# *ink* NOTES

## A resource guide for primary care

### Evidence-based guidelines for breast cancer patient surveillance and side effects

Erie St. Clair
Regional Cancer Program
in partnership with Cancer Care Ontario

# SUGGESTED MANAGEMENT AND REFERRAL FOR SELECT EVENTS

| Signs and Symptoms | Initial Assessment Steps | Results or Interpretation | Next Steps |
|---|---|---|---|
| **New palpable breast nodule or mass** | Mammogram +/- breast U/S<br>If suggested by radiologist:<br>• Breast MRI<br>• Image-guided biopsy | **Normal results** - If palpable abnormality persists → | **Refer to a breast surgeon** |
| | | **Other breast/chest wall skin changes** | **Refer to a breast surgeon** |
| | | **Abnormal results** | **Referral to breast surgeon arranged by BAP** |
| **New arm swelling on same side as breast cancer** | • Focused physical exam<br>• U/S +/- CT of axilla to rule out recurrence and/or<br>• Duplex U/S of arm to rule out DVT, especially if on tamoxifen | **Infection** | Treat with appropriate therapy |
| | | **Undefined axillary mass** | Refer to a general surgeon |
| | | **Local breast cancer recurrence** | **Refer back to Cancer Centre** |
| | | **Axillary vein thrombosis** | **STOP tamoxifen; treat the DVT. Refer back to Cancer Centre for AET review** |
| | | **Normal imaging results** | Consider lymphedema |
| **Bone pain** | • X-ray +/- Bone scan, CT<br>• Blood work: Alk Phos, Calcium, and Albumin | **Bone metastases** | **Refer back to Cancer Centre** |
| **Dyspnea / Shortness of breath / Cough / Chest pain** | • Focused physical exam<br>• Chest X-ray<br>• Consider Duplex U/S, D-dimer, V/Q scan or CT scan if on tamoxifen | **Pneumonia** | Treat with appropriate therapy |
| | | **DVT/Pulmonary embolus** | **STOP tamoxifen; treat DVT/ pulmonary embolus. Refer back to Cancer Centre for AET review** |
| | | **Lung metastases/cancer recurrence** | **Refer back to Cancer Centre** |
| **Post menopausal vaginal bleeding / spotting while on tamoxifen* or aromatase inhibitor** | • **Refer to gynaecologist** for assessment.**<br>• **STOP** tamoxifen or aromatase inhibitor<br>• **Initiate concomitant referral to Cancer Centre** | **Normal biopsy** | **Refer back to Cancer Centre for AET review** |
| | | **Atypical endometrial hyperplasia OR Endometrial cancer** | **Gynaecology and Cancer Centre coordinate gynaecology care and AET review** |
| | | In younger post menopausal women, vaginal bleeding may signify a return of ovulation, and decrease anti-cancer efficacy of the aromatase inhibitor. Advise patient of risk of pregnancy and, if needed, to use interim barrier contraception until assessed at Cancer Centre. | **Refer back to Cancer Centre for AET review** |
| **Fatigue / Dyspnea / Chest pain** | If a woman received adjuvant anthracycline and/or trastuzumab, consult her oncologist and/ or a cardiologist for guidance on ordering diagnostic tests for heart function and the need for specialist consultation. | | |

* *Premenopausal women treated with tamoxifen have no known increased risk of uterine cancer. If cause of vaginal bleeding or menopausal status is in doubt: refer for gynaecology assessment.*

** *Ultrasonography is poor at differentiating potential cancers from other tamoxifen-induced thickening because of the distorted endometrial architecture associated with long term use of tamoxifen.*

** *Transvaginal ultrasound can be ordered but should not delay referral to Gynaecologist.*

***U/S**=ultrasound, **MRI**=magnetic resonance imaging, **DVT**=deep vein thrombosis, **CT**=computed tomography, **Alk Phos**=alkaline phosphatase, **V/Q**=ventilation-perfusion, **AET**=adjuvant endocrine therapy*

# Surveillance Guidelines Section 1

| Post Diagnosis | Physical Exam | Mammogram (unless bilateral mastectomy) |
|---|---|---|
| 1–5 years | Every 4-6 months | Yearly |
| After 5 years | Yearly | Yearly |

History and physical exam should focus on symptoms of local or distant disease. Frequent sites of metastasis include liver, lung and bone.

