EJ, Gooren LJ, Netelenbos C (2004). "Effects of raloxifene on gonadotrophins, sex hormones, bone turnover and lipids in healthy elderly men" (<http://www.eje-online.org/content/150/4/539.full.pdf>) (PDF). *Eur. J. Endocrinol.* **150** (4): 539–46. doi:10.1530/eje.0.1500539 (<https://doi.org/10.1530%2Feje.0.1500539>). PMID 15080785 (<https://pubmed.ncbi.nlm.nih.gov/15080785>).
54. Smith MR, Fallon MA, Lee H, Finkelstein JS (2004). "Raloxifene to prevent gonadotropin-releasing hormone agonist-induced bone loss in men with prostate cancer: a randomized controlled trial" (<https://doi.org/10.1210%2Fjc.2003-032058>). *J. Clin. Endocrinol. Metab.* **89** (8): 3841–6. doi:10.1210/jc.2003-032058 (<https://doi.org/10.1210%2Fjc.2003-032058>). PMID 15292315 (<https://pubmed.ncbi.nlm.nih.gov/15292315>).
55. Ho TH, Nunez-Nateras R, Hou YX, Bryce AH, Northfelt DW, Dueck AC, Wong B, Stanton ML, Joseph RW, Castle EP (2017). "A Study of Combination Bicalutamide and Raloxifene for Patients With Castration-Resistant Prostate Cancer". *Clin Genitourin Cancer.* **15** (2): 196–202.e1. doi:10.1016/j.clgc.2016.08.026 (<https://doi.org/10.1016%2Fj.clgc.2016.08.026>). PMID 27771244 (<https://pubmed.ncbi.nlm.nih.gov/27771244>). S2CID 19043552 (<https://api.semanticscholar.org/CorpusID:19043552>).
56. Khodaie-Ardakani MR, Khosravi M, Zarinfard R, Nejati S, Mohsenian A, Tabrizi M, Akhondzadeh S (2015). "A Placebo-Controlled Study of Raloxifene Added to Risperidone in Men with Chronic Schizophrenia". *Acta Med Iran.* **53** (6): 337–45. PMID 26069170 (<https://pubmed.ncbi.nlm.nih.gov/26069170>).
57. Weickert TW, Weinberg D, Lenroot R, Catts SV, Wells R, Vercammen A, O'Donnell M, Galletly C, Liu D, Balzan R, Short B, Pellen D, Curtis J, Carr VJ, Kulkarni J, Schofield PR, Weickert CS (2015). "Adjunctive raloxifene treatment improves attention and memory in men and women with schizophrenia" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4444978>). *Mol. Psychiatry.* **20** (6): 685–94. doi:10.1038/mp.2015.11 (<https://doi.org/10.1038%2Fmp.2015.11>). PMC 4444978 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4444978>). PMID 25980345 (<https://pubmed.ncbi.nlm.nih.gov/25980345>).
58. Fujimura, Tetsuya; Takayama, Kenichi; Takahashi, Satoru; Inoue, Satoshi (2018). "Estrogen and Androgen Blockade for Advanced Prostate Cancer in the Era of Precision Medicine" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836061>). *Cancers.* **10** (2): 29. doi:10.3390/cancers10020029 (<https://doi.org/10.3390%2Fcancers10020029>). ISSN 2072-6694 (<https://www.worldcat.org/issn/2072-6694>). PMC 5836061 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836061>). PMID 29360794 (<https://pubmed.ncbi.nlm.nih.gov/29360794>).

