NICE National Institute for Health and Care Excellence

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Early and locally advanced breast cancer: diagnosis and management

Neoadjuvant and OFS update

Draft for consultation, February 2025

This guideline covers diagnosing and managing early and locally advanced breast cancer. It aims to help healthcare professionals offer the right treatments to people, taking into account the person's individual preferences.

This guideline will update NICE guideline NG101 (published July 2018).

Who is it for?

- Healthcare professionals
- Commissioners and providers of breast cancer services
- People with early and locally advanced breast cancer, their families and carers

What does it include?

- new and updated recommendations on neoadjuvant treatment and ovarian/testicular function suppression
- recommendations for research related to neoadjuvant treatment and ovarian/testicular function suppression
- the rationale and impact section that explains why the committee made the 2025 recommendations and how they might affect services.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on neoadjuvant treatment and ovarian/testicular function suppression. You are invited to comment on these new and updated recommendations only. These are marked as **[2025].**

We have not reviewed the evidence for the recommendations shaded in grey, which have been provided for context, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification or to bring recommendations in line with new content. These changes are highlighted in yellow.

Note that work is in progress to include links to relevant NICE technology appraisal guidance at relevant points in this guideline in line with our Interim process and methods statement for bringing together NICE guidance. This work is not included in this consultation, and we will include these links when the guideline update publishes.

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Systemic anti-cancer therapy planning

1.6.1 Consider systemic anti-cancer therapy (SACT) for people with invasive breast cancer, and ensure that recommendations are documented at the multidisciplinary team meeting. **[2009, amended 2025]**

1.6.2 Base recommendations about systemic anti-cancer therapy on multidisciplinary team assessment of the prognostic and predictive factors, and the possible benefits and risks of the treatment. Make decisions with the person after discussing these factors. **[2009, amended 2018]**

1.6.3 When discussing the benefits and risks of systemic anti-cancer therapy with people with invasive breast cancer, follow the recommendations on:

- enabling patients to actively participate in their care in NICE's guideline on patient experience in adult NHS services, and
- communicating risks, benefits and consequences in NICE's guideline on shared decision making. **[2025]**

Adjuvant endocrine therapy for ER positive invasive breast cancer

1.7.2 Offer adjuvant endocrine therapy to people with ER-positive invasive breast cancer. **[2025]**

People with female reproductive organs

The following recommendations apply to women, trans men and non-binary people who currently have ovaries.

1.7.3 Make a shared decision with premenopausal or perimenopausal people with ER-positive invasive breast cancer about the type of endocrine therapy that would be suitable for them. As part of this process:

- discuss the benefits and risks of using tamoxifen alone, or ovarian function suppression in combination with tamoxifen, or ovarian function suppression in combination with an aromatase inhibitor (see Table 1)
- explain that the use of ovarian function suppression (in combination with tamoxifen or an aromatase inhibitor) may be most beneficial for people who are at higher risk of disease recurrence
- provide information about the possible side effects of each treatment option, including what to expect and how these could be managed if they develop.

See also the recommendations on bone health **[2025]**

Table 1 The benefits and risks of using endocrine therapy in combination with ovarian function suppression (OFS)

Category	Effect of using OFS in combination with tamoxifen compared to tamoxifen alone	Effect of using OFS in combination with an aromatase inhibitor compared to tamoxifen alone	Effect of using OFS in combination with an aromatase inhibitor compared to OFS in combination with tamoxifen
Effect on overall survival	Using OFS in combination with tamoxifen improves overall survival compared to tamoxifen alone.	It was not possible from the evidence to differentiate between OFS in combination with an aromatase inhibitor compared to tamoxifen alone for overall survival.	It was not possible from the evidence (from 4 trials pooled) to differentiate for overall survival.
Effect on disease-free survival	Using OFS in combination with tamoxifen improves disease-free survival compared to tamoxifen alone.	Using OFS in combination with an aromatase inhibitor improves disease-free survival compared to tamoxifen alone.	It was not possible from the evidence (from 4 trials pooled) to differentiate for disease-free survival. However, the combined evidence reported in the SOFT and TEXT trials showed that OFS in combination with an aromatase inhibitor improves disease-free survival compared to OFS in combination with tamoxifen.
Side effects	Using OFS in combination with tamoxifen compared to tamoxifen may mean that the risk of having certain side effects are increased. These may include vaginal dryness, hot flushes, sleep disturbances or insomnia, depression symptoms, decreased libido or dyspareunia and	Using OFS in combination with an AI compared to tamoxifen may mean that the risk of having certain side effects are increased. These may include vaginal dryness, hot flushes, insomnia, depression symptoms, dyspareunia, fractures and osteoporosis. But they may	Using either OFS in combination with an AI or OFS in combination with tamoxifen may mean that the risk of having certain side effects are increased compared to having tamoxifen alone. (See the relevant column for potential side effects.) But they may vary in severity, and not everyone gets these.

