

**Guideline for the Non Surgical Treatment of Breast Cancer**  
incorporating former guidelines for systemic treatment, radiotherapy and aromatase inhibitors.

**Version History**

Version	Date	Comments
2.0	20.02.08	Endorsed by the Governance Committee
2.1	10.06.10	Discussed with Andrea Stevens (AS)
2.2	10.06.10	Following discussion with AS, guidelines for 'systemic treatment' 'radiotherapy' and 'aromatase inhibitors' incorporated into one document.
2.3	12.07.10	With AS comments after discussion with Dan Rea
2.4	02.08.10	Updated with AS comments\changes
2.5	13.08.10	Updated with further comments\changes by AS.
2.5	21.09.10	Circulated to the Breast NSSG and Oncologists for comment.
2.6	27.09.10	Following consultation – for final ratification by AS
2.7	5.11.10	With AS comments for submission to the Governance Subgroup 24/11/10
3.0	24.11.10	Finalised at Governance Sub Group.

<b>Date Approved by Network Governance</b>	<b>November 2010</b>
--	----------------------

<b>Date for Review</b>	<b>November 2013</b>
------------------------	----------------------

**Changes made between version 2 and version 3**

- Expanded section on role/indications for use of neoadjuvant treatment.
- Updated section on adjuvant endocrine treatment in light of recent prospective studies.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

## Contents

	<b>Page No.</b>	
1	Scope of the guideline	3
2	Background	3
3	Neo-adjuvant chemotherapy	3
4	Adjuvant cytotoxic chemotherapy	4
5	Adjuvant treatment with Trastuzumab	5
6	Adjuvant treatment with hormones	6
7	Adjuvant treatment with aromatase inhibitors	6
8	Radiotherapy	9
9	Management of isolated, operable loco-regional recurrence	10
10	Recurrent/metastatic disease	11
11	Patient information and counselling	12
12	Palliative care	12
13	Clinical trials	12
Appendix 1	Management of Bone Loss in Early Breast Cancer : <b>Algorithm 1</b>	16
Appendix 2	Management of Bone Loss in Early Breast Cancer – <b>Algorithm 2</b>	17

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

## 1 Scope of the Guideline

This guidance has been produced to support non-surgical treatment for patients with breast cancer. This includes:

- Neo adjuvant chemotherapy and endocrine treatment.
- Adjuvant chemotherapy.
- Adjuvant endocrine treatments including aromatase inhibitors.
- Radiotherapy.
- The clinical management of patients with relapsed disease.

## 2 Guideline Background

This guideline aims is to make sense of national and local documents within the context of Pan Birmingham Cancer Network, ensuring that up to date research, current thinking, and local expert opinion have been incorporated.

### Guideline Statements

## 3 Neo Adjuvant Treatment (Chemotherapy/Endocrine)

### 3.1 Advantages of Neoadjuvant Treatment

- a) To downstage tumours to make them operable/enable breast conservation/allow less extensive surgery.
- b) In-vivo sensitivity can be assessed and treatment tailored to response.

### 3.2 Patient Selection

3.2.1 The following patients should be considered for neoadjuvant treatment (chemotherapy or endocrine):

- a. Patients with inoperable cancers that can potentially be downstaged to enable surgery.
- b. Patients only suitable for mastectomy as they can be potentially downstaged to enable breast conserving surgery.
- c. Patients who require mastectomy, choose immediate reconstruction and who will clearly require chemotherapy or hormone therapy, to avoid any delay in systemic therapy that might arise from post operative recovery/complications.
- d. Patients who are suitable for breast conservation treatment at diagnosis but who clearly require chemotherapy or hormone therapy can also be considered for neoadjuvant treatment with its benefits of in vitro sensitivity and immediate systemic treatment.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

### 3.3 Chemotherapy regimens

An anthracycline and/or taxane based regimen is recommended. If there is no response after 3 cycles an alternative regimen should be commenced. All HER 2 positive patients should receive trastuzumab unless contraindicated.

### 3.4 Anti-oestrogen therapy

An aromatase inhibitor should be offered in post menopausal patients unless contra-indicated. In situations where a tumour has demonstrated sensitivity to a specific agent (tamoxifen or an aromatase inhibitor) patients should remain on that agent as an adjuvant therapy.

