A Pocket Guide

Nursing Management of Adverse Events With Oral Targeted Therapies for HR+/HER2– Breast Cancer

DECERA CLINICAL Education

Approved CDK4/6 Inhibitors: Indications, Dosing, and Administration

	Indications	Dosing	Administration	Warnings and Precautions
Abemaciclib	In combination with endocrine therapy (ET) (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive/HER2-negative, node-positive, early breast cancer (EBC) at high risk of recurrence In combination with an aromatase inhibitor (AI) as initial ET for the treatment of adult patients with HR-positive/HER2-negative advanced or metastatic breast cancer (BC) In combination with fulvestrant for the treatment of adult patients with HR-positive/HER2-negative advanced or metastatic BC with disease progression following ET As monotherapy for the treatment of adult patients with HR-positive/HER2-negative advanced or metastatic BC with disease progression following ET and prior chemotherapy in the metastatic setting In combination with imlunestrant for the treatment of adult patients with HR-positive/HER2-negative, *ESR1*-mutated advanced or metastatic BC with disease progression following ET	Combination dosing: 150 mg PO BID Monotherapy dosing: 200 mg PO BID	Tablets: With or without food	• Diarrhea • Neutropenia • Interstitial lung disease (ILD)/Pneumonitis • Hepatotoxicity • Venous thromboembolism (VTE) • Embryo-fetal toxicity
Palbociclib	For the treatment of adult patients with HR-positive/HER2-negative advanced or metastatic BC in combination with: • An AI as initial ET or • Fulvestrant in patients with disease progression following ET In combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, *PIK3CA*-mutated, HR-positive/HER2-negative advanced or metastatic BC following recurrence on or after completing adjuvant ET In combination with trastuzumab, with or without pertuzumab, and ET for the maintenance treatment of adult patients with HR-positive/HER2-positive advanced or metastatic BC following induction treatment	125 mg PO QD x 21 days followed by 7 days off treatment (28-day cycle)	Tablets: With or without food Capsules: With food	• Neutropenia • ILD/Pneumonitis • Embryo-fetal toxicity
Ribociclib*	In combination with an AI for the adjuvant treatment of adults with HR-positive/HER2-negative stage II and III EBC at high risk of recurrence For the treatment of adults with HR-positive/HER2-negative advanced or metastatic BC in combination with: • An AI as initial ET or • Fulvestrant as initial ET or following disease progression on ET	EBC: 400 mg PO QD x 21 days followed by 7 days off treatment (28-day cycle) Advanced or metastatic BC: 600 mg PO QD x 21 days followed by 7 days off treatment	Tablets: With or without food	• ILD/Pneumonitis • Severe cutaneous adverse reactions (SCARs) • QT interval prolongation • Hepatotoxicity • Neutropenia • Embryo-fetal toxicity

