NHS

National Institute for Health and Clinical Excellence

Quick reference guide

Issue date: February 2009

Early and locally advanced breast cancer

Diagnosis and treatment

This guideline updates and replaces NICE technology appraisal guidance 109 (docetaxel), 108 (paclitaxel) and 107 (trastuzumab)

NICE clinical guideline 80
Developed by the National Collaborating Centre for Cancer

About this booklet

This is a quick reference guide that summarises the recommendations NICE has made to the NHS in 'Early and locally advanced breast cancer: diagnosis and treatment' (NICE clinical guideline 80). The guideline updates and replaces NICE technology appraisal guidance 109 (published September 2006), 108 (published September 2006) and 107 (published August 2006).

Who should read this booklet?

This quick reference guide is for healthcare professionals and other staff who care for patients with early and locally advanced breast cancer.

Who wrote the guideline?

The guideline was developed by the National Collaborating Centre for Cancer, which is based at the Velindre NHS Trust in Cardiff. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

For more information on how NICE clinical guidelines are developed, go to www.nice.org.uk

Where can I get more information about the guideline?

The NICE website has the recommendations in full, reviews of the evidence they are based on, a summary of the guideline for patients and carers, and tools to support implementation (see page 18 for more details).

National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
London
WC1V 6NA

www.nice.org.uk

ISBN 1-84629-900-4

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Contents

Introduction

- Breast cancer is the most common cancer affecting women in England and Wales, with about 40,500 new cases diagnosed and 10,900 deaths recorded in England and Wales each year[1, 2].
- In men breast cancer is rare, with about 260 cases diagnosed and 68 deaths in England and Wales each year[1, 2].
- Of these new cases, a small proportion are diagnosed in the advanced stages, when the tumour has spread significantly within the breast or to other organs of the body.
- In addition, a significant number of women who have been previously treated with curative intent subsequently develop either a local recurrence or metastases.
- Early breast cancer is subdivided into two major categories: in situ ductal disease and invasive cancer.
- Over recent years there have been important developments in the investigation and management of breast cancer, including new chemotherapies and biological and hormonal agents.
- This clinical guideline helps to address practice variation across the country and inconsistent availability of certain treatments and procedures, and offers guidance on best practice.
- The guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, as there is good evidence to support that use. Unlicensed drugs are marked with a footnote.

Patient-centred care

Treatment and care should take into account patients' individual needs and preferences. Good communication is essential, supported by evidence-based information, to allow patients to reach informed decisions about their care. Follow Department of Health advice on seeking consent if needed. If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

[1] Office for National Statistics (2008) Cancer statistics registrations: registrations of cancer diagnosed in 2005, England. Series MB1 number 36. London: Office for National Statistics.
[2] Welsh Cancer Intelligence and Surveillance Unit (2008) Cancer incidence in Wales 1992–2002. Cardiff: Welsh Cancer Intelligence and Surveillance Unit.

Key priorities for implementation

Preoperative assessment of the breast

- Offer magnetic resonance imaging (MRI) of the breast to patients with invasive breast cancer:
  - if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
  - if breast density precludes accurate mammographic assessment
  - to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer.

Staging of the axilla

- Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.

Surgery to the axilla

- Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy is the preferred technique.

Breast reconstruction

- Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.

Adjuvant therapy planning

- Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery[3] in patients with early breast cancer having these treatments.

Aromatase inhibitors

- Postmenopausal women with oestrogen receptor-positive early invasive breast cancer who are not considered to be at low risk[4] should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is contraindicated or not tolerated.

continued

[3] Department of Health (2007). Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)

[4] Low-risk patients are those in the EPG or GPG (excellent or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have similar predictions using Adjuvant! Online.

Key priorities for implementation *continued*

Assessment of bone loss

- Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:
  - are starting adjuvant aromatase inhibitor treatment
  - have treatment-induced menopause
  - are starting ovarian ablation/suppression therapy.

Primary systemic therapy

- Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.

