East Kent Hospitals University NHS Foundation Trust

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

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

This leaflet is for women who have been told that they have a high risk of breast cancer because of their family history, and wish to discuss the use of Tamoxifen, Raloxifene, or aromatase inhibitors such as Anastrozole to decrease their risk. Having a high risk of developing breast cancer means a lifetime risk which is 1 in 3 (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 risk 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).

The other option is to try to decrease the risk of breast cancer. This can be done using tablets – chemoprevention – or by using surgery to remove healthy breast tissue before a breast cancer occurs. Surgery is the most effective way to decrease risk, and will reduce the risk of breast cancer below that of the general population. It is however, major surgery and not all women at high risk feel that surgery is right for them. This leaflet discusses the use of a tablet to decrease breast cancer risk.

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 risk of breast cancer because of a family history of breast cancer, should be offered medication to reduce their risk. 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 (https://www.macmillan.org.uk/cancer-information-and-support/breast-cancer/receptors-for-breast-cancer). These cancer cells have proteins called receptors, to which the oestrogen attaches. When oestrogen comes into contact with the receptors, it fits into them and stimulates the cancer cells to divide so that the tumour grows. 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 risk of oestrogen sensitive breast cancer in postmenopausal women at high risk by approximately 50%. Anastrozole 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 5 years. However, it is still the subject of ongoing research for the prevention of breast cancer, and is therefore currently unlicensed for this use in the UK.

Who is it for?

Anastrozole may be used to decrease the risk of breast cancer in post-menopausal women who are considered to have a high risk; unless they have severe osteoporosis.

The evidence for the benefit of drugs like Anastrozole taken by women with a known gene change in BRCA1 or BRCA2 who have a very high risk of breast cancer is limited. This is because not many women with a BRCA1/2 gene change were included in the studies.

Who should not take Anastrozole?

- Anastrozole is not recommended for women who have not reached their menopause (pre-menopausal).
- Women who have osteoporosis should not take Anastrozole; it does not improve bone density and may increase the risk of fracture.
- Women should not take HRT or Tamoxifen at the same time as Anastrozole.
- Not all women at increased risk will decide to take Anastrozole.

The potential benefits and side-effects should be considered and discussed with your doctor.

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 now evidence that it can also help to prevent 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 decreases the risk 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 5 years. However, it is still the subject of ongoing research for the prevention of breast cancer, and is therefore currently unlicensed for this use in the UK.

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 prevent breast cancer

There have been a number of studies researching the use of Tamoxifen to prevent breast cancer in women at increased risk. The IBIS-1 trial, which was carried out here in the UK, involved women with a family history of breast cancer, taking Tamoxifen or a placebo (inactive pill) for 5 years. The actual number of breast cancers they developed during the 5 years, and after was then compared. At the 5 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 which stopped after the tablet was stopped at 5 years.

Who is it for?

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

The evidence for the benefit of Tamoxifen taken by women with a known gene change in BRCA1 or BRCA2 who have a very high risk of breast cancer is limited. This is because not many women with a BRCA1/2 gene change were included in the studies. The evidence suggests that whilst it may be useful in BRCA2 gene carriers, the benefit for BRCA1 carriers is less certain.

Who should not take Tamoxifen?

Not all women at increased risk will decide to take Tamoxifen. The potential benefits and side-effects should be considered and discussed with your doctor.

- 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.
- Women who have had cancer of the womb should not take Tamoxifen for chemoprevention.
- Women should not take HRT at the same time as Tamoxifen.

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). Although nausea is quite common to start with, 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 to reduce the risk of blood clots.
- Cancer of the womb. Tamoxifen has been linked 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 5 years.
- Vision problems.
- Voice changes.

Effects of other drugs on taking Tamoxifen

There is some research that suggests some drugs – including the antidepressants Paroxetine (Seroxat®) and Fluoxetine (Prozac®) – may cause Tamoxifen to be less effective, but this isn't certain. 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.

How does Raloxifene 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.

Who is it for?

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

Who should not take Raloxifene?

Raloxifene is not recommended for women before the menopause. 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. Women who have had cancer of the womb or are currently being investigated for postmenopausal bleeding, should not take Raloxifene for chemoprevention.

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 risk of 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.

For all chemoprevention drugs, it is not recommended to continue taking them for more than 5 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 Anastrozole, Tamoxifen, or Raloxifene, you should talk to your GP 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.

Your healthcare professional can talk you through your options for chemoprevention, if appropriate. Decisions 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 (2017).**

This leaflet has been produced with and for patients.

If you would like this information in **another language, audio, Braille, Easy Read, or large print** please ask a member of staff. You can ask someone to contact us on your behalf.

Any complaints, comments, concerns, or compliments please speak to your doctor or nurse, or contact the Patient Advice and Liaison Service (PALS) on 01227 783145 (tel://+441227783145), or email ekh-tr.pals@nhs.net (ekh-tr.pals@nhs.net)

Patients should not bring large sums of money or valuables into hospital. Please note that East Kent Hospitals accepts no responsibility for the loss or damage to personal property, unless the property has been handed into Trust staff for safe-keeping.

Further patient leaflets are available via the East Kent Hospitals website (https://www.ekhuft.nhs.uk/information-for-patients/patient-information/).

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