For postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer (aBC or MBC), in combination with fulvestrant following progression on or after an endocrine-based regimen

Managing your patient on PIQRAY

Strategies for managing cutaneous adverse reactions, hyperglycemia, and other selected adverse reactions

Using this brochure

This brochure is designed to provide guidance on dose modifications and management of selected adverse reactions (ARs). It does not cover all ARs associated with PIQRAY® (alpelisib) tablets therapy. The management strategies presented here do not constitute medical advice and are not intended to take the place of your own clinical judgment based on each patient's particular presentation. Please refer to the full Prescribing Information for fulvestrant for dose modification guidelines and for relevant safety information.

PIQRAY®
(alpelisib) tablets
50 mg · 150 mg · 200 mg

The first and only therapy specifically for aBC patients with a PIK3CA mutation

Content is consistent with the Oncology Nursing Society Standards and Guidelines. The ONS Seal of Approval does not constitute medical advice, and does not imply product endorsement by ONS. Healthcare providers should exercise their own independent medical judgment. Website content or other resources referenced in these materials have not been reviewed for the ONS Seal of Approval.

Indication

PIQRAY® (alpelisib) tablets is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

Important Safety Information

PIQRAY is contraindicated in patients with severe hypersensitivity to it or any of its components.

Severe Hypersensitivity: Severe hypersensitivity reactions, including anaphylaxis and anaphylactic shock, can occur in patients treated with PIQRAY. Severe hypersensitivity reactions were manifested by symptoms including, but not limited to, dyspnea, flushing, rash, fever, or tachycardia. The incidence of grade 3 and 4 hypersensitivity reactions was 0.7%. Advise patients of the signs and symptoms of severe hypersensitivity reactions. Permanently discontinue PIQRAY in the event of severe hypersensitivity.

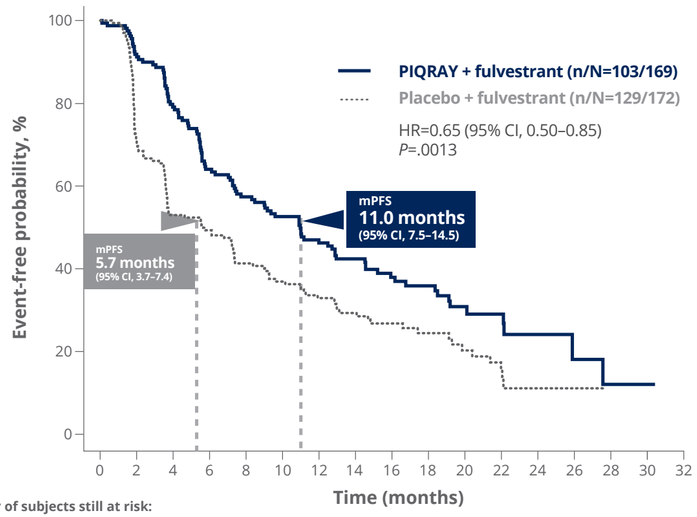
Please see additional Important Safety Information throughout and on pages 12-13.
Please click here for full Prescribing Information.

PIQRAY is **the first and only** therapy specifically for aBC patients with a PIK3CA mutation

~40%

of patients with HR+/HER2- aBC have a PIK3CA mutation[1-4]

Nearly doubled mPFS in patients with a PIK3CA mutation[5,6]



SOLAR-1 is a double-blind, placebo-controlled, multicenter phase 3 study in men and postmenopausal women with HR+/HER2- aBC or MBC with or without a PIK3CA mutation whose disease had progressed or recurred on or after AI-based treatment (N=572). In the PIK3CA mutation cohort (n=341), patients were randomized 1:1 to receive PIQRAY® (alpelisib) tablets 300 mg tablets orally once daily + fulvestrant 500 mg IM* or placebo + fulvestrant 500 mg IM.* The primary endpoint was PFS in patients with a PIK3CA mutation by investigator assessment per RECIST v1.1.

AI, aromatase inhibitor; PFS, progression-free survival; mPFS, median progression-free survival.