Follow-up imaging

- Offer annual mammography to all patients with early breast cancer, including ductal carcinoma in situ, until they enter the NHS Breast Screening Programme/Breast Test Wales Screening Programme. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

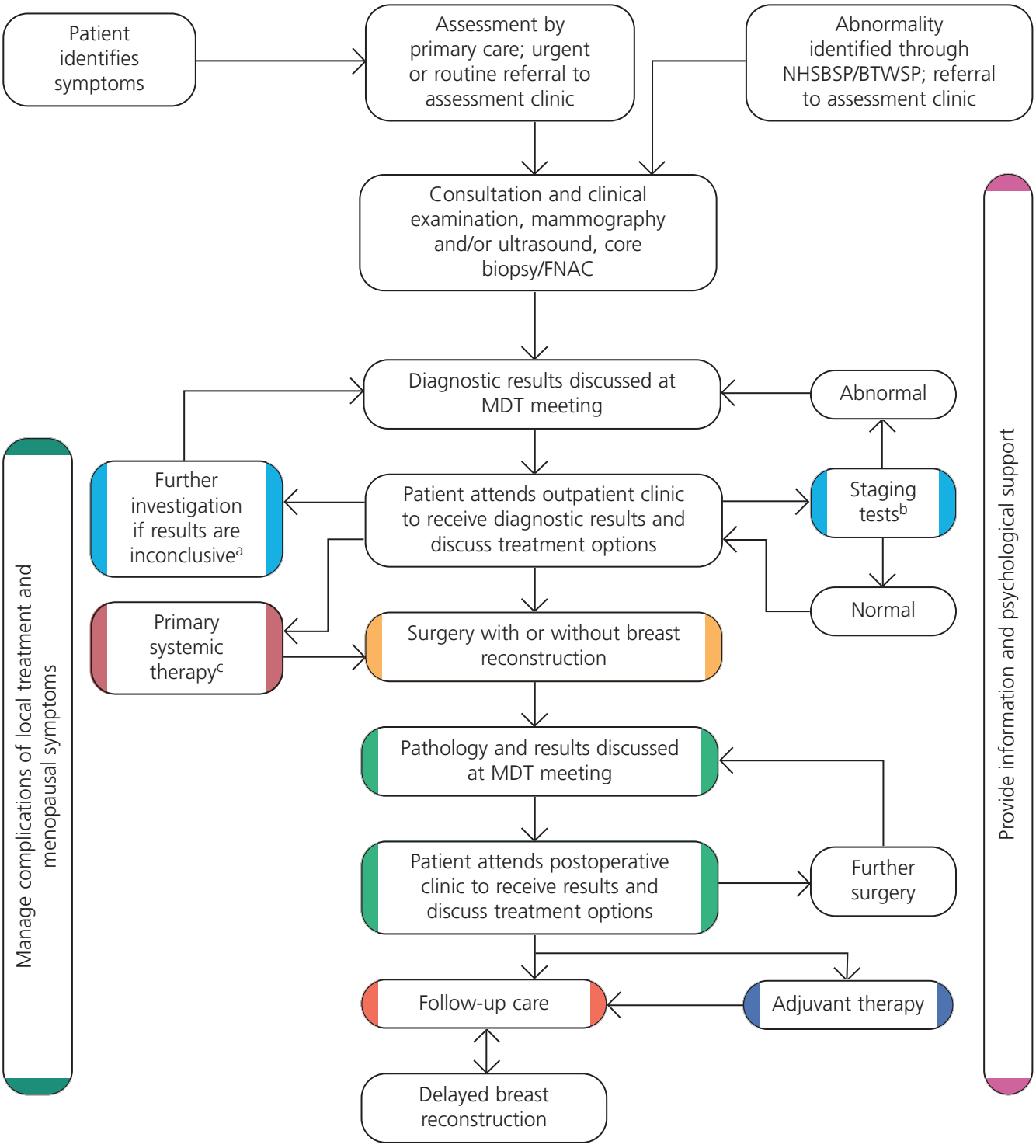
Clinical follow-up

- Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:
  - designated named healthcare professionals
  - dates for review of any adjuvant therapy
  - details of surveillance mammography
  - signs and symptoms to look for and seek advice on
  - contact details for immediate referral to specialist care, and
  - contact details for support services, for example support for patients with lymphoedema.

