MEDICAL MUTUAL®

MedicalPolicy

Policy:	**201717-CC**	**Initial Effective Date: 04/17/2017**
Code(s):	**HCPCS J9395**	**Annual Review Date: 04/19/2018**
SUBJECT:	**Faslodex® (fulvestrant injection for intramuscular)**	**Last Revised Date: 04/19/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Medical Policy.

OVERVIEW

Faslodex 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, Faslodex downregulates the ER protein in human breast cancer cells.

Faslodex is indicated 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 no previously treated with endocrine therapy; or for the treatment of patients with HR+ advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.[1] Faslodex is also FDA-approved for the treatment of HR+, HER2-negative advanced or metastatic breast cancer in combination with Ibrance® (palbociclib capsules). Verzenio™ (abemaciclib tablets), another cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated in combination with Faslodex for the treatment of women with HR+, HER2-negative, advanced or metastatic breast cancer with disease progression following endocrine therapy.[4]

The recommended dose of Faslodex 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 Faslodex and Ibrance should be treated with gonadotropin-releasing hormone (GnRH) agonists for ovarian suppression. The modified dose for hepatic impairment for monotherapy and combination therapy is Faslodex 250 mg IM (same days). The recommended dose of Ibrance is 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days of treatment. The recommended dose of Verzenio is 150 mg orally twice daily (BID) when used in combination with Faslodex.

Faslodex is available as 5-mL prefilled syringes containing 250 mg/5 mL.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 4.2017) recommends Faslodex in combination with Ibrance or Verzenio for the treatment of recurrent or metastatic ER+, HER2-negative disease that has progressed on endocrine therapy for postmenopausal women or in premenopausal women receiving ovarian suppression with a leutinizing hormone-releasing hormone (LHRH) agonist (e.g., Lupron® [leuprolide], Trelstar® [triptorelin], Zoladex) [both category 1].[2] Faslodex is also recommended for use in combination with Afinitor® (everolimus tablets) [category 2A]. As monotherapy, Faslodex is listed as one of the endocrine therapy options in

postmenopausal women with ER+ or PR+, HER2-negative recurrent metastatic or Stage IV breast cancer (category 1). 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 Faslodex monotherapy in men; however, there are no randomized prospective or retrospective trial data with the use of Afinitor or cyclin dependent kinase (CDK) 4/6 inhibitor in men.[4] In postmenopausal women with HR+/HER2-negative breast cancer, other endocrine therapy options for recurrent or Stage IV disease include nonsteroidal aromatase inhibitors (anastrozole, letrozole); steroidal aromatase inhibitors (exemestane or exemestane plus Afinitor); Afinitor plus tamoxifen; Ibrance plus aromatase inhibitor [category 1]; Kisqali [ribociclib tablets] plus aromatase inhibitor [category 1]; tamoxifen or Fareston® [toremifene tablets]); progestin (megestrol acetate); androgens (fluoxymesterone); single-agent Verzenio; and high-dose estrogen (ethinyl estradiol). Premenopausal women with HR+ disease should have ovarian ablation/suppression and follow the guidelines for postmenopausal patients. A survival benefit of aromatase inhibitors over other endocrine therapies has been suggested, but the advantage is small.

POLICY STATEMENT

This policy involves the use of Faslodex. Prior authorization is recommended for medical benefit coverage of Faslodex. Approval is recommended for those who meet the conditions of coverage in the **Criteria**, **Dosing**, **Initial or Extended Approval**, **Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Waste Management** applies for all covered conditions. **Conditions Not Recommended for Approval** is listed following the recommended authorization criteria and Waste Management section.

Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Faslodex, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Faslodex to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy.

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 are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Breast Cancer- Faslodex Monotherapy.[1]

Criteria. *Patient must meet the following criteria (A, B,C AND D)*:

A) Faslodex is prescribed by or in consultation with an oncologist; AND

B) Patient has advanced or metastatic hormone receptor (HR)-positive (i.e., estrogen receptor- [ER] or progesterone receptor [PR]-positive) disease; AND

C) Patient is postmenopausal; AND

D) Patient meets ONE of the following criteria (i or ii):

- **i.** Patient has disease progression following endocrine therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole); OR
- **ii.** Patient meets BOTH of the following criteria (a and b):
  - **a)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - **b)** Patient has not been previously treated with endocrine therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole)

Dosing in Advanced or Metastatic Breast Cancer. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter for both Faslodex monotherapy

Note: Dose modifications are recommended for hepatic impairment.[1] See the prescribing information for more detail.

Initial Approval/Extended Approval.

A) *Initial Approval:* Approve 6 months of therapy.

B) *Extended Approval:* Approve at additional 6-month intervals if the patient does not have disease progression, as determined by the prescribing physician.

Duration of Therapy in Advanced or Metastatic Breast Cancer. Indefinite if the patient does not have disease progression, as determined by the prescribing physician.

Labs/Diagnostics. Testing for HR status (ER or PR positive) and HER2 protein expression status is required for appropriate selection of patients for Faslodex therapy. See criteria above.

