NATIONAL BREAST CANCER CENTRE
Incorporating the Ovarian Cancer Program

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INFORMATION ABOUT

Hormonal therapies for women with early breast cancer

This information has been developed to help you understand and make decisions about hormonal therapies for the treatment of breast cancer. The information has been developed by a multidisciplinary working group and is based on the National Breast Cancer Centre *Recommendations for Aromatase Inhibitors as Adjuvant Endocrine Therapy for Post-Menopausal Women with Hormone Receptor-Positive Early Breast Cancer*. This document includes details of the research and references relating to this information.

To view or download a copy of the guideline go to www.nbcc.org.au/resources

This information replaces Chapter 8: Hormonal Therapies in the National Breast Cancer Centre's A Guide for Women with Early Breast Cancer (2003)

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WHAT ARE HORMONAL THERAPIES?

Hormonal therapies (also called endocrine therapies) are drugs used to treat women with breast cancer who have hormone receptors on their breast cancer cells. Hormone receptors are proteins on the surface of a cell that allow the cell to bind to hormones. When breast cancer cells have hormone receptors on them, this means the growth of the cancer cells is affected by female hormones. Breast cancer cells that have hormone receptors on them are said to be 'hormone receptor positive'. About two-thirds of women with breast cancer have hormone receptors on their breast cancer cells. Your pathology report shows whether your breast cancer cells are hormone receptor positive. You can ask your doctor for a copy of your pathology report. There are two types of hormone receptor – oestrogen receptors and progesterone receptors. Hormonal therapies may be suitable for women with either type of receptor on their breast cancer cells.

Hormonal therapies may be used in addition to surgery, radiotherapy and chemotherapy, or on their own.

Note: Hormonal therapies used to treat breast cancer are <u>not</u> the same as hormone replacement therapy used to manage symptoms of menopause.

MENOPAUSE AND OESTROGEN PRODUCTION

All women produce the hormone oestrogen; however, it is produced differently before and after menopause.

- **Before menopause (pre-menopause),** the ovaries are the main source of oestrogen.
- **Around the time of menopause (peri-menopause),** the ovaries stop producing female hormones, including oestrogen. This typically happens when women are in their late forties and early fifties. Women may experience a number of physical symptoms during menopause, including menstrual irregularities, hot flushes and sleep disturbances.
- **After menopause (post-menopause)**, monthly menstrual periods have stopped. The body still produces small amounts of oestrogen by converting hormones called androgens into oestrogen. Androgens are produced by the adrenal glands, which are above the kidneys. They are converted into oestrogen by a hormone called aromatase which is produced mainly by fatty tissue.

HOW DO HORMONAL THERAPIES WORK?

Hormonal therapies stop breast cancer cells with hormone receptors from growing by blocking either the production of female hormones or the ability of hormones to get into cancer cells.

Why take hormonal therapies?

Clinical trials have shown that hormonal therapies lower the risk of breast cancer coming back (in the breasts and in other parts of the body). The hormonal therapy tamoxifen and surgical removal of the ovaries have both been shown to lower the risk of dying from breast cancer. However, for newer drugs, such as the new (selective) aromatase inhibitors, there are not yet enough long-term results from clinical trials to measure the effect of treatment on the risk of dying.

WHEN SHOULD I START TAKING HORMONAL THERAPIES?

Hormonal therapies are usually taken once your other treatments for breast cancer, such as surgery, radiotherapy and chemotherapy, have finished.

WHO SHOULD I TALK TO ABOUT HORMONAL THERAPIES?

Your treating doctor or specialist will consider the most appropriate treatment options for you and will discuss whether hormonal therapies are recommended in your case. If you have any questions, you should refer these to your oncologist, breast care nurse or general practitioner.

It is important that you talk to your treating doctor or specialist about which hormonal therapies may be suitable for you, the possible side effects of treatment and ways of managing these side effects if they develop.

If you change general practitioners once you have started taking hormonal therapies, it is important to let him/her know what you are taking.

TYPES OF HORMONAL THERAPIES

There are different ways of reducing the level of female hormones in the body:

- anti-oestrogens, eg tamoxifen
- aromatase inhibitors, eg anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®)
- anti-ovarian treatments, eg surgery, radiotherapy, goserelin (Zoladex®).

ANTI-OESTROGENS

Anti-oestrogens work by stopping breast cancer cells from getting oestrogen. The most common anti-oestrogen is tamoxifen. Tamoxifen can be used to treat women of any age, regardless of whether they have reached menopause. Tamoxifen is taken as a single daily tablet, usually for 5 years.