## The history should include:

- Medication compliance if the patient is prescribed anti-estrogen therapy
- Return of menses unless previous hysterectomy
- Bone / chest / abdomen pain
- Fatigue / dyspnea
- Unexplained weight loss, GI complaints, abdominal pain, ascites
- Arm swelling on the affected side / breast or chest wall changes
- New headaches, neurological symptoms
- New nodules or masses
- Menopausal symptoms (hot flashes, vaginal dryness)
- Arthralgia

## The physical exam should include:

- Assessment of lymph nodes in the head and neck region
- Breast or chest wall examination including palpation of the scar and axillary nodes
- Assessment for lymphedema
- Respiratory and cardiac assessment
- Abdominal exam

# Surveillance Imaging — Section 2

## Mammograms:

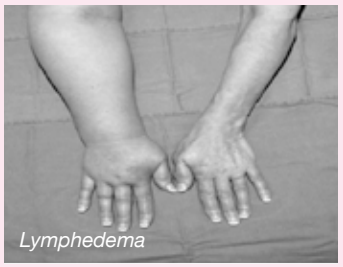
- Generally recommended to be done annually for at least ten years after diagnosis. Please refer to discharge instructions for the specific patient
- If patient has had reconstruction, mammograms are NOT recommended
- If an abnormality is detected on a clinical exam, it should be investigated further even in the context of a normal mammogram

Bloodwork and advanced imaging tests are NOT recommended for routine surveillance, unless index of suspicion for recurrence is high.

## Bone mineral density scans:

- Recommended for patients receiving treatment with aromatase inhibitors (anastrazole, exemestane, letrozole)
- Baseline scan is suggested at initiation of therapy and then 2–3 years later if first scan is normal

**Lymphedema** can occur any time after treatment, even years later.


*Lymphedema*

## Risk factors include:

- Being overweight
- Large number of nodes excised
- Radiation to axilla

First line treatment is a compression garment; lymphatic massage therapy may be helpful.

Patients are eligible through the Assistive Devices Program to receive 75% coverage for two garment sets every 4 months. **The initial prescription must be signed by a specialist** and subsequent renewals can be signed by the family practitioner.

## Assessment for Lymphedema:

- Consider circumferential measurements performed at a minimum of four (and up to six) points on both arms:
  1. Metacarpal-phalangeal joint
  2. Wrist
  3. 10 cm distal to the humerus lateral epicondyle
  4. 15 cm proximal to humerus lateral epicondyle
- For a difference of >1 cm between arms, arrange a follow-up visit in one month
- For a difference of >2 cm at any measurement point, refer for treatment to a specialized LE therapist
- Rule out other diagnoses for arm swelling
- **Patient self-reported symptoms without differences in measurement may still warrant referral**

## Fatigue / Dyspnea / Pain is a common side effect of cancer treatment.

- Routinely screen for cancer related fatigue (CRF):
  CRF is a persistent sense of tiredness (physically, mentally, emotionally) that interferes with usual day to day functioning. CRF is not proportional to the amount of activities undertaken. It affects 25-33% of breast cancer survivors. Studies have found that breast cancer survivors report similar levels of fatigue as age-matched women. One third of breast cancer survivors reported more severe fatigue. Fatigued women were more bothered by menopausal symptoms and were more likely to have received chemotherapy (with or without radiation therapy) than non-fatigued women. Women should be routinely screened for cancer related fatigue.

- Depression and pain are the strongest predictors of fatigue and are potentially treatable

## Recommendations:

- The only proven intervention for benign fatigue is exercise. Usually improves with time; if it persists longer than 6 months post treatment, other causes such as those listed below should be ruled out.
- Direct your patients to the patient-friendly symptom guides created by Cancer Care Ontario at: www.cancercare.on.ca/symptoms

## More serious cancer/treatment related causes of fatigue/dyspnea/pain can include:

- Thromboembolic events
- Recurrence of the disease
- Changes in heart function related to anthracycline chemotherapeutic agents and / or Herceptin

**Refer the patient back to the Cancer Centre for management of these issues.**

**Weight gain** is a common side effect for patients who have received:

- Chemotherapy
- Endocrine suppression therapy with tamoxifen, anastrazole, letrozole, or exemestane

It is potentiated by other side effects of treatment such as arthralgia and hot flashes. Other causes of weight gain (e.g. depression and thyroid dysfunction) should be ruled out.