*Not to be used in combination with tamoxifen

Key Adverse Events With CDK4/6 Inhibitors: Monitoring and Prevention

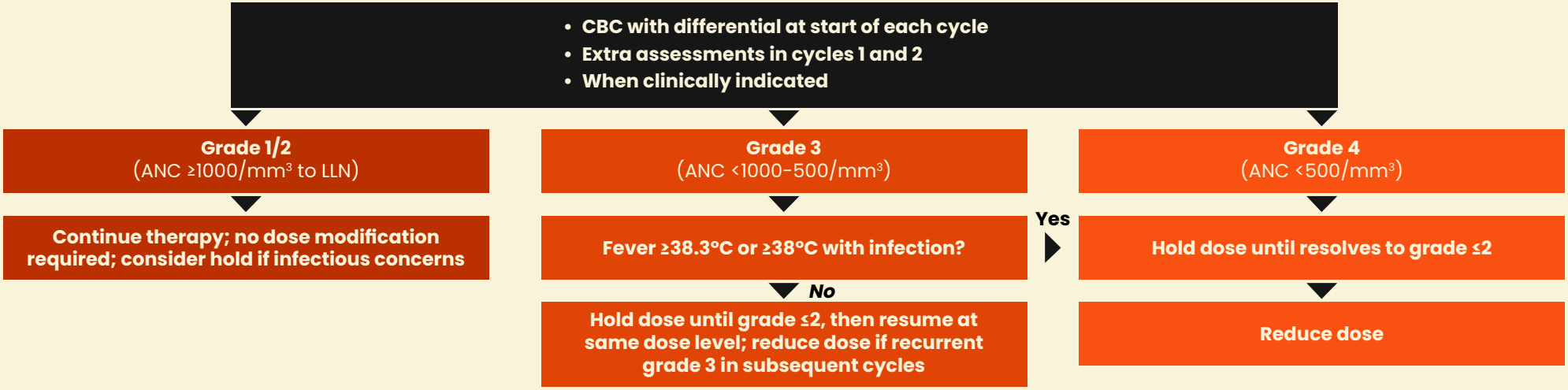
Adverse Event	Incidence	Median Time to Onset	Prevention, Monitoring, and Management
Diarrhea	Grade 3/4: Abemaciclib > Ribociclib, Palbociclib	6-8 days	• Assess at each visit • Patient education on notifying HCP at first sign/symptom • Antidiarrheal therapy • Increase oral hydration and replace electrolytes • Dietary modification: low fiber, low fat, smaller frequent meals
Hepatobiliary toxicity	Ribociclib > Abemaciclib > Palbociclib	8-12 wk	• Manage more conservatively in early-stage disease vs advanced disease • Greater concern if LFT elevations occur at lower starting dose of 400 mg for early-stage disease • Hepatotoxicity does not appear to be dose dependent; may recur after dose reduction • LFTs before starting treatment, Q2W x 2 mo, then: ○ Abemaciclib, QM x 2 mo, then as indicated ○ Ribociclib, at start of cycle x 4 cycles
Neutropenia	Ribociclib, Palbociclib > Abemaciclib	3-4 wk	• Educate patient on CBC schedule • Counsel on symptoms to report: fever, chills, flu-like symptoms • CBC before starting treatment, then: ○ Abemaciclib, Q2W x 2 mo, QM x 2 mo, then as indicated ○ Ribociclib and palbociclib, Q2W x 2 cycles, start of next 4 cycles, then as indicated
VTE	Abemaciclib (no grade 3 events)	8-12 wk	• Monitor for signs and symptoms of thrombosis and pulmonary embolism • Conduct patient education about what to report (SOB, unilateral swollen and painful extremity) or when to go to ED
ILD/Pneumonitis	Rare, but can be life-threatening*	8-12 wk	• Monitor for pulmonary symptoms indicative of ILD/pneumonitis (eg, hypoxia, cough, dyspnea)
QT Prolongation	Ribociclib (1.8% grade 3)	1-4 wk	• Monitor for signs and symptoms of QT prolongation • Monitor electrolytes • Monitor other medication use, avoid concomitant use of drugs known to prolong QT interval
Severe Cutaneous Adverse Reactions (SCARs)	Rare, but can be life-threatening (Ribociclib)**	—	• Monitor for signs of skin toxicity

*ILD/Pneumonitis: Severe, life-threatening, or fatal ILD/pneumonitis can occur with CDK4/6 inhibitor treatment. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Interrupt and evaluate patients with new or worsening respiratory symptoms suspected to be due to ILD/pneumonitis. Permanently discontinue CDK4/6 inhibitor in patients with recurrent symptomatic or severe ILD/pneumonitis.

**SCARs: SCARs including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) can occur with ribociclib. Permanently discontinue ribociclib in patients with SCARs or other life-threatening cutaneous reactions.