Abbreviations used in this booklet

AI:	aromatase inhibitor
ALND:	axillary lymph node dissection (also known as axillary clearance)
BTWSP:	Breast Test Wales Screening Programme
DCIS:	ductal carcinoma in situ
DEXA:	dual energy X-ray absorptiometry
ECG:	electrocardiograph
ER positive:	oestrogen receptor positive
FNAC:	fine needle aspiration cytology
HER2:	human epidermal growth factor receptor 2
HRT:	hormone replacement therapy
LVEF:	left ventricular ejection fraction
MDT:	multidisciplinary team
MRI:	magnetic resonance imaging
NHSBSP:	NHS Breast Screening Programme
SCF:	supraclavicular fossa
SLN:	sentinel lymph node
SLNB:	sentinel lymph node biopsy
SSRI:	selective serotonin re-uptake inhibitor

Overview of care pathway *(coloured boxes denote areas addressed in the guideline)*



[a] May include repeat core biopsy, open biopsy or MRI.
[b] Some patients may not require staging.
[c] Surgery may not be appropriate for all patients and for some patients primary systemic therapy precedes surgery.

Information and psychological support

- All members of the breast cancer clinical team should have completed an accredited communications skills training programme.
- All patients with breast cancer should:
  - be assigned to a named breast care nurse specialist who will support them throughout diagnosis, treatment and follow-up
  - be offered prompt access to specialist psychological support and, where appropriate, psychiatric services.

Assessment of the breast

- Routine MRI of the breast is not recommended for patients with biopsy-proven invasive breast cancer or DCIS.
- Offer MRI of the breast to patients with invasive breast cancer:
  - if there is discrepancy between the clinical and imaging assessment of disease extent
  - if breast density precludes accurate mammographic assessment
  - to assess tumour size if breast conserving surgery is being considered for invasive lobular cancer.

Assessment of the axilla

Patients with DCIS

Patient group	Actions
Having breast conserving surgery and not considered at high risk of invasive disease. Patients at high risk include those with a palpable mass or extensive microcalcifications	• Do not perform SLNB routinely.
Having mastectomy	• Offer SLNB.

Patients with early invasive breast cancer

Patient group	Actions
All being investigated	• Perform pretreatment ultrasound evaluation of the axilla. • If morphologically abnormal lymph nodes are identified, offer ultrasound-guided needle sampling.
No evidence of lymph node involvement on ultrasound, or negative ultrasound-guided needle biopsy	• Perform minimal surgery, rather than lymph node clearance. SLNB is the preferred technique. • SLNB should only be performed by a team that is validated in the use of the technique, as identified in the NEW START training programme[5]. • Perform SLNB using the dual technique with isotope and blue dye.
Macro- or micrometastases shown in SLN, or preoperative ultrasound-guided needle biopsy with histologically proven metastatic cancer	• Offer further axillary treatment. Axillary lymph node dissection (ALND) is the preferred technique because it gives additional staging information.
Only isolated tumour cells in SLNs	• Do not offer further axillary treatment. Regard as lymph node-negative.
All	• Breast units should audit their axillary recurrence rates.

[5] NEW START Sentinel Lymph Node Biopsy Training Programme, Royal College of Surgeons of England (www.rcseng.ac.uk/education/courses/new_start.html)

Surgery

Patients with DCIS

Patient group	Actions
Having breast conserving surgery	• A minimum of 2mm radial margin of excision is recommended, with pathological examination to NHSBSP reporting standards. • Consider re-excision if margin < 2mm after discussion of risks and benefits with patient. • Enter patients into the Sloane Project (UK DCIS audit) (www.sloaneproject.co.uk). • Breast units should audit their recurrence rates.

Patients with Paget's disease of the nipple

Patient group	Actions
Disease assessed as localised	• Offer breast conserving surgery with removal of the nipple–areolar complex as an alternative to mastectomy. • Offer oncoplastic repair techniques to maximise cosmesis.