## Recommendations:

- Encourge patients to follow Canada's Food Guide
- Regular cardiovascular exercise, preferably weight bearing
- Refer the patient for dietary counselling: www.eatrightontario.ca
- Refer to local exercise and fitness programs aimed at breast cancer survivors: www.csep.ca/guidelines
- Reference Cancer Care Ontario's new clinical guideline on exercise at: www.cancercare.on.ca/toolbox/qualityguidelines/clin-program/psychonc/

For the purpose of selecting adjuvant endocrine therapy for women with breast cancer, the most reliable definition of menopause is:

- Bilateral oophorectomy
- At least 12 months of amenorrhea prior to initiation of chemotherapy or tamoxifen

For women with breast cancer age ≤ 60 years who have ovaries and experience amenorrhea secondary to current or past adjuvant chemotherapy or tamoxifen, defining menopause is difficult and care must be taken when initiating an aromatase inhibitor (AI). Contact your Cancer Centre for guidance on determining menopausal status.

**Hot flashes** are related to hormonal changes as a result of chemotherapy, endocrine therapy or menopause. They usually improve over time though some women may experience difficulty for years.

## Recommendations:

**Lifestyle interventions:** Advise healthy lifestyle modifications first. These include reducing core body temperature (by clothing and bed linen choices), regular exercise, weight management, smoking cessation, and avoidance of known triggers such as hot beverages or alcohol. The Society of Obstetricians and Gynaecologists of Canada (SOGC) sponsored www.menopauseandu.ca provides an informative "Lifestyle Fact Sheet" for women.

**Pharmacological interventions** can include:

| Prescription non-hormonal therapy for hot flashes for women with a history of breast cancer | |
|---|---|
| **Medication** | **Suggested daily dose range: start low, go slow** |
| **Venlafaxine** (Effexor XR®) | 37.5 mg - 150 mg po daily |
| **Desvenlafaxine** (Pristiq®) | 50 mg - 100 mg po daily |
| **Citalopram** (Celexa®) | 10 mg - 20 mg po daily |
| **Escitalopram** (Cipralex®) | 10 mg - 20 mg po daily |
| **Gabapentin** (Neurontin®) | 100 mg po tid; titrate to 300 mg po tid |
| **Pregabalin** (Lyrica®) | 75 mg po bid |
| **Clonidine** (Dixarit®) 0.025 mg tab | 0.05 mg po bid |

*Other than clonidine 0.025 mg tab, none of the prescription non-hormonal therapies listed in this table are approved for the treatment of vasomotor symptoms in Canada. These are listed as therapeutic options in the SOGC Clinical Practice Guideline; Managing Menopause 2014. All are weak inhibitors of CYP2D6 therefore can be used with tamoxifen.*

- Menopause Hormone Therapy (MRT) (hormone replacement therapy) is **NOT recommended.**
- Custom compounded 'bio-identical' hormone therapy is **NOT recommended**.
- Complementary and alternative therapies: There is limited evidence of benefit for most complementary and alternative approaches to the management of hot flashes. Without good evidence for effectiveness, and with minimal data on safety, these approaches are **NOT recommended**. Some (e.g. ginseng, black cohosh, St. John's Wort) may interfere with tamoxifen activity.

## Dietary Phytoestrogens

| SAFE TO USE<br>Phytoestrogen rich food (with examples of 1 standard serving size) | | DO NOT USE<br>Concentrated phytoestrogen supplements |
|---|---|---|
| Flax seed (ground) | 1 tbsp | Soy isoflavones and protein extract and isolates<br>• may be listed as: genistein, daidzein, glycitein<br>Other concentrated phytoestrogens<br>• e.g. red clover isoflavones, wild yam root (diosgenin) |
| Tofu | 1/2 cup | |
| Edamame | 1/2 cup | |
| Soy milk | 1 cup | |

## Vaginal Bleeding While on Endocrine Suppression Therapy — Section 7

### Return of Menses:

In younger post menopausal women, vaginal bleeding may signify a return of ovulation, and decrease anti-cancer efficacy of the aromatase inhibitor. Advise patient of risk of pregnancy and, if needed, to use interim barrier contraception until assessed at Cancer Centre.

