

## SCA Drug Formulary

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### Appendix C

#### Definition of Menopause

Determination of menopausal status may be required to guide selection of endocrine therapy for breast cancer. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for Invasive Breast Cancer (v4.2023) defines menopause as no menses for 1 year in the absence of prior chemotherapy or tamoxifen use, or no menses after surgical removal of all ovarian tissue.

#### Additional information:

- Menopause is the permanent cessation of menses and includes a profound and permanent decrease in ovarian estrogen synthesis
- Menopause is usually a clinical diagnosis made after  $\geq 12$  months of amenorrhea; natural menopause is experienced between ages 42–58 years
- Breast cancer treatments may affect ovarian function and menses:
  - In those who are premenopausal at the beginning of chemotherapy and who develop chemotherapy-induced amenorrhea, ovarian function may still be intact despite amenorrhea or may resume over time; the likelihood of ovarian function resuming after chemotherapy is higher among those aged  $< 40$  years
  - Tamoxifen may cause amenorrhea without inducing menopause in premenopausal individuals
  - Ovarian function suppression induces amenorrhea and reduces ovarian estrogen synthesis without causing permanent menopause
- Twelve months of amenorrhea alone is insufficient to diagnose menopause with chemotherapy-induced amenorrhea or with tamoxifen  $\pm$  ovarian suppression; follicle-stimulating hormone (FSH) and estradiol levels are used to support the diagnosis of menopause, however, clear criteria to guide interpretation of FSH and estradiol in this population is lacking
  - Tamoxifen may alter FSH levels, limiting its utility in determination of menopausal status
- FSH and estradiol should be repeated serially to ensure menopausal status in patients with breast cancer with chemotherapy-induced amenorrhea
- Evidence-based criteria for the diagnosis of menopause in patients with breast cancer are lacking; clinical trials in breast cancer have utilized a variety of definitions of menopause, and reasonable criteria for determining menopause in patients with breast cancer include any of the following:
  - Prior bilateral oophorectomy
  - Age  $\geq 60$  years
  - Age  $< 60$  with amenorrhea for  $\geq 12$  months in the absence of prior chemotherapy, receipt of tamoxifen, toremifene, or ovarian suppression and estradiol and FSH in the post-menopausal range
  - Age  $< 60$  years: chemotherapy-induced amenorrhea for  $\geq 12$  months with FSH and estradiol in post-menopausal range on serial assessments
  - Age  $< 60$  years: on tamoxifen with FSH and estradiol level in post-menopausal range
- Menopausal status cannot be determined in those receiving ovarian function suppression