

***Title: Aromatase Inhibitors (Femara [letrozole] & Arimidex [anastrozole])***

<b>Origination:</b> 07/28/10	<b>Revised:</b>	<b>Annual Review:</b> 12/15/11
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**Purpose:**

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

**Background Information:**

***Medication Summary***

**Femara (Letrozole)**

- Letrozole is a nonsteroidal competitive inhibitor of the aromatase enzyme system; it inhibits the conversion of androgens to estrogens. In adult nontumor- and tumor-bearing female animals, letrozole is as effective as ovariectomy in reducing uterine weight, elevating serum LH, and causing the regression of estrogen-dependent tumors. In contrast to ovariectomy, treatment with letrozole does not lead to an increase in serum FSH. Letrozole selectively inhibits gonadal steroidogenesis but has no significant effect on adrenal mineralocorticoid or glucocorticoid synthesis.
- Letrozole inhibits the aromatase enzyme by competitively binding to the heme of the cytochrome P450 subunit of the enzyme, resulting in a reduction of estrogen biosynthesis in all tissues. Treatment of women with letrozole significantly lowers serum estrone, estradiol and estrone sulfate and has not been shown to significantly affect adrenal corticosteroid synthesis, aldosterone synthesis, or synthesis of thyroid hormones.
- Indications: adjuvant treatment of early breast cancer, extended adjuvant treatment of early breast cancer, first and second line treatment of advanced breast cancer.
- The recommended dose of Femara is one 2.5 mg tablet administered once a day, without regard to meals.

**Arimidex (Anastrozole)**

- Anastrozole is a potent and selective non-steroidal aromatase inhibitor. It significantly lowers serum estradiol concentrations and has no detectable effect on formation of adrenal corticosteroids or aldosterone.
- Arimidex is indicated for: adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer, first line treatment of postmenopausal women with hormone receptor-positive or hormone receptor unknown locally advanced or metastatic breast cancer, treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy.
- The dose of arimidex is one 1 mg tablet taken once a day. For Members with advanced breast cancer, arimidex should be continued until tumor progression. Arimidex can be taken with or without food.

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**Background Information, continued:**

***Reference Statement***

- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

***Eligibility Criteria***

- Member must be eligible and have applicable benefit coverage (i.e., self-injectable rider) within the specified date(s) of service.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

**Procedure:**

- 1.0 Request for *initiation of therapy* with **Aromatase inhibitors** for **breast cancer** requires documentation from the Member's medical records maintained by the requesting independent practitioner:
  - 1.1 Aromatase inhibitors are approvable for 12 months.
- 2.0 Request for initiation of therapy with Aromatase inhibitors for **infertility/ovulation induction** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 2.1 Member has infertility benefits per BDS (Miami-Dade POS only at this time);
  - 2.2 Documentation of recent negative pregnancy test **AND** normal liver function test;
  - 2.3 If criteria are met, approve for six (6) months (5-10 tablets / 28 days).

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**Procedure, continued:**

- 3.0 Request for *initiation of therapy* with Aromatase inhibitors for **short stature** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 3.1 Prescriber is an endocrinologist;
  - 3.2 Member is less than 18 years of age;
  - 3.3 Epiphyses are not fused;
  - 3.4 No active malignancy;
  - 3.5 More than one (1) year since completion of successful malignancy treatment;
  - 3.6 Member has not achieved a height consistent with mid-parental height (an average of mother's and father's heights);
  - 3.7 Growth rate greater than 2.5cm/year on growth hormone therapy;
  - 3.8 No hepatic impairment;
  - 3.9 Member must be male gender;
  - 3.10 Member must be in puberty and meet ALL of the following criteria:
    - 3.10.1 10 to 18 years of age;
    - 3.10.2 Tanner stage two (2) to five (5) OR Testis volume greater than 4 ml;
    - 3.10.3 Bone age greater than 14;

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**Procedure, continued:**

- 3.0 Request for *initiation of therapy* with Aromatase inhibitors for **short stature** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:
- 3.11 Member must have one (1) of the following diagnoses:
- 3.11.1 Growth hormone deficiency (GHD) AND meets the following criteria:
- 3.11.1.1 Two (2) growth hormone provocation tests (with insulin, propranolol, levodopa, arginine, clonidine, or glucagon) with post-stimulation peaks <10ng/ml (one (1) growth hormone provocation test if member has defined central nervous system pathology); AND
- 3.11.1.2 Height <3<sup>rd</sup> percentile; AND
- 3.11.1.3 Growth rate <4cm/year; AND
- 3.11.1.4 Bone age > 2 years behind actual age;
- 3.11.2 Small for gestational age (SGA) AND meets the following criteria:
- 3.11.2.1 Child's birth weight, birth length, or both more than two (2) SD below the mean normal values following adjustment for age and gender; AND
- 3.11.2.2 Age >2 years; AND
- 3.11.2.3 Current height  $\geq$ 2SD adjusted mean normal values;
- 3.11.3 Prader-Willi Syndrome (PWS) or Noonan Syndrome (NS) or Short stature homeobox-containing gene (SHOX) AND meets the following criteria:
- 3.11.3.1 Confirmed diagnosis by genetic testing;
- 3.11.3.2 Height <3<sup>rd</sup> percentile; AND
- 3.11.3.3 Growth rate <4cm/year; AND
- 3.11.3.4 Epiphyses confirmed open via wrist film;
- 3.12 If the above criteria are met, Aromatase Inhibitors are approvable for 12 months (30 tablets / 30 days).

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**Procedure, continued:**

- 4.0 Request for *continuation of therapy* with Aromatase inhibitors for **GHD, SGA, PWS, NS, SHOX** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 4.1 Prescriber is an endocrinologist;
  - 4.2 Member is less than 18 years of age;
  - 4.3 Epiphyses are not fused;
  - 4.4 No active malignancy;
  - 4.5 More than one (1) year since completion of successful malignancy treatment;
  - 4.6 Member has not achieved a height consistent with mid-parental height (an average of mother's and father's heights);
  - 4.7 Growth rate greater than 2.5cm/year on growth hormone therapy;
  - 4.8 No hepatic impairment;
  - 4.9 Member must be male gender;
  - 4.10 Member must be in puberty and meet ALL of the following criteria:
    - 4.10.1 Ten (10) to eighteen (18) years of age;
    - 4.10.2 Tanner stage two (2) to five (5) **OR** Testis volume greater than 4 ml;
    - 4.10.3 Bone age greater than 14;
  - 4.11 Member meets the following criteria:
    - 4.11.1 Pre-treatment growth rate doubled; **OR**
    - 4.11.2 Growth rate greater than 2.5cm/year; **AND**
    - 4.11.3 Epiphyses confirmed open via wrist film;
  - 4.12 Documentation has been submitted for lipid panel **AND** bone mineral density test;
  - 4.13 If above criteria are met, Aromatase Inhibitor is approvable for 12 months (30 tablets / 30 days).

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**References:**

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**Disclaimer Information:**

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.