



Electronic Health Record Treatment Plan Guide

Disclaimer:

This guide is intended to provide information to develop a drug record for Inluriyo and/or to assist users with creating a standard treatment template for use of Inluriyo as monotherapy or in combination with Verzenio for the treatment of adults with ER+, HER2-, *ESR1*m advanced or metastatic breast cancer with disease progression following at least one line of ET. Patients should be evaluated by a physician prior to the use of Inluriyo and deemed to meet both a confirmatory diagnosis of the above indication and be an appropriate candidate for the use of Inluriyo. Based on individual patient cases and unique scenarios, additional tests, assessments, and medications may be necessary for the proper care and treatment of patients receiving this regimen. This guide does not constitute a final order and may not meet the comprehensive needs of individual patients or institutions.

Indications

Inluriyo monotherapy is indicated:

- 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, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy¹

Inluriyo in combination with Verzenio is indicated:

- 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, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy^{1,2}

SELECT IMPORTANT SAFETY INFORMATION - DIARRHEA

Severe diarrhea associated with dehydration and infection occurred in patients treated with Verzenio. Instruct patients at the first sign of loose stools to initiate antidiarrheal therapy, increase oral fluids, and notify their healthcare provider. In EMBER-3, diarrhea occurred in 86% of patients who received Inluriyo in combination with Verzenio; Grade 3 or 4 diarrhea occurred in 9%. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

ER+=estrogen receptor-positive; *ESR1*m=estrogen receptor-1 mutated; ET=endocrine therapy; FDA=US Food and Drug Administration; HER2-=human epidermal growth factor receptor 2-negative.



Pharmacology¹

Class	ER antagonist
Mechanism of action	Inluriyo is an ER antagonist that binds to estrogen receptor α (ER α).

Treatment Medication¹

Dosing	Recommended dose is 400 mg orally once daily* Should be taken on an empty stomach; at approximately the same time every day; at least 2 hours before food or 1 hour after food
Dosage form and strength	Inluriyo is available as 200 mg tablets and is a white capsule-shaped tablet with “LILLY” on one side and “1717” with an elongated 4-point starburst on the other side.

Treatment¹

Category	Details
Regimen	Inluriyo days 1-28
FDA-approved indication	Inluriyo monotherapy is indicated: - for the treatment of adults with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, <i>estrogen receptor-1 (ESR1)</i>-mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy¹ Inluriyo in combination with Verzenio is indicated: - for the treatment of adults with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, <i>estrogen receptor-1 (ESR1)</i>-mutated advanced or metastatic breast cancer, as detected by an FDA-authorized test, with disease progression following at least one line of endocrine therapy^{1,2}

Treatment Schedule¹

Treatment days	Daily
Cycle length	28 days
Treatment duration	Continuously until disease progression or unacceptable toxicity

*Inluriyo is taken as two 200-mg tablets.¹

ER=estrogen receptor; *ESR1*=estrogen receptor-1; FDA=US Food and Drug Administration.

SELECT IMPORTANT SAFETY INFORMATION - NEUTROPENIA

Neutropenia, including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with Verzenio. In EMBER-3, neutrophil count decreased in 86% of patients who received Inluriyo in combination with Verzenio; Grade 3 or 4 decreases occurred in 21%. Monitor complete blood counts prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Monitoring¹

Recommended evaluations and immunizations prior to treatment initiation

- Monitor alanine aminotransferase (ALT)/aspartate aminotransferase (AST) during Inluriyo therapy as clinically indicated.
- Advise patients that hypercholesterolemia and hypertriglyceridemia may occur while taking Inluriyo. Inform patients that lipid profile monitoring will be performed prior to starting and periodically while taking Inluriyo.

Warnings and Precautions – Embryo-Fetal Toxicity

- Based on findings in animals and its mechanism of action, Inluriyo can cause fetal harm when administered to a pregnant woman. In an animal reproduction study, oral administration of imlunestrant to pregnant rats during the period of organogenesis led to embryo-fetal mortality and structural abnormalities at maternal exposures that were below the human exposure at the recommended dose based on area under the curve (AUC). Avoid the use of imlunestrant in pregnant women. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Inluriyo and for 1 week after the last dose.

