New Drug Overview

Inluriyo (imlunestrant)

PDL Category: Antineoplastics

Introduction

Disease Background:

- In females, breast cancer is the most common cancer diagnosed worldwide, with reports of more than 2 million cases yearly. Globally, more deaths are reported from this cancer in women than any other cancer (*Joe 2025*).
  - It is the most common cancer in women in the United States, and the second most frequent cause of cancer death in females.
- Breast cancer, a malignancy of the breast tissue, is characterized as either carcinoma in situ or invasive breast cancer. (*Henry et al 2025*).
  - Carcinoma in situ is also known as noninvasive carcinoma and is stage 0. This is defined as cancer cells that have not occupied outside of the basement membrane of the duct or lobule.
  - Invasive breast cancer is categorized as early breast cancer, locally advanced breast cancer, or advanced (metastatic) breast cancer.
    - Early breast cancer (invasive) includes stages I, IIA, and IIB, with no extension of tumor to the chest wall or skin and no distant metastases. There may be ipsilateral axillary lymph node metastases.
    - Locally advanced breast cancer (invasive) includes stages IIIA, IIIB, and IIIC, with metastases in the ipsilateral axillary lymph nodes and internal mammary lymph nodes. Tumor size is greater than 5cm and with direct extension to the chest wall or skin. There is no distant metastases.
    - Advanced (metastatic) breast cancer includes stage IV tumors with disease in a range that goes beyond the beast and axilla. Sites that are frequently metastasized to include the bone, liver, lung, and brain.
- In areas where there are recognized breast cancer screening programs, patients are generally asymptomatic when diagnosed. Nevertheless, diagnosis occurs in up to 15 percent of women because of clinical signs (eg, breast mass, nipple discharge, skin changes, axillary adenopathy, or other changes in the breast) that are not found during mammogram testing. This is known as mammographically occult disease. In addition, about 30 percent exhibit a breast mass found in between mammograms, known as interval cancers (*Joe 2025*).
- Upon diagnosis, it is essential for breast cancers to be tested for estrogen (ER) and progesterone (PR) receptor expression and for overexpression of human epidermal growth factor 2 (HER2) receptors. This is crucial for prognostic and therapeutic reasons (*Joe 2025*).
  - ER and PR are predictive for invasive breast cancer.
  - Data from a study that included 61,309 cases of breast cancer diagnosed between 1999 and 2004 suggested the following proportions with various receptor phenotypes:
    - Hormone receptor positive cancers (ER and/or PR) accounted for most cases, approximately 80%.
    - HER2 was overexpressed in about 23 percent; of these, 67% were hormone receptor-positive and 32% were hormone receptor-negative.
    - Triple negative cancers (ER, PR, and HER2-negative) accounted for about 13 percent.
  - The most frequent subtype of breast cancer is ER+, HER2- (*Jhaveri 2025*).
- Knowing the stage and subtype (ER, PR, or HER2) assists in the management of breast cancer (*Henry et al 2025, Joe 2025)*.
- Inluriyo was FDA approved in 2025.

Pharmacology/Usage

- Inluriyo (imlunestrant) is an estrogen receptor (ER) antagonist that binds to Erα. In vitro, imlunestrant induced degradation of Erα, leading to inhibition of ER-dependent gene transcription and cellular proliferation in ER+ breast

cancer cells. Imlunestrant demonstrated in vitro and in vivo anti-tumor activity in ER+ breast cancer xenograft models, including models with *ESR1* mutations.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Inluriyo (imlunestrant)
• For the treatment of adults with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *estrogen receptor-1* (*ESR1*)-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.	✔

(Prescribing information: Inluriyo 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Inluriyo (imlunestrant)	Film coated, capsule-shaped Tablets	Oral	Once daily until disease progression or unacceptable toxicity.	• Select patients for treatment of ER-positive, HER2-negative advanced or metastatic breast cancer with Inluriyo based on the presence of *ESR1* mutation(s) in a plasma specimen using an FDA-approved test. Information on FDA-approved tests for the detection of *ESR1* mutations is available online. • Take on an empty stomach. • Pre/perimenopausal women and men should receive a gonadotropin-releasing hormone agonist (GnRH) per current

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				clinical practice standards. • If miss a dose by 6 or more hours or if vomit, take the next dose the following day at its scheduled time. • There are recommended dosage modifications for adverse reactions. • Reduce the dose with moderate or severe hepatic impairment and monitor for increased adverse reactions.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Inluriyo was assessed in a randomized, open-label, active-controlled multicenter study (EMBER-3) that included adult patients (N=874) with ER+, HER2- locally advanced or metastatic breast cancer who were previously treated with an aromatase inhibitor either alone or in combination with a CDK4/6 inhibitor.
  - Patients were excluded if they were eligible to receive a PARP inhibitor.
- Patients were required to have progressed:
  - Within 12 months of completing neoadjuvant or adjuvant aromatase inhibitor therapy with no systemic treatment for recurrent disease, or
  - 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.
- Patients were randomized to Inluriyo 400mg once daily or investigator's choice of endocrine therapy (fulvestrant 500mg IM on days 1, 15, 29, and once monthly thereafter (N=111) or exemestane 25mg orally once daily (N=6)) or an additional investigational combination regimen.
  - Patients were treated until disease progression or unacceptable toxicity.
- Of the patients in the Inluriyo arm or investigator's choice of endocrine therapy who were positive for *ESR1*m (N=256), the median age was 61 years (range 28 to 85), while all patients were female, of which 11% were pre/perimenopausal. In addition, 61% were White, most patients had visceral metastasis (59%) at baseline, and the baseline Eastern Cooperative Oncology Group (ECOG) performance status was 0 in 63% of patients or 1 in 37% of patients. Of the enrolled patients, 21% had received no endocrine therapy and 79% had received one line of endocrine therapy in the advanced or metastatic setting. Overall, 70% of patients were treated with a prior CDK4/6 inhibitor, 2.3% treated in the adjuvant setting and 67% treated in the advanced or metastatic setting.
- The major efficacy outcome was investigator assessed progression-free survival (PFS) per RECIST v1.1.
  - Other efficacy measures included overall survival (OS), blinded independent review committee (BIRC)-assessed PFS, and objective response rate (ORR).
- The efficacy results are presented in the table below, which was adapted from the prescribing information.

