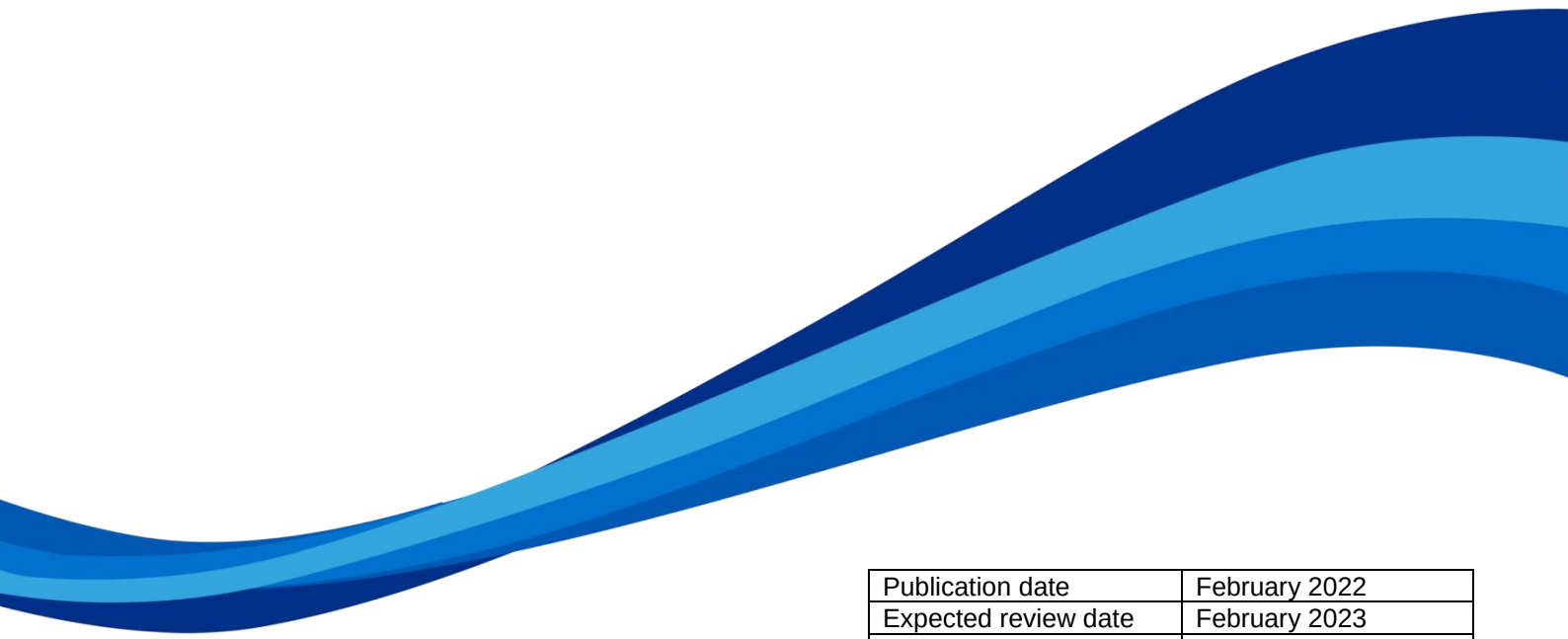
NHS
Kent and Medway
Cancer Collaborative

Oncological Treatment of Breast Cancer

Pathway of Care

Kent & Medway Cancer Collaborative



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1.0 ONCOLOGY PROVISION

1.1 Purpose

This document has been written to provide guidance on the treatment of breast cancer in the Kent & Medway Cancer Collaborative.

Radiotherapy schedules are as defined in the Kent Oncology Centre Quality System Clinical Protocols.

See KMCC chemotherapy prescribing protocols for details of chemotherapy / anti-cancer regimens.

All patients will be considered for entry into a clinical trial (see appendix C).

All patients should be discussed within a multidisciplinary team meeting before commencing initial treatment.

All chemotherapy regimens listed within this document are delivered at either Maidstone and Tunbridge Wells NHS Trust, Dartford and Gravesham NHS Trust, Medway NHS Foundation Trust or East Kent Hospitals University NHS Foundation Trust.

Please note, some of the drugs / doses recommended within this document are outside of the UK licensed marketing authorisation.

1.2 Details

The following information is needed at the time of referral:

- Age and menopausal status.
- Performance status.
- Full histology including grade and excision margins in early disease.
- ER and PgR status.
- HER2 status.

Recommendations for staging and pre-chemo investigations:

- All patients should have blood tests (U&E, LFTs, FBC).
- Patients receiving an anthracycline should have baseline ECG.
- Consider MUGA or ECHO pre-anthracycline for patients with cardiac history.
- Patients receiving trastuzumab should have MUGA / ECHO scans performed before and during treatment, see appendix B.
- Patients with T3, T4, N2 tumours and bilateral tumours should be fully staged to exclude liver, lung and bone metastases. Also consider in any patients felt clinically to be at high risk of metastases, e.g. high-risk TN, Her2+
- For adjuvant or neo-adjuvant carboplatin containing treatment, an EDTA should preferably be done before cycle 1.
- All patients being considered for fluoropyrimidine (i.e. capecitabine, 5-fluorouracil) based therapy should undergo pre-treatment pharmacogenomic screening for the four variants of DPYD associated with severe toxicity.

1.3 Ovarian Protection - Preservation of Fertility and/or Ovarian Function

For premenopausal women anxious to protect their fertility, early referral to a fertility specialist should be arranged for a full discussion of options. If no definitive fertility treatment is chosen, there is some evidence to suggest 4 weekly Zoladex 3.6mg SC started 10 days pre c1 of chemotherapy and continued throughout, may help preserve fertility.

2.0 ADJUVANT CHEMOTHERAPY

2.1 Risk Profiling

Adjuvant chemotherapy is based on discussion between clinician and patient balancing risks and benefits according to patient's risk profiling. Risk profiling is constructed from the following:

- Pre and post-menopausal patients who are ER+ HER2- and node- or micrometastases positive and, where patient and oncologist are undecided about the benefit of chemotherapy, should be offered tumour profiling testing according to NICE guidance. NICE guidance permits use of 2nd generation (ONCOTYPE) and 3rd generation (ENDOPREDICT or PROSIGNA) testing to guide chemotherapy decisions where there is immediate benefit to chemotherapy.
- Adjuvant chemotherapy should be discussed with patients according to the risk of relapse based on the most recent EBCTGG overview and other consensus documents.
- The Predict tool may also be used at www.predict.nhs.uk
- Histological phenotype.
- Co-morbidities.

There will exist a 'low risk' group of patients where the absolute benefit of adjuvant chemotherapy is so small that routine use is not recommended (<3% estimated benefit).

Adjuvant chemotherapy should be started as soon as clinically possible within 31 days of completion of surgery.

Consider the use of a frailty index assessment to assess fitness for chemotherapy; an example is given in appendix G.

2.2 Adjuvant Chemotherapy Regimens

Patients with following Phenotype	Preferred regimen	Alternatives
ER+ HER2- High risk	• Accelerated EC & accelerated paclitaxel (BRE-076)	• EC followed by Accelerated Paclitaxel (BRE-050) • EC x 4 (BRE-058) • Weekly paclitaxel x 12 (BRE-036) • TC x 4 (BRE-015)
Triple negative and/or BRCA +ve	• Accelerated EC followed by carboplatin (every 3 weeks) with weekly paclitaxel (BRE-077) • EC followed by accelerated paclitaxel (less toxicity) (BRE-050)	• EC followed by 3 weekly carboplatin & weekly paclitaxel. (BRE-059) • EC x 4 (BRE-058) • Accelerated EC followed by weekly carboplatin with weekly paclitaxel • Weekly paclitaxel x 12 (BRE-036) • TC x 4 (BRE-015)