### 3.5 Treatment of the axilla

No large prospective randomised trials have compared the sensitivity of sentinel node biopsy (SLNBX) pre and post neo-adjuvant treatment. The published evidence indicates that the procedure has equivalent sensitivity pre or post treatment. Therefore SLNBX pre or post treatment, or axillary clearance post treatment, should depend on individual unit/surgeon practice.

3.6 All patients should be considered for entry into randomised controlled trials (RCTs) for which they are eligible.

## 4 Adjuvant cytotoxic chemotherapy

4.1 Adjuvant chemotherapy should start within 6 to 8 weeks of the first definitive operation and this must be taken into account when patients are being considered for immediate reconstruction.

4.2 Adjuvant chemotherapy should be considered for patients where the magnitude of the expected benefit justifies the expense and anticipated toxicity of treatment. Factors to be considered include prognosis, age, co-morbidity and acceptability of the treatment to the patient. It is understood therefore that a considerable degree of variability in uptake is likely where the value of chemotherapy is considered to be marginal. Adjuvant chemotherapy should only be given when the social environment is considered to be safe.

4.3 Adjuvant chemotherapy should be multi-agent and include an anthracycline unless there is a clear medical contraindication. In the Pan Birmingham Cancer Network all patients undergoing adjuvant chemotherapy for breast cancer should be considered for the following 8 cycles of treatment in the first instance: sequential epirubicin x4, followed by CMF x4 (classical CMF or IV cyclophosphamide on D1 and D8). Other anthracycline based regimens such as FEC, or EC can be considered in appropriate circumstances.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

- 4.4 Adjuvant Taxanes are now an alternative for high risk node positive patients. However NICE has not recommended routine use of Paclitaxel. Docetaxel is sanctioned by NICE for node positive early breast cancer. Docetaxel containing regimens will incur greater toxicity and must only therefore be considered in highly motivated patients with excellent performance status and minimal co-morbidity. The registration regimen TAC is considered too toxic for routine use and it is recommended that it should be limited to clinical trials unless given with prophylactic GCSF and antibiotics. Therefore block sequential therapy with epirubicin x 3 docetaxel x 3 and CMF x 3 or FEC x 3 then Docetaxel x 3 are considered appropriate evidence based alternative docetaxel containing chemotherapy regimens that are a cost saving alternatives to TAC with growth factor support.
- 4.5 Maintenance of dose intensity is important in achieving maximal benefits from chemotherapy. Primary prophylaxis with antibiotics should be considered in patients at high risk of neutropenic complications such as patients with poorly healed surgical wounds or with a recent history of postoperative wound infection. Secondary prophylaxis with growth factors should also be considered to maintain dose intensity.
- 4.6 All patients should be considered for entry into RCTs for which they are eligible.

## 5 Adjuvant Treatment with Trastuzumab

- 5.1 Trastuzumab should be considered for all women with early stage Her2 positive breast cancer following surgery and chemotherapy (neoadjuvant or adjuvant) plus radiotherapy if applicable.
- 5.2 Cardiac function should be assessed prior to commencement of treatment. Trastuzumab should not be offered to women who have a left ventricular ejection fraction (LVEF) of 55% or less or who have any of the following:
- A history of documented congestive heart failure.
  - High-risk uncontrolled arrhythmias.
  - Angina pectoris requiring medication.
  - Clinically significant valvular disease.
  - Evidence of transmural infarction on electrocardiograph (ECG).
  - Poorly controlled hypertension.
- 5.3 Cardiac functional assessments should be repeated every 3 months during Trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50% (**or institutional lower limit of normal**) then trastuzumab treatment should be suspended. A decision to resume trastuzumab therapy should be based on a further cardiac assessment and a fully informed discussion of the risks and benefits between the individual patient and their clinician.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

5.4.1 Trastuzumab in the adjuvant setting is given using a 3 weekly regimen with loading for 1 year (**18** treatments) or until disease recurrence (which ever is the shorter period).

5.5 All patients should be considered for entry into RCTs for which they are eligible.

## **6 Adjuvant Treatment with Hormones**

6.1 All patients with hormone receptor positive tumours should be offered adjuvant hormone treatment for five years after primary therapy. If the patient is to receive chemotherapy, this should be delivered first and the endocrine treatment started on its completion.

6.2 Adjuvant hormone therapy should be Tamoxifen for pre-menopausal women.

6.3 The role of ovarian ablation remains unclear. Further RCTs are awaited.

6.4 Ovarian ablation may have a role in women less than 40 years if they are still menstruating post chemotherapy. As this remains uncertain individual patient decisions are required following discussion at the multidisciplinary team meeting. Entry into the RCTs investigating this should be offered.