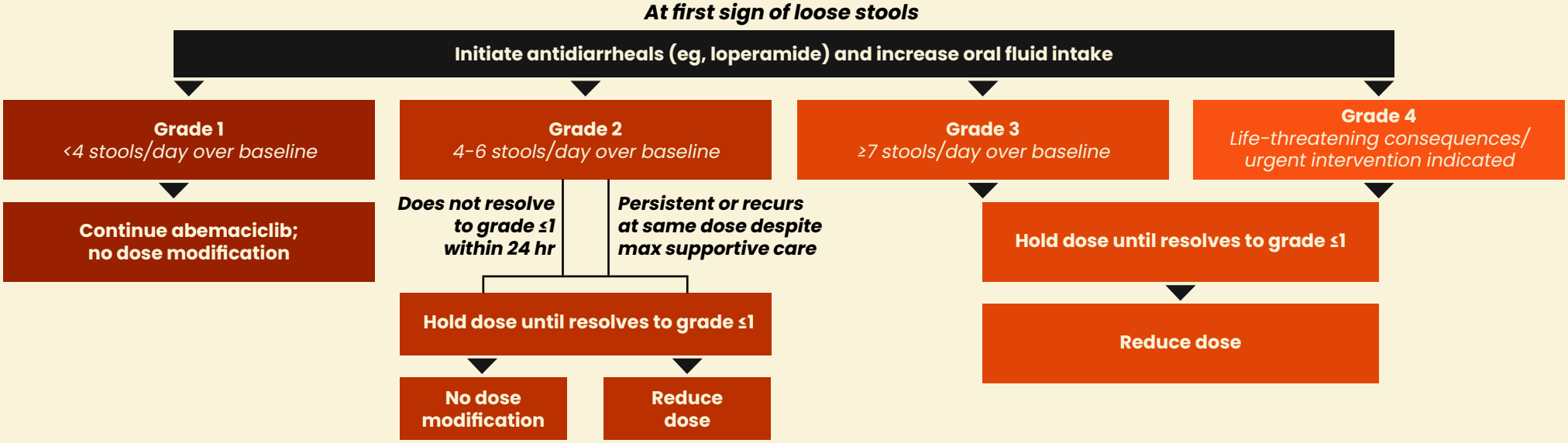
Managing CDK4/6 Inhibitor–Induced Neutropenia

- Neutropenia managed the same in early and advanced settings
- Generally reversible