59. Wang Q, Dong X, Wang Y, Li X (2017). "Raloxifene as an adjunctive treatment for postmenopausal women with schizophrenia: a meta-analysis of randomized controlled trials". *Arch Womens Ment Health*. **21** (1): 31–41. doi:10.1007/s00737-017-0773-2 (<https://doi.org/10.1007%2Fs00737-017-0773-2>). PMID 28849318 (<https://pubmed.ncbi.nlm.nih.gov/28849318>). S2CID 4524617 (<https://api.semanticscholar.org/CorpusID:4524617>).
60. Carneiro AL, de Cassia de Maio Dardes R, Haidar MA (July 2012). "Estrogens plus raloxifene on endometrial safety and menopausal symptoms--semisystematic review". *Menopause*. **19** (7): 830–4. doi:10.1097/gme.0b013e31824a74ce (<https://doi.org/10.1097%2Fgme.0b013e31824a74ce>). PMID 22549172 (<https://pubmed.ncbi.nlm.nih.gov/22549172>). S2CID 196380398 (<https://api.semanticscholar.org/CorpusID:196380398>).
61. Nordt CA, DiVasta AD (2008). "Gynecomastia in adolescents". *Curr. Opin. Pediatr*. **20** (4): 375–82. doi:10.1097/MOP.0b013e328306a07c (<https://doi.org/10.1097%2FMOP.0b013e328306a07c>). PMID 18622190 (<https://pubmed.ncbi.nlm.nih.gov/18622190>). S2CID 205834072 (<https://api.semanticscholar.org/CorpusID:205834072>).
62. Leung KC, Leung AC (2017). "Gynecomastia in Infants, Children, and Adolescents". *Recent Pat Endocr Metab Immune Drug Discov*. **10** (2): 127–137. doi:10.2174/1872214811666170301124033 (<https://doi.org/10.2174%2F1872214811666170301124033>). PMID 28260521 (<https://pubmed.ncbi.nlm.nih.gov/28260521>).
63. Lawrence SE, Faught KA, Vethamuthu J, Lawson ML (July 2004). "Beneficial effects of raloxifene and tamoxifen in the treatment of pubertal gynecomastia". *J. Pediatr*. **145** (1): 71–6. doi:10.1016/j.jpeds.2004.03.057 (<https://doi.org/10.1016%2Fj.jpeds.2004.03.057>). PMID 15238910 (<https://pubmed.ncbi.nlm.nih.gov/15238910>).
64. Kanakis, G. A.; Nordkap, L.; Bang, A. K.; Calogero, A. E.; Bártfai, G.; Corona, G.; Forti, G.; Toppari, J.; Goulis, D. G.; Jørgensen, N. (2019). "EAA clinical practice guidelines—gynecomastia evaluation and management" (<https://doi.org/10.1111%2Fandr.12636>). *Andrology*. **7** (6): 778–793. doi:10.1111/andr.12636 (<https://doi.org/10.1111%2Fandr.12636>). ISSN 2047-2919 (<https://www.worldcat.org/issn/2047-2919>). PMID 31099174 (<https://pubmed.ncbi.nlm.nih.gov/31099174>).
65. Sugiyama, Nobuhiro; Barros, Rodrigo P.A.; Warner, Margaret; Gustafsson, Jan-Åke (2010). "ERβ: recent understanding of estrogen signaling". *Trends in Endocrinology & Metabolism*. **21** (9): 545–552. doi:10.1016/j.tem.2010.05.001 (<https://doi.org/10.1016%2Fj.tem.2010.05.001>). ISSN 1043-2760 (<https://www.worldcat.org/issn/1043-2760>). PMID 20646931 (<https://pubmed.ncbi.nlm.nih.gov/20646931>). S2CID 43001363 (<https://api.semanticscholar.org/CorpusID:43001363>).

