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PHARMACY/MEDICAL POLICY – 5.01.618

Selective Estrogen Receptor Modulators and Down Regulators

Effective Date: **Feb. 5, 2027***	RELATED MEDICAL POLICIES:
Last Revised: Oct. 13, 2026	None
Replaces: N/A	
*This policy has been revised. Click here to view the current policy.	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Around two-thirds of breast cancers express the estrogen receptor (ER) alpha protein. These ER-positive tumors are dependent on the ER and its cognate ligand, estrogen, for their growth, survival, and progression. Selective estrogen receptor modulators (SERMs) and selective estrogen receptor down-regulators (SERDs) are two major classes of endocrine therapy drugs used for the treatment and/or prevention of ER-positive breast cancers. These therapies are all designed in one way or another to block ER function and signaling. Some SERMs also have estrogen activity in bone and, therefore, prevent bone loss, improve bone mineral density (BMD), and decrease the risk of vertebral fracture. This policy discusses when the use of brand SERMs and SERDs may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Fareston (toremifene)	**Fareston (toremifene) may be considered medically necessary for the treatment of metastatic breast cancer when all the following criteria are met:** • The individual is postmenopausal female **AND** • Diagnosed with estrogen receptor positive or unknown tumors **AND** • Has tried and had an inadequate response or intolerance to generic toremifene **AND** • The dose is limited to 60 mg per day
• **Cligavyx (fulvestrant)** • **Faslodex (fulvestrant)**	**Cligavyx (fulvestrant) and Faslodex (fulvestrant) may be considered medically necessary when the following criteria are met:** • The individual meets 1 of the following: ○ Treatment of hormone-receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative* advanced breast cancer in postmenopausal women not previously treated with endocrine therapy **OR** ○ Treatment of HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy **OR** ○ Treatment of HR-positive, HER2-negative* advanced or metastatic breast cancer in combination with ribociclib in postmenopausal women as initial endocrine-based therapy or following disease progression on endocrine therapy **OR** ○ Treatment of HR-positive, HER2-negative* advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression following endocrine therapy

Drug	Medical Necessity
	OR ○ Treatment in combination with Truqap (capivasertib) of adult individuals with HR-positive, HER2-negative* locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN*-alterations and has progressed on at least one endocrine-based regimen in the metastatic setting or had recurrence on or within 12 months of completing adjuvant therapy **AND** • The individual has tried and had an inadequate response or intolerance to generic fulvestrant *HER2-negative status is defined as 0 or 1+ intensity on immunohistochemical testing or 2+ intensity on immunohistochemical testing and no amplification on in situ hybridization.
Inluriyo (imlunestrant)	**Inluriyo (imlunestrant) may be considered medically necessary for the treatment of adults with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1- mutated advanced or metastatic breast cancer when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Diagnosed with ER-positive, HER2-negative, ESR1- mutated advanced or metastatic breast cancer **AND** • Has experienced disease progression following at least 1 line of endocrine therapy **AND** • Meets 1 of the following: ○ Inluriyo (imlunestrant) is used as monotherapy ○ Inluriyo (imlunestrant) is used in combination with abemaciclib **AND** • The dose is limited to 400 mg per day

Drug	Medical Necessity
	Note: HER2-negative status is defined as 0 or 1+ intensity on immunohistochemical testing or 2+ intensity on immunohistochemical testing and no amplification on in situ hybridization.
Orserdu (elacestrant)	**Orserdu (elacestrant) may be considered medically necessary for the treatment of estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1-mutated advanced or metastatic breast cancer when all the following criteria are met:** • The individual is postmenopausal female or male aged 18 years of age or older **AND** • Diagnosed with ER-positive, HER2-negative*, *ESR1*-mutated advanced or metastatic breast cancer **AND** • Has experienced disease progression following at least 1 line of endocrine therapy **AND** • The dose is limited to 345 mg per day *HER2-negative status is defined as 0 or 1+ intensity on immunohistochemical testing or 2+ intensity on immunohistochemical testing and no amplification on in situ hybridization.
Veppanu (vepdegestrant)	**Veppanu (vepdegestrant) may be considered medically necessary for the treatment of estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1-mutated advanced or metastatic breast cancer when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Diagnosed with ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic breast cancer **AND** • Has experienced disease progression following at least 1 line of endocrine therapy **AND** • Meets 1 of the following:

Drug	Medical Necessity
	○ Has tried and had an inadequate response or intolerance to elacestrant or imlunestrant ○ Documentation shows actual or anticipated gastrointestinal intolerance (e.g., history of colitis) or dyslipidemia with elacestrant or imlunestrant **AND** • The dose is limited to 200 mg daily

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in the policy may be approved up to 12 months.**
Re-authorization criteria	**All drugs listed in the policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation, and medication history

Coding

Code	Description
HCPCS	

Code	Description
J9395	Injection, fulvestrant, (Faslodex), 25 mg
J9999	Not otherwise specified, antineoplastic drugs (used to report Cligavyx)

Related Information

Benefit Application

Fareston (toremifene), Inluriyo (imlunestrant), Orserdu (elacestrant), and Veppanu (vepdegestrant) are managed through the pharmacy benefit.

Cligavyx (fulvestrant) and Faslodex (fulvestrant) are managed through the pharmacy and medical benefit.

Consideration of Age

Age limits specified in this policy are determined according to FDA-approved indications, where applicable.

Evidence Review

Background

Breast cancer remains the most commonly diagnosed cancer among women in the United States. In 2024, an estimated 310,720 new cases of invasive breast cancer are expected to be diagnosed, with approximately 16% occurring in women younger than 50 years of age. During the same year, an estimated 42,250 women will die from breast cancer, more than half of whom will be 70 years of age or older.

Breast cancer mortality has declined substantially over time. Since 1989, the death rate has decreased by 44%, largely attributable to advancements in treatment and earlier detection, resulting in an estimated 517,900 averted deaths. More recently, between 2013 and 2022, mortality rates remained stable among American Indian/Alaska Native and Asian

American/Pacific Islander women, while continuing to decline among Black women (1.4% per year), White women (1% per year), and Hispanic women (0.7% per year).

Following diagnosis, accurate assessment of disease extent is critical, as staging directly informs treatment planning and prognosis. Between 2018 and 2022, approximately two-thirds of breast cancer cases in women were diagnosed at a localized stage, indicating that the disease had not spread beyond the breast. In contrast, about one-quarter were identified at a regional stage, with spread to nearby lymph nodes or tissues, and approximately 6% were diagnosed at a distant stage, reflecting metastatic disease.

These stage distributions are strongly associated with outcomes. The 5-year relative survival rate exceeds 99% for localized breast cancer, when treatment is typically more effective and less intensive. However, survival declines to 87% for regional-stage disease and to 32% for cases diagnosed at a distant stage, underscoring the importance of early detection and timely intervention.

Summary of Evidence

Fareston (toremifene)

Efficacy

Three prospective, randomized, controlled clinical studies (North American, Eastern European, and Nordic) were conducted to evaluate the efficacy of Fareston for the treatment of breast cancer in postmenopausal women. The individuals were randomized to parallel groups receiving Fareston 60 mg (FAR60) or tamoxifen 20 mg (TAM20) in the North American Study or tamoxifen 40 mg (TAM40) in the Eastern European and Nordic studies. The North American and Eastern European studies also included high-dose toremifene arms of 200 and 240 mg daily, respectively. The studies included postmenopausal individuals with estrogen-receptor (ER) positive or estrogen-receptor (ER) unknown metastatic breast cancer. The individuals had at least one measurable or evaluable lesion. The primary efficacy variables were response rate (RR) and time to progression (TTP). Survival (S) was also determined. Ninety-five percent confidence intervals (95% CI) were calculated for the difference in RR between FAR60 and TAM groups and the hazard ratio (relative risk for an unfavorable event, such as disease progression or death) between TAM and FAR60 for TTP and S. Two of the 3 studies showed similar results for all effectiveness endpoints. However, the Nordic Study showed a longer time to progression for tamoxifen. The high-dose groups, toremifene 200 mg daily in the North American Study and 240 mg daily in the Eastern European Study, were not superior to the lower toremifene dose

groups, with response rates of 22.6% and 28.7%, median times to progression of 5.6 and 6.1 months, and median survivals of 30.1 and 23.8 months, respectively. The median treatment duration in the three pivotal studies was 5 months (range 4.2-6.3 months).

Safety/Tolerability

Toremifene has been shown to prolong the QTc interval in a dose-and concentration-related manner.

Hepatotoxicity, both increases in the serum concentration for grade 3 and 4 transaminitis and hyperbilirubinemia, including jaundice, hepatitis, and non-alcoholic fatty liver disease, have also been reported in clinical trials and postmarketing with Fareston.

