IBRANCE®

palbociclib | 125 mg capsules

DOSING AND ADMINISTRATION GUIDE

Indication

IBRANCE is a kinase inhibitor indicated in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

This indication is approved under accelerated approval based on progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Selected Safety Information

Neutropenia: Neutropenia is frequently reported with IBRANCE therapy. In the randomized phase II study, Grade 3 (57%) or 4 (5%) decreased neutrophil counts were reported in patients receiving IBRANCE plus letrozole. Febrile neutropenia can occur.

Monitor complete blood count prior to starting IBRANCE and at the beginning of each cycle, as well as Day 14 of the first two cycles, and as clinically indicated. For patients who experience Grade 3 neutropenia, consider repeating the complete blood count monitoring 1 week later. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Please see end of this document for additional Important Safety Information and full Prescribing Information.

IBRANCE® (palbociclib) Dosing

IBRANCE 125 mg once daily

FOR 21 CONSECUTIVE DAYS
followed by
7 DAYS OFF TREATMENT

+

LETROZOLE 2.5 mg once daily

GIVEN CONTINUOUSLY

IBRANCE should be taken with food in combination with letrozole

Patients should be encouraged to take their dose at approximately the same time each day

If the patient vomits or misses a dose, an additional dose should not be taken that day

— The next prescribed dose should be taken at the usual time

IBRANCE capsules should be swallowed whole (do not chew, crush, or open them prior to swallowing). No capsule should be ingested if it is broken, cracked, or otherwise not intact

Avoid coadministration of strong and moderate CYP3A inducers. Avoid coadministration of strong CYP3A inhibitors. Avoid grapefruit or grapefruit juice during IBRANCE treatment

— If patients must be coadministered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg once daily

— If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor

The dose of the sensitive CYP3A substrates with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure

Selected Safety Information

Pulmonary embolism (PE): PE has been reported at a higher rate in patients treated with IBRANCE plus letrozole (5%) compared with no cases in patients treated with letrozole alone. Monitor patients for signs and symptoms of PE and treat as medically appropriate.

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IBRANCE® palbociclib 125 mg capsules

Dose Modifications

Dose modification of IBRANCE® (palbociclib) is recommended based on individual safety and tolerability.

- Management of some adverse reactions may require temporary dose interruptions/delays and/or dose reductions, or permanent discontinuation

Recommended Dose Modification for Adverse Events

Dose Level	Dose	
Recommended starting dose	125 mg/day	
First dose reduction	100 mg/day	
Second dose reduction	75 mg/day*	

* If further dose reduction below 75 mg/day is required, discontinue the treatment.
Pills are not actual size.

- There is no known antidote for IBRANCE. The treatment of overdose of IBRANCE should consist of general supportive measures
- See manufacturer's prescribing information for the coadministered product, letrozole, dose-adjustment guidelines in the event of toxicity and other relevant safety information or contraindications

Selected Safety Information

Infections: Infections have been reported at a higher rate in patients treated with IBRANCE plus letrozole (55%) compared with letrozole alone (34%). Grade 3 or 4 infections occurred in 5% of patients treated with IBRANCE plus letrozole vs no patients treated with letrozole alone. Monitor patients for signs and symptoms of infection and treat as medically appropriate.

Pregnancy and lactation: Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females with reproductive potential to use effective contraception during therapy with IBRANCE and for at least 2 weeks after the last dose. Advise females to contact their healthcare provider if they become pregnant or if pregnancy is suspected during treatment with IBRANCE. Advise women not to breastfeed while on IBRANCE therapy because of the potential for serious adverse reactions in nursing infants from IBRANCE.

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Adverse Event Management

Monitor complete blood count prior to the start of IBRANCE® (palbociclib) therapy and at the beginning of each cycle, as well as on Day 14 of the first two cycles, and as clinically indicated

Dose Modification and Management—Hematologic Toxicities	
CTCAE Grade	**Dose Modifications**
Grade 1 or 2	No dose adjustment is required.
Grade 3†	No dose adjustment is required. Consider repeating complete blood count monitoring 1 week later. Withhold initiation of next cycle until recovery to Grade ≤2.
Grade 3 ANC (<1000 to 500/mm^3) + Fever ≥38.5 °C and/or infection	Withhold IBRANCE and initiation of next cycle until recovery to Grade ≤2 (≥1000/mm^3). Resume at next lower dose.
Grade 4†	Withhold IBRANCE and initiation of next cycle until recovery to Grade ≤2. Resume at next lower dose.
Dose Modification and Management—Nonhematologic Toxicities	
Grade 1 or 2	No dose adjustment is required.
Grade ≥3 nonhematologic toxicity (if persisting despite medical treatment)	Withhold until symptoms resolve to: • Grade ≤1; • Grade ≤2 (if not considered a safety risk for the patient) Resume at next lower dose.

