



# Postmenopausal women (aged over 50 years) at high risk of breast cancer

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## Information for patients from the UK Cancer Genetics Group (UKCGG)

This leaflet is for women who have a high lifetime risk of breast cancer and wish to discuss the use of medicines to reduce this. Medicines such as Tamoxifen, Raloxifene, or aromatase inhibitors such as Anastrozole can be taken to reduce the chance of developing breast cancer. Having a high risk means a lifetime chance of developing breast cancer which is one in three (approximately 30%) or higher.

### Breast cancer risk

Breast cancer risk means the chance of developing breast cancer in the future. Everyone has a chance of developing breast cancer, but this risk is increased if you have a family history of the disease. If you have an increased chance of developing breast cancer, there are a number of options available to you. This includes screening to detect cancer early using mammography and / or MRI (magnetic resonance imaging).

An additional option is to try to reduce the chance of developing breast cancer. One option for this is using tablets, called chemoprevention. Another option is having surgery to remove healthy breast tissue before a breast cancer occurs. This leaflet discusses the use of chemoprevention to reduce the chance of developing breast cancer.

### Chemoprevention and breast cancer risk

Guidelines produced by the National Institute for Health and Care Excellence (NICE) for familial breast cancer recommend that women at an increased lifetime chance of developing breast cancer because of a family history, should be offered medication to reduce their chance of developing breast cancer in the future. Options for breast cancer prevention in postmenopausal women at high risk include the drugs Anastrozole, Tamoxifen, or Raloxifene.

All the tablets that have been shown to decrease breast cancer risk have an effect on oestrogen. Oestrogen is a natural female hormone which is produced mainly by the ovaries in women before menopause. It is important for the functioning of the reproductive system. After menopause, the ovaries stop producing oestrogen, but low levels of the hormone continue to be produced in fat, liver, muscle, and breast tissue.

Many breast cancers rely on oestrogen to grow. These cancers are known as oestrogen-receptor positive (ER-positive) breast cancers. These cancer cells have proteins called receptors, to which the oestrogen attaches. If the receptor or the hormone itself is blocked, the cancer cells may grow more slowly or die. Cancers not sensitive to oestrogen are called oestrogen-receptor negative (ER-negative), and the tablets have not shown an effect on these cancers.

### **What is Anastrozole? and, how does it work?**

Anastrozole is an aromatase inhibitor. It reduces the level of the hormone oestrogen in the body by blocking an enzyme. It is used to treat breast cancer by reducing the risk of recurrence in women with cancers that are oestrogen receptor positive. Studies such as IBIS-II have shown it can reduce the chance of developing oestrogen sensitive breast cancer in postmenopausal women at high risk by approximately 50%. Anastrozole is usually prescribed as a tablet taken once a day by mouth. To reduce the chance of developing breast cancer, studies suggest it needs to be taken for five years. It is licensed for use as chemoprevention in the UK.

### **Who is it for?**

Anastrozole may be used to reduce the chance of developing breast cancer in post-menopausal women who are considered to have a high risk.

### **Who should not take Anastrozole?**

- Women who have not reached their menopause (pre-menopausal).
- Women who have osteoporosis (it does not improve bone density and may increase the risk of fracture).
- Women taking HRT or Tamoxifen.

### **Possible side-effects**

Anastrozole, like many medications, may cause unwanted side-effects. These side-effects may be worse for some than for others, as each person's reaction to any medicine is different. Some people have very few side-effects, while others may experience more. If you have side-effects you should discuss these with your GP.

Reported side-effects include:

- Hot flushes
- Joint aches and / or stiffness
- Vaginal dryness
- Headache

Anastrozole has not been shown to make a difference to your chance of getting a blood clot, or of developing cancer of the womb (see side effects for Tamoxifen and Raloxifene).

## What is Tamoxifen? and, how does it work?

Tamoxifen is a drug which blocks the action of oestrogen (it is sometimes called an anti-oestrogen drug) and has been used in the treatment of breast cancer for many years. There is evidence that it can also help to reduce the chance of breast cancer occurring. Four large studies have explored the use of Tamoxifen in women at increased risk of breast cancer and have shown that it reduces the chance by about 40%. Tamoxifen is usually prescribed as a tablet you take once a day by mouth. For breast cancer risk reduction, studies suggest it needs to be taken for five years. Tamoxifen is licensed for use as chemoprevention in women at moderate to high risk of breast cancer.

Tamoxifen reduces the effects of oestrogen in most areas of the body, including the breast. However, in the uterus, Tamoxifen acts like an oestrogen and encourages the growth of the lining of the uterus.

## Using Tamoxifen to reduce the chance of developing breast cancer

There have been a number of studies on the use of Tamoxifen to reduce the chance of developing breast cancer in women at increased lifetime risk. The IBIS-1 trial, which was carried out in the UK, involved women with a family history of breast cancer taking Tamoxifen or a placebo (inactive pill) for five years. The actual number of breast cancers they developed was then compared. At the five year point, the number of cancers had been reduced in women taking the Tamoxifen, but the complication (side-effect) rate was increased. At the 10 year point, the reduction in risk of breast cancer was 38%, and the benefit of Tamoxifen outweighed the complications. The side-effects went away after the tablet was stopped after five years.