Endometrial cancer, endometrial hypertrophy, hyperplasia, and uterine polyps have been reported in some individuals treated with Fareston. Endometrial hyperplasia of the uterus was observed in animals treated with toremifene.

Faslodex (fulvestrant)

Efficacy

Efficacy of Faslodex was established by comparison to the selective aromatase inhibitor anastrozole in two randomized, controlled clinical trials (one conducted in North America, Study 0021, NCT00635713; the other predominantly in Europe, Study 0020) in postmenopausal women with locally advanced or metastatic breast cancer. All individuals had progressed after previous therapy with an antiestrogen or progestin for breast cancer in the adjuvant or advanced disease setting. The effectiveness of Faslodex 250 mg was determined by comparing Objective Response Rate (ORR) and Time to Progression (TTP) results to anastrozole 1 mg, the active control. The two studies ruled out (by one-sided 97.7% confidence limit) inferiority of Faslodex to anastrozole of 6.3% and 1.4% in terms of ORR. There was no statistically significant difference in overall survival (OS) between the two treatment groups after a follow-up duration of 28.2 months in Study 0021 and 24.4 months in Study 0020.

The efficacy of Faslodex 500 mg in combination with palbociclib 125 mg was compared to Faslodex 500 mg plus placebo in PALOMA-3. PALOMA-3 (NCT-1942135) was an international, randomized, double-blind, parallel group, multi-center study of Faslodex plus palbociclib versus Faslodex plus placebo conducted in women with HR-positive, HER2-negative advanced breast cancer, regardless of their menopausal status, whose disease progressed on or after prior

endocrine therapy. Consistent PFS results were observed across individual subgroups of disease site, sensitivity to prior hormonal therapy, and menopausal status. After a median follow-up time of 45 months, the final OS results were not statistically significant.

The efficacy of Faslodex in combination with ribociclib was compared to plus placebo in MONALEESA-3. MONALEESA-3 (NCT 02422615) was a randomized double-blind, placebo-controlled study of Faslodex plus ribociclib versus Faslodex plus placebo conducted in postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment. Consistent results were observed in stratification factor subgroups of disease site and prior endocrine treatment for advanced disease.

The efficacy of Faslodex 500 mg in combination with abemaciclib 150 mg was compared to Faslodex 500 mg plus placebo in MONARCH 2. MONARCH 2 (NCT02107703) was a randomized, placebo-controlled, multi-center study conducted in women with HR-positive, HER2-negative metastatic breast cancer with disease progression following endocrine therapy treated with Faslodex plus abemaciclib versus Faslodex plus placebo. PFS assessment based on a blinded independent radiologic review was consistent with the investigator assessment. Consistent results were observed across individual stratification subgroups of disease site and endocrine therapy resistance for PFS and OS.

MONALEESA-3 (NCT 02422615) was a randomized double-blind, placebo-controlled study of Faslodex plus ribociclib versus Faslodex plus placebo conducted in postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment. Consistent results were observed in stratification factor subgroups of disease site and prior endocrine treatment for advanced disease.

Safety/Tolerability

The most frequently reported adverse reactions in the Faslodex 500 mg group were injection site pain (11.6% of individuals), nausea (9.7% of individuals), and bone pain (9.4% of individuals); the most frequently reported adverse reactions in the Faslodex 250 mg group were nausea (13.6% of individuals), back pain (10.7% of individuals), and injection site pain (9.1% of individuals).

Inluriyo

The efficacy of Inluriyo was evaluated in EMBER-3 (NCT04975308), a randomized, open-label, active-controlled, multicenter trial that enrolled 874 adult individuals with ER+, HER2- locally advanced or metastatic breast cancer of which 323 individuals had ESR1 mutations (ESR1m), who were previously treated with an aromatase inhibitor either alone or in combination with a CDK4/6 inhibitor. Individuals were excluded if they were eligible to receive a PARP inhibitor. Individuals were required to have progressed: 1) Within 12 months of completing neoadjuvant or adjuvant aromatase inhibitor therapy with no systemic treatment for recurrent disease or; 2) Greater than 12 months after neoadjuvant or adjuvant endocrine therapy or de novo metastatic disease and had progressed on only one line of aromatase inhibitor therapy. Individuals were randomized 1:1:1 to: 1) Inluriyo 400 mg orally once daily; 2) Investigator's choice of endocrine therapy [fulvestrant 500 mg intramuscularly on days 1, 15, 29, and once monthly thereafter or exemestane 25 mg orally once daily]; or 3) Inluriyo 400 mg once daily in combination with abemaciclib 150 mg orally twice daily. Randomization was stratified by previous treatment with CDK4/6 inhibitor (yes vs no), presence of visceral metastasis (yes vs no), and region (East Asia vs North America/Western Europe vs Others). ESR1m status was determined by blood circulating tumor deoxyribonucleic acid (ctDNA) analysis using the Guardant360 CDx assay and was limited to specific ESR1 mutations in the ligand binding domain. Individuals were treated until disease progression or unacceptable toxicity.