Grading according to CTCAE Version 4.0.
† Except lymphopenia (unless associated with clinical events, eg, opportunistic infections).
ANC=absolute neutrophil count; CTCAE=Common Terminology Criteria for Adverse Events.

Selected Safety Information

Additional hematologic abnormalities: Decreases in hemoglobin (83% vs 40%), leukocytes (95% vs 26%), lymphocytes (81% vs 35%), and platelets (61% vs 16%) occurred at a higher rate in patients treated with IBRANCE plus letrozole vs letrozole alone.

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Important Safety Information

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Pulmonary embolism (PE): PE has been reported at a higher rate in patients treated with IBRANCE plus letrozole (5%) compared with no cases in patients treated with letrozole alone. Monitor patients for signs and symptoms of PE and treat as medically appropriate.

Pregnancy and lactation: Based on the mechanism of action, IBRANCE can cause fetal harm. Advise females with reproductive potential to use effective contraception during therapy with IBRANCE and for at least 2 weeks after the last dose. Advise females to contact their healthcare provider if they become pregnant or if pregnancy is suspected during treatment with IBRANCE. Advise women not to breastfeed while on IBRANCE therapy because of the potential for serious adverse reactions in nursing infants from IBRANCE.

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Important Safety Information (continued)

Adverse reactions: The most common all causality adverse reactions (≥10%) of any grade reported in patients treated with IBRANCE® (palbociclib) plus letrozole vs letrozole alone in the phase II study included neutropenia (75% vs 5%), leukopenia (43% vs 3%), fatigue (41% vs 23%), anemia (35% vs 7%), upper respiratory infection (31% vs 18%), nausea (25% vs 13%), stomatitis (25% vs 7%), alopecia (22% vs 3%), diarrhea (21% vs 10%), thrombocytopenia (17% vs 1%), decreased appetite (16% vs 7%), vomiting (15% vs 4%), asthenia (13% vs 4%), peripheral neuropathy (13% vs 5%), and epistaxis (11% vs 1%).

Grade 3/4 adverse reactions reported (≥10%) occurring at a higher incidence in the IBRANCE plus letrozole vs letrozole alone group include neutropenia (54% vs 1%) and leukopenia (19% vs 0%). The most frequently reported serious adverse events in patients receiving IBRANCE were pulmonary embolism (4%) and diarrhea (2%).

General dosing information: The recommended dose of IBRANCE is 125 mg taken orally once daily for 21 days followed by 7 days off treatment in 28-day cycles. IBRANCE should be taken with food and in combination with letrozole 2.5 mg once daily continuously.

Patients should be encouraged to take their dose at approximately the same time each day.

Capsules should be swallowed whole. No capsule should be ingested if it is broken, cracked, or otherwise not intact. If a patient vomits or misses a dose, an additional dose should not be taken that day. The next prescribed dose should be taken at the usual time.

Management of some adverse reactions may require temporary dose interruption/delay and/or dose reduction, or permanent discontinuation. Dose modification of IBRANCE is recommended based on individual safety and tolerability.

Drug interactions: Avoid concurrent use of strong CYP3A inhibitors. If patients must be administered a strong CYP3A inhibitor, reduce the IBRANCE dose to 75 mg/day. If the strong inhibitor is discontinued, increase the IBRANCE dose (after 3-5 half-lives of the inhibitor) to the dose used prior to the initiation of the strong CYP3A inhibitor. Grapefruit or grapefruit juice may increase plasma concentrations of IBRANCE and should be avoided.

Avoid concomitant use of strong and moderate CYP3A inducers. The dose of the sensitive CYP3A substrates with a narrow therapeutic index may need to be reduced as IBRANCE may increase their exposure.

Hepatic and renal impairment: IBRANCE has not been studied in patients with moderate to severe hepatic impairment or in patients with severe renal impairment (CrCl <30 mL/min).

Please see end of this document for full Prescribing Information.

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Reference: IBRANCE® Prescribing Information. New York, NY: Pfizer Inc; 2015.