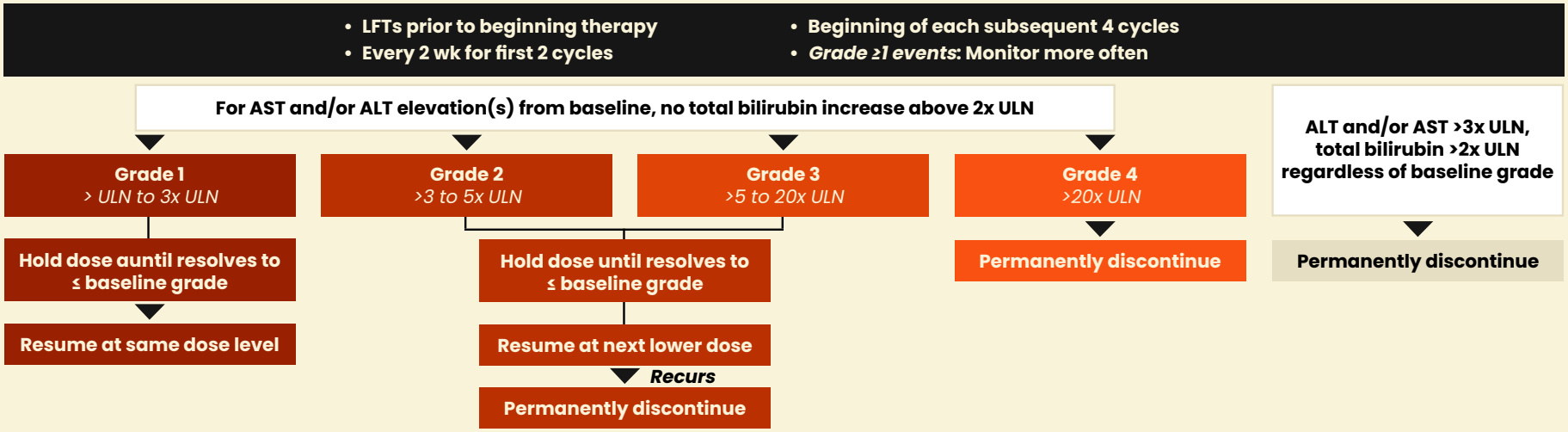


Managing Abemaciclib-Induced Diarrhea

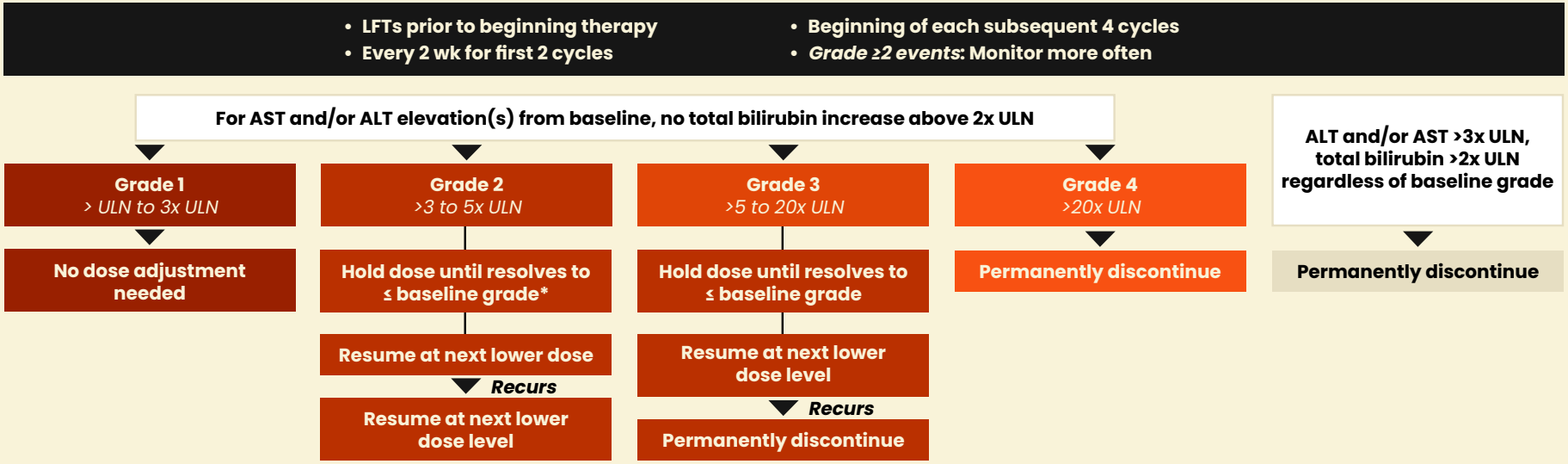
- Most patients experienced diarrhea during the first month of treatment; the median time to onset of the first diarrhea event ranged from 6-8 days



Managing Ribociclib-Induced Hepatotoxicity in Early-Stage BC



Managing Ribociclib-Induced Hepatotoxicity in Advanced BC



*Baseline at grade 2: no dose interruption.

Recommended Dose Reductions With CDK4/6 Inhibitors

	Abemaciclib		Palbociclib	Ribociclib	
	Combination	Monotherapy	Tablets or Capsules	EBC	Advanced or MBC
Recommended starting dose	150 mg BID	200 mg BID	125 mg QD	400 mg QD	600 mg QD
First dose reduction	100 mg BID	150 mg BID	100 mg QD	200 mg QD	400 mg QD
Second dose reduction	50 mg BID	100 mg BID	75 mg QD	Discontinue	200 mg QD
Third dose reduction	Discontinue	50 mg BID	Discontinue	Discontinue	Discontinue