AROMATASE INHIBITORS

Aromatase inhibitors work by blocking the conversion of androgens to oestrogen. They are only effective for women who have gone through menopause permanently. If you have not yet reached menopause, or if you are in the middle of menopause, your ovaries are still producing oestrogen, so aromatase inhibitors will not be effective for you. If you have become menopausal temporarily because of chemotherapy, aromatase inhibitors are not suitable for you because your ovaries may start producing oestrogen again. Aromatase inhibitors are taken as a single daily tablet, usually for 5 years.

ANTI-OVARIAN TREATMENTS

Anti-ovarian treatments work by stopping the ovaries from producing oestrogen. Drugs like goserelin stop the ovaries from producing oestrogen temporarily for the duration of taking the drug. A permanent method of stopping oestrogen production in women is to remove the ovaries or administer radiotherapy to the ovaries. Anti-ovarian treatments are only suitable for women who have not yet reached menopause.

SIDE EFFECTS OF HORMONAL THERAPIES

Hormonal therapies have some side effects in common, and others that differ. Also, different women may respond differently to the same treatment. For some of the newer drugs, such as aromatase inhibitors, clinical trials have not been running long enough to determine all of the long-term side effects.

When discussing your treatment options, ask your doctor about the possible side effects of the hormonal therapies recommended for you. Treatments are often available to help manage the side effects.

All hormonal therapies can cause menopausal symptoms such as hot flushes and vaginal dryness. All hormonal therapies can reduce your libido (sex drive). Treatments are available that can help with these problems – talk to your doctors or breast care nurse if you are troubled by them. The severity of these symptoms varies between women and treatments. These effects often improve after treatment stops.

Treatment with hormonal therapies can sometimes result in permanent menopause. It is important that women who have not yet reached menopause and for whom having children is important discuss their options with a specialist before starting treatment.

ADDITIONAL SIDE EFFECTS OF TAMOXIFEN

Rare side effects of tamoxifen include an increased risk of blood clots, stroke, cancer of the uterus and changes in vision. The risk of these side effects needs to be balanced against the fact that anti-oestrogens reduce the risk of breast cancer coming back and death from breast cancer. See your doctor immediately if you are concerned by any new or unusual symptoms, in particular if you have irregular vaginal bleeding, chest pain or warmth, pain, swelling or tenderness in an arm or leg.

Tamoxifen can also have some other benefits in addition to treating your cancer, including reducing the risk of osteoporosis and lowering your cholesterol level.

ADDITIONAL SIDE EFFECTS OF AROMATASE INHIBITORS

Aromatase inhibitors can cause pain in the bones and/or joints (arthralgia). They also increase the risk of fractures by speeding up the normal thinning of bones that occurs after menopause and with ageing (osteoporosis). If you are already at increased risk of osteoporosis, your doctor will consider this when recommending which hormonal therapy is most suitable for you. Talk to your doctor about how to reduce the risk of fractures and maintain bone strength.

Long-term side effects of aromatase inhibitors are still the subject of ongoing studies. For example, studies are investigating the effects of aromatase inhibitors on memory, concentration and heart disease.

ADDITIONAL SIDE EFFECTS OF ANTI-OVARIAN TREATMENTS

Removal of the ovaries by surgery or radiotherapy to the ovaries causes permanent menopause. Women who have had these treatments can no longer have children. Drugs that stop the ovaries from working also cause menopause, but this is usually temporary, lasting only as long as the drugs are continued. However, the effects of these drugs may be permanent in women who were close to having their natural menopause when they started treatment.

DECIDING WHETHER TO USE HORMONAL THERAPIES

Hormonal therapies are usually recommended for women who have hormone receptors on their breast cancer cells. Your doctor will also consider the risk of your breast cancer coming back, and your general health. Some of the things that affect your risk of breast cancer coming back include the size and grade of the breast cancer and whether it has spread to any lymph nodes. This information is listed in your pathology report. You can request a copy of your pathology report from your doctor.

The types of hormonal therapies recommended for an individual woman will depend on whether she has reached menopause. If you are not sure whether you have reached menopause, talk to your doctor.

IF YOU HAVE NOT YET REACHED MENOPAUSE AND YOUR CANCER CELLS HAVE HORMONE RECEPTORS

- It is usually recommended that you are treated with tamoxifen.
- If you are at very low risk of the breast cancer coming back (eg if your breast cancer is very small and has not spread to your lymph nodes) your doctor may not recommend tamoxifen for you.
- Your doctor may discuss taking part in international trials comparing different combinations of chemotherapy, anti-ovarian treatment and anti-oestrogens.
- Your doctor may recommend an anti-ovarian treatment; additional treatment with tamoxifen may also be recommended for you.

If you have not yet reached menopause and having children is important to you, you should discuss your options with your doctor before starting hormonal therapy.

