hepatotoxicity, infertility, neutropenia, pregnancy, pregnancy testing, reproductive risk, thromboembolic disease

DOSAGE AND ROUTES

HR-positive, HER2-negative advanced or metastatic breast cancer disease progression following endocrine therapy and prior chemotherapy, as monotherapy

• **Adult: PO** 200 mg bid until disease progression or unacceptable toxicity

HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy, in combination with fulvestrant

• **Adult: PO** 150 mg bid with fulvestrant (500 mg **IM** as two 250-mg [5 mL] injections, 1 injection in each buttock, on days 1, 15, 29, and q month thereafter) until disease progression or unacceptable toxicity. Pre- and perimenopausal women should also be treated with a gonadotropin-releasing hormone agonist

Therapeutic drug monitoring: dosage adjustments for treatment-related toxicities

Interrupt therapy per specific instructions. Restart as appropriate at the following reduced doses:

• **Starting dose:** Monotherapy, 200 mg bid; combination with fulvestrant, 150 mg bid

• **First occurrence:** Monotherapy, 150 mg bid; combination with fulvestrant, 100 mg bid

• **Second occurrence:** Monotherapy, 100 mg bid; combination with fulvestrant, 50 mg bid

• **Third occurrence:** Monotherapy, 50 mg bid; combination with fulvestrant, not applicable

Diarrhea

• **Grade 1:** Begin antidiarrheals, increase oral fluid intake. No change needed

• **Grade 2, first occurrence:** Begin antidiarrheals, increase oral fluid intake. If diarrhea does not resolve to grade ≤1 within 24 hr, hold therapy until resolution. No change needed unless grade 2 diarrhea persists; upon resolution to grade ≤1, resume at next lower dose level

• **Grade 2, recurrent despite maximal supportive measures:** Begin antidiarrheals, increase oral fluid intake. When diarrhea resolves to grade ≤1, resume at next lower dose level

• **Grade 3 or 4, or requires hospitalization:** Begin antidiarrheals, increase oral fluid intake. When diarrhea resolves to grade ≤1, resume at next lower dose level

Hematologic toxicities

• **Grade 3, first occurrence:** Hold; when toxicity resolves to grade ≤2, resume; dose reduction is not needed unless growth factor was needed. If treatment with growth factors is needed, additionally wait for at least 48 hr after the last dose of growth factor before resuming at the next lower dose level

• **Grade 3, recurrent, or grade 4:** Hold; when toxicity resolves to grade ≤2, resume at the next lower dose level. If treatment with growth factors is needed, additionally wait for at least 48 hr after the last dose of growth factor before resuming

Hepatic dose

• **Adult: PO**

Child-Pugh A or B: no change; **Child-Pugh C:** reduce dosing to once per day; **grade 1 (AST/ALT 1.1–3× the upper limit of normal [ULN]), without an increase in total bilirubin above 2× ULN:** no change; **grade 2, first occurrence (AST/ALT 3.1–5× ULN), without an increase in total bilirubin above 2× ULN:** no change; if grade 2 persists, hold; after resolution to baseline or grade 1, resume at the next lower dose level; **grade 2, recurrent (AST/ALT 3.1–5× ULN), without an increase in total bilirubin above 2× ULN:** hold; after resolution to baseline or grade 1, resume at the next