Approved Oral SERDs and PROTACs: Indications, Dosing, and Administration

	Indications	Dosing	Administration	Warnings and Precautions
Oral SERDs				
Elacestrant	Treatment of postmenopausal women or adult men with ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic BC with disease progression following at least 1 line of ET	345 mg PO QD	Tablets: With food	• Dyslipidemia • Embryo-fetal toxicity
Imlunestrant	Treatment of adults with ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic BC with disease progression following at least 1 line of ET In combination with abemaciclib for the treatment of adult patients with HR-positive/HER2-negative, *ESR1*-mutated advanced or metastatic BC with disease progression following ET	400 mg PO QD	Tablets: without food	• Embryo-fetal toxicity
Camizestrant	In combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) for the treatment of adults with HR-positive, HER2-negative advanced or metastatic BC upon detection of *ESR1* mutation during AI + CDK4/6 inhibitor therapy	75 mg PO QD	Tablets: with or without food	• QTc interval prolongation [Black Box Warning] • Bradycardia • Embryo-fetal toxicity
PROTAC				
Vepdegestrant	Treatment of adults with estrogen ER-positive, HER2-negative, *ESR1*-mutated advanced or metastatic BC with disease progression following at least 1 line of ET	200 mg PO QD	Tablets: With food	• QTc interval prolongation • Embryo-fetal toxicity

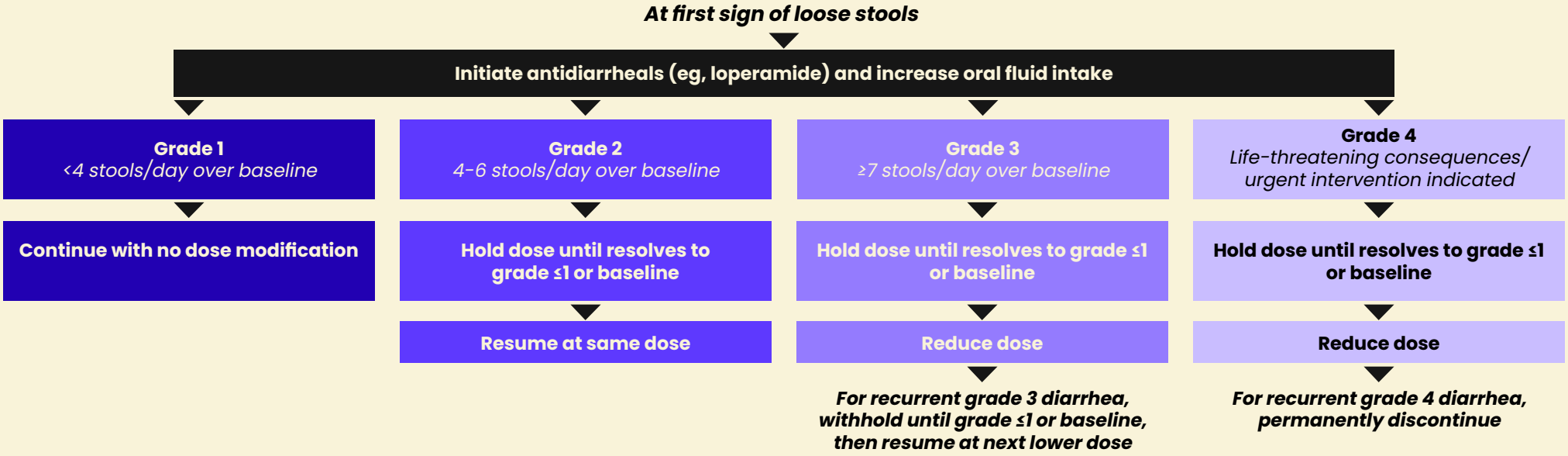
Emerging Oral SERDs

- Giredestrant: As of August 2026, giredestrant is under FDA review as adjuvant therapy for ER-positive/HER2-negative stage I-III breast cancer and, in combination with everolimus, for previously treated *ESR1*-mutated ER-positive/HER2-negative locally advanced or metastatic breast cancer. FDA decisions are expected by November 30 and December 18, 2026, respectively.