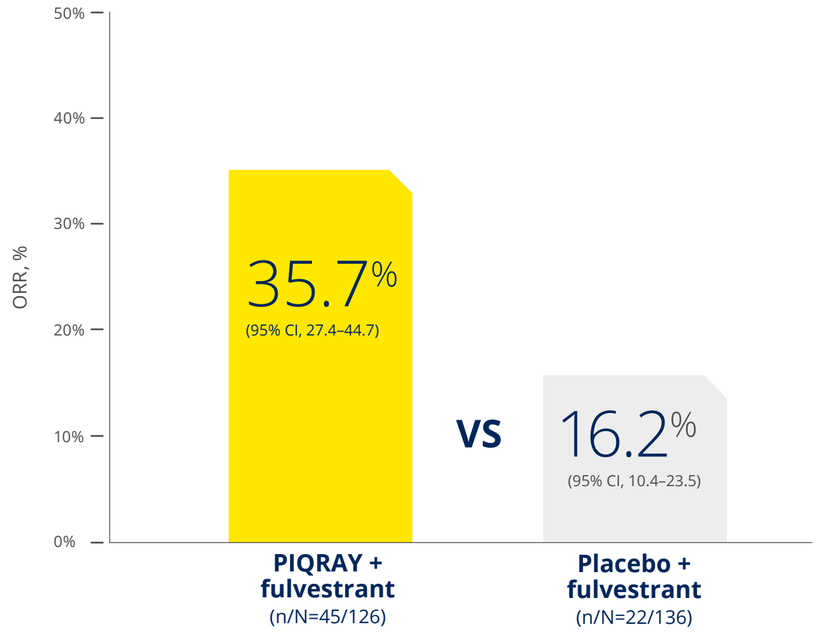
*Fulvestrant given on day 1 and day 15 of the first 28-day cycle, then day 1 of subsequent 28-day cycles.

Important Safety Information

Severe Cutaneous Adverse Reactions (SCARs): SCARs including Stevens-Johnson syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with PIQRAY. In the SOLAR-1 study, SJS and EM were reported in 0.4% and 1.1% of patients, respectively. DRESS was reported in patients in the postmarketing setting. If signs or symptoms of SCARs occur, interrupt PIQRAY until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended.

More than doubled the response rate[5,6]

Overall response rate (ORR) in patients with a PIK3CA mutation who had measurable disease[5,6]



ORR was defined as the percentage of subjects with confirmed complete response or partial response. Measurable disease was defined as the presence of at least one measurable nodal or non-nodal lesion as per RECIST v1.1 criteria.

Test for PIK3CA mutations to inform an up-front treatment plan.*
Information on FDA-approved tests for the detection of PIK3CA mutations in breast cancer is available at **www.fda.gov/CompanionDiagnostics**

*Test for PIK3CA mutations when an HR+/HER2- aBC patient presents with metastases from breast cancer following progression on or after an endocrine-based regimen.

Important Safety Information (cont)

Severe Cutaneous Adverse Reactions (SCARs) (cont): If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy).

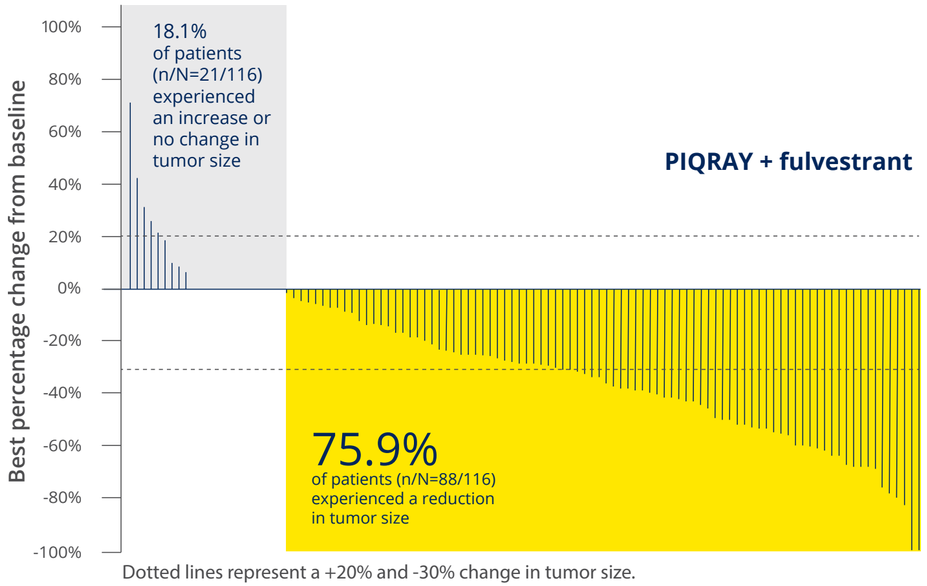
Please see additional Important Safety Information throughout and on pages 12-13. Please click here for full Prescribing Information.