## **7 Adjuvant Treatment with Aromatase inhibitors**

7.1 Aromatase inhibitors (AIs) should only be prescribed for postmenopausal women with ER positive disease. Caution should be exercised in women with chemotherapy induced menopause since ovarian function may recover.

7.2 Standard adjuvant therapy (up to 5 years)

7.2.1 Using AIs where Tamoxifen is contraindicated.

a. Patients for whom endocrine therapy is clearly indicated; but where clear contraindications to Tamoxifen are present or develop. This includes patients with a history or family history of spontaneous DVT or pulmonary embolus without identified and reversible cause such a trauma or surgery.

b. Patients for whom endocrine therapy is clearly indicated but where intolerance to Tamoxifen has required withdrawal of Tamoxifen.

These patients should commence AI therapy as soon as the indication arises and should complete 5 years of adjuvant therapy. Pre-menopausal women will require ovarian suppression when an AI is required.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

### 7.2.2 Low risk patients

Low risk T1 grade 1 N0 - Tamoxifen for 5 years unless toxicity or contraindications

### 7.2.3 Intermediate/high risk patients

- a. Node positive or PgR negative – AI for 5 years
- b. Others – Tamoxifen 2 – 3 years then switch to AI for remainder of 5 years

## 7.3 Extended adjuvant therapy

7.3.1 Women who have completed 5 years of adjuvant Tamoxifen with lymph node positive disease remain at increased risk of relapse and should be treated with an adjuvant aromatase inhibitor for 4 years, in keeping with the product licences (see below). This group can also be defined in terms of Nottingham Prognostic Indicator at an arbitrary value of 4.2, i.e. a 1cm grade II tumour with low lymph node involvement.

7.3.2 It is estimated that breast cancer recurrence in this group will be reduced by 5-7%.

## 7.4 Primary Endocrine treatment

Patients who are not fit for surgery due to co-morbidities (or those who decline) and who have endocrine receptor positive breast cancer should be offered primary endocrine treatment. This should be with an aromatase inhibitor (which show longer progression free survival than Tamoxifen). This should continue until disease progression.

## 7.5 Current Licences

Aromatase inhibitors should be used within specific licensed indications:

- a. Anastrozole and Letrozole are licensed for immediate use after surgery.
- b. Exemestane is licensed for use after 2-3 years prior Tamoxifen exposure in the adjuvant context.
- c. Anastrozole is licensed for use after 2 years prior Tamoxifen exposure in the adjuvant context.
- d. Letrozole is also licensed for use as neoadjuvant therapy and as therapy following the completion of 5 years adjuvant Tamoxifen.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

## 7.6 Other considerations

### 7.6.1 Safety

- a. Aromatase inhibitors have a number of differences in side effect profile compared to Tamoxifen, in general they are well tolerated and treatment withdrawal is less frequent than with Tamoxifen. They are associated with reduced gynaecological toxicity, incidence of vaginal discharge, vaginal bleeding and endometrial cancer is substantially reduced.
- b. Venous thrombosis is less common and in some studies hot flushes are less frequent although remain common. As with Tamoxifen, patients taking aromatase inhibitors who experience postmenopausal bleeding should be referred for gynaecological assessment.
- c. All the aromatase inhibitors are associated with increased bone mineral loss in comparison with Tamoxifen. This represents a combination of loss of protective effect seen with Tamoxifen and an additional increased loss over baseline as a result of oestrogen deprivation. More fractures are seen in women on aromatase inhibitors compared to women on Tamoxifen. A precautionary approach to management of bone health is recommended.