Oral SERD Adverse Event Considerations

Warning/Precautions	Recommendation			
Dyslipidemia	Monitor lipid profile before initiating treatment and periodically, as clinically indicated			
Hepatic Impairment	**Elacestrant**	**Imlunestrant**	**Camizestrant** + ribociclib	**Camizestrant** + abemaciclib or palbociclib
Moderate (Child-Pugh B)	Reduce the dosage to 258 mg once daily	Reduce dosage to 200 mg once daily	No adjustment needed	No adjustment needed
Severe hepatic impairment (Child-Pugh C)	Avoid use	Reduce dosage to 200 mg once daily	Reduce camizestrant dosage to 75 mg *every other day*	No adjustment needed

Management of Diarrhea With Elacestrant and Imlunestrant



Camizestrant QTc Interval Prolongation

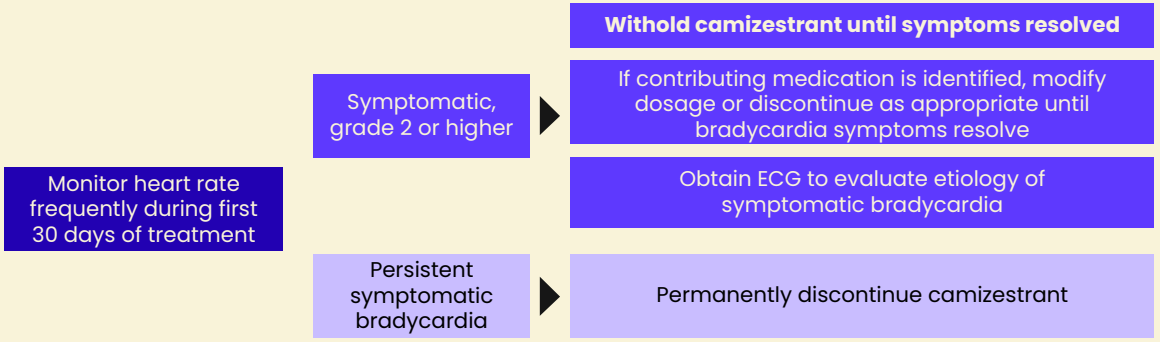
Black Box Warning: Arrhythmia risk with concomitant use of QTc interval prolonging drugs

- Camizestrant in combination with ribociclib, a QTc interval prolonging drug and a strong CYP3A inhibitor, or in combination with other QTc interval prolonging drugs, can increase the risk of Torsades de Pointes, other ventricular arrhythmias, and sudden death
- Avoid concomitant use of camizestrant with products (other than ribociclib) known to prolong the QTc interval and/or have a known risk of Torsades de Pointes. If concomitant use with other products cannot be avoided, monitor the QTc interval more frequently
- Obtain ECG prior to initiation and monitor heart rate and QTc interval during treatment. Assess and correct electrolyte abnormalities prior to initiation and during treatment. Withhold camizestrant until resolution of QTc interval prolongation and resume or permanently discontinue camizestrant based on severity

QTc Prolongation	Dose Modification and Management
QTc >500 or >480 ms and prolongation from baseline >60 ms	• Hold until QTc resolves to ≤480 ms • Identify and treat reversible causes (eg, hypokalemia and hypomagnesemia) • Re-assess eCGs weekly for the first two weeks of treatment and periodically during treatment as clinically indicated
QTc >500 or >60 ms change from baseline **and** associated with: Torsade de Pointes, polymorphic ventricular tachycardia, or serious arrhythmia	• Permanently discontinue