PIQRAY® (alpelisib) tablets
50 mg · 150 mg · 200 mg

Additional results: tumor shrinkage and quality of life

Tumor shrinkage observed in 3 out of 4 patients with a PIK3CA mutation[7]

Best percentage change in tumor size in patients with a PIK3CA mutation[7]



Dotted lines represent a +20% and -30% change in tumor size.

Reduction in tumor size was defined as any amount of tumor shrinkage from baseline. Results are based on best percentage change from baseline in sum of diameters per investigator assessment in the cohort with a PIK3CA mutation where only subjects with measurable disease at baseline are presented. Results reported were not prespecified and are observational in nature; as such, there was no prespecified statistical procedure controlling for type 1 error. Subjects for whom the best percentage change in target lesions was not available or was contradicted by an unknown overall lesion response were excluded from the analysis. Percent change in target lesion was contradicted by an overall lesion response of progressive disease in 6.0% of patients in the PIQRAY® (alpelisib) tablets + fulvestrant arm. A total of 43.5% (n/N=57/131) of patients in the placebo + fulvestrant arm experienced a reduction in tumor size.

During treatment, the EORTC QLQ-C30 global health status/QoL scores were similar in both arms in the PIK3CA mutant cohort[7]

- There was no difference between the two treatment arms in time to 10% deterioration (TTD) in EORTC QLQ-C30 global health/QoL status (HR=1.03; 95% CI, 0.72-1.48)[7]*†

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer core QoL questionnaire; QoL, quality-of-life.
*The EORTC QLQ-C30 was one of the questionnaires used to assess the secondary endpoint of health-related QoL.
†TTD was defined as a worsening in score by at least 10% compared to baseline, with no later improvement above this threshold observed during the treatment period, or death due to any cause.

Please see additional Important Safety Information throughout and on pages 12-13. Please click here for full Prescribing Information.

Safety profile

Serious ARs associated with PIQRAY include severe hypersensitivity, severe cutaneous adverse reactions (SCARs), hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.[5]

ARs occurring in >20% of the total population[5]

ARs	PIQRAY + fulvestrant (n=284)		Placebo + fulvestrant (n=287)	
	All grades (%)	Grade 3-4 (%)	All grades (%)	Grade 3-4 (%)
Gastrointestinal disorders				
Diarrhea	58	7*	16	0.3*
Nausea	45	2.5*	22	0.3*
Stomatitis[a]	30	2.5*	6	0*
Vomiting	27	0.7*	10	0.3*
General disorders and administration site conditions				
Fatigue[b]	42	5*	29	1*
Investigations				
Weight decreased	27	3.9*	2.1	0*
Metabolism and nutrition disorders				
Decreased appetite	36	0.7*	10	0.3*
Skin and subcutaneous tissue disorders				
Rash[c]	52	20*	7	0.3*

*No grade 4 ARs were reported.
[a]Including stomatitis, aphthous ulcer, mouth ulceration.
[b]Including fatigue, asthenia.
[c]Including rash, rash maculopapular, rash macular, rash generalized, rash papular, rash pruritic.

Laboratory abnormalities occurring in >30% of the total population[5]

Laboratory abnormality	PIQRAY + fulvestrant (n=284)		Placebo + fulvestrant (n=287)	
	All grades (%)	Grade 3-4 (%)	All grades (%)	Grade 3-4 (%)
Hematological parameters				
Lymphocyte count decreased	52	8	40	4.5†
Hemoglobin decreased	42	4.2†	29	1†
Biochemical parameters				
Glucose increased[a]	79	39	34	1
Creatinine increased	67	2.8†	25	0.7†
Gamma Glutamyl Transferase (GGT) increased	52	11	44	10
Alanine Aminotransferase (ALT) increased	44	3.5	34	2.4†
Lipase increased	42	7	25	6

[a]Glucose increase is an expected laboratory abnormality of PI3K inhibition.
†No Grade 4 laboratory abnormalities were reported.