Triple negative with residual disease following non-carboplatin containing neo-adjuvant chemotherapy or where neo-adjuvant carboplatin treatment is compromised and there is significant residual disease.	• Capecitabine x 8 (BRE-002)	
HER2+ node -ve	• EC followed by paclitaxel (weekly) and trastuzumab (SC) (3 weekly) followed by trastuzumab (SC) (BRE-064)	• FEC-T & trastuzumab (BRE-048 or BRE-049) • Weekly paclitaxel x 12 & trastuzumab (BRE-052)
HER2+ node +ve	• EC followed by paclitaxel (weekly) & Phesgo® (pertuzumab / trastuzumab SC) Adjuvant (BRE-081)	• TCPhesgo (adjuvant) (Phesgo® = pertuzumab/trastuzumab SC) (BRE-080)
HER2+ Node Positive post neoadjuvant SACT	Continue pertuzumab and trastuzumab to a total of 18 cycles (including cycles given in neo-adjuvant setting, see section 7)	
HER2+ with residual invasive disease following the combination of taxane-based and HER2-targeted neoadjuvant systemic therapy and surgery.	• Trastuzumab emtansine (Kadcyla®) x14	

NB:

- Abraxane (albumin paclitaxel) may be used as an alternative for patients who have documented taxane hypersensitivity.
- SC administration of pertuzumab/trastuzumab (Phesgo®) is the preferred formulation over IV administration. IV pertuzumab/trastuzumab regimens available on KMCC website.
- Triple Negative Tumours: It should be remembered that ER PR and HER2 negative tumours carry a worse prognosis and are a population often suitable for entry into clinical trials. Also triple negative patients under 60 years are suitable for referral for BRCA testing whatever their family history.
- For details on chemotherapy regimens and pre-treatment parameters, please refer to the KMCC Chemotherapy protocols.

3.0 ADJUVANT HORMONE THERAPY (FOR HORMONE RECEPTOR POSITIVE PATIENTS, ER AND/OR PGR

Adjuvant endocrine therapy should be started following the completion of chemotherapy, or following the oncology new patient appointment if chemotherapy is not appropriate. For patients with ER-positive advanced breast cancer who have neoadjuvant chemotherapy, offer endocrine therapy following the completion of chemotherapy and surgery. (reference NICE early breast cancer guidance : https://pathways.nice.org.uk/pathways/early-and-locally-advanced-breast-cancer#path=view%3A/pathways/early-and-locally-advanced-breast-cancer/early-and-locally-advanced-breast-cancer-overview.xml&content=view-index)

3.1 Tamoxifen

Patients with hormone receptor positive tumours, who are considered to be either low risk or in whom an aromatase inhibitor is not tolerated or contraindicated, should commence tamoxifen 20 mg daily for 5 years (after completion of chemotherapy and radiotherapy where indicated). Patients should be considered for extension of tamoxifen for up to 10 years where risk / benefit has been discussed with the patient.

The initiating physician must warn the patient about the small risk of endometrial cancer and venous thrombosis, and document that this has been done. For worrying symptoms, rapid access referral to Gynaecology should be arranged.

3.2 Aromatase Inhibitors (AIs)

NB: see appendix A for assessment of bone loss.

AIs are only licensed in **post**-menopausal women. When given pre-menopausal they cause heavy vaginal bleeding and can even induce ovulation and thus pregnancy. There is no good data on how to reliably define the menopause in patients; particular care should be taken in young women post chemotherapy in whom ovarian function can recover even after 2 years, despite amenorrhoea. AIs should not be prescribed to women under 40 who become amenorrhoeic following chemotherapy. For women under 60 it is mandatory to check the FSH at least and preferably oestradiol as well, (oestradiol is unhelpful in the presence of tamoxifen); FSH should be at least 35 **with** amenorrhoea for at least a year. Take advice from local laboratories.

3.2.1 Management of Side Effects

The side effects of AIs that are more common than tamoxifen are arthralgia and osteoporosis.

Glucosamine may help the arthralgia. Patients who can't tolerate AIs can go back to tamoxifen.

Patients not on adjuvant bisphosphonates on adjuvant AIs should have a bone density scan booked at the beginning of treatment and this is the responsibility of the initiating physician (see section 9.0 and appendix A). Oncologists are available to aid in the medical management of AIs.

3.2.2 Management of Menopausal Side Effects

For those in whom general advice and lifestyle management and counselling are not effective consider the use of SSRIs (fluoxetine, sertraline, citalopram / escitalopram, paroxetine) but fluoxetine and sertraline are contraindicated with tamoxifen.

- Do not offer soy, red clover, isoflavones, black cohosh, vitamin E, magnetic devices.
- Do not offer HRT, unless as a last resort and after the risks have been discussed.
- See appendix F for further guidance.

3.3 Extended Adjuvant Hormone Therapy

After 5 years, consider extended adjuvant therapy (i.e. additional 5 years of aromatase inhibitor or tamoxifen) treatment in high risk patients.

See Appendix E for further guidance.

3.4 Aromatase Inhibitors: Initial Therapy

3.4.1 Anastrozole and Letrozole

Initial adjuvant therapy with anastrozole or letrozole should be offered to all postmenopausal women.

3.5 Aromatase Inhibitors: Extended Therapy

3.5.1 Letrozole

Letrozole should be considered for node positive patients who have completed 5 years adjuvant tamoxifen. This should be given for a minimum of 3 years.

3.6 Goserelin or Leuprorelin Acetate

Monthly goserelin (3.6mg s/c) for up to 5 years in combination with tamoxifen or exemestane can be considered for intermediate or high-risk women with ER positive tumours who are pre-menopausal at diagnosis.

In pre-menopausal patients with low-risk ER positive cancers a combination of goserelin and tamoxifen may be considered as a substitute to chemotherapy.

NB: see appendix A for assessment of bone loss.

3 monthly Leuprorelin acetate (11.25mg s/c) where available on trust formularies may be considered as an alternative to goserelin on a case-by-case basis when monthly use is not feasible or accepted by the patient. Regular monitoring of FSH must be performed to ensure menopausal status has been secured.

4.0 ADJUVANT TARGETED THERAPY

4.1 Trastuzumab Adjuvant

This should be considered for all HER2+ive patients that are eligible according to NICE guidance. Full guidance on treatment should follow NICE 2018. The KMCC guidelines on managing cardiac toxicity for patients receiving trastuzumab should be followed (see Appendix B).

Trastuzumab should be initiated at the same time as the taxane based therapy. Testing and clinical pathways should follow those presented at the TSSG. Trastuzumab may be given SC or IV.

4.2 Adjuvant Trastuzumab Emtansine (Kadcyla®)

Should be considered for HER2+ with residual invasive disease following the combination of taxane-based and HER2-targeted neoadjuvant systemic therapy and surgery.

4.3 Adjuvant Neratinib

Patients with ER+ Her2+ breast cancer who are within 1 year of completing adjuvant trastuzumab **monotherapy** may be considered for 1 year of neratinib. Adequate cardiac function is necessary. This excludes patients with a pathological complete response to neo-adjuvant treatment or who have had previous adjuvant pertuzumab.

5.0 ADJUVANT BISPHOSPHONATES

Zoledronic acid is recommended as adjuvant treatment in post-menopausal natural (or treatment induced for a minimum of 3 months) women with a 10-year intermediate to high risk of breast cancer death.

Zoledronic acid every 6 weeks concurrent with adjuvant chemotherapy, then as a single agent every six months for three years (total of 9 doses).

Guidelines for Dental Procedures and patients presenting with ear symptoms, or thigh, hip or groin pain:

- A dental examination with appropriate preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with bisphosphonates
- Patients should be encouraged to have regular dental check-ups whilst on treatment
- Patients who develop osteonecrosis of the jaw should be referred to a maxillofacial surgeon.
- Caution is advised when zoledronic acid is administered with anti-angiogenic drugs (e.g. bevacizumab, sunitinib, pazopanib), as an increase in the incidence of ONJ has been observed in patients treated concomitantly with these medicinal products
- The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms including chronic ear infections.
- During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture.
- Resources are available from the UK chemotherapy board in relation to the management of medication related osteonecrosis of the jaw: https://www.rcplondon.ac.uk/guidelines-policy/medication-related-osteonecrosis-jaw-guidance-oncology-multidisciplinary-team
- http://www.sdcep.org.uk/published-guidance/medication-related-osteonecrosis-of-the-jaw/ is considered an acceptable tool for the guidance on ONJ.

6.0 POST-OPERATIVE RADIOTHERAPY

Adjuvant radiotherapy should be started as soon as clinically possible within 31 days of completion of surgery.

