Clinical Management Guideline for Breast Cancer
West of Scotland Cancer Network

Initial Evaluation
- Primary Diagnosis:
  - Mammography
  - History and physical
  - Fine needle aspiration
  - Core biopsy
  - Full blood count
  - Chest X-Ray
  - Biochemistry

Pre-Treatment Evaluation
- Operable by Conservation Surgery
- Candidate for Primary Medical Treatment
- Operable by Mastectomy

Clinical Stage
- Surgery
- Less than 4 positive lymph nodes
- 4 or more positive lymph nodes

Treatment and pathological stage
- HER2 Positive (see page 4)
- ER Negative
  - PR Negative
  - HER2 Negative (see page 5)
- If staging positive
- Metastatic disease (see page 7)

Adjuvant Treatment
- Radiotherapy
- Primary medical therapy (see page 6)

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<td><strong>Post-menopausal</strong></td>
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<td><strong>Pre-menopausal</strong></td>
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<td><strong>Node Positive</strong></td>
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<tr>
<td><strong>Node Negative</strong></td>
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- **High Risk:**
  - G3
    - **No**
    - Pre-menopausal
      - Tamoxifen
    - Post-menopausal
      - See page 3
  - **Yes**
    - Pre-menopausal
      - Chemotherapy^1
      - Tamoxifen 5 years
    - Post-menopausal
      - Consider Chemotherapy^1
      - See page 3

- **G1 or G2 1-3 nodes**
  - Pre-menopausal
    - Chemotherapy^1
    - See page 3

- **G3 and/or >4 Nodes**
  - Pre-menopausal
    - Chemotherapy^1
    - Tamoxifen 5 years
  - Post-menopausal
    - Chemotherapy^1
    - See page 3

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1. SEE PAGE 8
   AC x 4 or FEC80 x6
   TC if previous anthracyclines or cardiac issues
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**POSTMENOPAUSAL?**

**Menopausal Status - Definitions:**

- Post Menopausal: at time of diagnosis of breast cancer defined as:
  - Amenorrhea > 2 Years and > 50 years
- If amenorrhea <2 years and/or < 55 years check LH/FSH/Oestrodiol before chemotherapy

**CHEMOTHERAPY INDUCED AMENORRHOEA DOES NOT EQUAL POSTMENOPAUSAL**

And ovarian function tests are unreliable post chemotherapy/hormonal therapy

If pre-menopausal before chemotherapy with persisting chemo induced amenorrhoea following chemo then at the time of considering an AI:

- If < 50 years old exclude- unless ovarian ablation
- If 50-55 years use assessment of menopausal status pre chemotherapy
- If > 55 years class as postmenopausal

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**ANYONE OF:**

- Grade 3
- Node +ve¹
- ER poor²
- Her 2 +ve
- Path size ≥5cm (T3 & T4)
- Prev. neoadj AI with response

**ALL OF:**

- Grade 1 AND
- Node -ve¹ AND
- Size <2cm

**ALL THE REST i.e.**

- Grade 2 node –ve¹ Size<5cm
- Grade 1 node –ve¹ Size 2-5cm

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**Yes**

Aromatase Inhibitor³

5 years duration

**Yes**

Tamoxifen

5 years duration

**Yes**

Extended adjuvant³

(5yrs tam +3yearsAI)

OR

Switch³

(2.5 yrs tam +2.5years Al)

**No**

Ineligible for AI

Consider tamoxifen

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¹Micrometastases defined as 0.2-2mm = node positive, isolated tumour cells defined as <0.2mm = node negative

²ER poor defined as Allred 3-5

³Aromatase inhibitor as per current licenses. The choice of AI should be as per local Health Board policy and approvals
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**Pathological stage**

**Adjuvant Treatment**

1. **HER2 Positive**
   - **Node positive**
     - **Low risk: <1cm**
       - **Yes**
         - **ER positive?**
           - **No**
             - **No systemic therapy**
           - **Yes**
             - **Pre-menopausal**
               - **Tamoxifen**
             - **Post-menopausal**
               - **Aromatase inhibitor**
       - **No**
         - **Chemotherapy**
   - **No**
     - **Chemotherapy**

2. **HER2 Positive**
   - **Node negative**
     - **Low risk: <1cm**
       - **Yes**
         - **ER positive?**
           - **No**
             - **No systemic therapy**
           - **Yes**
             - **Pre-menopausal**
               - **Tamoxifen**
             - **Post-menopausal**
               - **Aromatase inhibitor**
       - **No**
         - **Chemotherapy**

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A. See Trastuzumab guideline, page 6

