

# What You Should Know About “Designer” Estrogens

**T**o many women, menopause meant the end of potential childbearing, freedom from the inconvenience of menstruation and the possibility of unplanned pregnancy, the beginning of physical decline and aging, or more likely some mixture of these reactions. Today, menopause presents women with a bewildering array of options and decisions. And now there’s a growing media buzz about “designer” estrogens that appear to offer the advantages of ERT/HRT without the risks—or do they?

## What are “designer” estrogens?

“Designer” estrogens, more properly called selective estrogen receptor modulators or SERMs, aren’t really estrogens at all. These drugs are unique because they behave like estrogens in some parts of the body, while having antiestrogen effects on other tissues and organs. The ideal SERM would have estrogen-like effects on the bones, blood vessels, heart, vagina, and urinary tract and anti-estrogen effects on the uterus and breasts—but such a compound remains to be developed. In general, SERMs help build bones like ERT and HRT, but do not increase the risk of breast and endometrial (uterine) cancer as ERT and HRT may do in susceptible women. Indeed, there is evidence that SERMs offer some protection against breast cancer.

Two SERMs marketed in the United States are raloxifene (Evista) and tamoxifen (Nolvadex).

## What are the main effects of raloxifene?

Raloxifene is taken as a tablet once a day, with or without food, and should only be used after menopause. It protects against osteoporosis by slowing bone loss and increasing bone growth, and it can be used as a treatment for women who already have osteoporosis. In addition, raloxifene doesn’t cause vaginal bleeding and breast tenderness, and it doesn’t increase the risk of breast or uterine cancer—all concerns associated with estrogen use. Thus, raloxifene has an estrogen-like effect on bone and an anti-estrogen effect on breast and uterine tissue.

With regard to cardiovascular effects, raloxifene lowers levels of total and low-density lipoprotein (LDL) cholesterol without raising triglycerides—another fatty substance that contributes to heart disease. Unlike estrogen, however, raloxifene doesn’t increase levels of high-density lipoproteins (HDL), a type of cholesterol that may protect the heart. So while raloxifene seems to have a

positive effect on the cardiovascular system overall, we are still waiting for study results to see whether it actually lowers the risk of heart disease.

Women who are using raloxifene shouldn’t take cholesterol-lowering drugs, and should only use blood thinners like warfarin (Coumadin) under close supervision by a doctor. They should also avoid using estrogen in any form, including injections, pills, and patches.

## What are the main effects of tamoxifen?

Tamoxifen is taken twice daily. It is used mainly by women at high risk of breast cancer and by breast cancer patients, and has been shown to reduce the risk of cancer in the unaffected breast by 40%. It opposes the action of estrogen in breast tissue, but actually has an estrogen-like effect on bone—helping to protect against osteoporosis and fractures. Tamoxifen is usually not prescribed for more than 5 years in women who have had breast cancer.

Tamoxifen does affect the cardiovascular system, lowering total and LDL cholesterol levels in the same manner as estrogen. However, a major study showed no effect on the death rate from heart disease, so any cardiovascular benefits remain to be established.

## What are the disadvantages of raloxifene and tamoxifen?

The side effects of raloxifene are usually mild, and may include hot flashes and leg cramps. In rare cases, women may develop blood clots in

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## Designer Estrogens

the veins. You should seek medical care immediately if you have calf pain, leg swelling, sudden chest pain, shortness of breath, a bloody cough, or disturbances in your vision. Tamoxifen may also increase the risk of developing blood clots, and (unlike raloxifene), it can raise the risk of uterine cancer.

The main problem with both raloxifene and tamoxifen is that they don't relieve hot flashes—a major source of distress and sleep disturbances in postmenopausal women that is often accompanied by headache and irritability as well. In addition, neither of these drugs alleviates the vaginal dryness that can lead to discomfort, painful sexual intercourse, and urinary problems that continue to worsen with age.

### Is there any way to address these disadvantages?

There are a number of ways to control hot flashes, but none seems to work quite as well as ERT/HRT. Hot flashes typically stop after 1 or 2 years, though, even without treatment. Medications that can help to reduce hot flashes include the antidepressants venlafaxine (Effexor) and paroxetine (Paxil), the blood pressure drug clonidine (Catapres, Duraclon), and the hormone megestrol (Megace) that is sometimes given to women who have had breast cancer.

Postmenopausal vaginal dryness is caused by a lack of estrogen, which leads to thinning of the vaginal lining. This can be relieved by regular use of vaginal moisturizers like Replens, while the application of water-based lubricants such as Lubrin or Astroglide can facilitate intercourse and enhance sexual pleasure.

Estrogen creams such as Premarin can be applied directly to the vagina, and vaginal estrogen tablets (Vagifem) are also available. The creams or tablets are used daily for 2 or 3 weeks,

### Comparison of Postmenopausal Medication Options\*

	ESTROGEN	RALOXIFENE	TAMOXIFEN
<b>Breast</b>	Stimulates breast tissues	Blocks effects of estrogen on breast tissues	Blocks effects of estrogen on breast tissues
<b>Uterine lining</b>	Increases uterine lining	No effect on uterine lining	Increases uterine lining
<b>Bone</b>	Increases bone mass	Increases bone mass	Slightly increases bone mass
<b>Cholesterol</b>	Increases HDL Decreases LDL	Decreases LDL	Decreases LDL

\*Modified from, Judith A Norris, OB/GYN, RNP. *Productive Times*. OBGYN.net (<http://www.obgyn.net>).

and then once or twice weekly thereafter. These preparations are usually more effective than moisturizers or lubricants for relieving vaginal dryness, urinary incontinence, and frequent urinary tract infections. Another alternative is the vaginal estrogen ring (Estring), which is inserted into the vagina and releases estrogen over a 3-month period.

### Who should consider using SERMs?

Guidelines have yet to be established for the use of raloxifene in postmenopausal women. Obvious candidates are those who cannot use estrogen because of recurrent blood clots, gallbladder disease, liver disease, or a very high risk of breast cancer—especially if they have signs of bone thinning.

Women who have had breast cancer must discuss the use of tamoxifen with their doctors; in general, it's prescribed for patients whose breast cancer was determined to be estrogen dependent. Breast cancer survivors may turn to antidepressants or clonidine for hot flashes. They can safely use vaginal moisturizers and lubricants for dryness, and the vaginal estrogen ring or low-dose estrogen creams are viable options as well.

If you are fearful about using estrogen, you might want to consider taking it for just 1 or 2 years—particularly

if you're experiencing hot flashes and/or vaginal dryness, or if you have been diagnosed with bone thinning. If osteoporosis is still a concern after this period, you can ask your doctor about switching to raloxifene. Certainly, any postmenopausal woman can discuss the use of raloxifene with her doctor, supplemented by other treatments for hot flashes and vaginal dryness as needed. If you have absolutely decided not to use estrogen, raloxifene offers a way to preserve bone health and a good quality of life.

### Who should not use SERMs?

You shouldn't use raloxifene if you're pregnant or can become pregnant, if you have a history of blood clots, if you have limited mobility (that is, if you're in a wheelchair or bedridden for a long time), or if you have liver disease.

Like ERT and HRT, SERMs are presenting postmenopausal women with almost as many questions as answers. But as women continue to have a wide range of symptoms, priorities, concerns, and needs, the development of additional options is always welcome. And remember that you're not committed to any choice for life; if you have problems with one therapy, you can discuss other options with your doctor to find one that is better suited to your requirements.