Post-operative radiotherapy to the conserved breast should be considered for patients with:

- Invasive carcinoma of the breast.
- For high risk, intermediate to high grade DCIS, see section 12.0
- Good prognosis metastatic patients with a high risk of locoregional recurrence.

Post-operative radiotherapy may be avoided after breast conservation and axillary surgery to patients with all of the following:

- Age ≥70yrs
- T1
- Grade 1 or 2
- N0
- ER strongly+ PR+ HER2-
- Willing to take endocrine therapy for 5 years
- Willing to have annual mammograms for 5 years and then 3 yearly to 10 years

Ref: PRIME 11 trial Lancet Oncology March 2015

A radiotherapy "boost" to the tumour bed should be considered for patients:

- With a close margin (<1mm).
- Age <50 years
- Age >50 years with high risk features e.g.:
    - Extensive intraduct component in an invasive tumour
    - Large grade 3 tumour
    - Lymphovascular invasion

Post-operative chest wall radiotherapy is recommended to patients with one or more 'major' criteria.
Major criteria:

- pT3 (>50mm).
- Histologically proven positive or close (<1mm) deep margin.
- 4 or more positive axillary nodes.

Post-operative chest wall radiotherapy can be considered for patients with one or more 'minor' criteria.
Minor criteria:

- 1-3 positive axillary nodes.
- Lymphovascular invasion.
- Grade 3

It may also be considered where margins are involved with DCIS.

Post-operative radiotherapy to the supraclavicular fossa can be considered where:

- 4 or more axillary nodes are involved.
- 1 node is clinically, radiologically or pathologically involved prior to neo-adjuvant therapy.
- The apical axillary node is involved.
- T3 tumour with 1-3 axillary nodes involved.

Post-operative radiotherapy to the axilla should be reserved for patients with:

- Residual macroscopic disease at operation.
- No axillary surgery but deemed to be at medium or high risk of axillary nodal involvement.

See Radiotherapy in breast cancer protocol for details of dose and fractionation available via Kent Oncology Centre Quality Management System.

7.0 NEOADJUVANT SACT (SYSTEMIC ANTI-CANCER THERAPY)

Neoadjuvant chemotherapy may be considered for:

- T2 and /or N+ HER2+ tumours (pertuzumab eligible)
- TNBC

Carefully consider neoadjuvant options in the ER+ HER2 negative population.
NB: Invasive ER+ lobular cancers are likely to respond better to neoadjuvant endocrine therapy.

- Consider CDK4/6 inhibitors (abemaciclib, palbociclib or ribociclib) plus aromatase inhibitor if locally advanced inoperable disease.
- Systemic chemotherapy.

Recommended management plan:

- Clinical assessment before each cycle of chemotherapy to exclude disease progression.
- Radiological reassessment (preferably with breast ultrasound) after 3 cycles.
- Proceed to definitive surgery and radiotherapy after chemotherapy where appropriate.
- Adjuvant hormone treatment as indicated.

7.1 Neo-Adjuvant Chemotherapy

Patients with following Phenotype	Preferred regimen	Alternatives
ER+ HER2- High risk	• Accelerated EC & accelerated paclitaxel (BRE-076)	• EC followed by accelerated paclitaxel (BRE-050) • Weekly paclitaxel x 12 (BRE-036)
Triple negative and/or BRCA positive	• Accelerated EC followed by carboplatin (every 3 weeks) with weekly paclitaxel (BRE-077)	• EC followed by 3 weekly carboplatin & weekly paclitaxel. (BRE-059) • EC followed by accelerated paclitaxel (BRE-50) or EC followed by weekly paclitaxel (BRE-058 followed by BRE-036) • Accelerated EC (BRE-083) followed by weekly carboplatin with weekly paclitaxel
HER2+	• TCPhesgo (Neo-adjuvant) (Phesgo® = pertuzumab/trastuzumab SC) (BRE-079) • Neo-adjuvant EC then paclitaxel (weekly) & Phesgo® (pertuzumab/trastuzumab SC) (BRE-082)	In exceptional circumstances, the following adjuvant protocol could be considered: Weekly paclitaxel and trastuzumab (BRE-052)
HER2+ node+ patients continuing to adjuvant treatment see adjuvant chemotherapy table**.**		

NB: SC administration of pertuzumab/trastuzumab (Phesgo®) is the preferred formulation over IV administration. IV pertuzumab/trastuzumab regimens available on KMCC website.

8.0 NEOADJUVANT ENDOCRINE THERAPY

Neoadjuvant endocrine therapy may be considered for patients with ER positive tumours in whom chemotherapy is contraindicated or not indicated.

Letrozole for post-menopausal patients *(Ellis 2003)*

Tamoxifen is appropriate for:

- Pre-menopausal patients.
- Post-menopausal patients in whom aromatase inhibitors are contraindicated.

9.0 ENDOCRINE TREATMENT IN ADVANCED DISEASE

9.1 Postmenopausal (Natural or Induced)

NB: Use ovarian suppression if patient is pre-menopausal at diagnosis.

9.1.1 1st Line Endocrine Therapy for Patients Who Have Received No Adjuvant Endocrine, or Who Have Progressed > 12 Months After Completing Adjuvant / Neo-Adjuvant Endocrine Therapy

Anastrozole or Letrozole should be offered first line, in combination with CDK 4/6 inhibitors (abemaciclib, ribociclib or palbociclib) as per NICE guidance and commissioning criteria in clinically suitable patients.

In selected cases aromatase inhibitors alone or tamoxifen may be considered.

9.1.2 1st Line Endocrine Therapy for Patients Who Have Progressive Disease Whilst Still Receiving Adjuvant or Neoadjuvant Endocrine Therapy or Progressive Disease Within </= 12 Months of Completing Adjuvant Endocrine Therapy

Palbociclib / Ribociclib & fulvestrant

9.1.3 2nd Line Endocrine Therapy

Palbociclib / Ribociclib & fulvestrant*

Abemaciclib and fulvestrant where exemestane and everolimus would otherwise have been considered*.

*NB: There should be no prior treatment with a CDK 4/6 inhibitor unless this has had to be stopped within 6 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.

9.1.4 Subsequent Lines of Therapy May Include:

- Fulvestrant single agent (funding approval pending)
- Everolimus and exemestane
- Exemestane
- Tamoxifen (including re-challenging patients treated with adjuvant tamoxifen)
- Megestrol Acetate

10.0 SYSTEMIC ANTI-CANCER THERAPY IN ADVANCED DISEASE

10.1 First Line Metastatic Therapy

For details on chemotherapy regimens and pre-treatment parameters, please refer to the KMCC Chemotherapy protocols.

10.1.1 HER2 Positive Patients

If patient suitable for triple therapy consider docetaxel plus trastuzumab plus pertuzumab.

Subcutaneous trastuzumab when used within the license may be used in place of intravenous trastuzumab in the metastatic setting.

Subcutaneous trastuzumab is not to be used in place of iv in the pertuzumab/ trastuzumab/ docetaxel regimen.

Taxane (depending on performance status and LFTs) plus Trastuzumab.

Alternative treatment regimens include:

- Vinorelbine plus trastuzumab.
- FEC 75 if not given with adjuvant intent.
- Patients not fit to receive chemotherapy should receive single agent trastuzumab.
- If patients have progressed within 6 months of completing treatment for early stage disease and have received previous treatment with trastuzumab and a taxane, and have a PS of 0-1, consider trastuzumab emtansine.
- Lapatinib could be considered if not fit for chemotherapy (funding approval required).

10.1.2 HER2 Negative Patients

- Triple negative breast cancer whose tumours have PD-L1 expression >/= 1% atezolizumab and Nab-paclitaxel
- An anthracycline containing regimen if not given with adjuvant intent.
- Docetaxel (depending on performance status and LFTs).
- Docetaxel in combination with Capecitabine should be considered for very fit young patients requiring a rapid response e.g. for life-threatening visceral metastases.
- Gemcitabine and Paclitaxel.

10.2 NICE approved 2nd or 3rd line treatments

- Capecitabine monotherapy - continue treatment until disease progression or unacceptable toxicity.
- Vinorelbine monotherapy.

10.2.1 Anti-HER2 Therapy Beyond Progression, Lapatinib & Trastuzumab Emtansine

NICE guidance states that trastuzumab should be discontinued at the time of disease progression outside of the central nervous system (CNS). Trastuzumab should be continued if disease progression is within the CNS alone.