- Among patients treated with PIQRAY and fulvestrant, 5% permanently discontinued both therapies and 21% permanently discontinued PIQRAY alone due to ARs[5]
- Dose reductions due to ARs occurred in 55% of patients receiving PIQRAY and fulvestrant[5]
  - The most common ARs leading to a dose reduction of PIQRAY were hyperglycemia (29% of patients), rash (9%), diarrhea (6%), stomatitis (4%), and mucosal inflammation (2%)[5]

The most common ARs leading to treatment discontinuation of PIQRAY in patients receiving PIQRAY + fulvestrant were[5]:

Hyperglycemia (6%) | Rash (4%) | Diarrhea (3%) | Fatigue (3%)

PIQRAY® (alpelisib) tablets
50 mg • 150 mg • 200 mg

Before treatment with PIQRAY

Antihistamines administered prior to rash onset may decrease incidence and severity of rash based on SOLAR-1 trial[5]

- A subgroup of 86 patients received prophylaxis, including antihistamines (eg, cetirizine), prior to onset of rash[5]
- In these patients, rash was reported less frequently than in the overall population as shown in the table below[5]

Effects of prophylactic treatment, including antihistamines, prior to onset of rash in patients receiving PIQRAY + fulvestrant[5]

Event	Patients receiving prophylactic treatment prior to onset of rash (n=86)	Overall population (n=284)
All grades rash	27%	54%
Grade 3 rash	12%	20%
Rash leading to permanent discontinuation of PIQRAY® (alpelisib) tablets	3.5%	4.2%

Please see additional Important Safety Information throughout and on pages 12-13.

Please click here for full Prescribing Information.

During treatment with PIQRAY

Advise patients of signs and symptoms of severe cutaneous adverse reactions (SCARs) and to immediately contact their health care provider should they occur[5]

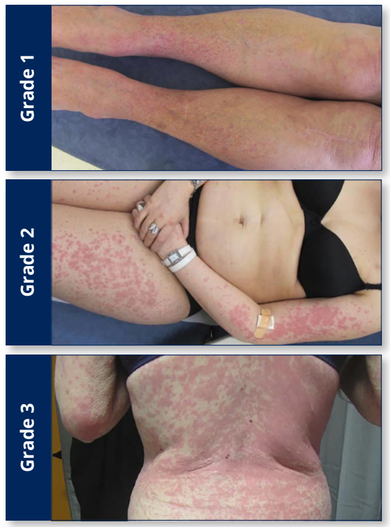
- Signs and symptoms include a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash or lymphadenopathy[5]

Monitor for different forms of rash

- Rash may present in different forms including rash, rash maculopapular, rash macular, rash generalized, rash papular, and rash pruritic[5]
- Maculopapular rash was reported as one of the most common types of rash[7]

Examples of maculopapular rash[8]
(photos are not from the SOLAR-1 trial)

Flat, red area covered with small confluent bumps[8]



Images provided by Prof. Dr. Siegfried Segaert (University Hospital Leuven, Leuven, Belgium).

SOLAR-1

12 days (range: 2-220 days)[7]

Median time to first onset of grade 2 or 3 rash[5]

If severe cutaneous adverse reactions (SCARs) or rash occur

SCARs in SOLAR-1 and postmarketing setting

- In the SOLAR-1 trial, Stevens-Johnson syndrome (SJS) and erythema multiforme (EM) were reported in 0.4% and 1.1% of the patients, respectively. Drug reaction with eosinophilia and systemic symptoms (DRESS) was reported in the postmarketing setting[5]

Rash in the SOLAR-1 trial

- Most events of rash were mild to moderate (grade 1 or 2). 52% of patients experienced all-grade rash with 20% reporting grade 3[5]

If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCAR during PIQRAY treatment[5]

Dose modifications and management for rash and SCARs[5]