### Post Menopausal Bleeding:

- Refer to gynaecologist for assessment
  - Normal biopsy - refer back to Cancer Centre for AET review
  - Atypical endometrial hyperplasia or endometrial cancer - Gynaecology and Cancer Centre coordinate gynaecology care and AET review
- Stop tamoxifen or aromatase inhibitor

**Tamoxifen:** development of endometrial carcinoma must be ruled out.

### Recommendations:

- Trans-vaginal ultrasound is highly recommended. Please refer the patient to the gynaecologist if endometrial thickness is more than 10 mm or if there is persistent bleeding
- Ensure adequate method of birth control

### Aromatase inhibitor: (anastrazole, exemestane, letrozole)

- Return of menses may signal return of ovarian function

### Recommendations:

- Stop the drug use immediately
- Ensure adequate method of birth control
- Refer back to the oncologist

## Sexuality and Intimacy

Sexual dysfunction is a common and distressing consequence of cancer treatment. For female breast cancer survivors, cancer treatments resulting in surgical and radiation therapy breast changes and treatment-induced menopause can all contribute to concerns about sexuality and intimacy. A first step for healthcare providers is to ask and acknowledge concerns about sexuality and intimacy.

Patient education material (example below) can be of assistance:

- Susan G. Komen®: FACTS FOR LIFE Sexuality & Intimacy https://ww5.komen.org/uploadedFiles/_Komen/Content/About_Breast_Cancer/Tools_and_Resources/Fact_Sheets_and_Breast_Self_Awareness_Cards/Sexuality%20and%20Intimacy.pdf

## Vaginal Health

Women who undergo abrupt treatment-induced menopause often find themselves in a vexing feedback loop in which they lose interest in sexual activity because it is painful and, consequently, vaginal atrophy and loss of desire become exacerbated with time. Vaginal changes including dryness, atrophic vaginitis and dyspareunia are more common with aromatase inhibitors than with tamoxifen.

**Interventions for vaginal changes** (e.g. dryness, atrophic vaginitis, dyspareunia):

- First rule out other causes (e.g. infection)
- Advise regular use of a moisturizer (e.g. Replens® three times weekly) as "maintenance therapy"
- Advise a water or silicone-based vaginal lubricant (e.g. K-Y® Brand, Astroglide®)
- Avoid use of oil-based lubricants (e.g. Vaseline®)
- Wear cotton underwear and pantyhose with ventilated lining
- Avoid wearing tight pants or tight shorts

The following strategies for maintaining vaginal health for female breast cancer survivors may also be considered:

- Mechanical stretching of tissue (vaginal dilators, pelvic floor muscle control)
- Increasing vaginal blood flow to help prevent atrophy (self-touch, use of vibrators)

**Estrogen containing intravaginal products (e.g. Premarin® cream Estring®, Vagifem® tablets)** are generally **NOT recommended**. Where conservative management has failed and there's an impact on quality of life, consider referral to the appropriate specialist.

## Contraception

- Hormone-based birth control is not recommended regardless of the hormone receptor status of the patient's breast cancer.

## Fertility and Pregnancy

- Adjuvant chemotherapy can impact the premenopausal woman's fertility.
- Amenorrhea usually occurs during chemotherapy, but it appears that the majority of women <35 years of age have a resumption of menses within two years of finishing chemotherapy.
- If a woman is considering pregnancy after treatment, it is advised she should have a discussion with her oncologist.

## Chemotherapy Induced Peripheral Neuropathy (CIPN)

Use of chemotherapeutic agents such as paclitaxel (Taxol) and docetaxel (Taxotere) may cause:

- Numbness
- Tingling
- "Pins and needles" pain affecting the fingers, toes and feet

Some patients may experience late onset. Usual treatments for neuropathic pain may not be effective. Usually peripheral neuropathy resolves over time – months to years.