	osteoporosis. But they may vary in severity, and not everyone gets these.	vary in severity, and not everyone gets these.	The risk of having some side effects may be higher with one combination treatment than the other, but there is some uncertainty about this because the analysis was not designed to look at this definitively.

For a short explanation of why the committee made the 2025 recommendations and how they might affect practice, see the rationale and impact section on adjuvant endocrine therapy for ER positive invasive breast cancer: people with female reproductive organs.

Full details of the evidence and the committee's discussion are in evidence review Q: ovarian function suppression.

1.7.4 Offer an aromatase inhibitor as the initial adjuvant endocrine therapy for postmenopausal people with ER-positive invasive breast cancer who are at medium or high risk of disease recurrence. Offer tamoxifen to people who are at low risk of disease recurrence, or if aromatase inhibitors are not tolerated or are contraindicated. **[2009, amended 2018]**

People with male reproductive organs

The following recommendations apply to men, trans women and non-binary people who currently have testes.

1.7.5 Offer tamoxifen as adjuvant endocrine therapy for people with ER-positive invasive breast cancer who have male reproductive organs. **[2009, amended 2025]**

1.7.6 Consider testicular function suppression in combination with an aromatase inhibitor if tamoxifen is not suitable or not tolerated for people with ER-positive invasive breast cancer who have male reproductive organs. **[2025]**

In February 2025, this was an off-label use for testicular function suppression and aromatase inhibitors. See NICE's information on prescribing medicines.

1.7.7 Do not use an aromatase inhibitor alone in people with ER-positive invasive breast cancer who have male reproductive organs. **[2025]**

1.7.8 Discuss the benefits and risks of the possible treatment options with people with ER-positive invasive breast cancer who have male reproductive organs. Ensure the discussion covers information about potential side effects of endocrine therapy, including side effects specific to people with male reproductive organs such as erectile dysfunction and gynaecomastia (with testicular function suppression in combination with an aromatase inhibitor). **[2025]**

1.7.9 On starting testicular function suppression in combination with an aromatase inhibitor, assess bone mineral density in people with ER-positive invasive breast cancer who have male reproductive organs (also see recommendations in the section on bone health). **[2025]**

For a short explanation of why the committee made the 2025 recommendations and how they might affect practice, see the rationale and impact section on adjuvant endocrine therapy for ER positive invasive breast cancer: people with male reproductive organs.

Full details of the evidence and the committee's discussion are in evidence review R: testicular function suppression.

Neoadjuvant treatment of HER2-positive breast cancer

1.11.2 Where chemotherapy is indicated, offer neoadjuvant chemotherapy to people with HER2-positive invasive breast cancer in line with the commissioning criteria for any related technology appraisals. **[2025]**

1.11.3 Pertuzumab in combination with trastuzumab is recommended as an option in NICE technology appraisal guidance for treating HER2-positive breast cancer in adults that is locally advanced, inflammatory, or early-stage with a high risk of recurrence. For full details, see the guidance on pertuzumab (TA424, 2016).

For a short explanation of why the committee made the 2025 recommendations and how they might affect practice, see the rationale and impact section on neoadjuvant treatment of HER2-positive breast cancer.