The major efficacy outcome for Inluriyo in combination with abemaciclib was investigator-assessed PFS according to RECIST v1.1 in the overall population. Other efficacy measures included OS, BIRC-assessed PFS, and ORR. While the comparison of PFS between Inluriyo in combination with abemaciclib and Inluriyo monotherapy in the overall population was statistically significant, a PFS improvement was not demonstrated for Inluriyo monotherapy compared to investigator's choice of endocrine therapy in either the overall or ESR1m not detected populations, indicating that the benefit for Inluriyo monotherapy was only observed in the ESR1m population. Therefore, exploratory analyses of PFS, OS and ORR in the ESR1m population comparing Inluriyo in combination with abemaciclib and Inluriyo monotherapy were performed. Among the individuals on the Inluryio in combination with abemaciclib arm or the Inluriyo monotherapy arm who were positive for ESR1m (n=159), the median age was 62 years (range: 31-85 years); all individuals were female, of which 12% were pre/perimenopausal; 60% were White, 27% Asian, 5% Black, 0.6% were American Indian or Alaskan Native, 0.6% multiple races, 7% missing, 12% were Hispanic/Latino, 75% not Hispanic/Latino, 13% not reported/missing; and all individuals had a baseline ECOG performance status of 0 (66%) or 1 (34%). Most individuals had visceral metastasis (58%) at baseline. Of the individuals enrolled, all received a prior line of endocrine therapy and 81% had received one line of endocrine therapy

in the advanced or metastatic setting. Overall, 79% of individuals were treated with a prior CDK4/6 inhibitor, 4.4% were treated in the adjuvant setting and 74% were treated in the advanced or metastatic setting. Among the individuals who had received prior CDK4/6 inhibitors, the specific CDK4/6 inhibitor received was palbociclib 65%, ribociclib 28%, and abemaciclib 6%. PFS assessment in the ESR1m population based on a BIRC was consistent with the investigator assessment. At the time of interim analysis, overall survival data was immature with 35% of deaths in the ESR1m population. Among the individuals treated with Inluriyo plus abemaciclib, ORR was 35% (95% CI, 22 to 48) in comparison to Inluriyo ORR was 15% (95% CI, 7-23).

Orserdu (elacestrant)

Efficacy

In the subgroup of individuals whose tumors had ESR1 mutations, Orserdu reduced the risk of progression or death by 45% (PFS 3.8 months versus 1.9 months; hazard ratio [HR] = 0.55, 95% confidence interval [CI]: 0.39, 0.77) versus SOC. A statistically significant difference in PFS was also observed for all individuals in the intention-to-treat (ITT) population versus SOC (PFS 2.8 months versus 1.9 months; HR = 0.70; 95% CI, 0.55 to 0.88; P = 0.002). However, an exploratory analysis of PFS in the 250 (52%) individuals without ESR1 mutations showed an HR of 0.86 (95% CI: 0.63, 1.19), indicating that the improvement in the ITT population was primarily attributed to the results seen in the ESR1-mutated population only.

Safety/Tolerability

Safety data were consistent with the other endocrine therapies. Most of the adverse events (AEs), including nausea and musculoskeletal pain, were Grade 1 and 2. No hematological safety signal was observed and none of the individuals in either of the two treatment arms had sinus bradycardia. The most common (>10%) AEs, including laboratory abnormalities, with Orserdu were musculoskeletal pain, nausea, increased cholesterol, increased aspartate transaminase, increased triglycerides, fatigue, decreased hemoglobin, vomiting, increased alanine transaminase, decreased sodium, increased creatinine, decreased appetite, diarrhea, headache, constipation, abdominal pain, hot flush, and dyspepsia.