Trastuzumab (IV & SC), pertuzumab and trastuzumab emtansine (Kadcyla®) may be continued if progression is within the CNS alone.

If patients have progressed during or after the most recent treatment for HER2 positive advanced stage disease, have received previous treatment with trastuzumab and a taxane, and have a PS of 0-1, consider trastuzumab emtansine.

Lapatinib in combination with capecitabine for HER2 positive patients may be considered for patients whose disease progresses following prior therapy for metastatic disease, (including anthracyclines (or anthracyclines contraindicated), taxanes and trastuzumab - funding approval required).

10.3 Subsequent Lines of Therapy

- Weekly Paclitaxel (80 mg/m2)
- Gemcitabine and Carboplatin
- Single agent carboplatin AUC5
- Eribulin
- CMF or other Anthracycline based chemotherapy if appropriate.
- Myocet (liposomal doxorubicin - funding approval required)
- Abraxane (paclitaxel albumin) – if documented hypersensitivity reaction to taxane.
- Vinorelbine (oral) and Capecitabine.

11.0 BISPHOSPHONATES FOR BONE METASTASES

Bisphosphonates reduce skeletal morbidity associated with bone metastases *(Hillner et al, 2000; Lipton et al, 2000).* All patients with bone metastases should be considered for treatment, especially those:

- Patients with lytic bone metastases on plain radiographs.
- Patients with symptomatic bone metastases (with appropriate use of palliative radiotherapy and analgesics).
- Patients who have suffered a previous skeletal event (pathological fracture, previous radiation to a painful bone metastasis).

Regular dental assessment is required to minimise the risk of osteonecrosis of the jaw (ONJ). http://www.sdcep.org.uk/published-guidance/medication-related-osteonecrosis-of-the-jaw and https://www.rcplondon.ac.uk/guidelines-policy/medication-related-osteonecrosis-jaw-guidance-oncology-multidisciplinary-team are considered acceptable resources for guidance on ONJ.

See section 5 Adjuvant bisphosphonate for further guidance.

Patients with well controlled sclerosing bone metastases who are asymptomatic may wish to start, or change to denosumab or zoledronic acid every 12 weeks.

Choice of drug:

- Denosumab is recommended as an option for preventing skeletal-related events in adults with bone metastases from breast cancer if bisphosphonates would otherwise be prescribed.
- Zolendronic acid is more effective than pamidronate at reducing skeletal complications *(Rosen et al, 2001)*.
- Oral bisphosphonates (Clodronate or Ibandronic acid) may be considered for patients with poor venous access or intolerance to intravenous bisphosphonates or patients on oral chemotherapy.
- Ibandronic Acid

Reference: Appendix D: Bisphosphonate guidelines incorporating prescribing in renal impairment.

12.0 USE OF ANTIBIOTICS AND GCSF

Prophylactic use of antibiotics is not recommended routinely in view of the risk of antibiotic resistant infections.
Prophylactic use of GCSF at clinical discretion after a neutropenic episode should be considered in order to maintain dose intensity and prevent delay in adjuvant chemotherapy regimens.
GCSF should be given as primary prophylaxis where indicated in the chemotherapy protocol. See KMCC GCSF guidelines for further information.

For further details, please see KMCC Prescribing Protocols.

13.0 MANAGEMENT OF DUCTAL CARCINOMA IN SITU (DCIS)

Consider mastectomy for multi-focal DCIS. Complete local excision with >1mm surgical margins is recommended for localised DCIS (*currently under review).*
The benefits and risks of post complete local excision radiotherapy should be discussed with patients with intermediate or high-grade DCIS.
ER testing should be undertaken on all intermediate and high-grade DCIS.

The routine use of adjuvant tamoxifen or an aromatase inhibitor should be considered after discussion of potential benefits and risks in:

- Patients who didn't receive radiotherapy with ER positive DCIS
- High risk women who are <50yrs
- High grade DCIS or large area ER positive DCIS
- Close margins post-mastectomy.

14.0 MANAGEMENT OF MALE BREAST CANCER: ASCO GUIDELINES 2020

Many of the management approaches used for men with breast cancer are like those used for women. Men with hormone receptor–positive breast cancer who are candidates for adjuvant endocrine therapy should be offered tamoxifen for an initial duration of five years; those with a contraindication to tamoxifen may be offered a gonadotropin-releasing hormone agonist/antagonist plus aromatase inhibitor. Men who have completed five years of tamoxifen, have tolerated therapy, and still have a high risk of recurrence may be offered an additional five years of therapy.

Early-stage disease should not be treated with bone-modifying agents to prevent recurrence, but men could still receive these agents to prevent or treat osteoporosis.

Men with advanced or metastatic disease should be offered endocrine therapy as first-line therapy, except in cases of visceral crisis or rapidly progressive disease. Targeted systemic therapy may be used to treat advanced or metastatic cancer using the same indications and combinations offered to women. Ipsilateral annual mammogram should be offered to men with a history of breast cancer treated with lumpectomy regardless of genetic predisposition; contralateral annual mammogram may be offered to men with a history of breast cancer and a genetic predisposing mutation. Breast magnetic resonance imaging is not recommended routinely. Genetic counselling and germline genetic testing of cancer predisposition genes should be offered to all men with breast cancer.

There is an association between male breast cancer and BRCA inheritance and careful family history should be recorded with appropriate genetic referral.

15.0 MANAGEMENT OF BREAST CANCER DURING PREGNANCY

Please refer to Breast TSSG Pathway of Care document.
With regards to oncological treatment the following principles should be followed:

General Principles

	Oncological Treatment
1st trimester	• Not recommended either Chemo or RT • Biological agents not recommended at any stage of pregnancy
2nd trimester	• Chemo can now be utilised; AVOID CMF (Cyclophosphamide, methotrexate, 5- Flurouracil). • Taxanes can now be considered. • Adjuvant RT not recommended. • Biological agents not recommended at any stage of pregnancy
3rd trimester	• Chemo can be used throughout but with final cycle to be timed according to delivery. • If diagnosed in 3rd trimester attempt to give 2 cycles of chemo pre-delivery. • Adjuvant RT not recommended • Biological agents not recommended at any stage of pregnancy

16.0 USE OF THE MIRENA® COIL IN PATIENTS WITH OESTROGEN RECEPTOR POSITIVE TUMOURS

Due to the lack of safety data, patients with oestrogen receptor positive breast cancer that have a Mirena® coil in situ should have the device removed. Occasionally it may be used if no alternative method of controlling gynaecological symptoms exists, after an appropriate discussion of risks and benefits with the patient, oncologist and gynaecologist.

17.0 APPENDIX A: ASSESSMENT OF BONE LOSS

See algorithms 1 and 2 below on the management of bone loss in early breast cancer.
Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:

- Start adjuvant aromatase inhibitors
- Have treatment-induced menopause under 45 years
- Start ovarian ablation / suppression therapy

It is the responsibility of the initiating doctor to arrange a baseline DEXA scan and then to communicate the results of the scan to the patient and the GP. It should be made clear when the next scan is due and who is to arrange it. Algorithms for managing bone health exist *(NCRI Breast Study Group and National Osteoporosis Society Guidelines 11/2007)*.

For MTW and Medway, if the planned duration of an AI is stated on the form, Dr Ryan and Dr A'Costa will usually advise whether a repeat scan is indicated and when. Other units may need to follow the algorithms below. If it is unclear following first DEXA result when the next scan is due, the general rule is 2 years if there is no significant osteopenia.
If there is borderline osteoporosis at any point, advice should be sought from the local osteoporosis specialist. AIs can often still be given following advice with bisphosphonates and calcium supplementation. As trials have reported increase in cardiac events and lipids, patients should report any new cardiac events whilst on an AI and medical advice sought if concerned when starting or continuing an AI.

