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Patient information: Medications for the prevention of breast cancer (Beyond the Basics)

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INTRODUCTION

Approximately 210,000 women in the United States are newly diagnosed with breast cancer each year. Certain risk factors may increase the likelihood that a woman will develop breast cancer, including advancing age, a strong family history of breast cancer, and having a precancerous breast condition, such as lobular carcinoma in situ (LCIS).

Based upon a careful risk assessment, healthcare providers sometimes recommend therapy with one of several medications to reduce the chance of developing breast cancer for women at increased risk. These medications are called selective estrogen receptor modulators (SERMs), of which there are two: tamoxifen and raloxifene. Another group of medications, called the aromatase inhibitors (AIs), such as exemestane, are also being studied for breast cancer prevention, though none are approved for this indication.

These medications only work to prevent tumors that are known to be responsive to female hormones, which can be identified by the presence of hormone receptors. Tumors that have hormone receptors are called either ER-positive (short for estrogen receptor-positive) or PR-positive (short for progesterin receptor-positive).

The following is a discussion of studies evaluating the effectiveness of both SERMs and AIs for breast cancer prevention in women without a history of breast cancer, possible adverse effects of treatment, and information about which women should consider taking one of these agents. The role of SERMs and AIs in women with a history of breast cancer is covered separately. (See "[Patient information: Early stage breast cancer treatment in postmenopausal women \(Beyond the Basics\)](#)" and "[Patient information: Early stage breast cancer treatment in premenopausal women \(Beyond the Basics\)](#)".)

HOW DO PREVENTIVE AGENTS WORK?

The preventive agents all work by interfering with the effects of the female hormone estrogen. Selective estrogen receptor modulators (SERMs) work by blocking the effects of estrogen on breast tissue. Aromatase inhibitors (AIs) work by blocking an enzyme (aromatase) that is responsible for producing estrogen within the body in postmenopausal women (or women after menopause).

EFFECTIVENESS

SERMs

Tamoxifen — Multiple studies have examined the effectiveness of tamoxifen for the prevention of breast cancer. Overall, these studies suggest that tamoxifen can prevent hormone-positive breast cancers from developing in women at risk for the disease. In general, tamoxifen, given daily for five years, reduces the risk of developing breast cancer by about one-half. Tamoxifen can be used in women before and after menopause.

Despite the evidence that it reduces the risk of developing breast cancer in high-risk women, tamoxifen has not been widely accepted for breast cancer prevention. That is largely because there is no evidence that tamoxifen improves survival when given as a preventive treatment and because the medication has a small risk of serious adverse events, including uterine cancer and blood clots in the legs or lungs.

Raloxifene — Raloxifene is currently used for the prevention and treatment of osteoporosis (low bone density) in postmenopausal women. Several studies suggest that in postmenopausal women at high risk of developing breast cancer, raloxifene can reduce the risk of developing an invasive hormone-positive (estrogen receptor-positive) breast cancer.

In the STAR Breast Cancer Prevention Trial that directly compared tamoxifen and raloxifene, raloxifene was slightly less effective than tamoxifen at preventing breast cancer. On the other hand, raloxifene was associated with fewer of the most serious side effects associated with tamoxifen, including a lower risk of uterine cancer. Raloxifene has been tested only in postmenopausal women; its benefit in premenopausal women is unknown.

Precautions — Tamoxifen and raloxifene are not recommended for some women, including those who:

- Have a history of blood clots in the legs or lungs (known as “deep vein thrombosis” or “pulmonary embolism”)
- Require anticoagulant or blood-thinning medications
- Smoke
- Are pregnant, planning on becoming pregnant, or breastfeeding (tamoxifen may cause birth defects if taken during pregnancy)

Women who use tamoxifen prior to menopause should use a non-hormonal method of birth control (such as condoms and a diaphragm), since hormonal methods of birth control, such as oral contraceptives, may alter the effectiveness of tamoxifen. A woman should immediately notify her doctor if she becomes pregnant while on tamoxifen. (See ["Patient information: Birth control; which method is right for me? \(Beyond the Basics\)".](#))

Women who use tamoxifen or raloxifene should be closely monitored by their healthcare provider. In particular, women should:

- Have an annual gynecologic examination, including a breast examination and, if recommended, a yearly mammogram and Pap smear (screening of the cervix for cancerous or precancerous cells). Any woman who finds a new breast lump should speak with her healthcare provider about the need for diagnostic testing (mammogram, ultrasound, biopsy).
- Immediately report any abnormal gynecologic symptoms, such as menstrual irregularities, abnormal vaginal bleeding or spotting, staining, or pelvic pressure or pain. (See "[Patient information: Abnormal uterine bleeding \(Beyond the Basics\)](#)".)
- Seek immediate medical care if they develop signs or symptoms of a blood clot, such as calf tenderness, swelling, pain, or severe, unexplained breathlessness or a fast heart rate.