See Warnings and Precautions (5.1) for more complete information.

Administration Considerations¹

Administration

- Take tablets at approximately the same time daily
- Swallow tablets whole. Do not split, crush, or chew the tablets
- Take on an empty stomach, at least 2 hours before food or 1 hour after food
- Pre-/perimenopausal women and men should receive a gonadotropin-releasing hormone agonist (GnRH) according to current clinical practice standards
- If patient misses a dose by 6 or more hours or vomits, instruct the patient to take the next dose the following day at its scheduled time

SELECT IMPORTANT SAFETY INFORMATION – INTERSTITIAL LUNG DISEASE (ILD)/PNEUMONITIS

Severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis can occur in patients treated with Verzenio and other CDK4/6 inhibitors. In EMBER-3, ILD or pneumonitis occurred in 2.9% of patients who received Inluriyo in combination with Verzenio. Monitor for clinical symptoms or radiological changes indicative of ILD/pneumonitis. Permanently discontinue Verzenio in all patients with Grade 3 or 4 ILD or pneumonitis. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Recommended Inluriyo dosage modifications for adverse reactions (except hepatotoxicity)¹

Grade	Inluriyo Dosage Modifications
Persistent or recurrent Grade 2 that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1	Withhold until toxicity resolves to baseline or $\leq$ Grade 1. Resume Inluriyo at the same dose .
Grade 3 or 4 (except nonhepatic asymptomatic laboratory changes)	Withhold until toxicity resolves to baseline or $\leq$ Grade 1. Resume Inluriyo at next lower dose .

If dosage reduction is necessary, decrease the dose by 200 mg. Discontinue Inluriyo for patients unable to tolerate 200 mg once daily.¹

Recommended Inluriyo dosage modifications for hepatotoxicity¹

Monitor ALT/AST during Inluriyo therapy as clinically indicated.

Liver Transaminase	Inluriyo Dosage Modifications
Persistent or recurrent: AST/ALT >3.0 – $5.0 \times$ ULN	Withhold until toxicity resolves to baseline or to $>ULN - 3.0 \times ULN$. Resume Inluriyo at the same dose .
If AST/ALT at baseline is within the normal range: AST/ALT >5.0 – $20 \times$ ULN or If AST/ALT at baseline is above ULN: AST/ALT $\geq 3 \times$ baseline (if AST/ALT $\geq 1.5 \times$ ULN at baseline) or AST/ALT $>8 \times$ ULN (whichever is the lower threshold)	Withhold until toxicity resolves to baseline or to $>ULN - 3.0 \times ULN$. Resume Inluriyo at next lower dose or discontinue if receiving 200 mg daily .
AST/ALT $>20.0 \times$ ULN OR AST/ALT $\geq 3 \times$ ULN concurrent with TBL $\geq 2 \times$ ULN (if AST/ALT $<1.5 \times$ ULN at baseline), in the absence of cholestasis OR AST/ALT $\geq 2 \times$ baseline concurrent with TBL $\geq 2 \times$ ULN (if AST/ALT $\geq 1.5 \times$ ULN at baseline), in the absence of cholestasis	Permanently discontinue Inluriyo.

Dosage in Patients with Hepatic Impairment¹

- The recommended dosage of Inluriyo for patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment is 200 mg once daily. Monitor for increased adverse reactions. No dosage modification is recommended for patients with mild hepatic impairment (Child-Pugh A)

Dosage Modifications for Drug Interactions¹

- Strong CYP3A Inhibitors:** Avoid concomitant use with strong CYP3A inhibitors. If concomitant use cannot be avoided, decrease the Inluriyo dosage to 200 mg once daily
- Strong CYP3A Inducers:** Avoid concomitant use with strong CYP3A inducers. If concomitant use cannot be avoided, increase the Inluriyo dosage to 600 mg once daily

CYP3A=cytochrome P450 3A; TBL=total bilirubin level; ULN=upper limit of normal.