1. See page 8
   - AC (node negative and unfit)
   - FEC80 (node negative)
   - FEC100 > DH (node positive)
   - TC + Herceptin (not suitable for anthracyclines)

*a Aromatase inhibitor as per current licence & Health Board policy*
• ER Negative
• PR Negative
• HER2 Negative

Node Negative

Low risk:
G1 & <2cm

Yes

No systemic therapy

Chemotherapy ¹

Pathological stage

Adjuvant Treatment

Node Positive

¹ SEE PAGE 8
FEC80 (node negative)
AC (node negative and unfit)
FEC100 > D (node positive)
TC (not suitable for anthracyclines)
Primary medical therapy

Her2 NEG ER Positive
- Premenopausal
  - Fscore X 3 >
  - Docetaxel 100 x 3 or TCx4
- Postmenopausal
  - Letrozole 2.5mg od 4-6 months

Her2 POS Any ER
- Premenopausal
  - Fscore X 3 >
  - Docetaxel 100 x 3 + Herceptin 2-3 or TC + Herceptin x 4
- Postmenopausal
  - No further tx

Premenopausal
- ER/PR positive
  - Docetaxel 100mg/m² x 3
- ER/PR negative
  - Complete 5 yrs letrozole

Postmenopausal
- ER/PR positive
  - Tamoxifen 5 yrs + OS if HER2 pos
- ER/PR negative
  - No further tx

Surgery + 3 or 4 field radiotherapy

HER 2 Positive > Add 14-16 cycles Trastuzumab

For chemotherapy schedules see page 9
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Evaluation for metastases

Primary Diagnosis:
- Mammography
- History and physical
- Fine needle aspiration
- Core biopsy
- Full blood count
- Chest X-Ray
- Biochemistry

Metastatic Diagnosis:
- Bone Scan
- CT chest and abdomen

Metastatic Diagnosis:
- Bone Metastases
- ER positive
- ER negative

Treatment of metastases:

- Other (e.g., Megestrol)

- Aromatase inhibitor
  - Good response
  - Poor response

- Alternative AI
  - Good response
  - Poor response

- Hormone treatment candidate
  - No

- Suitable for chemotherapy
  - Yes
  - No

- Previous adjuvant treatment
  - Yes
  - No

- >2 years ago
  - Yes
  - No

- <2 years ago
  - Yes

- Relapse

- Previous Taxane
  - Yes
  - No

- Relapse

- Palliative therapy

- Fluorouracil/epirubicin/cyclophosphamide or
  - Epirubicin
  - See note B, page 9

- Taxane and
  - Trastuzumab (if HER2 Positive)
  - See note A, page 9

- Taxane and
  - Trastuzumab (if HER2 Positive)
  - See note A, page 9

- Capecitabine or
  - Vinorelbine
  - See note C, page 9

- Consider 3rd/4th line therapies
  - See note D, page 9

- No

- Relapse

- Relapse

- Relapse

- Relapse

- Relapse

- Relapse

- Relapse

- Relapse
Adjuvant chemotherapy regimens

For full details please refer to relevant WoSCAN chemotherapy protocol

Clinical trials should be considered in all cases. Acceptable regimens for adjuvant chemotherapy:

AC : Doxorubicin (Adriamycin) 60mg/m² + Cyclophosphamide 600mg/m², 3 weekly x 4 cycles
For women > 70 or low risk or patients need chemotherapy but thought not able to tolerate more intensive regimen

FEC 80: Fluorouracil 600mg/m² + Epirubicin 80mg/m² + Cyclophosphamide 600mg/m², 3 weekly x 6 cycles
Standard anthracycline based schedule. ER + / HER2 negative as adjuvant therapy.

FEC > D: 5-FU 500mg/m² Epirubicin 100mg/m² Cyclophosphamide 500mg/m² x 3 cycles 3 weekly > Docetaxel 100mg/m² x 3 cycles,3 weekly. Requires primary prophylaxis with GCSF
Taxane based chemotherapy preferred option [triple negative] < 65 years, performance status 0,1

FEC > DH: 5-FU 500mg/m² Epirubicin 100mg/m² Cyclophosphamide 500mg/m² x 3 cycles 3 weekly > Docetaxel 100mg/m² x 3 cycles,3 weekly + Herceptin 8mg/kg / 6mg/kg. Requires primary prophylaxis with GCSF. Start Herceptin at cycle 4 or 5.
Taxane based chemotherapy preferred option [HER2 positive] < 65 years, performance status 0,1