### 7.6.2 Bone Health Recommendations

#### All Patients

- a. Guidelines being considered by the British Osteoporosis Society recommend routine calcium and vitamin D replacement for all patients on adjuvant AIs. Sufficient replacement should be given to ensure 100% RDA intake.
- b. For patients with premature menopause at age <45 years
  - i) The UK Management Algorithm for the National Osteoporosis Society / National Cancer Research Institute should be followed (see appendix one).
  - ii) In summary all patients should receive:
    - Baseline DEXA scan and risk assessment
    - Lifestyle advice and adequate calcium and vitamin D
      - 1g calcium and 800iu vitamin D
    - Risk adapted strategy
    - Reassure if T score > -1 and not on concomitant AI
      - No monitoring required
    - Monitoring of BMD
      - Perform every 2 years if:
        - T score < -1 without an AI
        - All patients if concomitant AI

**ENDORSED BY THE GOVERNANCE COMMITTEE**



- Intervention with bisphosphonates (alendronic acid (Fosamax) 70mg once per week or ibandronic acid (Bonviva) 150mg once per month)
  - Concomitant AI and T score < -1
  - T score < -2 either at baseline or on follow-up
  - Annual bone loss >4% on serial BMD monitoring

c. For post-menopausal women >age 45 years

- The UK Management Algorithm for the National Osteoporosis Society / National Cancer Research Institute should be followed (see appendix two).
- In summary all patients should receive:
  - Baseline DEXA scan and risk assessment if for AI therapy
  - Risk adapted strategy
  - Lifestyle advice and adequate calcium and vitamin D
    - 1 g calcium and 800iu vitamin D
  - Reassure if T score > -1 and no risk factors
    - No monitoring required
  - Monitor BMD of osteopaenic patients every 2 years
    - Baseline T score <-1
    - Intervention with bisphosphonates (alendronic acid (Fosamax) 70mg once per week or ibandronic acid (Bonviva) 150mg once per month)
      - > age 75 and > 1 risk factor for osteoporotic fracture
      - T score < -2 either at baseline or on follow-up
      - T score < -1 at baseline and annual bone loss >4%

### 7.6.3 Ischaemic Cardiac Disease

Two out of five registration studies have indicated a possible increased risk of ischaemic cardiac disease with aromatase inhibitors. If this is a real effect it is small and may reflect a loss of Tamoxifen associated cardio protection rather than a true toxicity. However, patients on adjuvant AIs should be reminded to have cardiac risk factors such as hypertension and hyperlipidaemias addressed according to routine practice in primary care.

### 7.6.4 Randomised Controlled Trials

All patients should be considered for entry into RCTs for which they are eligible.

## 8 Radiotherapy

- Radiotherapy should be considered for all patients with breast cancer who have had breast conserving surgery for high grade Ductal Carcinoma Insitu (DCIS) or invasive carcinoma.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

- 8.2 Radiotherapy should be considered for all patients with breast cancer who have had a mastectomy if they are considered to have a high risk of local recurrence. This will normally include those with a tumour greater than 5 cm or who are lymph node positive.
- 8.3 40Gy is administered in 15 fractions over 3 weeks. Arm B of the START trials has not yet reported (comparative dose/ fraction study) but Arm A (40Gy in 15 fractions versus 50Gy in 25 fractions) demonstrates shorter fractionation to be equivalent and possibly superior to longer schedules (i.e. 50Gy in 25 fractions). All patients will also receive a boost to the tumour bed when radiotherapy is given after breast conserving surgery.
- 8.4 Patients should commence their radiotherapy treatment within 4 weeks of the definitive decision to proceed. This will normally be the consultation with the clinical oncology team when radiotherapy is formally discussed with the patient by the appropriate specialist team and written consent from the patient obtained.
- 8.5 Radiotherapy to the axilla is not normally given following an axillary clearance (see note below), but should be offered to patients following axillary sampling if the patient is node positive (unless axillary clearance is proposed as an alternative).
- 8.6 Where there are more than 10 lymph nodes involved in the axilla with extracapsular extension patients may have to be considered for adjuvant radiotherapy to the axilla. In these cases the patient must be fully aware of the likelihood of increased toxicity.
- 8.7 Radiotherapy to the supraclavicular fossa (SCF) should be considered when more than 4 axillary nodes are involved (or other risk factors for SCF relapse are present).
- 8.8 CT based radiotherapy planning has been implemented at the radiotherapy centre and is used where clinically appropriate. Conventional simulation and planning remains available for those not suitable for a CT based approach.
- 8.9 All patients should be considered for entry into RCTs for which they are eligible.
- 8.10 Patients who have received neo-adjuvant treatment should be discussed on an individual basis in the MDT with regard to radiotherapy to the chest wall after mastectomy and nodal radiotherapy taking into account factors such as response to treatment, tumour size and grade at diagnosis, evidence of axillary nodal involvement at diagnosis (imaging +/-histology/cytology). Patients who have had wide local excision after neo-adjuvant treatment should all receive radiotherapy to intact breast.**

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

## **9 Management of isolated, operable loco-regional recurrence**

- 9.1 Isolated local recurrence should be managed by surgical resection where possible.
- 9.2 Systemic treatment should be reviewed in the light of the pathology and discussed at the MDT for each individual patient.