SELECT IMPORTANT SAFETY INFORMATION - HEPATOTOXICITY

Increases in serum transaminase levels have been observed. Perform liver function tests (LFTs) before initiating treatment with Verzenio. Monitor LFTs every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated with Verzenio. Monitor ALT and AST during treatment with Inluriyo as clinically indicated. In EMBE-3, ALT increase occurred in 33% for all grades (Grade 3 or 4: 5%) and AST increase occurred in 36% for all grades (Grade 3 or 4: 2.5%) of patients who received Inluriyo in combination with Verzenio. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Patient Counseling

Adverse reactions¹

Inluriyo

- Adverse reactions reported in at least 10% of patients and at a higher frequency than standard of care (fulvestrant or exemestane) in EMBER-3 were the following:
 - Musculoskeletal pain (3.7% Grades 3 or 4)
 - Fatigue (0.3% Grades 3 or 4)
 - Gastrointestinal disorders (diarrhea [0.6% Grades 3 or 4], nausea [0.3% Grades 3 or 4], constipation, abdominal pain [0.3% Grades 3 or 4])
- Select lab abnormalities reported in $\geq 10\%$ in patients treated with Inluriyo in EMBER-3:
 - Hemoglobin decreased (1.2% Grades 3 or 4)
 - Neutrophils decreased (4% Grades 3 or 4)
 - Platelets decreased (1.8% Grades 3 or 4)
 - Calcium decreased
 - AST increased (1.9% Grades 3 or 4)
 - ALT increased (1.3% Grades 3 or 4)
 - Triglycerides increased
 - Cholesterol increased

Inluriyo in combination with Verzenio

- Adverse reactions reported in at least 10% of patients and at a higher frequency than Inluriyo alone in EMBER-3 were the following:
 - Gastrointestinal disorders (diarrhea [9% Grades 3 or 4], nausea [1.9% Grades 3 or 4], vomiting [0.5% Grades 3 or 4], abdominal pain [1.9% Grades 3 or 4])
 - Fatigue (5% Grades 3 or 4)
 - Infections (7% Grades 3 or 4)
 - Musculoskeletal pain (1.4% Grades 3 or 4)
 - Decreased appetite (1.0% Grades 3 or 4)
 - Rash (1.4% Grades 3 or 4)
 - Cough
 - Headache (0.5% Grades 3 or 4)
 - Weight decreased
- Select lab abnormalities reported in $\geq 10\%$ in patients treated with Inluriyo in combination with Verzenio in EMBER-3:
 - Neutrophil count decreased (21% Grades 3 or 4)
 - Hemoglobin decreased (9% Grades 3 or 4)
 - Lymphocyte count decreased (9% Grades 3 or 4)
 - Platelet count decreased (2.4% Grades 3 or 4)
 - Triglycerides increased (2.3% Grades 3 or 4)
 - AST increased (2.5% Grades 3 or 4)
 - Creatinine increased (1.1% Grades 3 or 4)
 - ALT increased (5% Grades 3 or 4)
 - Cholesterol increased

See *Clinical Trial Experience (Section 6.1)* for more complete information.

SELECT IMPORTANT SAFETY INFORMATION - VENOUS THROMBOEMBOLISM

Deaths due to venous thromboembolism have been reported in patients treated with Verzenio. In EMBER-3, venous thromboembolic events occurred in 4.8% of patients who received Inluriyo in combination with Verzenio. Monitor patients for signs and symptoms of thrombosis and pulmonary embolism and treat as medically appropriate. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Patient Counseling (continued)