17.1 Bone Health in the Under 45s

Any baseline premenopausal patient <45 years and not on bone protection will require a DEXA scan if:

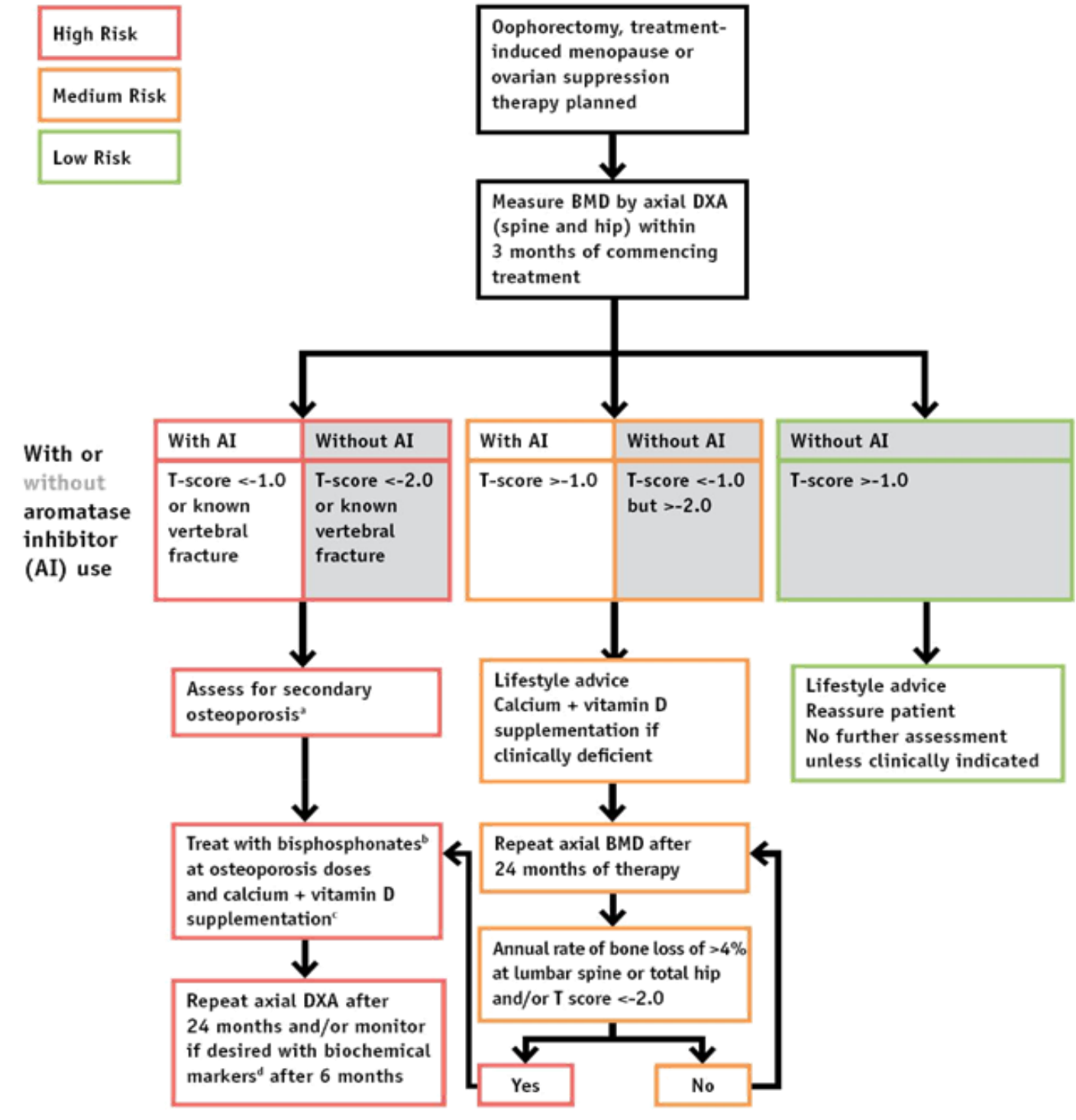
- Rendered menopausal by treatment
- For patients on tamoxifen follow algorithm 2

17.2 Bone Health After Zoledronic Acid

Given the increasing use of extended aromatase inhibitors in early breast cancer, a post-zoledronic acid bone mineral density DEXA scan after zoledronic acid treatment is complete should be considered.

Until further guidance is available use suggested guidance below.

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 / ↓GT), serum creatinine, endomysial antibodies, serum thyroid stimulating hormone

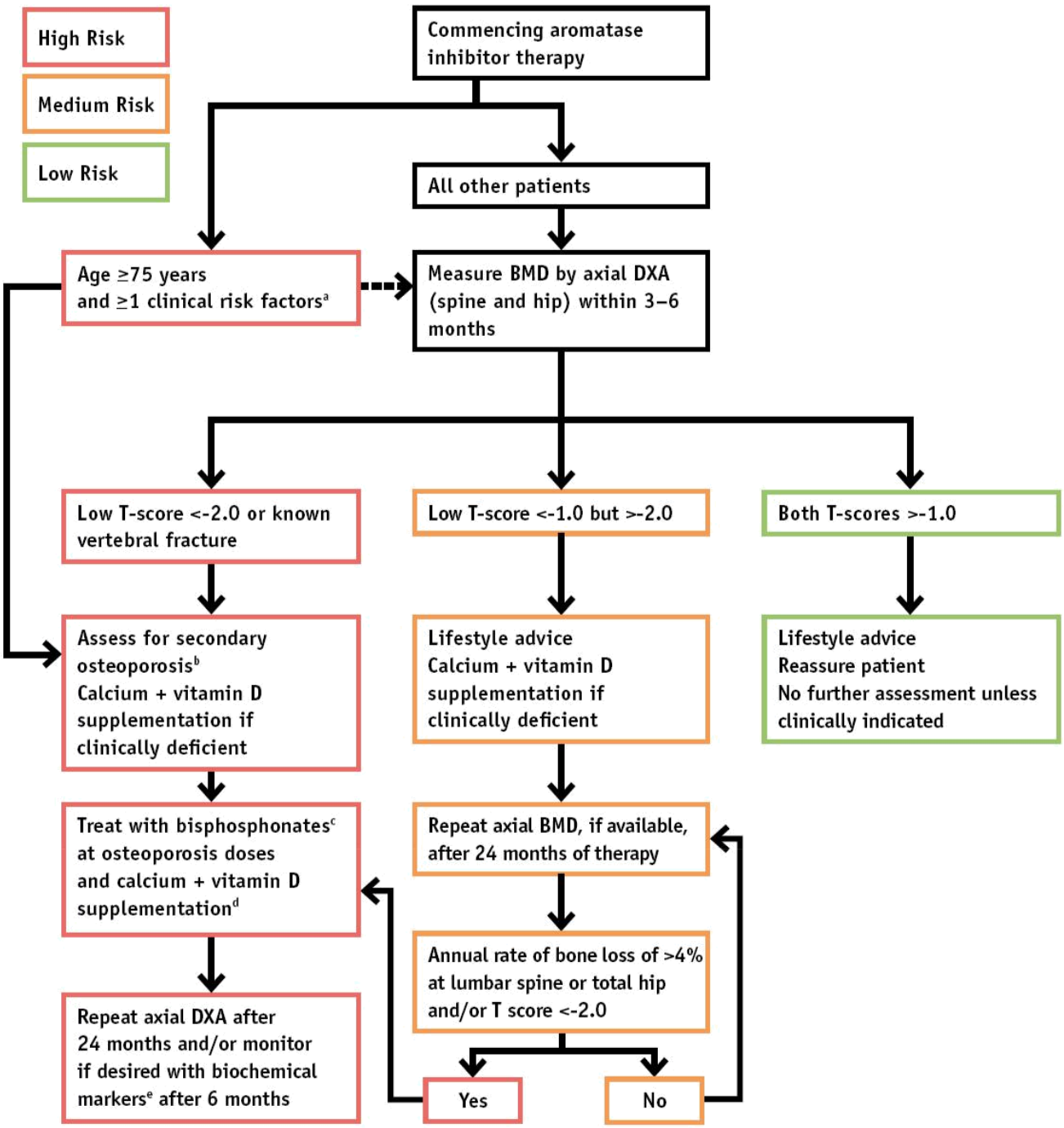
b Alendronate 70 mg per week, risedronate 35 mg per week, ibandronate (150 mg po monthly or 3 mg iv 3-monthly), zoledronic acid 4 mg iv 6-monthly

c To be given as ≥1 g of calcium + ≥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

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 / γGT), 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 ≥1 g of calcium + ≥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