## **10 Recurrent / Metastatic Disease**

- 10.1 Treatment will depend on previous response to treatment, site of disease recurrence, symptoms and interval from initial diagnosis.
- 10.2 The treatment aim is to relieve symptoms, improve quality of life and survival.
- 10.3 Endocrine treatment after Tamoxifen failure will be a reversible AI (second line) and an irreversible AI (third line) in post-menopausal women. For pre-menopausal women, second line endocrine treatment will normally be induction of menopause (e.g. Zoladex) with the aromatase inhibitors used third line concurrently with the ovarian ablation treatment.
- 10.4 Cytotoxic agents should be considered for
  - a. ER-ve patients
  - b. Those that fail to respond to hormone therapy.
  - c. Patients with life threatening visceral disease or;
  - d. Those with a short disease free interval from the completion of adjuvant treatment to relapse.
- 10.5 Agents that may be used include, Anthracyclines, Taxanes, Vinka Alkaloids Antimetabolites and alkylating agents. NICE guidance exists for the use of Taxanes, Vinorelbine, Capecitabine and taxanes as monotherapy or in combination with Gemcitabine.
- 10.6 Chemotherapy should normally be no more than 6 cycles and treatment should be stopped if the disease continues to progress (early assessment of response after 2 -3 cycles should be made) or if side effects cannot be adequately controlled. Patients responding to treatment and tolerating therapy with a history of rapid progression after prior therapy may be considered for extended courses of treatment.
- 10.7 All patients developing relapsed disease should have the HER 2 status of the original breast cancer checked unless there is a clear medical contraindication to the use of Trastuzumab. Where this is positive, use of Trastuzumab should be considered in line with NICE guidance:

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

NICE has recommended that trastuzumab be available for women with HER2 positive advanced breast cancer either:

- in combination with paclitaxel for women whose HER2 protein is measured as 3+.who have not had chemotherapy and for whom anthracycline treatment is not appropriate.
- or on its own for women with breast cancer and HER2 levels of 3+ who have had at least two chemotherapy treatments for metastatic breast cancer. Previous chemotherapy must have included at least an anthracycline drug and a Taxane drug where these treatments are appropriate. It should also have included hormonal therapy in patients sensitive to oestrogen.

10.8 Bisphosphonates should be considered for all patients with bony metastatic disease.

10.9 All patients should be considered for entry into RCTs for which they are eligible.

## 11 Patient Information and Counselling

11.1 All patients, and with their consent, their partners, will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the Breast MDT at all times.

11.2 Access to psychological support will be available if required. All patients should be offered an holistic needs assessment and onward referral as required.

## 12 Palliative Care

Palliative care services will be made available to all patients as deemed appropriate by the MDT.

## 13 Clinical Trials

13.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.

13.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: [PBCRN@westmidlands.nhs.uk](mailto:PBCRN@westmidlands.nhs.uk)

13.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

## Monitoring of the Guideline

Compliance with the guidance will be considered as a topic for audit by the NSSG in 2012.

## References (Chemotherapy)

1. NICE 2002. Guidance on the use of Trastuzumab for the treatment of advanced breast cancer. Technology Appraisal 34.
2. NICE – Technology Appraisal Guidance 107
3. NICE – Adjuvant Trastuzumab
4. NICE – Adjuvant Taxotere
5. Pan Birmingham Cancer Network Aromatase inhibitors Guidance
6. 'The Cancer Centre Medical Treatment Portfolio' (2007) held by the University Hospital Birmingham Foundation NHS Trust.