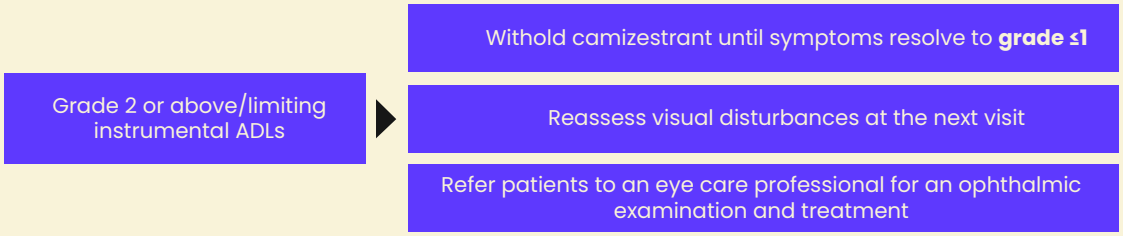
Camizestrant Monitoring and Management of Bradycardia

- Monitor heart rate more frequently during the first 30 days of treatment with camizestrant in patients with bradycardia (resting heart rate <60 bpm) at baseline and those on concomitant medications known to lower heart rate



Camizestrant Visual Disturbances

- Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia and visual perseveration.
- Among patients who reported experiencing a visual disturbance while receiving camizestrant + a CDK4/6 inhibitor, episodes were typically < 1 minute and occurred < 3 days per week



Vepdegestrant QTc Interval Prolongation

- Monitor ECGs and electrolytes prior to initiation of treatment
- Correct hypokalemia and hypomagnesemia prior to and during treatment
- Repeat ECG approximately 4 wk after initiating treatment and as clinically indicated

QTc Prolongation	Dose Modification and Management
QTc >480 ms or >60 ms increase from baseline (and QTc ≤500 ms)	• Withhold until QTc resolves to ≤480 ms and ≤60 ms above baseline, then resume vepdegestrant at the same dose • Identify and treat reversible causes (eg, hypokalemia and hypomagnesemia) • Initiate more frequent ECG monitoring
QTc >500 ms	• Withhold until QTc resolves to ≤480 ms and ≤60 ms above baseline, then: ○ Resume at the same dose if reversible cause is identified and corrected (eg, hypokalemia and hypomagnesemia) ○ Resume at the reduced dose if no reversible cause is identified • Initiate more frequent ECG monitoring • Permanently discontinue if QTc >500 ms recurs
Torsade de pointes, polymorphic ventricular tachycardia, or signs/ symptoms of serious arrhythmia	• Permanently discontinue

Recommended Dose Reductions With Oral SERDS and PROTACS

	Elacestrant	Imlunestrant	Camizestrant	Vepdegestrant
Recommended starting dose	345 mg QD	400 mg QD	75 mg QD	200 mg QD
First dose reduction	258 mg QD	200 mg PO QD	Not Recommended	100 mg QD
Second dose reduction	172 mg QD	Discontinue	Not Recommended	Discontinue

Approved Oral PI3K/AKT Pathway Inhibitors: Indications, Dosing, and Administration

	Indications	Dosing	Administration	Warnings and Precautions
Alpelisib	In combination with fulvestrant for the treatment of adults with HR-positive/HER2-negative, *PIK3CA*-mutated, advanced or metastatic BC following progression on or after an endocrine-based regimen	300 mg PO QD	Tablets: With food	• Severe hypersensitivity • SCARs • Hyperglycemia • Pneumonitis • Diarrhea or colitis • Embryo-fetal toxicity
Capivasertib	In combination with fulvestrant for the treatment of adult patients with HR-positive/HER2-negative advanced or metastatic BC with 1 or more *PIK3CA/AKT1/PTEN* alteration following progression on at least 1 endocrine-based regimen in the metastatic setting or recurrence on or within 12 mo of completing adjuvant therapy	400 mg PO BID x 4 days followed by 3 days off	Tablets: With or without food	• Hyperglycemia • Diarrhea • Cutaneous adverse reactions • Embryo-fetal toxicity
Inavolisib	In combination with palbociclib and fulvestrant for the treatment of adults with endocrine-resistant, *PIK3CA*-mutated, HR-positive/HER2-negative advanced or metastatic BC following recurrence on or after completing adjuvant endocrine therapy	9 mg PO QD	Tablets: With or without food	• Hyperglycemia • Stomatitis • Diarrhea • Embryo-fetal toxicity