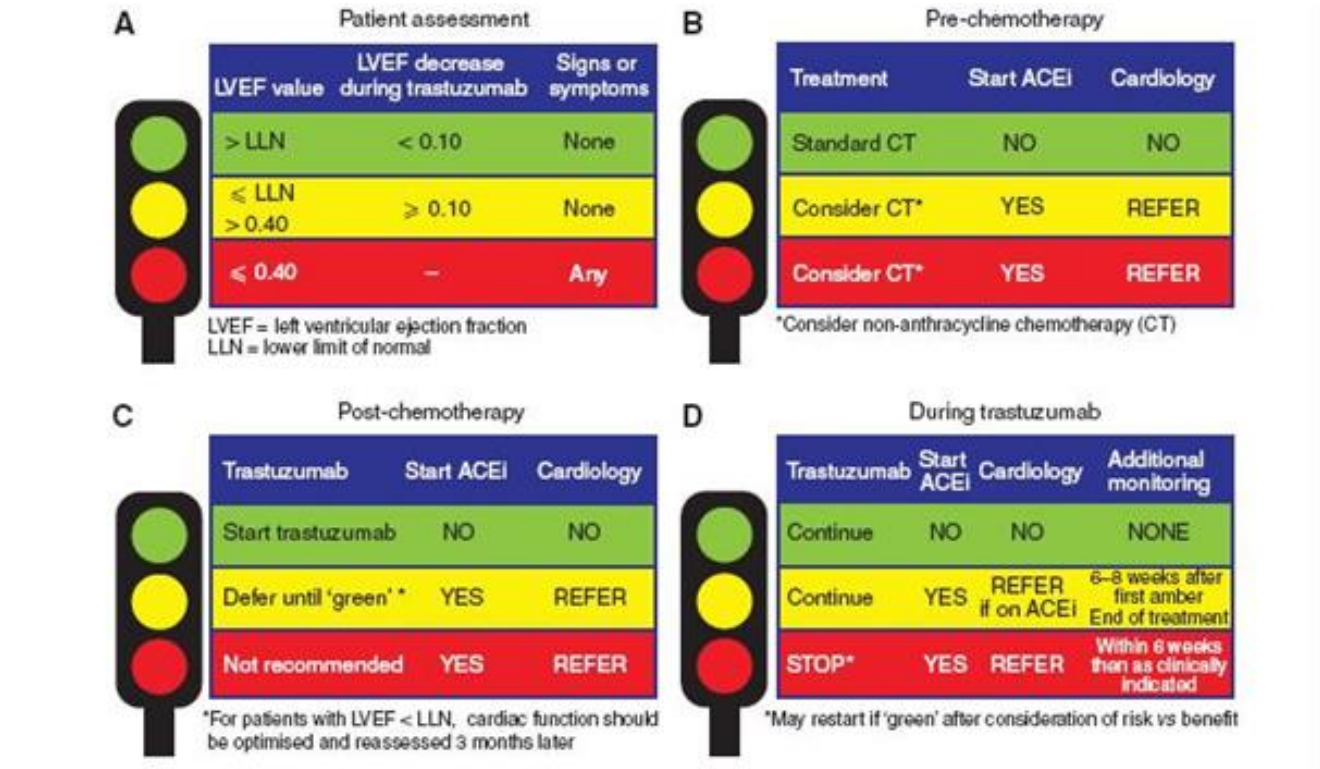
The algorithm has been reviewed and supported by the National Cancer Research Institute Breast Cancer Study Group and the National Osteoporosis Society

18.0 APPENDIX B: KMCC GUIDELINES ON MANAGING CARDIAC TOXICITY FOR PATIENTS RECEIVING TRASTUZUMAB

18.1 Guidelines for Patients Receiving Trastuzumab in the Adjuvant Setting

These guidelines have been reproduced from recommendations made by *Jones et al BJC (2209) 100; 684-692*.

- The same monitoring modality should be used throughout the course of treatment and, where possible, this should also include the same operator, machine, and calculation algorithm. Each institution should establish a normal range for the methods used. On the basis that an echocardiogram exposes the patient to less radiation and is usually less expensive than a MUGA scan, the NOG recommend this as the method used to assess cardiac function. ECHOs are reported as a range not an absolute figure, but it is generally accepted that the lower limit of normal (LLN) for cardiac function when measured by an ECHO is 55%.
- Patients developing signs and symptoms of heart failure should have their trastuzumab treatment interrupted, have ACE inhibitor therapy initiated by the oncologist and be referred to a cardiologist. Investigation and treatment are recommended in accordance with present guidelines *(NICE, 2003; Bonow et al 2005; Swedberg et al 2005)*.
- It is the prescriber's responsibility to check that the ECHO/MUGA is satisfactory before continuing treatment.
- An ECHO/ MUGA should be carried out at the following timepoints:
  - Pre-cytotoxic chemotherapy (if indicated clinically)
  - Pre trastuzumab
  - At 4 months
  - At 8 months
  - 3-4 weeks after the end of treatment
- The minimum number of LVEF assessments when following this recommendation is 4 compared with 5 previously



NB When an ECHO is used to measure cardiac function, LLN can be assumed to be 55%. For MUGA scans, the LLN for the institution should be used.

18.2 Guidelines for Patients Receiving Trastuzumab in the Metastatic Setting

Cardiac function should be monitored at baseline (ECHO/MUGA and ECG) and then every 6 months (ECHO or MUGA) during treatment or as clinically indicated. Follow traffic light system outlined above ('during trastuzumab').

19.0 APPENDIX C: CLINICAL TRIALS

Refer to the local research team who will provide on request an orientation handbook, list of current trials and associated trial protocols and summaries.

Contact numbers:

MTW – Clinical Trials Office	01622 225033
Darent Valley Hospital – Clinical Trials Office	01322 428100 ext. 4810
Medway Maritime Hospital – Clinical Trials Office	01634 825094
East Kent Hospitals – Clinical Trials Office:	
Solid Tumours (excluding Gynae)	01227 866393
Gynae Clinical Trials	01843 234343
Haematology Clinical Trials	01227 864129

20.0 APPENDIX D: BISPHOSPHONATE GUIDELINES INCORPORATING PRESCRIBING IN RENAL IMPAIRMENT

BEFORE TREATMENT

1) **Renal, liver and bone profile MUST be reviewed at baseline and prior to the administration of EACH dose of bisphosphonate**

AT THE START OF TREATMENT

2) **Prescribe Initial Bisphosphonate dose based on baseline creatinine clearance**

Baseline creatinine clearance (ml/min)	Zoledronic Acid dose	Pamidronate dose	Oral Ibandronate dose/frequency
>60	4.0mg	90mg	50mg/daily
50 – 60	3.5mg	90mg	50mg/daily
40 – 49	3.3mg	90mg	50mg on alternate days
30 – 39	3.0mg	90mg	50mg on alternate days
<30	Not recommended per SPC- consider IBANDRONIC acid	Discuss with consultant. Reduce rate of administration to 20mg/hr in impaired renal function. (90mg/270min)	50mg/weekly

DURING TREATMENT

3) **Following initiation of therapy, review serum creatinine (SrCr) prior to each dose.**

- **Modify the dose of bisphosphonate as follows:**

  Zoledronic Acid[1]:

Baseline serum creatinine	WITHHOLD TREATMENT IF CREATININE INCREASES BY	INFORM CONSULTANT IF CREATININE INCREASES BY
<124µmol/L	**44µmol/L**	**44µmol/L**
>124µmol/L	**88µmol/L**	**44µmol/L**

- **Following a dose delay, repeat bloods after 4 weeks and recommence when SrCr is below or within + 10% of baseline[1]**
- **Above table is only for use with Zoledronic Acid. If Pamidronate is used discuss any significant rise in serum creatinine with consultant.**

Management of hypocalcaemia

Patients with a corrected serum calcium below 2.2mmol/l should be discussed with the consultant, to consider extra calcium supplementation.

Cycle No	1	2	3	4	5	6	7	8
Date:								
Serum Creatinine (SrCr) umol/l								
Creatinine Clearance (CrCl) ml/min								
Phosphate IU/l								
Magnesium Mmol/l								

NB: For calculation of creatinine clearance refer to the KOC intranet Cockcroft Gault calculator.