## Who is it for?

Tamoxifen can be used to reduce the chance of developing breast cancer in women with an increased lifetime risk, whether or not they have gone through menopause. The best age to start taking Tamoxifen is not known. It will vary between women depending on their level of risk. For most women the chance of developing breast cancer, and therefore the benefit of Tamoxifen, will be low before the age of 35. All the research studies using Tamoxifen started from 35 years of age, or older.

## Who should not take Tamoxifen?

- Women who have had cancer of the womb
- Women taking HRT
- Women who have a personal or family history of blood clots, for example deep vein thrombosis (DVT), should let their doctor know as Tamoxifen may not be suitable.

## Possible side-effects

Tamoxifen, like many medications, may cause unwanted side-effects. Often, Tamoxifen causes symptoms similar to the menopause. These side-effects may be worse for some than for others, as each person's reaction to any medicine is different. Some people have very few side-effects, while others may experience more. If you have side-effects you should discuss these with your GP. Very rarely, if the side-effects are severe, you may have to stop taking Tamoxifen.

## Common side-effects

- Hot flushes and sweats
- Feeling sick (nausea): nausea is quite common initially, it usually improves after a few weeks
- Gynaecological problems (vaginal discharge, itching or dryness). Any vaginal bleeding after the menopause should be reported to your GP
- **Leg cramps: if your leg becomes red, hot, or swollen, tell your doctor immediately.**

## Less common side-effects

- Headaches
- Blood clots (thrombosis): the risk of blood clots doubles whilst a woman takes Tamoxifen, but returns to usual population level once tablets are stopped. Women should stop Tamoxifen six weeks before any planned surgery.
- Cancer of the womb: Tamoxifen has been associated with an increased risk of cancer of the womb, approximately three extra women out of every 1000 will develop a cancer if they take Tamoxifen for five years.
- Vision problems
- Voice changes.

## Effects of other drugs on taking Tamoxifen

Research suggests some drugs – including the antidepressants Paroxetine (Seroxat®) and Fluoxetine (Prozac®) – cause Tamoxifen to be less effective. Tell your doctors about any other medicines you are taking so that they can check whether it is safe for you to use them alongside Tamoxifen.

## What is Raloxifene? and, how does it work?

Raloxifene is another anti-oestrogen drug. It is prescribed in tablet form, to be taken by mouth once a day for 5 years. Like Tamoxifen, Raloxifene works by blocking the effects of oestrogen in the breast and other tissues. However, unlike Tamoxifen, Raloxifene does not have oestrogen-like effects on the womb. Clinical trials have shown that Raloxifene reduces breast cancer risk to a similar level as Tamoxifen in postmenopausal women. It is currently unlicensed for use as chemoprevention in the UK.

## Who is it for?

Raloxifene may be used to reduce the chance of developing breast cancer in women at increased risk who are past the menopause (postmenopausal).

## Who should not take Raloxifene?

- Women who have not reached the menopause.

- Women who have had cancer of the womb or are currently being investigated for postmenopausal bleeding.
- Women who have a personal or family history of blood clots or deep vein thrombosis (DVT) should let their doctor know, as Raloxifene may not be suitable.

### Other benefits

Raloxifene reduces the risk of fracture because it stimulates bone formation. It may also reduce the number of migraine attacks in some sufferers.

### Side-effects

Side-effects can be similar to those described for Tamoxifen.

### Anastrozole versus Tamoxifen versus Raloxifene

For postmenopausal women, Anastrozole has been shown to reduce the chance of developing breast cancer most significantly in a small number of studies. It has not been shown to affect the risk of blood clots or cancer of the womb. Current evidence suggests that Tamoxifen reduces the risk of breast cancer by a larger amount than Raloxifene. There is a slightly higher risk of blood clots with Tamoxifen than with Raloxifene, and Raloxifene has not been shown to increase the risk of cancer of the womb.

The benefit of taking any of these drugs when someone has a known pathogenic / likely pathogenic gene variant in a breast cancer predisposition gene (such as BRCA1 or BRCA2) is unknown. This is because no studies have been conducted on the benefit of chemoprevention in patients with a known pathogenic variant in a cancer predisposition gene. The evidence suggests that it may be useful in women who carry variants in certain genes like BRCA2 as these women have an increased risk of oestrogen-positive breast cancers. However, it is not routinely recommended where there is a high risk of oestrogen-negative breast cancers, such as with BRCA1.

Not all women at increased risk will decide to take chemoprevention. The potential benefits and side-effects should be considered. For all chemoprevention drugs, it is not recommended to continue taking them for more than five years for women with no personal history of breast cancer.

### What should I do next?

If you have previously had your risk of breast cancer assessed and you fall into the high risk category and wish to consider taking chemoprevention you should talk to your genetics team or breast clinic about this. If you have not had your risk of breast cancer assessed, you should ask your GP to refer you either to the local breast cancer family history clinic or your local genetics service. Decision aids to help women, along with a healthcare professional, make a more informed choice about which tablet, if any, is right for them are available on the National Institute for Health and Care Excellence (NICE) web site (<https://www.nice.org.uk/guidance/cg164/resources>).

Produced with grateful acknowledgement to the UK Cancer Genetics Group and their **Leaflet for postmenopausal women (aged over 50 years) at high risk of breast cancer (last reviewed November 2023)**.

**This leaflet has been produced with and for patients.**

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