Veppanu (vepdegestrant)

Efficacy

The efficacy of Veppanu was evaluated in VERITAC-2 (NCT05654623), a randomized, open-label, active controlled, multicenter trial that enrolled 624 adult individuals with ER-positive, HER2-negative, advanced or metastatic breast cancer, of whom 270 individuals had tumors carrying ESR1 mutations. Individuals were required to have disease progression on 1 to 2 prior lines of endocrine therapy, including 1 line with a CDK4/6 inhibitor. Progression during or within 12 months from the end of adjuvant therapy was counted as 1 line of endocrine therapy for advanced/metastatic setting. Pre-menopausal and peri-menopausal women and men received a gonadotropin-releasing hormone (GnRH) agonist. Individuals were excluded if they had received chemotherapy for advanced or metastatic disease or fulvestrant in any line of therapy, or if progression on the most recent line of endocrine therapy occurred within the first 6 months.

Individuals were randomized 1:1 to receive Veppanu 200 mg orally once daily (N=313), or fulvestrant 500 mg intramuscularly on Days 1 and 15 of Cycle 1 and then once monthly thereafter (N=311). Randomization was stratified by ESR1 mutation status (detected vs. not detected) and visceral metastasis (yes vs. no). ESR1 mutational status was determined by blood circulating tumor deoxyribonucleic acid (ctDNA) using central or local testing. Individuals were treated until disease progression or unacceptable toxicity. Among the individuals whose tumors had ESR1 mutations (N=270), the median age was 60 (range: 26 to 87) years; all but 1 were female; 47% were White; 41% Asian; 3.3% Black; 8% unknown/not reported; 7% were Hispanic/ Latino, 83% were Not Hispanic or Latino and 10% not reported. Of the 269 women, 20% were pre/perimenopausal. Baseline Eastern Cooperative Oncology Group (ECOG) performance status was 0 (57%) or 1 (43%). Most individuals (68%) had visceral disease; 81% had received 1 line of endocrine therapy and 19% had received 2 lines of endocrine therapy in the advanced or metastatic setting. All individuals had received prior treatment with a CDK4/6 inhibitor. The major efficacy outcome was progression-free survival (PFS) as assessed by blinded independent central review (BICR) in the population of individuals whose tumors had an ESR1 mutation and in the overall population evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. Additional efficacy outcomes were overall survival (OS) and objective response rate (ORR) as assessed by BICR. A statistically significant difference in PFS by BICR was observed for the individuals whose tumors had ESR1 mutations for Veppanu compared with fulvestrant.

Among individuals with *ESR1*-mutated disease, Veppanu significantly improved progression-free survival (PFS) compared with fulvestrant. Median PFS was 5.0 months (95% CI, 3.7–7.4) versus 2.1 months (95% CI, 1.9–3.5), respectively (hazard ratio, 0.57; 95% CI, 0.42–0.77; P = 0.0001). The

objective response rate (ORR) was 19% with Veppanu compared to 4% with fulvestrant. Overall survival data were immature, with 16% of deaths reported in this population at the time of PFS analysis.

Safety/Tolerability

QTc interval prolongation is a clinically meaningful safety consideration, occurring in ~10% of individuals (grade 3: 1.6%). It requires electrocardiogram (ECG) and electrolyte monitoring at baseline, approximately 4 weeks after initiation, and periodically as clinically indicated during treatment.

Most common (≥10%) adverse reactions with Veppanu, including laboratory abnormalities, were decreased white blood cells, increased AST, musculoskeletal pain, fatigue, decreased hemoglobin, decreased neutrophils, increased ALT, increased alkaline phosphatase, nausea, decreased blood potassium, increased bilirubin, decreased appetite, electrocardiogram QT prolonged, decreased platelets, and constipation.

US Preventive Services Task Force Recommendations

The USPSTF recommends offering risk-reducing medications to women at increased risk for breast cancer and at low risk for adverse medication effects (B recommendation) and recommends against routine use of risk-reducing medications in women not at increased risk (D recommendation). The current recommendation now includes aromatase inhibitors among medications that can reduce risk of breast cancer.

Various methods are available to identify women at increased risk for breast cancer, including formal clinical risk assessment tools or assessing breast cancer risk factors without using a formal tool. The USPSTF does not endorse any particular risk-prediction tool. The National Cancer Institute Breast Cancer Risk Assessment Tool and the Breast Cancer Surveillance Consortium Risk Calculator are based on models tested in US populations and are publicly available. There is no single cutoff for defining increased risk for all women.