Aromatase inhibitors — Of the aromatase inhibitors (AIs) used in the treatment of breast cancer (anastrozole, letrozole, exemestane), only one trial that looked at exemestane has been published. In this trial, exemestane reduced the risk of breast cancer by approximately 65 percent. Questions remain as to long-term effects of these drugs on bone loss and cardiovascular risk. Furthermore, joint and muscle symptoms associated with AIs may limit patient acceptance of this medication for preventive purposes. However, none of the AIs, including exemestane, is approved for breast cancer prevention.

SUMMARY

Who should consider medication for breast cancer prevention? — Guidelines from expert groups recommend that the risks and benefits of breast cancer prevention be discussed with premenopausal and postmenopausal women who are at high risk for the disease [[1-3](#)].

Appropriate candidates for breast cancer prevention include the following groups:

- Women over the age of 60.
- Women with certain high-risk conditions found on breast biopsy, such as lobular carcinoma in situ (LCIS) or atypical ductal or lobular hyperplasia.
- Women between the ages of 35 and 59 years who have a calculated five-year risk of developing breast cancer of 1.66 percent or higher, according to a system called the Gail model. The Gail model uses a woman's current age, age at first menstrual period, age at first live birth, the number of first-degree relatives with breast cancer, and the number and pathologic findings of any breast biopsies to estimate the probability of breast cancer over time.

A program called the Breast Cancer Risk Assessment Tool is available to calculate an individual woman's risk according to the Gail model [[4](#)]. Risk assessment tools such as these were developed for health professionals; patients who use them on their own should speak with their clinician for help interpreting the results. In addition, the presence of breast cancer risk factors does **not** mean that cancer is inevitable. Many women with risk factors never develop breast cancer.

An important issue is that the Gail model does not consider the risk of cancer associated with inherited breast cancer-predisposing genes such as BRCA1 and BRCA2. Preliminary data suggest that tamoxifen helps reduce the risk of breast cancer in women with BRCA mutations, but benefit may be limited to certain women who inherit these mutations. (See "[Patient information: Genetic testing for breast and ovarian cancer \(Beyond the Basics\)](#)".)

Choice of agent: tamoxifen, raloxifene, or an aromatase inhibitor?

For women who choose to pursue breast cancer prevention, the choice of agent depends on a number of factors, including her menopausal status, the side effects expected with each agent, and cost.

Postmenopausal women have the choice between tamoxifen or raloxifene. There are no studies comparing them against each other as primary prevention. In addition, aromatase inhibitors (AIs) are not approved for primary prevention. Questions remain as to long-term effects of an aromatase inhibitor on bone loss and cardiovascular risk.

If a selective estrogen receptor modulator (SERM) is chosen, tamoxifen appears to be more effective than raloxifene in preventing breast cancer. However, raloxifene has fewer serious side effects. Models to assess benefit and risk of tamoxifen versus raloxifene in individual women are available. (See "[Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention](#)".)

Tamoxifen is the only option for premenopausal women who choose to pursue breast cancer prevention. At present, raloxifene is not used for breast cancer prevention in premenopausal women because of the lack of data regarding safety in this population. In addition, aromatase inhibitors are generally not used in premenopausal women because they can actually increase estrogen production in women whose ovaries are still producing the hormone.

WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

[Patient information: Genetic testing for breast and ovarian cancer \(The Basics\)](#)

[Patient information: Ductal carcinoma in situ \(DCIS\) \(The Basics\)](#)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

[Patient information: Factors that modify breast cancer risk in women \(Beyond the Basics\)](#)

[Patient information: Bone density testing \(Beyond the Basics\)](#)

[Patient information: Osteoporosis prevention and treatment \(Beyond the Basics\)](#)

[Patient information: Deep vein thrombosis \(DVT\) \(Beyond the Basics\)](#)

[Patient information: Birth control; which method is right for me? \(Beyond the Basics\)](#)

[Patient information: Abnormal uterine bleeding \(Beyond the Basics\)](#)

[Patient information: Genetic testing for breast and ovarian cancer \(Beyond the Basics\)](#)

Professional-level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

[Factors that modify breast cancer risk in women](#)

[Genetic testing for hereditary breast and ovarian cancer syndrome](#)

[Managing the side effects of tamoxifen](#)

[Management of hereditary breast and ovarian cancer syndrome and patients with BRCA mutations](#)

[Postmenopausal hormone therapy and the risk of breast cancer](#)

[BRCA1 and BRCA2: Prevalence and cancer risks for breast and ovarian cancer](#)

[Screening for breast cancer: Strategies and recommendations](#)

[Selective estrogen receptor modulators and aromatase inhibitors for breast cancer prevention](#)

The following organizations also provide reliable health information.

- National Comprehensive Cancer Network

www.nccn.com)

- Website of the American Society of Clinical Oncology

www.cancer.net)

- National Cancer Institute

1-800-4-CANCER

www.nci.nih.gov)

- American Cancer Society

1-800-ACS-2345

www.cancer.org)

- Susan G. Komen Breast Cancer Foundation

www.komen.org)

Literature review current through: Oct 2013. | This topic last updated: Jun 4, 2013.