2. Breast Cancer – Faslodex Combination Therapy

Criteria. *Patient must meet the following criteria (A, B, C, D, E, AND F):*

A) Faslodex is prescribed by or in consultation with an oncologist; AND

B) Patient has advanced or metastatic hormone receptor (HR)-positive (i.e., estrogen receptor- [ER] or progesterone receptor [PR]-positive) disease; AND

C) Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND

D) Patient has disease progression after endocrine therapy (e.g., tamoxifen, anastrozole, exemestane, megestrol acetate, fluoxymesterone); AND

E) Faslodex will be used in combination with Ibrance (palbociclib capsules), Verzenio (abemaciclib tablets), or Afinitor® (everolimus tablets); AND

F) Patient meets ONE of the following criteria (i or ii):

i. Patient is postmenopausal; OR

ii. Patient is premenopausal and is receiving ovarian suppression with a gonadotropin- releasing hormone (GnRH) agonist (e.g., Zoladex [goserelin], Lupron [leuprolide], Trelstar [triptorelin]) or has had ovarian ablation (e.g., surgical bilateral oophorectomy or ovarian irradiation).

Dosing in Advanced or Metastatic Breast Cancer. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter for Faslodex combination therapy with Ibrance, Verzenio, or Afinitor.[1]

Note: Dose modifications are recommended for hepatic impairment.[1] See the prescribing information for more detail.

Initial Approval/Extended Approval.

C) *Initial Approval:* Approve 6 months of therapy.

D) *Extended Approval:* Approve at additional 6-month intervals if the patient does not have disease progression, as determined by the prescribing physician.

Duration of Therapy in Advanced or Metastatic Breast Cancer. Indefinite if the patient does not have disease progression, as determined by the prescribing physician.

Labs/Diagnostics. Testing for HR status (ER or PR positive) and HER2 protein expression status is required for appropriate selection of patients for Faslodex therapy. See criteria above.

Other Uses with Supportive Evidence

3. Breast Cancer in Men*- Faslodex Monotherapy.[2-4]

Criteria. *Patient must meet the following criteria (A, B,C AND D)*:

A) Faslodex is prescribed by or in consultation with an oncologist; AND

B) The patient has advanced 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 has disease progression following endocrine therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole); OR
- **ii.** Patient meets BOTH of the following criteria (a and b):
  - **a)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - **b)** Patient has not been previously treated with endocrine therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole); AND

D) Patient is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Zoladex [goserelin], Lupron [leuprolide], Trelstar [triptorelin]) if on concomitant aromatase inhibitor therapy (e.g., letrozole tablets, exemestane, anastrozole).

* Refer to the Policy Statement.

Dosing in Advanced or Metastatic Breast Cancer. 500 mg intramuscularly (IM) as two 5 mL injections, on Days 1, 15, 29 and once monthly thereafter for both Faslodex monotherapy

Note: Dose modifications are recommended for hepatic impairment.[1] See the prescribing information for more detail.

Initial Approval/Extended Approval.

A) *Initial Approval:* Approve 6 months of therapy.

B) *Extended Approval:* Approve at additional 6-month intervals, as determined by the prescribing physician.

Duration of Therapy in Breast Cancer. Indefinite as determined by the prescribing physician.

Labs/Diagnostics. Testing for HR status (ER or PR positive) and HER2 protein expression status is required for appropriate selection of patients for Faslodex therapy. See criteria above.

4. Patient has been Started on Faslodex.

Criteria. *The patient must meet the following criteria (A AND B):*

A) Patient meets the conditions for coverage required for **Dosing**, **Extended Approval**, **Duration of Therapy**, and **Labs/Diagnostics** for an approved use in this *Faslodex Utilization Review* policy; AND

B) Patient meets ONE of the following criteria (i or ii):

i. If using Faslodex as monotherapy, the patient has HR-positive breast cancer; OR

ii. If using Faslodex in combination with Ibrance (palbociclib capsules) or Verzenio (abemaciclib tablets), or Afinitor (everolimus tablets) the postmenopausal or premenopausal patient has HR-positive, HER2-negative breast cancer.

5. **Other Cancer Indications.** Forward to the Medical Director for review on a case-by-case basis. Other indications supported in *NCCN Compendium*[3] with category 2A or category 2B recommendations include: Faslodex used in combination with or without Herceptin® (trastuzumab for injection) in HR+ and HER2-positive breast cancer in postmenopausal patients, and for endometrial carcinoma.

Waste Management for All Indications.
The dose is 500 mg IM as two 5 mL injections on Days 1, 15, 29, and once monthly thereafter. Faslodex is available 5 mL prefilled syringes containing 250 mg/5 mL.

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.

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

Prior approval is required for HCPCS Codes J9395

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 4.2017). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 11, 2018.
3. The NCCN Drugs and Biologics Compendium. © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on March 11, 2018. 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.

HCPCS Code(s):	
J9395	Injection, Fulvestrant, 25 mg