Patients advised to have mastectomy

Patient group	Actions
All	• Discuss immediate breast reconstruction, except where comorbidities or adjuvant therapy may preclude this option. • Offer and discuss all breast reconstruction options with patients, irrespective of whether they are all available locally.

Postoperative assessment

All patients with early invasive breast cancer

- Use standardised and qualitatively assured methodologies to assess ER and HER2 status.
- Assess ER status using immunohistochemistry and report the result quantitatively.
- Ensure results of ER and HER2 status assessment are available and recorded at the MDT meeting at which guidance about systemic treatment is made.
- Do not routinely assess progesterone receptor status.

Systemic therapy

Patients with early invasive breast cancer

Patient group	Actions
All, irrespective of age	• Treat with surgery followed by adjuvant systemic therapy (rather than with endocrine therapy alone) unless significant comorbidity prevents surgery.
Considering breast conserving surgery that is not advisable at presentation	• Preoperative systemic therapy can be offered. • Discuss with the patient the increased risk of local recurrence with breast conserving surgery and radiotherapy rather than mastectomy after systemic therapy.

Patients with locally advanced or inflammatory breast cancer

Patient group	Actions
Have been treated with chemotherapy	• Offer local treatment by mastectomy (or, in exceptional cases, breast conserving surgery) followed by radiotherapy.

Adjuvant therapy planning

All patients with early invasive breast cancer

- After surgery, consider adjuvant therapy at the MDT meeting. Record all decisions.
- Make decisions about adjuvant therapy based on assessment of prognostic and predictive factors and potential benefits and side effects of the treatment. Make decisions following discussion of these factors with the patient.
- Consider using Adjuvant! Online (www.adjuvantonline.com) to support estimations of individual prognosis and absolute benefit of adjuvant treatment.

All patients with early breast cancer

- Start adjuvant chemotherapy or radiotherapy as soon as clinically possible and within 31 days of surgery[6].

Assessment and treatment of bone loss in patients starting adjuvant treatment

- Offer baseline DEXA to patients with early invasive breast cancer who:
  - are starting adjuvant AI treatment
  - have treatment-induced menopause
  - are starting ovarian ablation/suppression therapy.
- Do not offer DEXA to patients with early invasive breast cancer who are receiving tamoxifen alone, regardless of pretreatment menopausal status.
- Offer bisphosphonates to patients identified by algorithms 1 and 2 in 'Guidance for the management of breast cancer treatment-induced bone loss. A consensus position statement from a UK expert group'[7].

[6] Department of Health (2007). Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)
[7] Reproduced in appendix 2 of the full guideline. See www.nice.org.uk/CG80

Adjuvant therapy

Endocrine therapy

Patient group	Actions
ER-positive early invasive breast cancer, premenopausal women	• Do not offer ovarian ablation/suppression to women having tamoxifen and chemotherapy. • Offer ovarian ablation/suppression in addition to tamoxifen to women who have been offered chemotherapy but chosen not to have it.
ER-positive early invasive breast cancer, postmenopausal women who are not at low risk[8]	• Offer AI, either anastrozole or letrozole, as initial adjuvant therapy. Offer tamoxifen if AI is not tolerated or contraindicated.
ER-positive early invasive breast cancer, postmenopausal women who are not at low risk[8] and who have been treated with tamoxifen for 2–3 years	• Offer AI, either exemestane or anastrozole, instead of tamoxifen.
ER-positive, lymph-node positive early invasive breast cancer, postmenopausal women who have been treated with tamoxifen for 5 years	• Offer additional treatment with the AI letrozole for 2–3 years.
ER-positive early invasive breast cancer, postmenopausal women	• The AIs anastrozole, exemestane and letrozole, within their licensed indications, are recommended as options for adjuvant treatment[9].
ER-positive early invasive breast cancer	• Discuss with women the risks and benefits of each treatment option. Consider previous treatment with tamoxifen, licensed indications and side-effect profiles of individual drugs and, in particular, assessed risk of recurrence[9].
DCIS after breast conserving surgery	• Do not offer tamoxifen.