IF YOU HAVE REACHED MENOPAUSE AND YOUR CANCER CELLS HAVE HORMONE RECEPTORS

- It is usually recommended that you are treated with either tamoxifen or with an aromatase inhibitor.
- If the risk of breast cancer coming back is very low (for example, if your breast cancer is very small and has not spread to any lymph nodes) your doctor may not recommend hormonal therapy for you.

AFTER MENOPAUSE: WHICH HORMONAL THERAPY?

When deciding which hormonal therapy to recommend for your individual situation, your doctor will consider the likely benefits and possible side effects (both known and unknown) of the different treatments.

The long-term benefits and risks of taking tamoxifen are well established. Tamoxifen reduces the risk of breast cancer coming back and lowers the risk of dying from breast cancer.

Studies have shown that treatment with an aromatase inhibitor reduces the risk of breast cancer coming back more than tamoxifen. These studies have not been going long enough to say whether aromatase inhibitors improve survival more than tamoxifen. Also, the long-term side effects of aromatase inhibitors are not yet known.

For women with a higher risk of their breast cancer coming back, the short-term benefits of treatment with an aromatase inhibitor are already sufficient to outweigh the risks of side effects (both known and unknown).

For women with a lower risk of their breast cancer coming back, it is still possible that long-term side effects of aromatase inhibitors (as yet unknown) will outweigh the short-term benefits of treatment compared with tamoxifen.

WHAT IF I AM ALREADY RECEIVING TAMOXIFEN?

If you have reached menopause and started tamoxifen less than 5 years ago, then you may benefit from changing your treatment to an aromatase inhibitor. The decision about whether to change to an aromatase inhibitor will depend on your level of risk of breast cancer coming back – the higher your risk, the more likely it is that your doctor will recommend that you change treatments.

If you have reached menopause and have recently completed 5 years of treatment with tamoxifen, then you may benefit from receiving further treatment with an aromatase inhibitor. The decision about whether to have further treatment with an aromatase inhibitor will depend on your level of risk of breast cancer coming back – the higher your risk, the more likely it is that your doctor will recommend that you have further treatment.

QUESTIONS YET TO BE ANSWERED ABOUT AROMATASE INHIBITORS

As with many drugs available to treat breast cancer, there are important things that we still don't know about aromatase inhibitors. Clinical trials to answer these questions are ongoing and more information will become available in the future.

Some of these questions include:

- the ideal length of time for which an aromatase inhibitor should be taken (at the moment aromatase inhibitors are usually prescribed for 5 years)
- whether it's better to use tamoxifen and an aromatase inhibitor in sequence (one after the other) and if so, in which order
- the effects of aromatase inhibitors on memory, concentration and heart disease
- how best to manage the loss in bone strength caused by aromatase inhibitors
- whether hormonal therapies can be used to prevent breast cancer in women who have not been diagnosed with the disease.

QUESTIONS TO ASK YOUR DOCTOR ABOUT HORMONAL THERAPIES

The following questions may be useful for you when discussing hormonal therapies with your oncologist, breast care nurse or general practitioner.

Before treatment

- How can I benefit from hormonal therapy?
- Which hormonal therapies are suitable for me? Why?
- What does the hormonal therapy you are recommending involve?
- How much will the hormonal therapy you are recommending cost?
- What are the most common and rarer side effects of the hormonal therapy you are recommending?
- Who should I contact if side effects develop?
- How can I manage side effects if they develop?
- Will the side effects stop when I finish treatment?
- When will I start hormonal therapy if I am having other treatments?
- Will hormonal therapy affect my ability to have children?
- Do I still need to use contraception if I am having hormonal therapy?

Once treatment has started

If you decide to take a hormonal therapy such as tamoxifen or an aromatase inhibitor, you will probably be advised to take it for 5 years. During this time, you may have questions about side effects. It is important that you discuss any questions or concerns you have with your oncologist or general practitioner – even if these questions arise several years after you start treatment. Listed below are some frequently asked questions that may be relevant for you in the coming years.

Question: If I experience side effects, can I lower my dose of hormonal therapy?
Answer: The recommended doses are the only ones tested – taking lower doses or less frequent doses is not a good idea. If you have side effects, it is important that you discuss them with your oncologist, surgeon or general practitioner.

Question: If I run out of my script, can my GP renew it?
Answer: Yes.

Question: If I am planning to have surgery (including dental surgery) can I continue to take my hormonal therapy?
Answer: Some hormonal therapies can increase the risk of blood clots. If you are likely to be confined to bed or have limited movement, your doctor may recommend that you stop taking your hormonal therapy for a period of time before surgery and that you do not start taking it again until you are fully mobile after surgery.

Question: If I miss a dose of my hormonal therapy, should I take a double dose?
Answer: No. Just take the next dose as normal.

Question: If I change from tamoxifen to an aromatase inhibitor, can I change back later if side effects worry me?
Answer: Yes.

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