Patient counseling information^{1,2}

Inluriyo

- Advise patients to read the FDA-approved patient labeling (Patient Information)
- **Dyslipidemia:** Advise patients that hypercholesterolemia and hypertriglyceridemia may occur while taking Inluriyo. Inform patients that lipid profile monitoring will be performed prior to starting and periodically while taking Inluriyo
- **Embryo-Fetal Toxicity:**
 - Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy
 - Advise females of reproductive potential to use effective contraception during treatment and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the last dose
- **Lactation:** Advise women not to breastfeed during treatment with Inluriyo and for 1 week after the last dose
- Refer to the Prescribing Information of abemaciclib when administered in combination with Inluriyo for (pregnancy and contraception/lactation) information. When used in combination, advise patients to use effective contraception during treatment and for the longest post-treatment duration recommended in the Prescribing Information of the individual products
- **Infertility:** Advise males and females of reproductive potential that Inluriyo may impair fertility
- **Drug Interactions:** Advise patients to inform their healthcare provider of all concomitant medications, including prescription medications, over the counter drugs, herbal products
- **Dosing Instructions:**
 - Instruct patients to take Inluriyo at approximately the same time each day swallowing the tablet(s) whole. Tablets should not be chewed, crushed, or split prior to swallowing
 - Advise patients to take Inluriyo without food, either 2 hours before food or 1 hour after food
 - Instruct patient that if a dose of Inluriyo is missed by more than 6 hours or vomiting occurs, skip the dose and take the next dose the following day at its regularly scheduled time

See *Dosage and Administration (Section 2.2)* for more complete information.

Verzenio

- Advise the patient to read the FDA-approved patient labeling (Patient Information)
- **Diarrhea:** Verzenio may cause diarrhea, which may be severe in some cases
 - Early identification and intervention is critical for the optimal management of diarrhea. Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy (for example, loperamide) and notify their healthcare provider for further instructions and appropriate follow-up
 - Encourage patients to increase oral fluids
 - If diarrhea does not resolve with antidiarrheal therapy within 24 hours to $\leq$ Grade 1, suspend Verzenio dosing
- **Neutropenia:** Advise patients of the possibility of developing neutropenia and to immediately contact their healthcare provider should they develop a fever, particularly in association with any signs of infection
- **Interstitial Lung Disease/Pneumonitis:** Advise patients to immediately report new or worsening respiratory symptoms
- **Hepatotoxicity:** Inform patients of the signs and symptoms of hepatotoxicity. Advise patients to contact their healthcare provider immediately for signs or symptoms of hepatotoxicity

SELECT IMPORTANT SAFETY INFORMATION - EMBRYO-FETAL TOXICITY

Inluriyo and Verzenio can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to initiating treatment. Advise females of reproductive potential to use effective contraception during treatment with Inluriyo in combination with Verzenio and for 3 weeks after the last dose of Verzenio or 1 week after the last dose of Inluriyo, whichever is longer. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the last dose of Inluriyo.

For Inluriyo monotherapy, advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Inluriyo and for 1 week after the last dose.

Patient Counseling (continued)

Patient counseling information (continued)^{1,2}

Verzenio (continued)

- **Venous Thromboembolism:** Advise patients to immediately report any signs or symptoms of thromboembolism such as pain or swelling in an extremity, shortness of breath, chest pain, tachypnea, and tachycardia
- **Embryo-Fetal Toxicity:**
 - Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy
 - Advise females of reproductive potential to use effective contraception during Verzenio treatment and for 3 weeks after the last dose
- **Lactation:** Advise lactating women not to breastfeed during Verzenio treatment and for at least 3 weeks after the last dose
- When used in combination, advise patients to use effective contraception during treatment and for the longest post-treatment duration recommended in the Prescribing Information of the individual products
- **Infertility:** Inform males of reproductive potential that Verzenio may impair fertility
- **Dosing Instructions:**
 - Instruct patients to take the doses of Verzenio at approximately the same times every day and to swallow whole (do not chew, crush, or split them prior to swallowing)
 - Instruct patients that if a dose is missed, take the next dose at the next scheduled time
 - Instruct patients that if they vomit after taking the dose an additional dose should not be taken. The next dose of Verzenio should be taken at the next scheduled time
 - Advise the patient that Verzenio may be taken with or without food

See *Dosage and Administration (Section 2.1)* for more complete information.