## References (Aromatase inhibitors)

1. Winer EP, Hudis C, Burstein HJ, et al: American Society of Clinical Oncology technology assessment on the use of Aromatase inhibitors as adjuvant therapy for postmenopausal women with hormone receptor-positive breast cancer: status report 2004. J Clin Oncol 23:619-29, 2005
2. Baum M, Budzar AU, Cuzick J, et al: Anastrozole alone or in combination with Tamoxifen versus Tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial. [see comment][erratum appears in Lancet 2002 Nov 9;360(9344):1520]. Lancet. 359:2131-9, 2002
3. Coombes RC, Hall E, Gibson LJ, et al: A Randomized Trial of Exemestane after Two to Three Years of Tamoxifen Therapy in Postmenopausal Women with Primary Breast Cancer. New England Journal of Medicine 350:1081 - 1092, 2004
4. Coombes RC HE, Snowdon CF, Bliss JM.: The Intergroup Exemestane Study: a randomised trial in postmenopausal patients with early breast cancer who remain disease free after two to three years of Tamoxifen-updated survival analysis. Breast Cancer Res Treat SABCS supplement:Abstract 3, 2004
5. Goss PE, Ingle JN, Martino S, et al: A randomized trial of letrozole in postmenopausal women after five years of Tamoxifen therapy for early-stage breast cancer. N Engl J Med 349:1793-802, 2003
6. Goss PE: A placebo controlled trial of letrozole following Tamoxifen as adjuvant therapy in postmenopausal women with breast cancer. ASCO WEBB SITE Slides available at:[http://www.asco.org/ac/1,1003,12-002511-00\\_18-0026-00\\_19-0011301,00.asp](http://www.asco.org/ac/1,1003,12-002511-00_18-0026-00_19-0011301,00.asp), 2004
7. Howell A, Cuzick J, Baum M, et al: Results of the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet 365:60-2, 2005

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

8. Howell et al: ATAC ('Arimidex', Tamoxifen, Alone or in Combination) completed treatment analysis: Anastrozole demonstrates superior efficacy and tolerability compared with Tamoxifen. Breast cancer Research and treatment, 2004
- 9 Switching of postmenopausal women with endocrine-responsive early breast cancer to anastrozole after 2 years' adjuvant Tamoxifen: combined results of ABCSG trial 8 and ARNO 95 trial. Jakesz R KM, Gnant M, Jonat W et al Lancet. 2005 Aug 6-12;366(9484):455-62.
10. Thurlimann B: Letrozole as adjuvant endocrine therapy for postmenopausal women with receptor positive breast cancer. St Galen Breast Cancer Consensus Conference, 2005
11. Use of lutenising hormone releasing hormone agonists as advuvant treatment in pre-menopausal patients with hormone receptor positive patients breast cancer: a meta-analysis of individual patient form randomised adjuvant trials. The lancet. V369, issue 9574, pages 1711-1723, 19<sup>th</sup> May 2007.

### References (Radiotherapy)

1. All oncological statements are with reference to 'The Cancer Centre Medical Treatment Portfolio' (2007) held by the University Hospital Birmingham Foundation NHS Trust.
2. 'Effect of radiotherapy fraction size on tumour control in patients with early stage breast cancer after local tumour excision: long term results of a randomised trial.' Owen JR, Ashton A, Bliss JM et al. Lancet Oncol. 2006 Jun; 7(6):467-71.
3. Clin Oncol (R Coll Radiol). 1999;11(3):S90-133. [Links](#)

### Authors

Andrea Stevens	Consultant Clinical Oncologist
Dan Rea	Consultant Medical Oncologist
Lara Barnish	Deputy Director of Nursing