## Interventions:

- Duloxetine (Cymbalta®) 30-60 mg daily (max dose = 120 mg) (beware of interactions with Tamoxifen)
- TCA's (optional):
    - Notriptyline (Aventyl®) 10-25 mg QHS (max = 100 mg daily)
    - Amitryptyline (Elavil®) 25-50 mg QHS (max = 100 mg daily)
- Gabapentin (Neurontin®) 300mg PO tid and titrate up to a max dose of 3600mg/day
- Pregabalin (Lyrica®) 75mg PO bid and titrate up to a maximum of 600mg/day

## Aromatase Inhibitor-Induced Arthralgia (AIA):

Arthralgia and myalgia are common complaints in patients receiving therapy with aromatase inhibitors (letrozole, anastrazole, and exemestane)

- Described as joint stiffness, pain in the wrists, hips, knees and ankles (symmetrical) improving over the day
- Median time of onset is 1.6 months – symptoms peak at 6 months after initiation of aromatase inhibitors. Discontinuation relieves symptoms within 8-10 weeks.
- Usually decreases over the first 1-2 years of treatment

## Recommendations:

- Maintain an exercise program
- Physiotherapy
- Massage therapy
- Anti-inflammatories or acetaminophen
- Acupuncture

**Some patients may require a change in therapy to another agent – please refer back to the oncologist.**

## Normal changes post radiation:

- Hyper pigmentation in the treated area
- Small broken blood vessels called telangiectasia can appear (even years later)
- Thickened skin with increased density of the breast tissue for patients with lumpectomy
- Adherence of skin to the underlying fascia for patients with mastectomy
- Defined thickening around the scar can be present initially and gradually subsides over time as surgical changes resolve
- Some patients may have persistent seromas
- Axillary cording may develop and be observed as a thick visible cord stretching from the anterior axilla to the upper arm or even distally beyond the elbow





Figure 1: Telangiectasia
Figure 2: Axillary Cording
Figure 3: Seroma
Figure 4: Hyper-pigmentation

## Side effects reported up to 5 years following breast adjuvant radiation therapy are:

- Mild breast erythema (6%)
- Mild breast edema (3%)
- Moderate to severe breast induration (2%)
- Mild (13%) to moderate to severe (1%) telangiectasia of the breast, especially in the area of radiation therapy boost
- Localized fat necrosis may occur in high boost areas (1-8%), is self-limiting and harmless, but may be confused with local recurrence

## Abnormal changes:

- New lumps in the breast tissue, scar, axilla or neck nodes
- New erythema
- New pain
- New nipple retraction or dimpling

## Recommendations:

- Please refer the patient for imaging and to a surgeon for assessment / biopsy
- If unsure about thickening of skin, please refer to the surgeon

# Low Bone Mineral Density (BMD) / Osteoporosis



## Accelerated bone loss can be caused by:

- Chemotherapy
- Use of aromatase inhibitors such as anastrozole, letrozole or exemestane

## Recommendations:

- For **women on AIs** with a **baseline Low Risk BMD**, the next BMD while still on an AI is usually **1-3 years.**
- For **women on AIs** with a **baseline Moderate Risk BMD**, the next BMD while still on an AI is generally recommended at **one year**, whether initiated on osteoporosis medication or not.
- Cessation of smoking, weight-bearing exercise, if appropriate, and limited caffeine intake
- Sufficiency of elemental calcium in diet and / or use of supplements
  - 500 mg daily if risk of heart disease
  - 1200 mg daily if osteopenic or osteoporotic - **preferably through diet**
  - Vitamin D: 1000 – 2000 units daily

## Osteoporosis medication (OM) initiation:

www.osteoporosis.ca recommends OM be initiated when:

- The BMD result is **High Risk** (10 year fracture rate is >20%) OR
- Prior personal fragility fracture of hip or spine OR
- More than one fragility fracture, including sites other than hip or spine

**Earlier OM initiation** for breast cancer patients may be considered if the BMD test is **Moderate Risk** (10 year fracture rate is 10-20%) AND the patient is still on an aromatase inhibitor, or if there is rapid bone loss between interval BMDs.

## Treatments:

- **Oral bisphosphonates:** alendronate (Fosamax®), risedronate (Actonel®)
- **Denosumab** (Prolia® and Xgeva®). Refer to the Ontario Drug Benefit (ODB) for Limited Use (LU) criteria
- **Intravenous bisphosphonates:** zoledronic acid (Aclasta®). Refer to ODB for LU criteria

# Psychosocial Concerns Section 12

**Psychosocial concerns** can include anxiety / depression, fear of recurrence, relationship concerns, body image, genetic risk, spirituality, and other specific issues. Some primary care providers may wish to use a quick screening tool (e.g. **Your Symptoms Matter - General Symptoms** and **Canadian Problem Checklist**) along with **Cancer Care Ontario's Symptom Management Guidelines** in their own evaluation to identify any concerns that emerge post treatment. In some cases, multiple vague physical symptoms and complaints may be an indicator of poor post treatment psychosocial adjustment.