Drug interactions^{1,2}

Inluriyo

- Advise patients to avoid concomitant use of Inluriyo with strong CYP3A inhibitors. If concomitant use cannot be avoided, reduce the dosage of Inluriyo
- Advise patients to avoid concomitant use of Inluriyo with strong CYP3A inducers. If concomitant use cannot be avoided, increase the dosage of Inluriyo
- Advise patients to avoid concomitant use unless otherwise recommended in the Prescribing Information for the P-gp or BCRP substrates where minimal concentration changes may lead to serious adverse reactions

See *Drug Interactions (Sections 7.1 and 7.2)* for more complete information.

Verzenio

- Inform patients to avoid concomitant use of ketoconazole. Dose reduction may be required for other strong CYP3A inhibitors or for moderate CYP3A inhibitors
- Grapefruit may interact with Verzenio. Advise patients not to consume grapefruit products while on treatment with Verzenio
- Advise patients to avoid concomitant use of strong and moderate CYP3A inducers and to consider alternative agents
- Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products

See *Drug Interactions (Sections 2.2 and 7.1)* for more complete information.

BCRP=Breast Cancer Resistance Protein; CYP3A=cytochrome P450 3A; P-gp=P-glycoprotein.

SELECT IMPORTANT SAFETY INFORMATION - INCREASED SERUM CREATININE WITHOUT AFFECTING RENAL FUNCTION

Verzenio can increase serum creatinine. These increases were not associated with changes in glomerular function. In EMBE-3, creatinine increased for all grades in 36% (Grade 3 or 4: 1.1%) of patients who received Inluriyo in combination with Verzenio. During Verzenio treatment, use alternative measures that are not based on serum creatinine to assess renal function, such as BUN, cystatin C, or calculated GFR.

How Supplied¹

Tablet Strength*	Quantity of Tablets per Bottle	NDC	Days' Supply
200 mg	28	0002-1717-28	28 days
200 mg	56	0002-1717-56	

*The standard dose for Inluriyo is two 200 mg tablets once daily, dispensed in a 56-count bottle for a 28-day supply. Inluriyo is also available in 28-count bottles for patients who require dose modifications.¹

Storage and Handling

Strength¹	200 mg tablets
Hazardous classification³	Physical Hazards: Not classified Health Hazards: Carcinogenicity (Category 2), reproductive toxicity (Category 1B), reproductive toxicity (effects on or via lactation) OSHA defined hazards: Not classified
Hazard statements³	May damage fertility. May damage the unborn child. (H360FD) May cause harm to breast-fed children. (H362) Suspected of causing cancer. (H351) Very toxic to aquatic life with long-lasting effects. (H410)
Storage and handling¹	- Store at 20°C to 25°C (68°F to 77°F) - Excursions between 15°C to 30°C (59°F to 86°F) are permitted
Disposal¹	Dispose unused medication via a take-back option, if available. Otherwise, follow FDA instructions for disposing medication in the household trash. Do NOT flush down toilet.
Stability and reactivity³	- Reactivity: Not water reactive - Chemical stability: This material should not be exposed to temperatures above 83°C (181.4°F). This temperature is based on a laboratory test (DSC) and assumes near atmospheric pressures and quantities of less than 500 kg (1100 lb) or 208 L (55 gal) - Possibility of hazardous reactions: Hazardous polymerization does not occur

DSC=differential screening calorimetry; NDC=National Drug Code; OSHA=Occupational Safety and Health Administration.

SELECT IMPORTANT SAFETY INFORMATION – SERIOUS AND FATAL ADVERSE REACTIONS FOR INLURIYO IN COMBINATION WITH VERZENIO

Serious adverse reactions occurred in 21% of patients who received Inluriyo in combination with Verzenio. Serious adverse reactions in >1% of patients who received Inluriyo in combination with Verzenio included pneumonia (2.4%), abdominal pain, and renal failure (each 1.4%). **Fatal adverse reactions** occurred in 3.8% of patients who received Inluriyo in combination with Verzenio, including pneumonia (1.4%), myocardial infarction, interstitial lung disease, and sepsis (0.5% each).

Additional Resources

Lilly Support Services™

- [Medical.Lilly.com](https://www.Medical.Lilly.com)
- [Lilly.com/about/contact](https://www.Lilly.com/about/contact)
- [provider.lilly.com](https://www.provider.lilly.com)
- [inluriyo.lilly.com/hcp/savings-support](https://www.inluriyo.lilly.com/hcp/savings-support)

- Savings Card: <https://www.inluriyo.lilly.com/hcp/savings-support>

Governmental beneficiaries excluded, terms and conditions apply.