## Further reading

- Barrett-Connor E (2001). "Raloxifene: risks and benefits". *Ann N Y Acad Sci*. **949** (1): 295–303. Bibcode:2001NYASA.949..295B (<https://ui.adsabs.harvard.edu/abs/2001NYASA.949..295B>). doi:10.1111/j.1749-6632.2001.tb04036.x (<https://doi.org/10.1111%2Fj.1749-6632.2001.tb04036.x>). PMID 11795366 (<https://pubmed.ncbi.nlm.nih.gov/11795366>). S2CID 41412601 (<https://api.semanticscholar.org/CorpusID:41412601>).
- Heringa M (2003). "Review on raloxifene: profile of a selective estrogen receptor modulator". *Int J Clin Pharmacol Ther*. **41** (8): 331–45. doi:10.5414/cpp41331 (<https://doi.org/10.5414%2Fcpp41331>). PMID 12940590 (<https://pubmed.ncbi.nlm.nih.gov/12940590>).
- Sporn MB, Dowsett SA, Mershon J, Bryant HU (2004). "Role of raloxifene in breast cancer prevention in postmenopausal women: clinical evidence and potential mechanisms of action". *Clin Ther*. **26** (6): 830–40. doi:10.1016/s0149-2918(04)90127-0 (<https://doi.org/10.1016%2Fs0149-2918%2804%2990127-0>). PMID 15262454 (<https://pubmed.ncbi.nlm.nih.gov/15262454>).
- Vogel VG (2009). "The NSABP Study of Tamoxifen and Raloxifene (STAR) trial" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2785111>). *Expert Rev Anticancer Ther*. **9** (1): 51–60. doi:10.1586/14737140.9.1.51 (<https://doi.org/10.1586%2F14737140.9.1.51>). PMC 2785111 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2785111>). PMID 19105706 (<https://pubmed.ncbi.nlm.nih.gov/19105706>).



- Wickerham DL, Costantino JP, Vogel VG, Cronin WM, Cecchini RS, Ford LG, Wolmark N (2009). "The use of tamoxifen and raloxifene for the prevention of breast cancer" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5110043>). *Recent Results Cancer Res.* *Recent Results in Cancer Research.* **181**: 113–9. doi:10.1007/978-3-540-69297-3\_12 ([https://doi.org/10.1007%2F978-3-540-69297-3\\_12](https://doi.org/10.1007%2F978-3-540-69297-3_12)). ISBN 978-3-540-69296-6. PMC 5110043 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5110043>). PMID 19213563 (<https://pubmed.ncbi.nlm.nih.gov/19213563>).
- Vogel VG (2011). "Update on raloxifene: role in reducing the risk of invasive breast cancer in postmenopausal women" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3846694>). *Breast Cancer: Targets and Therapy.* **3**: 127–37. doi:10.2147/BCTT.S11288 (<https://doi.org/10.2147%2FBCTT.S11288>). PMC 3846694 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3846694>). PMID 24367182 (<https://pubmed.ncbi.nlm.nih.gov/24367182>).
- Yang ZD, Yu J, Zhang Q (2013). "Effects of raloxifene on cognition, mental health, sleep and sexual function in menopausal women: a systematic review of randomized controlled trials". *Maturitas.* **75** (4): 341–8. doi:10.1016/j.maturitas.2013.05.010 (<https://doi.org/10.1016%2Fj.maturitas.2013.05.010>). PMID 23764354 (<https://pubmed.ncbi.nlm.nih.gov/23764354>).

## External links

---

- "Raloxifene" (<https://druginfo.nlm.nih.gov/drugportal/name/raloxifene>). *Drug Information Portal.* U.S. National Library of Medicine.
  - "Raloxifene hydrochloride" (<https://druginfo.nlm.nih.gov/drugportal/name/raloxifene%20hydrochloride>). *Drug Information Portal.* U.S. National Library of Medicine.
- 

Retrieved from "<https://en.wikipedia.org/w/index.php?title=Raloxifene&oldid=1079920821>"

---

**This page was last edited on 29 March 2022, at 10:12 (UTC).**

Text is available under the Creative Commons Attribution-ShareAlike License 3.0; additional terms may apply. By using this site, you agree to the Terms of Use and Privacy Policy. Wikipedia® is a registered trademark of the Wikimedia Foundation, Inc., a non-profit organization.