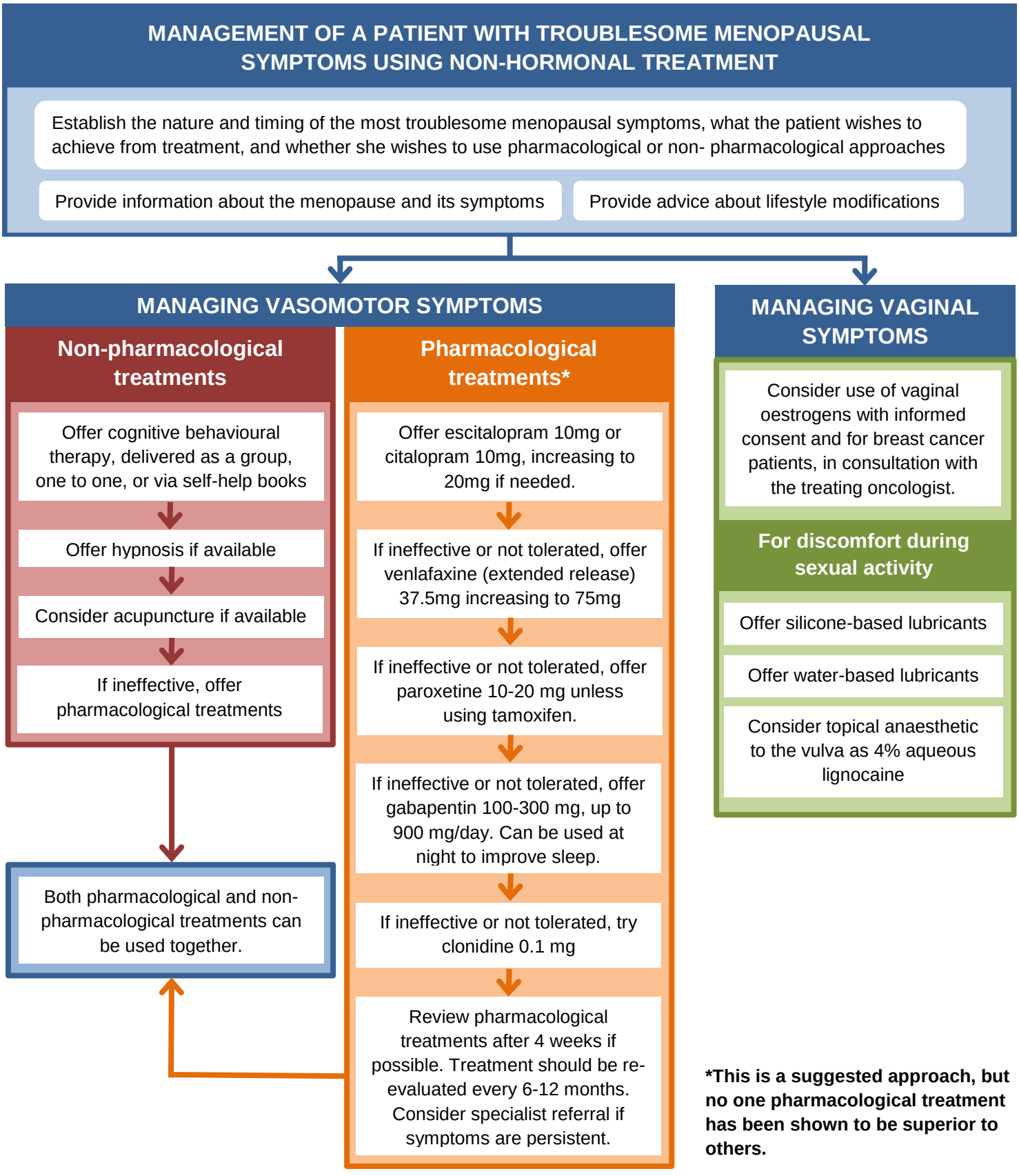
References 1. Zometa© Zoledronic Acid (accessed online 01/05/2018) Summary of Product Characteristics 2. Pamidronate (accessed online 01/05/2018) Summary of Product Characteristics 3. ZICE Protocol (Zoledronate versus Ibandronate Comparative Evaluation) (07/2007) 4. Bondronat© Ibandronate Oral (accessed online 01/05/2018) Summary of Product Characteristics.

21.0 APPENDIX E: EXTENDED ADJUVANT HORMONE THERAPY

	Pre-Menopausal	Post-Menopausal
Lower Risk patients	Tamoxifen for 5-10 years	AI for 5 years. If not tolerated or relative contraindication (e.g. osteoporosis, high cholesterol, arthritis) then Tamoxifen for 5-10 years.
Higher Risk patients	LHRH agonist + Exemestane (or tamoxifen if poorly tolerated) for 5 years. If post-menopausal after 5 years of tamoxifen, consider switch to AI	5 years AI then consider either switch to tamoxifen or a further 2-5 years of an AI

22.0 APPENDIX F: PATIENTS WITH MENOPAUSAL SYMPTOMS

Suggested algorithm for using non-hormonal treatment for a patient with problematic menopausal symptoms.



***This is a suggested approach, but no one pharmacological treatment has been shown to be superior to others.**

Ref:BMJ 2017;359:j5101 doi: 10.1136/bmj.j5101 (published 23 Nov 2017)

23.0 APPENDIX G: CLINICAL FRAILTY SCALE

Clinical Frailty Scale*

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 Managing Well – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 Vulnerable – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

24.0 APPENDIX H: ADJUVANT / NEO-ADJUVANT PERTUZUMAB BASED CHEMOTHERAPY FOR PATIENTS WITH HER2+ BREAST CANCER

Indication at start of treatment	Nodal Status	Aria regimen(s)	Blueteq form	Nodal status after surgery	Change Aria regimen to	Start at cycle	Blueteq form
	PRE-SURGERY (neo-adjuvant)			POST-SURGERY (adjuvant)			
Neo-adjuvant	+	**BRE-061 (Neo-adjuvant)** • TCH-P: Docetaxel, Carboplatin, trastuzumab (IV) and pertuzumab C1-6 • Trastuzumab (SC) C7-18	PER2a	+	**BRE-066 (adjuvant)** • TCH-P: Docetaxel, Carboplatin, trastuzumab (IV) and pertuzumab C1-6 • Trastuzumab (IV) & pertuzumab C7-18	7+	PER4a
		BRE-079 (Neo-adjuvant) • TC Phesgo® C1-6			**BRE-069 (adjuvant)** • EC (90) C1-4 • Weekly paclitaxel, trastuzumab and pertuzumab C5-8 • Trastuzumab (IV) & pertuzumab C9-22	9+	
		BRE-082 (Neo-adjuvant) • EC C1-4 • Weekly paclitaxel & Phesgo® C5-8			**BRE-080 (adjuvant)** • TC Phesgo® C1-6 • Phesgo C7-18	7+	
					BRE-081 (adjuvant) • EC C1-4 • Weekly paclitaxel & Phesgo® C5-8 • Phesgo® C9-22	9+	
Neo-adjuvant	-	As above	PER2b	+	As above		PER4b
Neo-adjuvant	-	As above	PER2b	-	If patient is on: BRE-061 continue regimen BRE-079 switch to BRE-034 starting at cycle 7 BRE-082 switch to BRE-034 starting at cycle 9 Do not change Blueteq form. Not eligible for adjuvant pertuzumab.		

Indication at start of treatment	Nodal Status	Aria regimen(s)	Blueteq form	Nodal status after surgery	Change Aria regimen to	Start at cycle	Blueteq form
	POST-SURGERY No prior Neo-adjuvant treatment						
Adjuvant	+	**BRE-066 (adjuvant)** • TCH-P: Docetaxel, Carboplatin, trastuzumab (IV) and pertuzumab C1-6 • Trastuzumab (IV) & pertuzumab C7-18	PER3				
		BRE-069 (adjuvant) • EC (90) C1-4 • Weekly paclitaxel, trastuzumab and pertuzumab C5-8 • Trastuzumab (IV) & pertuzumab C9-22					
		BRE-080 (adjuvant) • TC Phesgo® C1-6 • Phesgo C7-18					
		BRE-081 (adjuvant) • EC C1-4 • Weekly paclitaxel & Phesgo® C5-8 • Phesgo® C9-22					

25.0 PERSONNEL AND CONTACT INFORMATION

A comprehensive, up to date list of MDM contact details can be requested by NHS professionals by contacting the Kent & Medway Cancer Collaborative. Their contact telephone number is 01233 651905.