- Interim Access Program for Lilly oral oncology medication(s), Assistance Determining Insurance Coverage, Field Reimbursement Managers: <https://www.inluriyo.lilly.com/hcp/savings-support>

Sample Letter of Medical Necessity, Sample Letter of Appeals, and Access, Distribution, and Reimbursement Guide: <https://www.inluriyo.lilly.com/hcp/savings-support>

Important Safety Information for Inluriyo® (imlunestrant) as Monotherapy and in Combination with Verzenio® (abemaciclib)

Diarrhea: Severe diarrhea associated with dehydration and infection occurred in patients treated with Verzenio. Instruct patients at the first sign of loose stools to initiate antidiarrheal therapy, increase oral fluids, and notify their healthcare provider. In EMBER-3, diarrhea occurred in 86% of patients who received Inluriyo in combination with Verzenio; Grade 3 or 4 diarrhea occurred in 9%. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Neutropenia: Neutropenia, including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with Verzenio. In EMBER-3, neutrophil count decreased in 86% of patients who received Inluriyo in combination with Verzenio; Grade 3 or 4 decreases occurred in 21%. Monitor complete blood counts prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Interstitial Lung Disease (ILD)/Pneumonitis: Severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis can occur in patients treated with Verzenio and other CDK4/6 inhibitors. In EMBER-3, ILD or pneumonitis occurred in 2.9% of patients who received Inluriyo in combination with Verzenio. Monitor for clinical symptoms or radiological changes indicative of ILD/pneumonitis. Permanently discontinue Verzenio in all patients with Grade 3 or 4 ILD or pneumonitis. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Hepatotoxicity: Increases in serum transaminase levels have been observed. Perform liver function tests (LFTs) before initiating treatment with Verzenio. Monitor LFTs every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated with Verzenio. Monitor ALT and AST during treatment with Inluriyo as clinically indicated. In EMBER-3, ALT increase occurred in 33% for all grades (Grade 3 or 4: 5%) and AST increase occurred in 36% for all grades (Grade 3 or 4: 2.5%) of patients who received Inluriyo in combination with Verzenio. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Venous Thromboembolism: Deaths due to venous thromboembolism have been reported in patients treated with Verzenio. In EMBER-3, venous thromboembolic events occurred in 4.8% of patients who received Inluriyo in combination with Verzenio. Monitor patients for signs and symptoms of thrombosis and pulmonary embolism and treat as medically appropriate. Follow specific dose modification and management instructions located in the Prescribing Information for each drug.

Embryo-Fetal Toxicity: Inluriyo and Verzenio can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify pregnancy status in females of reproductive potential prior to initiating treatment. Advise females of reproductive potential to use effective contraception during treatment with Inluriyo in combination with Verzenio and for 3 weeks after the last dose of Verzenio or 1 week after the last dose of Inluriyo, whichever is longer. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the last dose of Inluriyo.

For Inluriyo monotherapy, advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Inluriyo and for 1 week after the last dose.

Increased Serum Creatinine Without Affecting Renal Function: Verzenio can increase serum creatinine. These increases were not associated with changes in glomerular function. In EMBER-3, creatinine increase occurred in 36% for all grades (Grade 3 or 4: 1.1%) of patients who received Inluriyo in combination with Verzenio. During Verzenio treatment, use alternative measures that are not based on serum creatinine to assess renal function, such as BUN, cystatin C, or calculated GFR.

Serious and Fatal Adverse Reactions for Inluriyo in combination with Verzenio: Serious adverse reactions occurred in 21% of patients who received Inluriyo in combination with Verzenio. Serious adverse reactions in >1% of patients who received Inluriyo in combination with Verzenio included pneumonia (2.4%), abdominal pain, and renal failure (each 1.4%).