Assess grade*†	Initial dose modification	Administer medical management‡	Monitor and implement as clinically appropriate
Grade 1 (<10% body surface area [BSA] with active skin toxicity)	No PIQRAY dose adjustment **If the etiology is SCAR,** permanently discontinue PIQRAY	Initiate topical corticosteroid treatment Consider adding oral antihistamine to manage symptoms	
Grade 2 (10%-30% BSA with active skin toxicity)	No PIQRAY dose adjustment **If the etiology is SCAR,** permanently discontinue PIQRAY	Initiate or intensify topical corticosteroid and oral antihistamine treatment Consider low-dose systemic corticosteroid treatment	
Grade 3 (eg, severe rash not responsive to medical management) (>30% BSA with active skin toxicity)	**If the etiology is not SCAR,** interrupt PIQRAY **If the etiology is SCAR,** permanently discontinue PIQRAY	Initiate or intensify topical/ systemic corticosteroid and oral antihistamine treatment	**If the etiology is not SCAR:** Once improved to ≤ grade 1, resume PIQRAY at the same dose level for first occurrence of rash, or at next lower dose level in case of second occurrence
Grade 4 (eg, severe bullous, blistering, or exfoliating skin conditions) (any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences)	Permanently discontinue PIQRAY		

*Grading according to CTCAE version 5.0.
†For all grades of rash, consider consultation with a dermatologist.
‡Antihistamines administered prior to rash onset may decrease incidence and severity of rash based on the SOLAR-1 trial.

Examples of medication used to manage rash in the SOLAR-1 trial[7,a]

Topical corticosteroids
- Triamcinolone 3x-4x daily
- Betamethasone 3x-4x daily

Oral antihistamines
- Diphenhydramine 25-50 mg 3x daily
- Hydroxyzine 25 mg 3x-4x daily
- Fexofenadine 180 mg daily or 60 mg 3x daily
- Cetirizine

Low-dose oral corticosteroids
- Prednisone 20-40 mg daily or equivalent

[a]The management plan of each patient should be based on the individual benefit/risk assessment.

92% (141/153)

of patients who experienced rash had resolution of rash[5]

PIQRAY® (alpelisib) tablets
50 mg • 150 mg • 200 mg

Before treatment with PIQRAY

Assess FPG and HbA1c[5]

Optimize blood glucose[5]

- In the SOLAR-1 trial, patients with controlled type 2 diabetes and prediabetes were included if they had an FPG of ≤140 mg/dL (7.7 mmol/L) and HbA1c ≤6.4% (both criteria had to be met)[7]

FPG, fasting plasma glucose; HbA1c, hemoglobin A1c.

Assess patient's past medical history

- The safety of PIQRAY® (alpelisib) tablets in patients with type 1 and uncontrolled type 2 diabetes has not been established as these patients were excluded from the SOLAR-1 trial. Patients with a medical history of type 2 diabetes were included[5]
- Patients with a history of diabetes mellitus may require intensified diabetic treatment. Closely monitor patients with diabetes

Glucose increase, including hyperglycemia, is an expected, on-target effect of PI3K inhibition[5,9]

In the SOLAR-1 trial

- Hyperglycemia was reported in 65% of patients treated with PIQRAY. Grade 3 and grade 4 hyperglycemia was reported in 33% and 3.9% of patients, respectively[5]
- Glucose increased (all grades) was reported in 79% of patients treated with PIQRAY + fulvestrant[5]

Please see additional Important Safety Information throughout and on pages 12-13.

Please click here for full Prescribing Information.

During treatment with PIQRAY

Advise patients of signs and symptoms of hyperglycemia and to contact their health care provider immediately should they occur[5]

- Signs and symptoms include excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss[5]

Monitor for hyperglycemia throughout your patient's treatment

- The only laboratory monitoring needed for patients on PIQRAY is for fasting glucose (FPG or fasting blood glucose) and HbA1c[5]

Fasting glucose

When monitoring fasting glucose, measure FPG or fasting blood glucose

First 2 weeks
At least 1x per week[5]

After first 2 weeks
At least once every 4 weeks and as clinically indicated for the duration of treatment[5]

HbA1c

Duration of treatment
Once every 3 months and as clinically indicated[5]

SOLAR-1

15 days (range: 5-517 days)[5]

Median time to first occurrence of grade ≥2 (FPG 160-250 mg/dL) hyperglycemia[5]

Median time to improvement* of grade ≥2 hyperglycemia (n=153) was 8 days (range: 2-65 days)[5]

*Improvement by at least 1 grade from time of first event.

