

POLICY: Oncology – Fulvestrant (Faslodex injection for intramuscular use – AstraZeneca; generics)

DATE REVIEWED: 05/06/2020

OVERVIEW

Fulvestrant is an estrogen receptor (ER) antagonist that binds to the estrogen receptor in a competitive manner.¹ Its affinity to the ER is comparable to that of estradiol. By binding to the ER, fulvestrant downregulates the ER protein in human breast cancer cells.

Fulvestrant is indicated for the following:

- As monotherapy, for the treatment of hormone receptor-positive (HR+) [i.e., ER+ or progesterone receptor (PR+)], human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy; or
- As monotherapy, for the treatment of patients with HR+ advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.¹
- Fulvestrant is indicated in combination with Kisqali® (ribociclib tablets) as initial endocrine based therapy or following disease progression on endocrine therapy for HR+, HER2-negative advanced or metastatic breast cancer in postmenopausal women.
- Fulvestrant is indicated in combination with Ibrance® (palbociclib capsules) or Verzenio™ (abemaciclib tablets) in women with disease progression after endocrine therapy for HR+, HER2-negative advanced or metastatic breast cancer.

The recommended dose of fulvestrant as monotherapy and for combination therapy is 500 mg administered intramuscularly (IM) as two 5 mL injections (one to two minutes per injection) on Days 1, 15, 29, and once monthly thereafter. Pre/perimenopausal women treated with the combination fulvestrant and cyclin dependent kinase 4/6 (CDK4/6) inhibitors [Ibrance, Kisqali, Verzenio) should be treated with gonadotropin-releasing hormone (GnRH) agonists for ovarian suppression. The modified dose for moderate hepatic impairment (Child-Pugh class B) for monotherapy and combination therapy is fulvestrant 250 mg IM as one 5 mL injection on Days 1, 15, 29, and once monthly thereafter. Fulvestrant is available as 5-mL prefilled syringes containing 250 mg/5 mL.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 3.2020 – March 6, 2020) recommends fulvestrant in combination with cyclin dependent kinase 4/6 inhibitors (i.e., Ibrance, Kisqali, Verzenio) and non-steroidal aromatase inhibitors (i.e., anastrozole, letrozole) for the treatment of recurrent or metastatic HR+, HER2-negative disease (category 1 preferred regimen).² The guidelines note that CDK4/6 inhibitors or anastrozole/letrozole in combination with fulvestrant may be considered as a treatment option for first-line therapy for women who are postmenopausal or premenopausal (receiving ovarian suppression or ablation). If CDK4/6 inhibitor was not previously used, fulvestrant + CDK4/6 inhibitor is a category 1, preferred regimen as second/subsequent-line therapy. It is also recommended as a second/subsequent-line therapy, category 1, preferred regimen for *PIK3CA* mutated tumors in combination with Piqray (alpelisib tablets). Fulvestrant in combination with everolimus (category 2A) is another option for second/subsequent-line therapy. As monotherapy, fulvestrant is listed as one of the preferred options (category 2A) for second/subsequent-line therapy. Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.²⁻³ Based on a review article, there are limited data to support the

use of fulvestrant monotherapy in men; however, there are no randomized prospective or retrospective trial data with the use of everolimus or cyclin dependent kinase (CDK) 4/6 inhibitor in men.⁴

The NCCN compendium for fulvestrant and the respective guidelines support fulvestrant use for low-grade serous carcinoma (ovarian/fallopian tube/primary peritoneal cancer), uterine sarcoma, and endometrial carcinoma.³

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of fulvestrant. Approval is recommended for those who meet the Criteria and Dosing for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the of the specialized skills required for evaluation and diagnosis of patients treated with fulvestrant, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires fulvestrant to be prescribed by or in consultation with a physician who specializes in the condition being treated.

In the approval indication, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: men/males are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression. Female/women are defined as individuals with the biological traits of a woman, regardless of the individual's gender identity or gender expression.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of fulvestrant is recommended in those who meet one of the following criteria:

FDA-Approved Indications

- 1. Breast Cancer – Fulvestrant Monotherapy.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
 - A)** The medication is prescribed by or in consultation with an oncologist; AND
 - B)** Patient has recurrent or metastatic hormone receptor (HR)-positive (i.e., estrogen receptor- [ER] or progesterone receptor [PR]-positive) disease; AND
 - C)** Patient meets one of the following criteria (i or ii):
 - i.** Patient is a postmenopausal female* or a male* ; OR
 - ii.** Patient is premenopausal and is receiving ovarian suppression with a gonadotropin-releasing hormone (GnRH) agonist or has had ovarian ablation.
Note: Examples of GnRH agonists are Zoladex (goserelin), Lupron (leuprolide), Trelstar (triptorelin) and examples of ovarian ablation are surgical bilateral oophorectomy or ovarian irradiation.

* Refer to the Policy Statement.

