CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Fulvestrant (Faslodex®)

Version: 1.0

EFFECTIVE DATE: 12/1/2024

NantHealth® | Eviti®

Please note the following:

Fulvestrant (Faslodex®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Fulvestrant (Faslodex): Discussion

Fulvestrant acts by binding, blocking, and degradation of estrogen receptors, which in turn leads to the complete cessation of estrogen signaling through the estrogen receptors in the body. Fulvestrant acts as a complete antagonist at the estrogen receptor, compared with the previously used drugs, namely the selective estrogen receptor modulators (SERMs), for example, tamoxifen, which had partial agonist activity.[1]

The most common adverse reactions reported were injection site pain, nausea, bone pain, arthralgia, headache, back pain, fatigue, pain in the extremities, hot flashes, vomiting, anorexia, asthenia, musculoskeletal pain, cough, dyspnea, fetal harm, and constipation. Hypersensitivity reactions include urticaria and angioedema.[2]

Fulvestrant is approved by the Food and Drug Administration (FDA) for breast cancer.

The National Comprehensive Cancer Network (NCCN) endorses fulvestrant in the following cancer types: breast, fallopian tube, and uterine.[3,4,5]

Fulvestrant: Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

Fulvestrant: Policy

Note: Coverage of fulvestrant will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Fulvestrant will be considered for coverage when the following criteria are met:

Breast Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Hormone receptor (HR) therapy; OR
4. HR positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy; OR
5. HR positive, HER2 negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib, as initial endocrine based therapy or following disease progression on endocrine therapy; OR
6. HR positive, HER2 negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy[2]; OR

Invasive Breast Cancer and Inflammatory Breast Cancer

For **NCCN** required criteria coverage:

7. Therapy for recurrent unresectable (local or regional) or stage IV (M1) hormone receptor positive disease in postmenopausal women or for premenopausal women treated with ovarian ablation and suppression for one of the following:
   a) Abemaciclib, palbociclib or ribociclib) for HER2 negative disease with no visceral crisis if disease progression on adjuvant endocrine therapy (ET) or with early disease relapse within 12 months of adjuvant ET completion
   b) First-line therapy in combination with inavolisib and palbociclib if PIK3CA activating mutation positive for HER2 negative disease with no visceral crisis after disease progression on adjuvant endocrine therapy or disease relapse within 12 months of adjuvant endocrine therapy completion
   c) First-line or subsequent-line therapy as a single agent for human epidermal growth factor receptor 2 HER2 negative disease with no visceral crisis
   d) Second-line or subsequent-line therapy in combination with everolimus for HER2 negative disease with no visceral crisis
   e) Second-line or subsequent-line therapy in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib or ribociclib) for HER2 negative disease with no visceral crisis if a CDK4/6 inhibitor was not previously used
   f) Second-line or subsequent-line therapy in combination with capivasertib for HER2 negative disease with no visceral crisis if PIK3CA or AKT1 activating mutations or PTEN alterations are present after disease progression or recurrence after one or

more prior lines of endocrine therapy, including one line containing a CDK4/6 inhibitor
   g) Single agent for HER2 positive disease
   h) In combination with trastuzumab for HER2 positive disease; OR
8. Emerging biomarkers to identify novel therapies for patients with stage IV (M1) disease: Activity in HER2 activating mutations in combination with neratinib with or without trastuzumab for one of the following:
   a) Hormone receptor positive human epidermal growth factor receptor 2 (HER2) negative disease in patients who have already received a CDK4/6 inhibitor therapy
   b) Triple negative disease.[3]

Note: Men with breast cancer should be treated similarly to postmenopausal women; however, the use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.

Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer

Grade 1 Endometrioid Carcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Hormone therapy as a single agent as primary adjuvant treatment for pathologic stage IC-IV disease

Low-Grade Serous Carcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Hormone therapy as a single agent for platinum-sensitive or platinum-resistant recurrence of low-grade serous.[4]

Uterine Neoplasms

Endometrial Carcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Primary treatment as single agent hormonal therapy used for lower grade endometrioid histologies, preferably in patients with small tumor volume or an indolent growth pace for one of the following:
   a) Disease that is not suitable for primary surgery in patients with suspected or gross cervical involvement
   b) With or without external beam radiation therapy (EBRT), stereotactic body radiation therapy, and/or total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO) for distant metastases that is suitable for primary surgery
   c) With or without external beam radiation therapy (EBRT), stereotactic body radiation therapy, and/or total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO) for distant metastases that is suitable for primary surgery
   d) For locoregional extrauterine disease or distant metastases that is not suitable for primary surgery; OR
4. Adjuvant treatment for surgically staged patients as single-agent hormonal therapy with or without external beam radiation therapy (EBRT) and with or without vaginal brachytherapy for stage IV disease; OR
5. Single agent hormonal therapy typically used for lower grade endometrioid histologies, preferably in patients with small tumor volume or an indolent growth pace for one of the following:
   a) Isolated metastases
   b) Disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
   c) With sequential EBRT and with or without brachytherapy for locoregional recurrence in patients with no prior RT to the site of recurrence, or previous vaginal brachytherapy
   d) After surgical exploration, with sequential EBRT for locoregional recurrence in patients with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
   e) After surgical exploration, with or without sequential EBRT for locoregional recurrence in patients with upper abdominal or peritoneal disease
   f) With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in patients who have received prior EBRT to the site of recurrence

Uterine Sarcoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Single agent therapy for low-grade endometrial stromal sarcoma (ESS), or adenosarcoma without sarcomatous overgrowth, or estrogen receptor/progesterone receptor positive (ER/PR+) uterine sarcomas in patients with small tumor volume or an indolent growth pace for one of the following:
   a) Primary treatment of known or suspected extrauterine disease diagnosed by biopsy or myomectomy
   b) Primary treatment of disease that is not suitable for primary surgery

c) As additional therapy following total hysterectomy with bilateral salpingo-oophorectomy (TH + BSO) for stage II-IV low-grade ess or adenosarcoma without sarcomatous overgrowth (recommended for residual measurable disease)
d) Additional therapy following TH + BSO for stage II-IV ER/PR+ adenosarcoma with sarcomatous overgrowth
e) Additional therapy following TH ± BSO for stage II-III ER/PR+ high grade ESS, undifferentiated uterine sarcoma (UUS), leiomyosarcoma (LMS), or other sarcomas
f) Additional therapy following TH ± BSO for stage IV ER/PR+ high grade ESS, UUS, LMS, or other sarcomas
g) Preoperatively or postoperatively for recurrent disease with resectable isolated metastases
h) Recurrent disease with unresectable isolated metastases or disseminated disease
i) Radiologically isolated vaginal/pelvic recurrence if no prior radiation therapy, given in combination with RT
j) For a radiologically isolated vaginal/pelvic recurrence if prior RT is given with or without RT.[5]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Fulvestrant: References

1. Farooq et al. Fulvestrant. https://www.ncbi.nlm.nih.gov/books/NBK560854/. Accessed December 12, 2024.
2. Fulvestrant (Faslodex) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021344s044lbl.pdf. Accessed December 12, 2024.
3. National Comprehensive Cancer Network. Breast Cancer. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 12, 2024.
4. National Comprehensive Cancer Network. Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed December 12, 2024.
5. National Comprehensive Cancer Network. Uterine Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed December 12, 2024.

Fulvestrant: Coding (CPT®, ICD 10, and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C50.9	Malignant neoplasm of the breast
C54.1	Malignant neoplasm of the endometrium
C55.0	Malignant neoplasm of the uterus
C56.9	Malignant neoplasm of the ovary
J9395	Fulvestrant

Fulvestrant: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	12/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	12/21/2024
6	Revision Changes:	