imlunestrant (Inluriyo™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO337

Description

Imlunestrant (Inluriyo) is an orally administered estrogen receptor antagonist.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
imlunestrant (Inluriyo)	ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer	200 mg tablets	56 tablets/28 days

Initial Evaluation

I. **Imlunestrant (Inluriyo)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Medication will not be used in combination with any other oncology therapy; **AND**
   D. A diagnosis of **advanced or metastatic breast cancer** when the following are met:
      1. Breast cancer is hormone receptor (HR)-positive and human epidermal growth factor receptor 2 (HER2)-negative; **AND**
      2. Documentation of an ESR1 mutation; **AND**
      3. The member had disease progression on at least one prior endocrine therapy in the advanced or metastatic breast cancer setting (e.g., fulvestrant, letrozole, anastrozole, exemestane, tamoxifen); **AND**
      4. The member had disease progression on, or after, treatment with a CDK4/6 inhibitor (e.g., palbociclib [Ibrance], abemaciclib [Verzenio], ribociclib [Kisqali], etc.)*

*Please note: medications notated with an asterisk may require additional review.

II. Imlunestrant (Inluriyo) is considered investigational when used for all other conditions, including but not limited to:
   A. Imlunestrant (Inluriyo) used in combination with another oncology therapy
   B. ESR1 wild type tumors

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. The medication will not be used in combination with any other oncolytic therapy; **AND**
IV. Member has exhibited response to the treatment defined by stabilization of disease or decrease in tumor size or tumor spread.

Supporting Evidence

I. Imlunestrant (Inluriyo) is FDA approved in adults aged 18 years of age and older. Use in members younger than 18 years of age is not appropriate due to lack of established efficacy and safety.
II. Given the complexities involved with the diagnosis, treatment approaches, and management of therapy for the indicated population, treatment with imlunestrant (Inluriyo) should be initiated by, or in consultation with, an oncologist.
III. Imlunestrant (Inluriyo) is not FDA approved and has not been well studied in combination with other oncolytic therapies at this time. The EMBER-3 clinical trial studied imlunestrant (Inluriyo) in combination with abemaciclib (Verzenio), which improved median progression free survival (PFS) to 9.4 months compared to 5.5 months for standard of care (SOC) endocrine therapy. However, the results of this cohort are not fully mature and this combination therapy has not been approved by the FDA at this time, until that occurs, imlunestrant (Inluriyo) should remain limited to the FDA-approved indication.
IV. Imlunestrant (Inluriyo) was studied in one Phase 3, open-label, active-controlled, randomized clinical trial (EMBER-3) in 874 adults. Treatment arms included imlunestrant (Inluriyo), oral exemestane or fulvestrant as the standard of care arm and imlunestrant (Inluriyo) in combination with abemaciclib (Verzenio) as the exploratory cohort. Enrolled participants had confirmed ER-positive, HER2-negative locally advanced or metastatic breast cancer following disease progression on an aromatase inhibitor (AI) alone or in combination with a cyclin-dependent kinase (CDK) 4/6 inhibitor (e.g., ribociclib [Kisqali]) as neoadjuvant or adjuvant treatment or within 12 months after adjuvant treatment or while receiving first-line treatment for advanced breast cancer (BC). The median age was 61 years, all were female, 61% were White. Of the patients enrolled, 256 had an ESR1 mutation, the majority (79%) had received one line of endocrine therapy and CDK4/6i (67%) in the advanced or metastatic setting. The primary endpoint was progression-free survival, secondary endpoints included overall survival (OS) and objective response rare (ORR). Progression free survival was superior for imlunestrant (Inluriyo) compared to standard of care endocrine therapy (ET) only in the ESR1 mutated population, 5.5 months vs. 3.8 months, $p<0.001$. Clinical trial data is considered of low quality due to use of a surrogate endpoint (PFS) as the primary endpoint, immature survival data, and unknown impact

on symptoms, quality of life, functionality, or morbidity. The chosen comparator, fulvestrant or exemestane no longer represents a standard of care option in the first line setting for advanced disease; therefore, applicability of the data for imlunestrant (Inluriyo) in this setting is uncertain.

V. The EMBER-3 clinical trial demonstrated superior PFS for the imlunestrant (Inluriyo) monotherapy arm only in the ESR1 mutated cohort. The FDA approved indication is also only in the ESR1 mutated cohort. The results in the non-mutated cohort (including ESR1 wild type, all patients) were not statistically significant (5.6 months vs 5.5 months, p=0.12 for imlunestrant (Inluriyo) vs standard of care endocrine therapy).

VI. Treatment with a CDK4/6 inhibitor +/- ET is required as this provides the strongest evidence for overall survival benefit. While the FDA-approved label does not require prior use of a CDK4/6i, and EMBER-3 did include patients without prior CDK4/6i exposure, CDK4/6 +/- ET remains the standard of care, are recommended with a category 1 recommendation by the NCCN and should be utilized first. Endocrine therapy in the advanced or metastatic setting is required to be tried as this reflects the current standard of care where ET + CDK4/6i is recommended with a category 1 recommendation. Additionally, this reflects how imlunestrant (Inluriyo) was studied, as EMBER-3 enrolled participants with most recent endocrine therapy in the advanced breast cancer setting (73%) as opposed to adjuvant therapy (29%).

Investigational or Not Medically Necessary Uses

I. Imlunestrant (Inluriyo) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Imlunestrant (Inluriyo) used in combination with another oncology therapy
      i. Imlunestrant (Inluriyo) has not been sufficiently studied in combination with any other oncology therapy at this time. EMBER-3 clinical trial studied imlunestrant (Inluriyo) with abemaciclib (Verzenio), however, the results of this cohort are considered immature at this time.
   B. ESR1 wild type tumors
      i. The safety and effectiveness of imlunestrant (Inluriyo) has not been established in patients without ESR1 mutated tumors. EMBER-3 clinical trial demonstrated a lack of statistical superiority in all patients (including ESR1 wild type) when compared to standard of care endocrine therapy. The results of the combination cohort of imlunestrant (Inluriyo) and abemaciclib (Verzenio) are considered immature at this time.

References

1. Inluriyo product dossier. Eli Lilly, Inc; November 2025.
2. Inluriyo. Package Insert. Eli Lilly Inc; September 2025.
3. National Comprehensive Cancer Network. Breast Cancer. NCCN. October 16, 2025. Accessed December 16, 2025. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
4. Jhaveri KL, Neven P, Casalnuovo ML, et al. Imlunestrant with or without Abemaciclib in Advanced Breast Cancer. N Engl J Med. 2025;392(12):1189-1202. doi:10.1056/NEJMoa2410858

Related Policies

Policy Name	Disease state
elacestrant (Orserdu)	ESR1 mutated, HR+, HER2- advanced or metastatic breast cancer

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	02/2025