If hyperglycemia occurs
Hyperglycemia was generally manageable and reversible

In the SOLAR-1 trial

- **87% (163/187) of patients with hyperglycemia were managed with antihyperglycemic medication[5]**
  - Most patients (76%, 142/187) reported use of metformin as a single agent or in combination with other antihyperglycemic medication* (ie, insulin, dipeptidyl peptidase-4 [DPP-4] inhibitors, and sulfonylureas)[5]
- **Among patients with elevated FPG who continued fulvestrant treatment after discontinuing PIQRAY (n=54), 96% (n=52) of patients had FPG levels that returned to baseline[5]**

*The maximum dose of metformin allowed in SOLAR-1 was 2000 mg per day.

Dose modifications and management should only be based on fasting glucose values (FPG or fasting blood glucose)[5]

Dose modifications and management for hyperglycemia[1,2]

Assess grade†	Initial dose modification	Administer medical management	Monitor and implement as clinically appropriate
Grade 1 Fasting glucose >ULN-160 mg/dL	No PIQRAY dose adjustment	Initiate or intensify antihyperglycemic treatment[a]	
Grade 2 Fasting glucose >160-250 mg/dL	No PIQRAY dose adjustment	Initiate or further intensify antihyperglycemic treatment[a]	**If fasting glucose does not decrease to ≤160 mg/dL within 21 days under appropriate antihyperglycemic treatment:** → Reduce dose by 1 level and follow fasting glucose value-specific recommendations
Grade 3 >250-500 mg/dL	Interrupt PIQRAY	Initiate or intensify oral antihyperglycemic treatment[a] and consider additional antihyperglycemic medications[b] for 1-2 days until hyperglycemia improves Administer IV hydration and consider appropriate treatment including intervention for electrolyte/ ketoacidosis/hyperosmolar disturbances	**If fasting glucose decreases to ≤160 mg/dL within 3-5 days under appropriate antihyperglycemic treatment:** → Resume at 1 lower dose level **If fasting glucose does not decrease to ≤160 mg/dL within 3-5 days under appropriate antihyperglycemic treatment:** → Consultation with a physician with expertise in the treatment of hyperglycemia is recommended **If fasting glucose does not decrease to ≤160 mg/dL within 21 days following appropriate antihyperglycemic treatment[a]:** → Permanently discontinue
Grade 4 >500 mg/dL	Interrupt PIQRAY	Initiate or intensify appropriate antihyperglycemic treatment[a] Administer IV hydration and consider appropriate treatment including intervention for electrolyte/ketoacidosis/ hyperosmolar disturbances	**Re-check fasting glucose within 24 hours and as clinically indicated** **If fasting glucose decreases to ≤500 mg/dL within 24 hours:** → Follow fasting glucose value-specific recommendations for grade 3 **If fasting glucose is confirmed at >500 mg/dL:** → Permanently discontinue

CTCAE, Common Terminology Criteria for Adverse Events; ULN, upper limit of normal.
†FPG/fasting blood glucose/grade levels reflect hyperglycemia grading according to CTCAE version 4.03.
[a]Initiate applicable antihyperglycemic medications, including metformin and insulin sensitizers (such as thiazolidinediones or DPP-4 inhibitors), and review respective prescribing information for dosing and dose titration recommendations, including local diabetic treatment guidelines. See below for metformin recommendations from SOLAR-1.
[b]As recommended in the SOLAR-1 clinical trial, insulin may be used for 1 to 2 days until hyperglycemia resolves. However, this may not be necessary in the majority of PIQRAY-induced hyperglycemia, given the short half-life of PIQRAY and the expectation of glucose levels normalizing after interruption of PIQRAY.