- There was a statistically significant difference in investigator-assessed PFS in the *ESR1*m population for Inluriyo compared to investigator's choice of endocrine therapy.
- PFS assessment based on a BIRC was consistent with the investigator assessment.
- At the time of PFS analysis, overall survival data was immature with 31% of deaths in the *ESR1*m population.

Table 3. Efficacy results for patients with *ESR1*m

	Inluriyo (N=138)	**Fulvestrant or exemestane (N=118)**
Progression-free Survival (PFS)		
# of PFS Events, n (%)	109 (79%)	102 (86%)
Median in months	5.5	3.8
Hazard Ratio (HR)	0.62	
p-value	0.0008	
Objective Response Rate (ORR)		
Patients with measurable disease	112	91
ORR	14.3	7.7
Complete Response Rate, %	0.9	0
Parital Response Rate, %	13.4	7.7

Clinical guidelines

- **National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Breast Cancer** (*NCCN 2026*). The NCCN guidelines were last updated in January 2026 and include Inluriyo (imlunestrant). It was added as a category 2A, as other recommended treatment (for NCCN category of preference) in HR+, HER2- with an *ESR1m.* Elacestrant is also in this same category.

Safety summary

- **Contraindications:** None.
- **Box Warning:** None.
- **Warnings and precautions:**
  - This product has a warning regarding embryo-fetal toxicity.
- **Common adverse drug reactions:** Listed % incidence for adverse drug reactions= reported % incidence for drug (Inluriyo) minus reported % incidence for fulvestrant or exemestane for all grades. Please note that an incidence of 0% means the incidence was the same as or less than comparator.

- The most frequently reported adverse events included musculoskeletal pain (1%), fatigue (9%), diarrhea (10%), nausea (4%), constipation (4%), and abdominal pain (4%).
- Select laboratory abnormalities include hemoglobin decreased (0%), neutrophils decreased (0%), platelets decreased (2%), calcium decreased (7%), aspartate aminotransferase increased (0%), alanine aminotransferase increased (0%), triglycerides increased (0%), and cholesterol increased (0%).

- **Drug interactions:**
  - Imlunestrant is a CYP3A substrate.
    - Avoid concomitant use of Inluriyo with strong CYP3A inhibitors. If concomitant use cannot be avoided, reduce the dosage of Inluriyo.
    - Avoid concomitant use of Inluriyo with strong CYP3A inducers. If concomitant use cannot be avoided, increase the dosage of Inluriyo.
  - Imlunestrant inhibits both P-gp and breast cancer resistance protein (BCRP).
    - Avoid concomitant use unless otherwise recommended in the prescribing information for P-gp or BCRP substrates where minimal concentration changes may lead to serious adverse reactions.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that based on findings in animals and its mechanism of action, Inluriyo can cause fetal harm when given to a pregnant women. There are no available human data on use in pregnant women to inform the drug-associated risk. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.
    - Verify the pregnancy status in females of reproductive potential prior to starting treatment.
    - Advise females of reproductive potential and male patients with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the last dose.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- In the United States, breast cancer is the most frequent cancer in females, and is the second most frequent cause of cancer death in females (*Joe 2025*).
- Inluriyo is an estrogen receptor antagonist indicated for the treatment of adults with ER-positive, HER2-, *estrogen receptor-1* (*ESR1*)-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.
- The efficacy of Inluriyo was assessed in a randomized, open-label, active-controlled, multicenter trial that included adult patients with ER+, HER2- locally advanced or metastatic breast cancer, who were previously treated with an aromatase inhibitor either alone or in combination with a CDK4/6 inhibitor.
  - The major efficacy outcome was investigator assessed PFS per RECIST v1.1.
  - Results of the study suggested that there was a statistically significant difference in investigator-assessed PFS in the *ESR1*m population for Inluriyo compared to investigator's choice of endocrine therapy (fulvestrant or exemestane).
- NCCN guidelines have been updated to include Inluriyo.

- It is recommended that Inluriyo should be non-recommended in order to confirm the appropriate diagnosis and clinical parameters for use.

- **PDL Placement:**
  - ☐ Recommended
  - ☒ Non-Recommended with Conditions

References

- Inluriyo Package insert. Lilly USA, LLC; September 2025.
- Henry NL, Scheer AS, Ko YJ et al. Female Breast Cancer. Dynamed Web site. Updated January 22, 2026. Accessed January 29, 2026. www.dynamed.com.
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- National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Breast Cancer v1.2026- January 16, 2026. Accessed January 29, 2026. nscl.pdf.

Publication Date: February 2026.