[8] Low-risk patients are those in the EPG or GPG (excellent or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have similar predictions using Adjuvant! Online.
[9] This recommendation is from 'Breast cancer (early) – hormonal treatments' (NICE technology appraisal guidance 112).

Chemotherapy

Patient group	Actions
Lymph node-positive breast cancer	• Offer docetaxel as part of adjuvant chemotherapy regimen. • Do not offer paclitaxel.

Biological therapy

Patient group	Actions
HER2-positive early invasive breast cancer following surgery, chemotherapy, and radiotherapy when applicable	• Offer trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is shortest). • Assess cardiac function before starting treatment with trastuzumab. Do not offer if any of the following are present: – LVEF ≤ 55% – history of documented congestive heart failure – high-risk uncontrolled arrhythmias – angina pectoris requiring medication – clinically significant valvular disease – evidence of transmural infarction on ECG – poorly controlled hypertension. • Repeat cardiac functional assessments every 3 months during trastuzumab treatment. • If LVEF drops by ≥ 10 percentage (ejection) points from baseline and to < 50%, stop trastuzumab. Restart trastuzumab only after further cardiac assessment and fully informed discussion with the patient about the risks and benefits.

Radiotherapy (breast) for patients with early invasive breast cancer

Patient group	Actions
After breast conserving surgery	• Patients should have breast radiotherapy.
After breast conserving surgery or mastectomy	• Use external beam radiotherapy, giving 40Gy in 15 fractions as standard practice.
After breast conserving surgery and breast radiotherapy, at high risk of local recurrence	• Offer external beam boost to the site of local excision. • Inform patients that cosmesis is likely to be worse, particularly in women with larger breasts.
After mastectomy, at high risk of local recurrrence[10]	• Offer chest wall radiotherapy.
After mastectomy, at intermediate risk[11] of local recurrence	• Consider entering patients into SUPREMO trial assessing value of postoperative radiotherapy (www.supremo-trial.com).
After mastectomy, at low risk of local recurrence[12]	• Do not offer radiotherapy.

[10] Includes patients with ≥ 4 positive axillary lymph nodes or involved resection margins.
[11] Includes patients with 1–3 involved lymph nodes, lymphovascular invasion, histological grade 3 tumours, ER-negative tumours, and those aged < 40 years.
[12] For example, most patients who are lymph node-negative.

Radiotherapy (breast) for patients with DCIS

Patient group	Actions
After breast conserving surgery (see Surgery, page 10)	• Offer breast radiotherapy. Discuss with patients the potential benefits and risks.

Radiotherapy (nodal) for patients with early breast cancer

Patient group	Actions
Lymph-node negative	• Do not offer radiotherapy to the axilla or SCF.
After ALND	• Do not offer radiotherapy to the axilla.
Positive axillary SLNB or 4-node sample; ALND not possible	• Offer radiotherapy to the axilla. (See Assessment of the axilla, page 9).
Lymph node-positive, ≥ 4 involved nodes	• Offer radiotherapy to the SCF.
Lymph node-positive, 1–3 involved nodes and other poor prognostic factors (for example, T3 and/or histological grade 3 tumours), and good performance status	• Offer radiotherapy to the SCF.
After breast surgery	• Do not offer radiotherapy to the internal mammary chain.

Complications of local treatment and menopausal symptoms

Complication	Information and advice	Actions
Lymphoedema	• Inform patients about the risk and give them written information before offering surgery and radiotherapy. • Give advice on how to prevent infection or trauma.	• Ensure rapid access to a specialist lymphoedema service.
Arm mobility	• Give instructions on functional exercises, which should start the day after surgery, to patients having axillary surgery. This should include relevant written information from a member of the breast or physiotherapy team.	• Identify pre-existing shoulder conditions preoperatively. • Refer patients to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment. • Breast units should have written local guidelines agreed with the physiotherapy department for postoperative physiotherapy regimens.
Menopausal symptoms	• Offer information and counselling about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment.	• Discontinue HRT in women diagnosed with early breast cancer. • Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. • HRT[13] may, in exceptional cases, be given to women with early breast cancer who have severe menopausal symptoms, as long as the woman has been fully informed about the associated risks. • SSRI antidepressants (paroxetine[14] and fluoxetine[14]) may be used to relieve menopausal symptoms, particularly hot flushes, but not in women taking tamoxifen. • Clonidine, venlafaxine[14] and gabapentin[14] should only be used to treat hot flushes after the woman has been fully informed of the significant side effects. • Tibolone, progestogens, soy (isoflavone), red clover, black cohosh, vitamin E and magnetic devices are not recommended to treat menopausal symptoms.