TC : Docetaxel 75mg/m² + Cyclophosphamide 600mg/m², 3 weekly x 4 cycles
For patients who need chemotherapy but not suitable for anthracycline due to cardiac history, previous anthracycline or taxane based chemotherapy preferred [triple receptor negative or HER2 positive] but not fit enough for FEC > D or > 65 years of age. If HER-2 positive start Herceptin with chemotherapy (18 cycles in total)
Neo-Adjuvant chemotherapy regimens

For full details please refer to relevant WoSCAN chemotherapy protocol

Clinical trials should be considered in all cases. Acceptable regimens for primary chemotherapy:

**FEC 100**: Fluorouracil 500mg/m2 + Epirubicin 100mg/m2 + Cyclophosphamide 500mg/m2, 3 weekly x 6 cycles
Standard anthracycline based schedule. ER+ / HER2 neg. Peg-GCSF required all cycles
If no response after 3 cycles change to **Docetaxel 100 mg/m2 for a further 3 cycles**.

**FEC > D or FEC > DH**, 3 weekly x 6 cycles
Triple negative: Fluorouracil 500mg/m2 + Epirubicin 100mg/m2 + Cyclophosphamide 500mg/m2, 3 weekly x 3 cycles followed by Docetaxel 100mg/m2 x 3 cycles. Peg-GCSF required all cycles.
HER2 positive: Fluorouracil 500mg/m2 + Epirubicin 100mg/m2 + Cyclophosphamide 500mg/m2, 3 weekly x 3 cycles followed by Docetaxel 100mg/m2 x 3 cycle + Herceptin 8mg/kg / 6mg/kg. Start Herceptin at cycle 4 or 5. Peg-GCSF required all cycles.

**TC**: Docetaxel 75mg/m2 / Cyclophosphamide 600mg/m2 3 weekly x 4 cycles
For patients who need chemotherapy but not suitable for anthracycline due to cardiac history, previous anthracycline.
Taxane based chemotherapy preferred [triple negative or HER2 positive] but not fit enough for FEC> D or > 65 years of age.
**Metastatic chemotherapy regimens**

*For full details please refer to relevant WoSCAN chemotherapy protocol*

The choice of metastatic therapies are dictated by the individual patient’s previous therapy, general health, liver/renal/bone marrow function, response to previous treatments and sites of disease. Definitive recommendations can therefore not be made.

**Clinical trials should be considered in all cases.**

A. Acceptable regimens:
   - Paclitaxel 80mg/m² weekly; Paclitaxel 175mg/m² 3 weekly; Docetaxel 100mg/m² 3 weekly.
   - Trastuzumab either 4mg/kg loading dose then 2mg/kg weekly or 8mg/kg loading followed by 6mg/kg 3 weekly.

B. Acceptable regimens:
   - Epirubicin 30mg/m² weekly; Epirubicin 100mg/m² 3 weekly; FEC 600/60/600mg/m² 3 weekly.

C. Acceptable regimens:
   - Capecitabine 1000mg/m² bd days 1-14, 3 weekly; Vinorelbine 25mg/m² IV or 60 mg/m² oral days 1+8, 3 weekly,

D. Phase 1 or 2 trials should be considered. Otherwise suitable options include:
   - Vinorelbine or Capecitabine if not previously received
   - Weekly Paclitaxel if responded to previous Docetaxel
   - Mitoxantrone
   - Low-dose oral Cyclophosphamide

E. Bisphosphonates as per WoS guidelines.
Radiotherapy Algorithm

**Axillary Sample or +ive SLNB**
- **Node Positive**
  - Further Surgery Axillary Dissection
    - **Yes**
      - Conservation or Reconstruction
        - 50Gy in 25# (boost if Conservation & ≤60 yrs)
      - Mastectomy
        - 45Gy in 20#
    - **No**
      - Mastectomy with 1-3 nodes positive plus one of:
        - LVI
        - Multifocality
        - Grade 3
        - OR T3 / T4
      - Conservation
        - 2 Field
          - **Yes**
            - 400.5Gy in 15# (boost if Conservation & ≤60 yrs)
          - **No**
            - Nil or Trial
      - Mastectomy
        - 50Gy in 25#
  - **Inadequate axillary surgery (Non-SLNB sample with < 4 nodes)**

- **Node Negative**
  - Axillary Sample or +ive SLNB
  - Conservation or Reconstruction
    - 50Gy in 25# (boost if Conservation & ≤60 yrs)
  - Mastectomy
    - 45Gy in 20#
  - Reconstruction
    - 2 Field
      - **Yes**
        - 400.5Gy in 15# (boost if Conservation & ≤60 yrs)
      - **No**
        - Nil or Trial