26.0 GLOSSARY

Acronyms in common usage throughout KMCC documentation

BNF	British National Formulary
BOPA	British Oncology Pharmacist Association
CNB	Cancer Network Board
COSHH	Control of substances hazardous to health regulations.
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
DGT	Dartford and Gravesham NHS Trust
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
EPS	Electronic Prescribing System
FP10(HNC)	Prescriptions issued by hospital doctors for dispensing in the community
GP	General Practitioner
HoP	High Level Operational Policy

IOSC	Improving Outcomes: A Strategy for Cancer
IV	Intravenous
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
KOMS	Kent Oncology Management System
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NHS	National Health Service
NMP	Non-medical prescriber
NPSA	National Patient Safety agency
NOG	Non-Surgical Oncology Group *(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)*
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)
QoL	Quality of life
QSIS	Quality service information system
QST	Quality Surveillance Team
RAT	Research and Trial Group *(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)*
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
SACT	Systemic Anti-Cancer therapy
SACT regimen	Systemic Anti-cancer prescription on the electronic prescribing system
SACT protocol	Systemic Anti-cancer protocol on KMCC website
TTO	Treatment to take home
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

27.0 DOCUMENT ADMINISTRATION

Document Title	Oncological Treatment of Breast Cancer
Principle author	Breast NOG
Co-author(s)	Caroline Waters
Current version number	30
Current status	Final
Expected review date by	2022

Enquiries:	
[[1] DOG, NOG, CCG Chair [2] DOG, NOG, CCG Vice Chair	Russell Burcombe and Jennifer Glendenning – Breast NOG chair Caroline Waters – KMCC Lead Pharmacist

Revision History			
Date of revision	New Version Number	Nature of Revision	Confirmation of Accuracy by
15/09/2005	001	Draft: All sections reviewed New flow chart	Andrew Jackson
25/09/2005	002	Follow-up revisions	Rosemary Toye Jenny Weeks
23/01/06	003	Updated version from collated comments since December 2005 DOG	Andrew Jackson
03/02/06	04a	Revised oncology section Updates from e-mail comments on 3rd draft	Catherine Harper-Wynne Andrew Jackson Sue Green
07/02/06	5	Final amendments agreed DOG 6th Feb	Andrew Jackson
28/02/2008	6	Amendments to oncology section	Andrew Jackson Charlotte Abson
16/05/08	7	Changes to pages 11 & 12 following e-mail from Charlotte Abson	Andrew Jackson Charlotte Abson
02/09	8	Oncological treatment as standalone POC	K Nathan
Jan 2010	8.1 – 8.8	Overall review, numerous changes – record of changes on file KMCC	C Waters C Abson
June 2010	9	Published	Breast NOG
September 2010 –March 2011	9.1 – 9.4	Changes to neo-adjuvant chemotherapy Addition of triple negative treatment options Addition of Appendix D – Bisphosphonate guidelines Addition of liposomal doxorubicin (Myocet) and Nab-paclitaxel as treatment options	Breast NOG
May 2011	10	Published	
June 2011	10.1	Addition of Eribulin to treatment options in section 8.3 Addition of reference ranges from all 4 trusts to the Bisphosphonate guidelines appendix	Breast NOG
September 2011	11	Published	
December 2011	11.1	Section 7.1 updated to reflect changes in funding arrangements for Fulvestrant.	Breast NOG
February 2012	11.2	Addition of Denosumab in bisphosphonate sec 9 Addition of FEC-T as treatment option for high risk node negative patients sec 5 Addition of Bevacizumab with weekly Paclitaxel as treatment option in advanced disease for triple negative patients –sec 8	Breast NOG
April 2012	12	Published	Breast NOG
October - November 2012	12.1 – 12.2	Draft Addition of Everolimus & Exemestane to section 8.1 Addition of new cohort of patients to be considered for FEC-T (section 2.2)	Breast NOG
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January 2013	13.1	Minor amendments – funding of denosumab	Breast NOG
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June 2013	15.1	Funding arrangements for abraxane (metastatic) updated	
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Oct –Dec 2013	16.1	Draft – whole document revised	C Abson / C Waters /Breast NOG
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February – August 2016	19.2-19.3	Updated in line with NCDF changes. Section added for adjuvant bisphosphonates. Adjuvant SACT revised. Guidelines for managing cardiac toxicity in adjuvant trastuzumab updated.	C Abson
November 2016	19.4	Final draft – addition of neo-adjuvant pertuzumab	C Abson
November 2016	20	Published	
February 2017	20.1	Addition of Section 3.3 – extended adjuvant hormone therapy. Addition of TCH-P and FEC-T plus pertuzumab & trastuzumab to neo-adjuvant chemotherapy options.	
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August 2017	21.1	Document revised following NOG. Information on oncological management of breast cancer in pregnancy added. Appendix E added.	
October 2017	22	Published	C Abson / Breast NOG
April 2018	22.8	Following NOG Breast meeting additions and/or amendments made to sections: 1.2 Test information amended 1.3 Title amended 2.2 High risk regimens added 3.5 Aromatase switch therapy removed 6.0 Radiotherapy boost information added 7.0 ER + lobular cancer/T2 information added. ECx4 for triple negative patients amended. 8.0 Minor wording amendment 9.1 Postmenopausal information added 10.1.1 Trastuzumab funding information removed. 10.2.1 Trastuzumab info added Appendix B: Echo/Muga 4/8 months info added Appendix E: Post-Menopausal High-Risk Patients.	Breast NOG
April 2018	23	CIRCULATED BUT NOT SIGNED OFF	P Williams
June 2018	23.1	16.0 Updated weblink Appendix D Updated	C Waters
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July 2018	24	Published	NOG
October 2018	24.1	Updates to section 1.2, 11 and appendix D following discussion in NOG	NOG M. Archer

December 2018	25	Published	C. Abson
January 2019	V25.1 draft	Amendments made during NOG	
January 2019	V25.2 draft	Oncological guidelines re formatted. Amendments to: Section 1.0 Section 1.2 Section 2.1 Section 2.2 Section 3.2.1 Section 3.4.1 Section 3.6 Section 5.0 Section 7.0 Section 10.3 Section 13.0 Section 14.0 New section 3.2.2 Addition of Appendix F	Updates following Breast NOG M. Archer
February 2019	V26	Published	C. Abson
July 2019	V26.2	Amendments made to: Section 1.2 Section 2.0 Section 4.0 Section 7.0 Section 9.1 Section 10.1.2 Section 10.3 Section 11 Appendix A	Amended following NOG 16/07/19 and reviewed at NOG 15/10/2019
Nov 2019	V27	Published Jan 2020 Section 10.1.2 Triple negative breast cancer whose tumours have PD-L1 expression >/= 1% consider atezolizumab and Nab-paclitaxel (EAMS). Removed as expired.	C. Abson approved
Jan 2020	V27.2	Amendments made to: Section 3.2 change of age limit and removal of cardiovascular risk/events on AI paragraph Section 3.4.1 Section 5: addition of UK chemotherapy board guidance web link re ONJ	Amended following NOG 28/01/20
	V28 not published		COVID pandemic
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September 2020	V29	Published	Approved: J. Glendenning
November 2020	V29.1-v29.2.1	Section 2.0 ADJUVANT chemotherapy: Tx table updated	Updated following NOG

		3.6 Goserelin or Leuprorelin acetate 7.0 Neoadjuvant SACT (systemic anti-cancer therapy): Tx table updated 10.1.1 HER2 positive patients	
February 2021	V29.3-29.6.1	Section 2 risk profiling updated ADJUVANT chemotherapy: Tx table updated 3.6 Goserelin or Leuprorelin acetate 7.0 Neoadjuvant SACT (systemic anti-cancer therapy): Tx table updated Section 9.1 updated and reformatted Appendix A bone health after zoledronic acid. 15.0 Management of Breast cancer during pregnancy: updated in line with TSSG document Document reformatted by R. Patel	
July	29.7	Update to tables appendix H neoadjuvant and adjuvant prescribing tables	M.Archer/C.Waters
October	30	Published	Approved: R.Burcombe
January	31	Published: minor amendment	Approved CWaters
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