Full details of the evidence and the committee's discussion are in evidence review P: neoadjuvant chemotherapy for people with HER2 positive breast cancer.

Neoadjuvant treatment of triple-negative breast cancer

1.11.4 For people with triple-negative invasive breast cancer where neoadjuvant chemotherapy is indicated, offer a regimen that contains a platinum, taxane and an anthracycline. Discuss the benefits and risks of this approach (see table 2), taking into account the person's circumstances, needs and preferences. **[2025]**

Table 2 Benefits and risks of adding a platinum to neoadjuvant chemotherapy for triple-negative invasive breast cancer

Category	Effect of using a platinum-containing neoadjuvant chemotherapy
Effect on survival	Using a platinum-containing neoadjuvant chemotherapy regimen improves overall survival compared to a neoadjuvant chemotherapy regimen without a platinum. • With a minimum follow up of 3 years, when people had non-platinum-containing neoadjuvant chemotherapy then 81 out of 100 survived. • When people had platinum-containing neoadjuvant chemotherapy then 85 out of 100 survived (an additional 4 people).
Effect on disease free survival	Using platinum-containing neoadjuvant chemotherapy regimen and improves disease-free survival compared to a neoadjuvant chemotherapy regimen without a platinum. • With a minimum follow up of 3 years, when people had non-platinum-containing neoadjuvant chemotherapy then 75 out of 100 were disease free. • When people had platinum-containing neoadjuvant chemotherapy then 82 out of 100 were disease free (an additional 7 people).
Effect on pathological complete response rate (no residual cancer found at surgery)	Using a platinum-containing neoadjuvant chemotherapy regimen improves the chances of a pathological complete response in the breast and lymph nodes in the axilla, compared to a neoadjuvant chemotherapy regime without platinum. • When people had non-platinum-containing neoadjuvant chemotherapy then 33 out of 100 had a pathological complete response. • When people had platinum-containing neoadjuvant chemotherapy then 48 out of 100 had a pathological complete response (an additional 15 people).
Effect on breast conservation rate	No increase in the rates of breast conserving surgery was seen with platinum-based therapy.
Side effects	Using a platinum-containing neoadjuvant chemotherapy may mean that that the risks of having certain side effects are increased, but they may vary in severity and not everyone gets them. Neutropenic sepsis (reported as febrile neutropenia in the studies, see note below), neutropenia, thrombocytopenia, and anaemia are seen more frequently with platinum-based chemotherapy.

Category	Effect of using a platinum-containing neoadjuvant chemotherapy
Additional information	• Data comes from trials with 3 to 8 years follow-up. • Data comes from trials with younger people (median age ranged from 45 to 52 years old) with few comorbidities and good performance status. • Data comes from trials that either have predominantly or entirely recruited people with female reproductive organs. The effects on people with male reproductive organs are unclear, but they may also benefit from platinum based neoadjuvant chemotherapy. The effects on pregnant women are also unclear as no data was identified for this population. • The data recorded in the trials was for febrile neutropenia and no data was identified specifically for neutropenic sepsis. The committee noted the partial overlap of this outcome with that of neutropenic sepsis and agreed that the potential for an increased risk of neutropenic sepsis (as a result of the detected increased risk of febrile neutropenia) was important to highlight as this could have a very severe outcome if left untreated. However, some people with febrile neutropenia will not have sepsis and not everyone with neutropenic sepsis will have a fever. (See the NICE clinical knowledge summary on neutropenic sepsis for more information and see also the NICE guideline on Neutropenic sepsis: prevention and management in people with cancer.)

For a short explanation of why the committee made the 2025 recommendations and how they might affect practice, see the rationale and impact section on neoadjuvant treatment of triple-negative breast cancer.

Full details of the evidence and the committee's discussion are in evidence review O: platinum based neoadjuvant chemotherapy.

Research recommendations

Neoadjuvant treatment of triple-negative breast cancer

1. What is the clinical and cost effectiveness of adding a platinum to a neoadjuvant chemotherapy regimen in people with invasive breast cancer who have a germline BCRA mutation, but who do not have triple-negative breast cancer?