Dosing. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter.¹

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- 2. Breast Cancer – Fulvestrant Combination Therapy.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
- A)** The medication is prescribed by or in consultation with an oncologist; AND
 - B)** Patient has recurrent or metastatic hormone receptor (HR)-positive (i.e., estrogen receptor- [ER] or progesterone receptor [PR]-positive) disease; AND
 - C)** Patient meets ONE of the following criteria (i or ii):
 - i.** Patient is a postmenopausal female* or a male*; OR
 - ii.** Patient is premenopausal and is receiving ovarian suppression with a gonadotropin-releasing hormone (GnRH) agonist or has had ovarian ablation.
Note: Examples of GnRH agonists are Zoladex (goserelin), Lupron (leuprolide), Trelstar (triptorelin). Examples of ovarian ablation are surgical bilateral oophorectomy or ovarian irradiation; AND
 - D)** Patient meets one of the following criteria (i or ii):
 - i.** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer and meets one of the following criteria (a or b):
 - a)** The patient meets both of the following criteria (1 and 2):
 - (1)** The patient has progressed on or after at least one prior endocrine-based therapy.
Note: Examples of endocrine therapy are tamoxifen, anastrozole, letrozole, exemestane; AND
 - (2)** The patient has *PIK3CA*-mutated tumor and the medication is used in combination with Piqray (alpelisib tablets); OR
 - b)** The medication will be used in combination with one of: cyclin dependent kinase 4/6 (CDK 4/6) inhibitor, non-steroidal aromatase inhibitor (i.e., anastrozole or letrozole), or everolimus.
Note: Examples of CDK4/6 inhibitors are Kisqali [ribociclib tablets], Ibrance [palbociclib capsules], Verzenio [abemaciclib tablets]); OR
 - ii.** Patient has human epidermal growth factor receptor 2 (HER2)-positive breast cancer and the medication is used in combination with trastuzumab products.

Dosing. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter.¹

Other Uses with Supportive Evidence

- 3. Ovarian/Fallopian Tube/Primary Peritoneal Cancer.** Approve for 1 year if the patient meets the following criteria (A and B):
- A)** The medication is prescribed by or in consultation with an oncologist; AND
 - B)** The medication is used as recurrence therapy for low-grade serous carcinoma.

Dosing. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter.

Limited dosing is available. The dose listed is recommended in the product labeling for approved uses.¹

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- 4. Uterine Sarcoma.** Approve for 1 year if the patient meets the following criteria (A and B):
- A) The medication is prescribed by or in consultation with an oncologist; AND
 - B) Patient meets one of the following criteria (i or ii):
 - i. Patient has low-grade endometrial stromal sarcoma; OR
 - ii. Patient has hormone receptor-positive uterine leiomyosarcoma.

Dosing. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter.

Limited dosing is available. The dose listed is recommended in the product labeling for approved uses.¹

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- 5. Endometrial Carcinoma.** Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Dosing. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter.

Limited dosing is available. The dose listed is recommended in the product labeling for approved uses.¹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

- 1. Other Indications (Non-Cancer).** Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications and Other Uses with Supportive Evidence). Criteria will be updated as new published data are available.

REFERENCES

1. Faslodex[®] injection for intramuscular use [prescribing information]. Wilmington, DE: AstraZeneca; November 2017.
2. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (Version 3.2019 – September 6, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 30, 2019.
3. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on April 8, 2019. Search term: fulvestrant.
4. Losurdo A, Rota S, Gullo G, et al. Controversies in clinicopathological characteristics and treatment strategies of male breast cancer: a review of the literature. *Crit Rev Oncol Hematol*. 2017;113:283-291.

HISTORY

Type of Revision	Summary of Changes*	Date Reviewed
New policy	New criteria	02/22/2017
Selected revision	Added new indication for Faslodex use as monotherapy in postmenopausal patients not previously treated with endocrine therapy.	09/27/2017
Selected revision	Added Verzenio to criteria for use in combination with Faslodex	10/11/2017
Annual revision	Separated out criteria for “Faslodex Monotherapy” and “Faslodex Combination Therapy” to make it easier to read. Deleted criteria for combination therapy in men due to lack of data. Added Afinitor as an option for combination therapy with Faslodex based on guidelines. Added criteria for Faslodex Monotherapy that men treated for breast cancer should be on gonadotropin-releasing hormone agonist. Matched up Extended Approval duration criteria and Duration of Therapy criteria in Breast Cancer in Men section to that of women. Added other compendium supported indication for Medical Director review under Other Cancer Indications.	03/14/2018
Annual revision	Deleted Breast Cancer in Men – Faslodex Monotherapy criteria since this is addressed together with postmenopausal/premenopausal women. Added criteria in both breast cancer indications to require gonadotropin releasing-hormone agonist use in pre/perimenopausal women. Deleted criteria requiring Faslodex use after disease progression on endocrine therapy. For combination use, added approval for all cyclin dependent kinase 4/6 (CDK4/6) inhibitors and listed products as examples. Also added approval for Faslodex use in combination with trastuzumab products for HER2-positive disease. Deleted Initial/Extended approval, Duration of Therapy, and Labs/Diagnostics sections for all indications since these are addressed within criteria. Deleted Patient has started on Faslodex condition to be in line with other policies. Deleted Other Cancer Indications since these are listed as approval conditions separately. Added new conditions of approval based on compendium/guideline supported use for: uterine sarcoma, endometrial carcinoma, and ovarian/fallopian tube/primary peritoneal cancer.	04/10/2019
Selected revision	Name of policy changed to Oncology – Fulvestrant due to availability of generics. For Breast Cancer – Fulvestrant Combination Therapy, added criteria for combination use with Piqray if patient has tried prior endocrine regimen. Based on guidelines, fulvestrant and CDK4/6 inhibitor use does not require prior endocrine regimen. Faslodex now has generics available; so changed reference from brand name to generic name where applicable.	10/02/2019
Annual revision	For Breast Cancer - Fulvestrant Combination Therapy indication, added non-steroidal aromatase inhibitors (i.e., letrozole or anastrozole) as one of the agents that could be used in combination with fulvestrant.	05/06/2020