Oral PI3K and AKT Inhibitors Toxicity Overview

Adverse Event	Incidence	Time to Onset (Median)	Monitoring/Management
Hyperglycemia	Grade 3/4: alpelisib > inavolisib > capivasertib	1-2 wk	• Monitor fasting glucose levels and A1C (see PI for specific monitoring for each agent) • Consider prophylactic metformin (based on results of METALLICA trial) • Insulin sensitizers (eg, metformin) preferable to insulin secretagogues (eg, sulfonylurea)
Stomatitis	Grade 3/4: inavolisib > alpelisib > capivasertib	2 wk	• Consider corticosteroid-containing mouthwash as prophylaxis
Rash	Grade 3/4: alpelisib > capivasertib > inavolisib	2-4 wk	• Topical steroids (3-4x daily) and oral antihistamines recommended for treatment • Consider prophylaxis with oral nonsedating antihistamine
Diarrhea	Grade 3/4: inavolisib > alpelisib > capivasertib	8 days (capivasertib), 15 days (inavolisib), 46 days (alpelisib)	• Supportive medications (such as loperamide PRN)

Hyperglycemia Management

- Ensure proactive monitoring, consider prophylactic metformin

Grade 1: FBG > ULN to 160 mg/dL or A1C >7% (for capivasertib)	**Alpelisib, capivasertib, and inavolisib:** continue and initiate or intensify antihyperglycemic regimen
Grade 2: FBG >160-250 mg/dL	**Alpelisib:** continue; if FBG does not decrease to ≤160 mg/dL within 21 days, reduce dose by 1 level **Capivasertib:** hold until FBG ≤160 mg/dL; if recovery in ≤28 days, resume at same dose, but if >28 days, resume at 1 lower dose **Inavolisib:** hold until FBG ≤160 mg/dL, then resume at same dose; if FBG persists >200-250 mg/dL for 7 days, consider endocrine consult
Grade 3: FBG >250-500 mg/dL	**Alpelisib:** hold; if FBG ≤160 mg/dL within 3-5 days, resume at reduced dose; if not resolved within 21 days, permanently d/c **Capivasertib:** hold until FBG ≤160 mg/dL; if recovery occurs ≤28 days, resume at 1 lower dose, but if >28 days, permanently d/c **Inavolisib:** hold; if FBG ≤160 mg/dL within 7 days, resume at same dose; if FBG ≤160 mg/dL in ≥8 days, resume at 1 lower dose; if FBG >250-500 mg/dL recurs within 30 days, hold until ≤160 mg/dL, then resume at 1 lower dose
Grade 4: FBG >500 mg/dL	**Alpelisib:** hold; if FBG ≤500 mg/dL, follow recommendations for grade 3; if FBG confirmed at >500 mg/dL, permanently d/c **Capivasertib:** hold; if life-threatening sequelae or if FBG persists at ≥500 mg/dL after 24 hr, permanently d/c; if FBG ≤500 m/dL within 24 hr, follow guidance as above for relevant grade **Inavolisib:** hold; if FBG ≤160 mg/dL, resume at 1 lower dose; if FBG >500 mg/dL recurs within 30 days, permanently d/c

Recommended Dose Reductions With Oral PI3K/AKT Pathway Inhibitors

	Alpelisib	Capivasertib	Inavolisib
Recommended starting dose	300 mg QD	400 mg BID x 4 days followed by 3 days off	9 mg QD
First dose reduction	250 mg QD	320 mg BID x 4 days followed by 3 days off	6 mg QD
Second dose reduction	200 mg QD	200 mg BID x 4 days followed by 3 days off	3 mg QD

References

- Abemaciclib PI.
- Alpelisib PI.
- Camizestrant PI
- Capivasertib PI.
- Elacestrant PI
- Imlunestrant PI.
- Inavolisib PI.
- Palbociclib PI.
- Ribociclib PI.
- Vepdegestrant PI.

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