2. What is the real-world evidence on clinical and cost effectiveness of adding a platinum to a neoadjuvant chemotherapy regimen in people with invasive breast cancer that is triple negative and/or with a germline BRCA mutation who are often excluded from clinical trials, such as:

    - people 65 years and older, or
    - people who are pregnant, or
    - people with male reproductive organs?

Adjuvant endocrine therapy for ER positive invasive breast cancer

People with female reproductive organs (women, trans men and non-binary people who currently have ovaries)

3. What is the real-world evidence on the long-term adverse events and effects on quality of life of using ovarian function suppression in combination with either tamoxifen or an aromatase inhibitor in premenopausal people with ER-positive invasive breast cancer?

People with male reproductive organs (men, trans women and non-binary people who currently have testes)

4. What is the real-world evidence on the clinical and cost effectiveness of testicular function suppression in combination with an aromatase inhibitor compared to tamoxifen alone or an aromatase inhibitor alone in people with ER-positive invasive breast cancer who have male reproductive organs?

5. What is the real-world evidence on the types of side effects (and severity) that people with ER-positive invasive breast cancer who have male reproductive organs experience with tamoxifen alone or testicular function suppression in combination with an aromatase inhibitor?

Terms used in this guideline

Triple negative breast cancer is defined as ER/PR/HER2 where each has been scored as negative according to local multidisciplinary team guidelines.

Rationale and impact

Adjuvant endocrine therapy for ER positive invasive breast cancer

Why the committee made the recommendations

The committee noted that, in the 2018 version of this guideline, there were separate recommendations to offer endocrine therapy to people with ER-positive invasive breast cancer who are premenopausal or perimenopausal or who have male reproductive organs, and for people who are postmenopausal. They agreed that it would be clearer to have a single overarching recommendation on endocrine therapy before giving advice about which therapy is suitable for each population separately, and so revised the recommendations accordingly.

People with female reproductive organs (women, trans men and non-binary people who currently have ovaries)

The evidence showed improvements in disease-free survival and reduced local or locoregional recurrence with ovarian function suppression (OFS) in combination with tamoxifen or OFS in combination with an aromatase inhibitor (AI) compared to tamoxifen alone for premenopausal people who have ER-positive invasive breast cancer. For overall survival the evidence could not differentiate when OFS in combination with tamoxifen was compared to OFS in combination with an AI, but there was an improvement with OFS in combination with tamoxifen compared to tamoxifen alone. There was a reduced risk of new contralateral disease with OFS in combination with an AI compared to tamoxifen alone, but the evidence could not differentiate between OFS in combination with tamoxifen compared to tamoxifen alone.

However, the evidence also showed an increased risk of some side effects with these treatments when compared to tamoxifen alone.

The committee agreed that the benefits in terms of cancer-related outcomes from using OFS in combination with an AI or OFS in combination with tamoxifen compared to tamoxifen alone were clear enough to recommend the option of OFS as part of initial endocrine therapy as well as retaining the option of treatment with tamoxifen alone.

The committee agreed that, for some premenopausal people with ER positive invasive breast cancer, the balance of benefits in terms of improvements in cancer-related outcomes from taking OFS in combination with an AI or in combination with tamoxifen compared to taking tamoxifen alone would outweigh the side effects and their impact on quality of life as a result of inducing a menopausal state. This includes people at higher risk of disease recurrence. However, they agreed that some people at lower risk would also choose to accept this treatment, and other people at low or high risk may choose to take tamoxifen instead. They therefore made a recommendation on making a shared decision about which type of endocrine therapy would be suitable.

The committee highlighted that perimenopausal people were not excluded by any of the included trials, and that most of these trials defined premenopausal status in a way that could be interpreted that perimenopausal people were also included. Therefore, the committee agreed that the evidence could be extrapolated to include perimenopausal people.