Alternatively, clinicians may use combinations of risk factors to identify women at increased risk. Some examples of combinations of multiple risk factors in women at increased risk include (but are not limited to): age 65 years or older with 1 first-degree relative with breast cancer; age 45 years or older with more than 1 first-degree relative with breast cancer or 1 first-degree relative who developed breast cancer before age 50 years; age 40 years or older with a first-degree

relative with bilateral breast cancer; presence of atypical ductal or lobular hyperplasia or lobular carcinoma in situ on a prior biopsy.

When considering prescribing breast cancer risk-reducing medications, the potential benefit of risk reduction of breast cancer must be balanced against the potential harms of adverse medication effects.

Tamoxifen, raloxifene, and aromatase inhibitors all reduce primary breast cancer risk in post-menopausal women. Use of raloxifene and aromatase inhibitors is indicated only in postmenopausal women; only tamoxifen is indicated for risk-reduction of primary breast cancer in premenopausal women.

2021 Update

Reviewed prescribing information for all drugs in policy. No new information was identified that would result in changes to policy statements.

2022 Update

Reviewed prescribing information for all drugs in policy. No new information was identified that would result in changes to policy statements.

2023 Update

Reviewed prescribing information for all drugs in policy. Added criteria for Orserdu (elacestrant) for the treatment of breast cancer.

2024 Update

Reviewed prescribing information for all drugs in policy. Updated Faslodex (fulvestrant) to include coverage criteria for the treatment of certain individuals with breast cancer in combination with Truqap (capivasertib).

2025 Update

Reviewed prescribing information for all drugs in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

2026 Update

Reviewed prescribing information for all drugs in policy. Updated criteria for Fareston (toremifene) adding the quantity is limited to 30 tablets per 30 days. Updated criteria for Orserdu (elacestrant) adding a quantity limit per 30 days. Removed reference to non-formulary exception reviews.

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History

Date	Comments
11/01/20	New policy, approved October 13, 2020. Added criteria for Arimidex (anastrozole) for the treatment of breast, endometrial, ovarian, and uterine cancers. Added criteria for Aromasin (exemestane) for the treatment of breast cancer. Added criteria for Evista (raloxifene) for the treatment and prevention of osteoporosis and for the treatment of breast cancer. Added criteria for Fareston (toremifene) for the treatment of breast cancer. Added criteria for Faslodex (fulvestrant) for the treatment of breast cancer. Added criteria for Femara (letrozole) for the treatment of breast cancer and ovarian cancer.
01/01/22	Annual Review, approved December 2, 2021. No changes to policy statements.
11/01/22	Annual Review, approved October 24, 2022. No changes to policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
04/01/23	Annual Review, approved March 14, 2023. Added criteria for Orserdu (elacestrant) for the treatment of breast cancer.

Date	Comments
03/01/24	Annual Review, approved February 26, 2024. Updated Faslodex (fulvestrant) to include coverage criteria for the treatment of certain individuals with breast cancer in combination with Truqap (capivasertib).
11/01/24	Interim Review, approved October 21, 2024. Updated Faslodex (fulvestrant) coverage criteria to apply to the pharmacy and medical benefit. Added HCPCS code J9395 for Faslodex.
04/01/25	Annual Review, approved March 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.
01/01/26	Interim Review, approved December 9, 2025. Added coverage criteria for Inluriyo (imlunestrant) for the treatment of adults with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy. Removed criteria for Arimidex (anastrozole), Aromasin (exemestane), Evista (raloxifene), and quantity limits moved to policy 5.01.656 Drug Quantity Management.
07/01/26	Annual Review, approved June 22, 2026. Updated criteria for Fareston (toremifene) adding the quantity is limited to 30 tablets per 30 days. Updated criteria for Orserdu (elacestrant) adding a quantity limit per 30 days. Removed reference to non-formulary exception reviews.
11/01/26	Interim Review, approved October 13, 2026. Added coverage criteria for Veppanu (vepdegestrant) for the treatment of ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic breast cancer. Updated criteria for Inluriyo (imlunestrant) adding requirement Inluriyo is used as monotherapy or in combination with abemaciclib. Removed quantity limits for Fareston (toremifene), Inluriyo (imlunestrant) and Orserdu (elacestrant) as quantity limits are addressed in policy 5.01.656 Drug Quantity Management. The following policy change is effective February 5, 2027, following 90-day provider notification. Added Cligavyx (fulvestrant) to the policy with the same criteria as Faslodex (fulvestrant). Added HCPCS code J9999.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member

benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.