Fatal adverse reactions occurred in 3.8% of patients who received Inluriyo in combination with Verzenio, including pneumonia (1.4%), myocardial infarction, interstitial lung disease, and sepsis (0.5% each).

Most Common Adverse Reactions for Inluriyo in combination with Verzenio: The most common (≥10%) adverse reactions with Inluriyo in combination with Verzenio, including laboratory abnormalities, were decreased neutrophils, diarrhea, decreased hemoglobin, decreased lymphocytes, nausea, decreased platelets, fatigue, increased triglycerides, infections, increased AST, increased creatinine, increased ALT, vomiting, musculoskeletal pain, abdominal pain, decreased appetite, increased cholesterol, rash, cough, headache, and decreased weight.

Serious and Fatal Adverse Reactions for Inluriyo Monotherapy: Serious adverse reactions occurred in 10% of patients who received Inluriyo. Serious adverse reactions in >1% of patients included pleural effusion (1.2%). **Fatal adverse reactions** occurred in 1.8% of patients who received Inluriyo, including cardiac arrest, acute myocardial infarction, right ventricular failure, hypovolemic shock, and upper gastrointestinal hemorrhage (each 0.3%).

Important Safety Information for Inluriyo® (imlunestrant) as Monotherapy and in Combination with Verzenio® (abemaciclib) (continued)

Most Common Adverse Reactions for Inluriyo Monotherapy: The most common (≥10%) adverse reactions with Inluriyo monotherapy, including laboratory abnormalities were decreased hemoglobin, musculoskeletal pain, decreased calcium, decreased neutrophils, increased AST, fatigue, diarrhea, increased ALT, increased triglycerides, nausea, decreased platelets, constipation, increased cholesterol, and abdominal pain.

Drug Interactions – Inluriyo:

- Avoid concomitant use with **strong CYP3A inhibitors**. If concomitant use cannot be avoided, decrease the Inluriyo dosage. Avoid concomitant use with **strong CYP3A inducers**. If concomitant use cannot be avoided, increase the Inluriyo dosage. See Prescribing Information for recommended dosage modifications.
- Imlunestrant inhibits both **P-gp** and **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.

Drug Interactions – Verzenio:

- **CYP3A Inhibitors:** Avoid concomitant use of ketoconazole. Reduce the Verzenio dose with concomitant use of other strong and moderate CYP3A inhibitors. Monitor for adverse reactions and follow the specific dose modification instructions located in the Prescribing Information. Patients should avoid grapefruit products.
- **CYP3A Inducers:** Avoid concomitant use of strong and moderate CYP3A inducers and consider alternative agents.

Lactation: Because of the potential for serious adverse reactions in the breastfed child, advise lactating women to not breastfeed during treatment with Inluriyo in combination with Verzenio and for 3 weeks after the last dose of Verzenio or 1 week after the last dose of Inluriyo, whichever is longer.

For Inluriyo monotherapy, advise lactating women to not breastfeed during treatment with Inluriyo and for 1 week after the last dose.

Hepatic Impairment: With **Inluriyo**, reduce the dose in patients with moderate or severe **hepatic impairment**. The recommended dosage for patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment is 200 mg once daily. No dosage modification is recommended for patients with mild hepatic impairment (Child-Pugh A).

With **Verzenio**, reduce the dosing frequency to once daily in patients with severe **hepatic impairment** (Child-Pugh C). No dosage adjustments are necessary in patients with mild or moderate hepatic impairment (Child-Pugh A or B).

Inluriyo may impair fertility in females and males of reproductive potential.

Verzenio may impair fertility in males of reproductive potential.

Inluriyo (imlunestrant) is available as 200 mg tablets.

Verzenio (abemaciclib) is available as 50 mg, 100 mg, 150 mg, and 200 mg tablets.

Please click to access Prescribing Information for [Inluriyo](#) and [Verzenio](#).

IN VZ HCP ISI Combo+Mono APPR

References: **1.** Inluriyo. Prescribing Information. Lilly USA, LLC. **2.** Verzenio. Prescribing Information. Lilly USA, LLC. **3.** Inluriyo Safety Data Sheet. Lilly USA, LLC.

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