The committee also acknowledged the importance of taking the individual's circumstances, needs and preferences into account as part of the decision-making process. To help the person make an informed decision, the committee recommended that there should be a discussion with them about the benefits of this type of endocrine treatment, such as improving overall survival and disease-free survival, as well as risks, such as side effects of this treatment and included a table to support this. They also emphasised the possible side effects of each treatment option should be discussed. Some of

these can be managed with support or other treatments, and the committee agreed that it was important for people to be aware of this before they made their decision. However, the long-term consequences of these treatments and effects on quality of life from inducing the menopause prematurely are unclear. Therefore, the committee made a research recommendation to gather evidence on this topic.

How the recommendations might affect practice

It is not expected that the recommendations to offer endocrine therapy using tamoxifen alone, or ovarian function suppression in combination with either tamoxifen or an AI, will significantly increase resource use as many locations are already using these types of endocrine therapy in routine practice. The recommendations should also encourage standardisation of practice across the UK.

People with male reproductive organs (men, trans women and non-binary people who currently have testes)

Why the committee made the recommendations

The committee agreed that, based on their experience, they would continue to recommend tamoxifen as the initial endocrine therapy for people with male reproductive organs who have ER-positive invasive breast cancer.

It was not possible to differentiate between testicular function suppression (TFS) in combination with an AI compared to either tamoxifen alone or an AI alone from the evidence. However, the committee were aware that there was other evidence from studies in healthy people with male reproductive organs suggesting that an AI alone does not reduce the levels of this hormone enough that it could be used to exert an effect on oestrogen sensitive processes. Although this evidence is not directly relevant for people with ER-positive breast cancer, it means that an AI alone is unlikely to be sufficient to block the effects of oestrogen on ER-positive breast cancer in people with male reproductive organs. Therefore, the committee recommended that an AI should not be used alone to treat ER-positive breast cancer in people with male reproductive organs.

Although the evidence was limited, the committee agreed that TFS in combination with an AI could be an alternative when tamoxifen is not suitable or is not tolerated. However, they also highlighted that TFS is given as injections every 4 weeks or every 12 weeks (which could be inconvenient for some people) and that more side effects are expected with TFS in combination with an AI. The committee extrapolated from the evidence for people with female reproductive organs that showed an increased risk of adverse events with ovarian function suppression (OFS) in combination with an AI compared to tamoxifen alone, and agreed that there were no biological reasons that the effect of this combined therapy would be different in terms of causing an increased risk of adverse events for people with male reproductive organs. However, they expected there to be some male-specific side effects such as erectile dysfunction and gynaecomastia that should be discussed when considering treatment options as part of making a shared decision.

The committee also agreed that bone mineral density should be assessed in people with male reproductive organs who have ER-positive invasive breast cancer and who start adjuvant endocrine therapy with TFS in combination with an AI because the use of an AI is associated with the risk of bone density loss. There is an existing recommendation (recommendation 1.9.4 in the section on bone health) that covers this for women who are taking an AI and the committee agreed that to prevent the introduction of a health inequality they should recommend a similar assessment for people with male reproductive organs.

The committee noted the lack of evidence in people with male reproductive organs who have ER-positive invasive breast cancer, and made a recommendation for research that could be carried out using real-world evidence because of the expected difficulty recruiting to randomised controlled trials. They also noted that side effects in people with male reproductive organs who have ER-positive invasive breast cancer are expected to be similar to those in premenopausal or perimenopausal people with ER-positive invasive breast cancer, but agreed more evidence was needed to understand this and inform discussions around treatment options

for people with male reproductive organs. Therefore, they made a research recommendation to gather evidence about side effects and their severity from using tamoxifen alone or using TFS in combination with an AI in people with male reproductive organs.

How the recommendations might affect practice

The recommendations should encourage standardisation of practice across the UK. Both tamoxifen alone and TFS in combination with an AI are associated with adverse effects that can have cost and quality of life impacts, and because of the different mechanism of action, the side effect profiles will be different and therefore differences in the resources needed to manage these effects may arise. However, very few people are expected to receive TFS in combination with an AI because the population of people with male reproductive organs and breast cancer is very small. This should mean that the resource impact from using TFS in combination with an AI and of testing bone mineral density is also small.