**Approval Date of Network Site Specific Group: Septemebr 2010**

**Date Approval by the Clinical Governance Team: November 2010**

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

**Approval Signatures:**

**Pan Birmingham Cancer Network Governance Committee Chair**

**Pan Birmingham Cancer Network Governance Committee Chair**

Name: Doug Wulff

Signature 

Date 24 November 2010

**Pan Birmingham Cancer Network Manager**

Name: Karen Metcalf

Signature 

Date 24 November 2010

**Network Site Specific Group Chair**

Name Alan Jewkes

Date 24 November 2010

Signature 

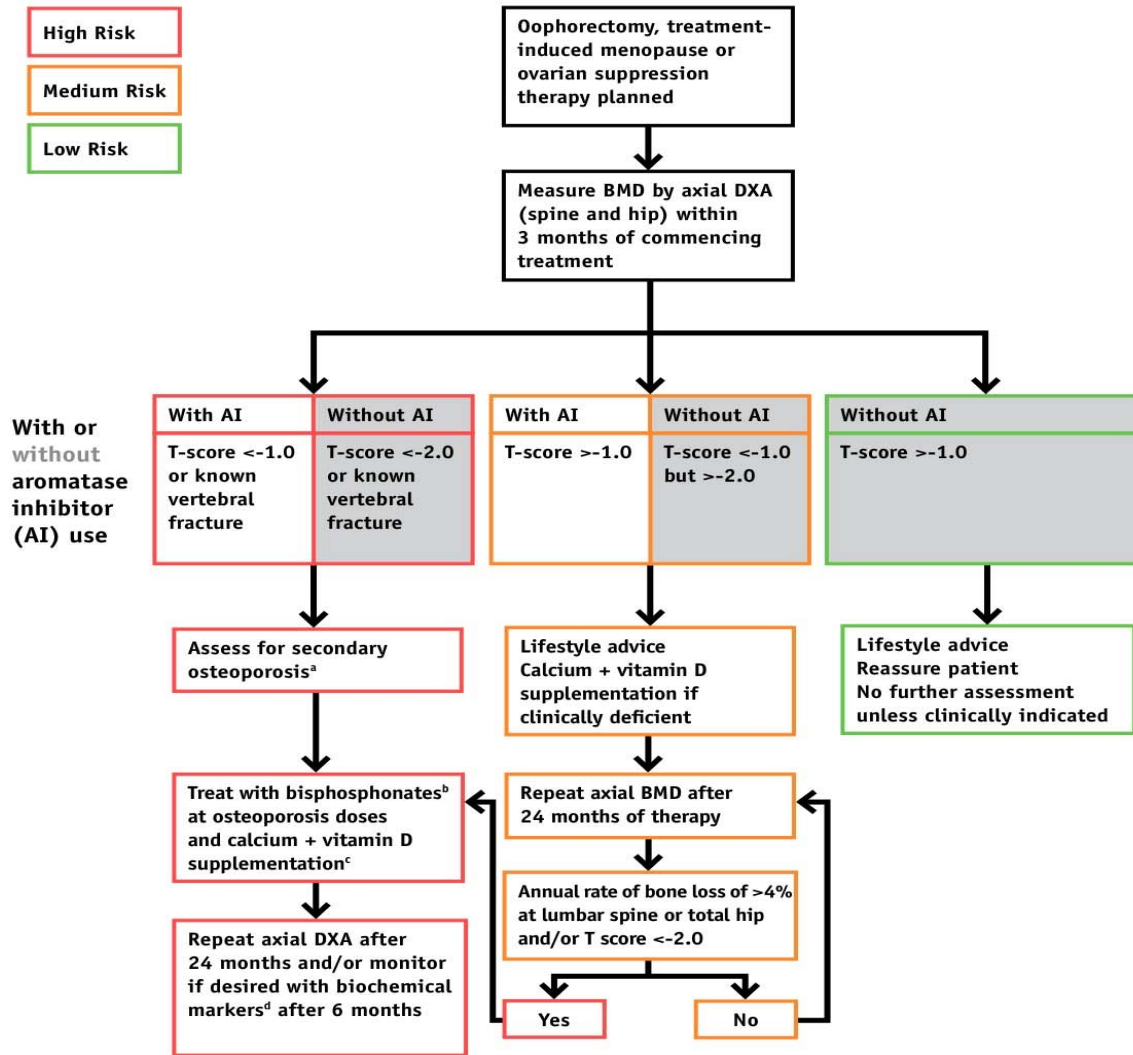
Date 24 November 2010

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc

Management of bone loss in early breast cancer

Algorithm 1: Adjuvant treatment associated with ovarian suppression/failure with or without concomitant aromatase inhibitor use in women who experience premature menopause



a ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST /  $\gamma$ GT), serum creatinine, endomysial antibodies, serum thyroid stimulating hormone  
 b Alendronate 70 mg per week, risedronate 35 mg per week,

ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly  
 c To be given as  $\geq 1$  g of calcium +  $\geq 800$  IU of vitamin D  
 d Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen

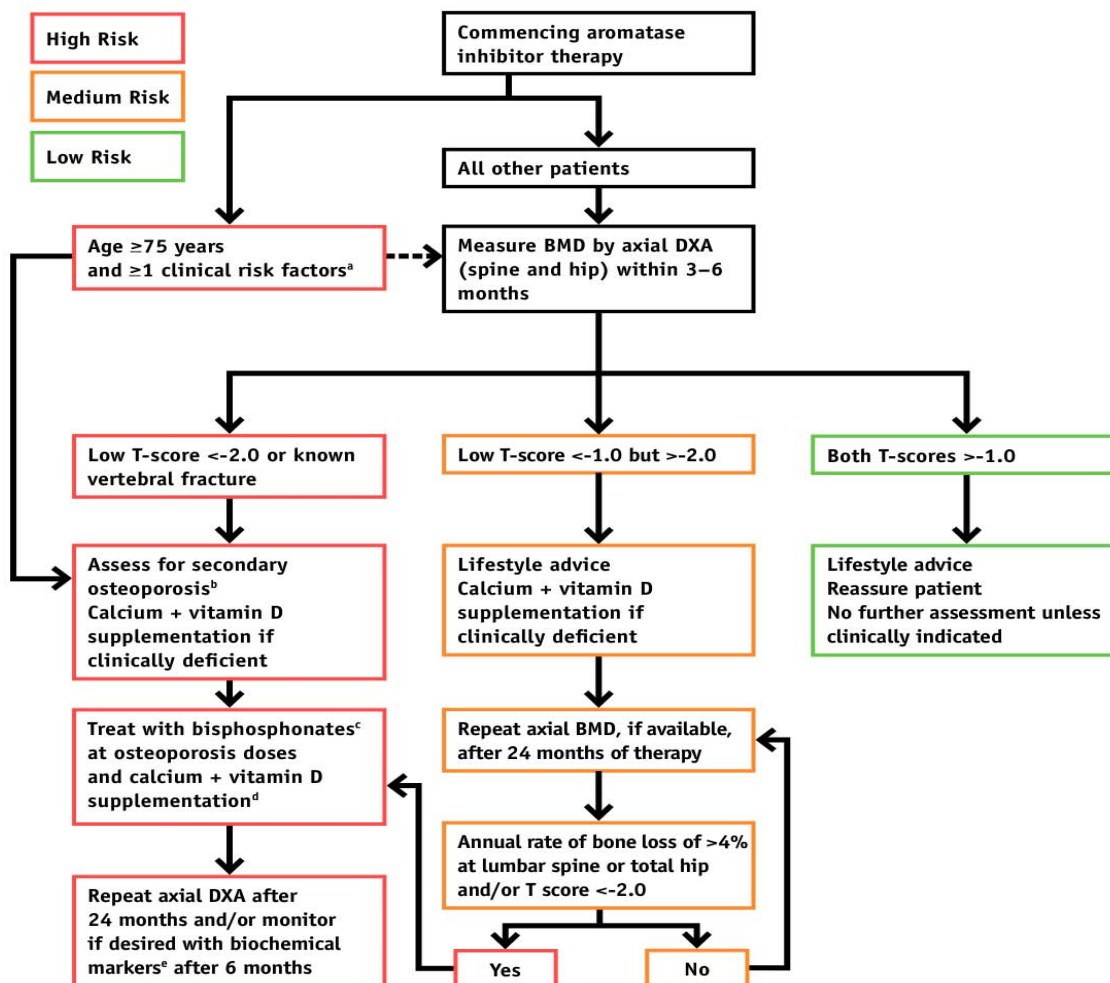
The algorithm has been reviewed and supported by the National Cancer Research Institute Breast Cancer Study Group and the National Osteoporosis Society

**ENDORSED BY THE GOVERNANCE COMMITTEE**



## Management of bone loss in early breast cancer

### Algorithm 2: Postmenopausal adjuvant treatment with aromatase inhibitors



**a** Previous low-trauma fracture after age 50, parental history of hip fracture, alcohol intake of >4 units/day, diseases associated with secondary osteoporosis, prior corticosteroids for >6 months, low BMI (<22)

**b** ESR, FBC, bone and liver function (calcium, phosphate, alkaline phosphatase, albumin, AST /  $\gamma$ GT), serum creatinine, endomysial antibodies, serum thyroid stimulating hormone

**c** Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

**d** To be given as  $\geq 1$  g of calcium +  $\geq 800$  IU of vitamin D  
**e** Biochemical markers such as serum C-terminal telopeptide of type I collagen or urinary N-telopeptide of type I collagen

The algorithm has been reviewed and supported by the National Cancer Research Institute Breast Cancer Study Group and the National Osteoporosis Society

**ENDORSED BY THE GOVERNANCE COMMITTEE**

S:\Cancer Network\Guidelines 2011\Guidelines and Pathways by Speciality\Breast\Current Approved Versions (Word and PDF)\Guidelines Breast Non Surgical Treatment Version 3.doc