[13] The summaries of product characteristics state that HRT is contraindicated in women with known, past or suspected breast cancer. Informed consent should be obtained and documented.
[14] These drugs are not licensed for the stated use. Informed consent should be obtained and documented.

Follow-up care

Follow-up imaging

- Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP.
- Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years[15].
- Do not offer mammography of the ipsilateral soft tissues after mastectomy.
- Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have had early invasive breast cancer or DCIS.

Clinical follow-up

- After adjuvant treatment (including chemotherapy and/or radiotherapy, where indicated) is completed, discuss with patients where they would like follow-up to be undertaken. They may choose primary, secondary or shared care.
- Patients should follow an agreed, written care plan, recorded by a named healthcare professional (or professionals). A copy should be sent to the GP and a copy given to the patient. It should include:
  - designated named healthcare professionals
  - dates for review of any adjuvant therapy
  - details of surveillance mammography
  - contact details for immediate referral to specialist care, and
  - contact details for support services, for example, support for patients with lymphoedema.

[15] For patients who have entered the NHSBSP/BTWSP, or who have had 5 years of annual mammography follow-up, we recommend the NHSBSP/BTWSP stratify screening frequency in line with risk category.

Further information

Ordering information

You can download the following documents from www.nice.org.uk/CG80

- The NICE guideline – all the recommendations.
- A quick reference guide (this document) – a summary of the recommendations for healthcare professionals.
- 'Understanding NICE guidance' – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1792 (quick reference guide)
- N1793 ('Understanding NICE guidance').

Related NICE guidance

For information about NICE guidance that has been issued or is in development, see www.nice.org.uk

Published

Advanced breast cancer: diagnosis and treatment. NICE clinical guideline 81 (2009). Available from www.nice.org.uk/CG81

Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal guidance 161 (2008). Available from www.nice.org.uk/TA161

Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. NICE technology appraisal guidance 160 (2008). Available from www.nice.org.uk/TA160

Brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision. NICE interventional procedure guidance 268 (2008). Available from www.nice.org.uk/IPG268

Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer. NICE technology appraisal guidance 112 (2006). Available from www.nice.org.uk/TA112

Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of NICE clinical guideline 14). NICE clinical guideline 41 (2006). Available from www.nice.org.uk/CG41

Endoscopic axillary lymph node retrieval for breast cancer. NICE interventional procedure guidance 147 (2005). Available from www.nice.org.uk/IPG147

Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/CG27

Interstitial laser therapy for breast cancer. NICE interventional procedure guidance 89 (2004). Available from www.nice.org.uk/IPG89

Improving supportive and palliative care for adults with cancer. Cancer service guidance (2004). Available from www.nice.org.uk/csgsp

Improving outcomes in breast cancer – manual update. Cancer service guidance (2002). Available from www.nice.org.uk/csgbc

Under development

Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. NICE clinical guideline (publication date to be confirmed).

Updating the guideline

This guideline will be updated as needed, and information about the progress of any update will be posted on the NICE website (www.nice.org.uk/CG80).

Implementation tools

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG80).

- Slides highlighting key messages for local discussion.
- Audit support for monitoring local practice.
- Costing tools:
  - costing report to estimate the national savings and costs associated with implementation
  - costing template to estimate the local costs and savings involved.

National Institute for
Health and Clinical Excellence
MidCity Place
71 High Holborn
London
WC1V 6NA

www.nice.org.uk

N1792 1P 75k Feb 09

ISBN 1-84629-900-4