Neoadjuvant treatment of HER2-positive breast cancer

Why the committee made the recommendations

The committee looked at evidence comparing the use of a platinum and a taxane based neoadjuvant chemotherapy regimen to an anthracycline and a taxane based regimen for people with HER2-positive invasive breast cancer. There was limited evidence available, and it was not able to differentiate between the 2 neoadjuvant chemotherapy regimens for key outcomes including pathological compete response, all-cause mortality and recurrence. The committee therefore concluded that there was insufficient evidence to support recommending one regimen over the other.

The committee noted that neoadjuvant therapy is not necessary for some small HER2-positive tumours, and that people who neoadjuvant therapy is suitable for are identified in line with criteria set out in related NICE technology appraisals (TAs). Although there is only one related TA at the time of publication, the committee agreed the recommendation should make allowances for other options as they become available in future.

The committee agreed that, although the evidence came from trials that recruited women with breast cancer, this recommendation would also apply to people with male reproductive organs because the biological mechanism of action of neoadjuvant chemotherapy is expected to be the same as for people with female reproductive organs.

How the recommendations might affect practice

It is not expected that the recommendation will increase resource use, as it is likely that many clinicians are already using these regimens in routine practice already.

Neoadjuvant treatment of triple-negative breast cancer

Why the committee made the recommendations

The committee recommended that people with triple negative breast cancer (TNBC) be offered a neoadjuvant chemotherapy regimen that contains a platinum, a taxane and an anthracycline because the evidence showed clinically meaningful improvements in overall survival, disease free survival and pathological complete response (signs of cancer disappearing in both the breast and lymph nodes in the axilla at surgery) after this treatment, compared to a regimen that contained a taxane and an anthracycline without a platinum. However, the evidence also showed an increased risk of some specific side effects with this regimen: anaemia, neutropenia (low numbers of white blood cells), thrombocytopenia (low number of platelets), and febrile neutropenia (a low number of neutrophils and temperature of 38°C or above on one occasion).

The committee agreed that the decision about which neoadjuvant chemotherapy regimen was the best option for a person with TNBC would be determined after a discussion with them on the balance of benefits (improvements to pathological complete response and survival) and harms (potential side effects, and their effects on quality of life). The committee also acknowledged the importance of taking the individual's circumstances, needs and preferences into account as part of the decision-making process.

Where people have TNBC and BRCA germline mutations, the committee agreed that they should be offered the same neoadjuvant chemotherapy options as other people with TNBC (that is, a regimen that contains a platinum, a taxane and an anthracycline) as there was no evidence to support treating them differently based on their BRCA germline mutation status. As a result, they did not make a separate recommendation for this population. However, for people with BRCA germline mutations of any receptor subtype other than triple negative (this could be any combination of positive or negative oestrogen receptor, progesterone receptor or human epidermal growth factor receptor 2) the committee were unable to determine whether treatment with a neoadjuvant chemotherapy regimen containing a platinum, a taxane and an anthracycline was beneficial in terms of improved survival and other important outcomes, so they made a recommendation for research to cover this gap in the evidence.

There was only limited evidence for people who were 60 years and older and no evidence for people with breast cancer who have male reproductive organs or people who are pregnant. The committee noted that these groups are often not recruited into RCTs, but real-world evidence is available in databanks such as SAIL and Systemic Anti-Cancer Therapy Dataset that could be used to address these gaps. They therefore made a research recommendation for a study using this RWE to look at the clinical and cost-effectiveness of platinum based neoadjuvant chemotherapy for these groups of people. The committee agreed that despite the lack of direct evidence, people aged 60 years and older and people with male reproductive organs may also benefit from platinum based neoadjuvant chemotherapy.

How the recommendations might affect practice

The committee agreed that neoadjuvant chemotherapy including a platinum-based chemotherapy is already current practice in many locations across the UK. The recommendation may increase this figure and might lead to an initial increase in NHS spending. However, downstream savings caused by fewer recurrences will likely offset the higher costs of increased use of this neoadjuvant treatment.

The recommendations should also encourage standardisation of practice across the UK.