## Recommendations:

- Rule out underlying physical diagnosis
- Treat anxiety / depression. For patients receiving Tamoxifen, please keep in mind that many antidepressants can reduce the efficacy. Venlafaxine/ desvenlafaxine and citalopram/escitalopram are usually less likely to cause a problem
- Non-pharmacological resources can include referral to counselling or psychotherapy, relaxation training, cognitive behavioural therapy, supportive-expressive therapy, or psycho-educational interventions

## Community counselling agencies and other resources:

| | |
|---|---|
| **Canadian Cancer Society Peer Support** | 1-800-263-6750 • www.cancer.ca |
| **Willow Breast Cancer Support Canada** | 1-888-778-3100 • www.willow.org |
| **Canadian Breast Cancer Network** | www.cbcn.ca |
| **Cancer Chat Canada** | www.cancerchatcanada.ca |
| **Windsor Hospice Wellness Programs** | 519-251-2590 • www.thehospice.ca |
| **Windsor Regional Cancer Centre** | 519-253-5253 |
| **RENEW: A Life After Cancer Educational Series** | 519-253-5253<br>renew@wrh.on.ca |
| **RENEW Back to Fitness Program** | 519-253-5253<br>renew@wrh.on.ca |

Check with patient to see if they have private counselling coverage through Employer Benefits.

# Genetic Assessment Section 13

For most women with breast cancer, during care with oncology, their family history will have been reviewed and if appropriate, a genetic assessment referral may have been initiated/completed (may include genetic testing, if eligible). During breast cancer well follow-up care, if the appropriate genetic assessment has not been initiated, consider discussing a referral.

## Hereditary Breast Cancers

About 5-10% of breast cancers are thought to be hereditary, resulting from a gene mutation that has been inherited from a parent (e.g. BRCA1, BRCA2).

- Women with a known hereditary breast cancer gene mutation or who are at a high lifetime risk of developing breast cancer as assessed by predictive risk tools (e.g. IBIS, BOADICEA) are defined as high risk and tend to develop breast cancer at an earlier age, and their breast cancer tends to be more aggressive than breast cancer found in women in the general population.
- Women with a hereditary breast cancer gene mutation have up to an 80% risk of developing breast cancer and up to a 50% risk of developing ovarian cancer in their lifetime.
- Women with a hereditary breast cancer gene mutation, if already diagnosed with breast cancer in one breast, have up to 65% risk of developing breast cancer in the other breast.

## Referral Criteria:

If your patient meets any of the following criteria (published by the Ontario Ministry of Health and Long-Term Care), and they have not previously been referred, a referral should be discussed.

1. Multiple cases of breast cancer (particularly where diagnosis occurred at less than 50 years of age) and/or ovarian* cancer (any age) in the family - especially in closely related relatives in more than one generation
2. Age at diagnosis of breast cancer less than 35 years
3. A family member diagnosed with both breast and ovarian* cancer
4. Breast and/or ovarian* cancer in Jewish families
5. Family member(s) with primary cancer occurring in both breasts, especially if one or both cancers were diagnosed before the age of 50
6. A family member diagnosed with invasive serous ovarian* cancer
7. Presence of male breast cancer in the family
8. A family member with an identified BRCA1 or BRCA2 mutation
9. Presence of other associated cancers or conditions suggestive of an inherited cancer syndrome

*includes cancer of the fallopian tubes and primary peritoneal cancer

## Windsor Cancer Genetics Clinic:

Windsor Regional Hospital – Cancer Centre
519-254-5577 x58601

Erie St. Clair Regional Cancer Program

# SURVEILLANCE/SURVIVORSHIP PRIMARY CARE GUIDES:

1. Pink Notes (Breast)
2. Blue Notes (Colorectal)
3. Prostate Notes

To access any of the above online
or to request a hard copy, call:
519-254-5577 x 58620

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