Adjust monitoring schedule

If a patient experiences hyperglycemia
Monitor fasting glucose as clinically indicated and ***at least 2x per week*** until fasting glucose decreases to normal levels.[5]
Consider consultation with a health care provider with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.[5]

During treatment with antihyperglycemic medication

First 8 weeks
Monitor fasting glucose at least 1x per week[5]

After first 8 weeks
Monitor fasting glucose every 2 weeks and as clinically indicated[5]

In SOLAR-1, metformin was recommended with the following guidance if hyperglycemia occurred[5]

1. Initiate metformin 500 mg once daily
2. Increase dose to 500 mg twice daily, based on tolerability
3. Increase dose to 500 mg with breakfast and 1000 mg with dinner, based on tolerability
4. Increase dose to 1000 mg twice daily if needed, based on tolerability

Other insulin sensitizers such as thiazolidinediones or DPP-4 inhibitors can also be used as antihyperglycemic treatment.

Management in the event of diarrhea and other toxicities

In the SOLAR-1 trial

- Most patients (58%) experienced diarrhea during treatment with PIQRAY® (alpelisib) tablets[5]
- Grade 3 diarrhea occurred in 7% (n=19) of patients. Among patients with grade 2 or 3 diarrhea (n=71), the median time to onset was 46 days (range: 1-442 days)[5]

Dose modifications and management for diarrhea[5]

Grade*	Modify dose	Administer medical management and monitor as clinically indicated
Grade 1	No PIQRAY dose adjustment	Initiate appropriate medical therapy and monitor as clinically indicated
Grade 2	Interrupt PIQRAY dose until recovery to grade ≤1, then resume PIQRAY at same dose level	Initiate or intensify appropriate medical therapy and monitor as clinically indicated
Grades 3 + 4	Interrupt PIQRAY dose until recovery to grade ≤1, then resume PIQRAY at the next lower dose level	Initiate or intensify appropriate medical therapy and monitor as clinically indicated

*Grading according to CTCAE version 5.0.

Dose modifications and management for other toxicities[5]

Grade†	Modify dose	Administer medical management and monitor as clinically indicated
Grades 1 or 2	No PIQRAY dose adjustment[a,b]	Initiate appropriate medical therapy and monitor as clinically indicated
Grade 3	Interrupt PIQRAY dose until recovery to grade ≤1, then resume PIQRAY at the next lower dose level	
Grade 4	Permanently discontinue PIQRAY	

†Grading according to CTCAE version 5.0.
[a]For grade 2 and 3 pancreatitis, interrupt PIQRAY dose until recovery to grade <2 and resume at next lower dose level. Only one dose reduction is permitted. If toxicity reoccurs, permanently discontinue PIQRAY treatment.
[b]For grade 2 total bilirubin elevation, interrupt PIQRAY dose until recovery to grade ≤1 and resume at the same dose if resolved in ≤14 days or resume at the next lower dose level if resolved in >14 days.

Refer to the full Prescribing Information of fulvestrant for dose modification guidelines and for other relevant safety information.

Dosing and administration

PIQRAY is given in combination with fulvestrant[5,6]

PIQRAY
Starting dose: 300 mg daily
(Two 150-mg tablets)

Once-daily continuous oral dosing
Should be swallowed whole and taken with food, at approximately the same time each day*

+

FULVESTRANT
Recommended dose: 500 mg

Administered on days 1, 15, and 29, and once monthly thereafter
Please refer to the full Prescribing Information for fulvestrant

Continue treatment until disease progression or unacceptable toxicity occurs

*Tablets should not be chewed, crushed, or split prior to swallowing. No tablet should be ingested if it is broken, cracked, or otherwise not intact.

Certain ARs may require dose modifications[5]

- Dose interruptions may be required prior to dose reductions[5]
- The PIQRAY dose may be reduced in increments of 50 mg[5,†]
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY[5]

Please refer to the full Prescribing Information for dose interruption, reduction, or discontinuation of PIQRAY in specific ARs. The management plan of each patient should be based on the individual benefit/risk assessment.

†Only one dose reduction is permitted for pancreatitis.

Blister pack is designed to help patients stay on track with treatment

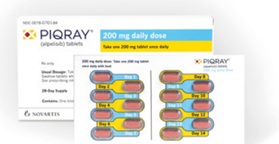
300 mg
(Two 150-mg tablets once daily)

NDC 0078-0708-02

250 mg
(One 200-mg tablet + one 50-mg tablet once daily)

NDC 0078-0715-02

200 mg
(One 200-mg tablet once daily)



NDC 0078-0701-84

Please see additional Important Safety Information throughout and on pages 12-13. Please click here for full Prescribing Information.

PIQRAY® (alpelisib) tablets
50 mg · 150 mg · 200 mg

Important Safety Information

Indication

PIQRAY® (alpelisib) tablets is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

Important Safety Information

PIQRAY is contraindicated in patients with severe hypersensitivity to it or any of its components.

Severe Hypersensitivity: Severe hypersensitivity reactions, including anaphylaxis and anaphylactic shock, can occur in patients treated with PIQRAY. Severe hypersensitivity reactions were manifested by symptoms including, but not limited to, dyspnea, flushing, rash, fever, or tachycardia. The incidence of grade 3 and 4 hypersensitivity reactions was 0.7%. Advise patients of the signs and symptoms of severe hypersensitivity reactions. Permanently discontinue PIQRAY in the event of severe hypersensitivity.

Severe Cutaneous Adverse Reactions (SCARs): SCARs including Stevens-Johnson syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with PIQRAY. In the SOLAR-1 study, SJS and EM were reported in 0.4% and 1.1% of patients, respectively. DRESS was reported in patients in the postmarketing setting. If signs or symptoms of SCARs occur, interrupt PIQRAY until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended.

If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy).

Hyperglycemia: Severe hyperglycemia, including ketoacidosis, can occur in patients treated with PIQRAY. Hyperglycemia was reported in 65% of patients treated with PIQRAY. Grade 3 (FPG >250-500 mg/dL) and grade 4 (FPG >500 mg/dL) hyperglycemia were reported in 33% and 3.9% of patients, respectively. Ketoacidosis was reported in 0.7% of patients (n=2) treated with PIQRAY.

Before initiating treatment with PIQRAY, test fasting plasma glucose (FPG), HbA1c, and optimize blood glucose. After initiating treatment with PIQRAY, monitor fasting glucose (FPG or fasting blood glucose) at least once every week for the first 2 weeks, then at least once every 4 weeks, and as clinically indicated. Monitor HbA1c every 3 months and as clinically indicated. If a patient experiences hyperglycemia after initiating treatment with PIQRAY, monitor fasting glucose as clinically indicated, and at least twice weekly until fasting glucose decreases to normal levels. During treatment with antidiabetic medication, continue monitoring fasting glucose at least once a week for 8 weeks, followed by once every 2 weeks and as clinically indicated. Consider consultation with a health care practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.

The safety of PIQRAY in patients with type 1 and uncontrolled type 2 diabetes has not been established as these patients were excluded from the SOLAR-1 trial. Patients with a medical history of type 2 diabetes were included. Patients with a history of diabetes mellitus may require intensified diabetic treatment. Closely monitor patients with diabetes.

Based on the severity of the hyperglycemia, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients of the signs and symptoms of hyperglycemia (eg, excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss).

Pneumonitis: Severe pneumonitis, including acute interstitial pneumonitis and interstitial lung disease, can occur in patients treated with PIQRAY. Pneumonitis was reported in 1.8% of patients treated with PIQRAY.

Pneumonitis (cont): In patients who have new or worsening respiratory symptoms or are suspected to have developed pneumonitis, interrupt PIQRAY immediately and evaluate the patient for pneumonitis. Consider a diagnosis of noninfectious pneumonitis in patients presenting with nonspecific respiratory signs and symptoms such as hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams and in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations.

Permanently discontinue PIQRAY in all patients with confirmed pneumonitis. Advise patients to immediately report new or worsening respiratory symptoms.

Diarrhea: Severe diarrhea, including dehydration and acute kidney injury, can occur in patients treated with PIQRAY. Most patients (58%) experienced diarrhea during treatment with PIQRAY. Grade 3 diarrhea occurred in 7% (n=19) of patients. Based on the severity of the diarrhea, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients to start antidiarrheal treatment, increase oral fluids, and notify their health care provider if diarrhea occurs while taking PIQRAY.

Embryo-Fetal Toxicity: Based on findings in animals and its mechanism of action, PIQRAY 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. Advise females of reproductive potential to use effective contraception during treatment with PIQRAY and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use condoms and effective contraception during treatment with PIQRAY and for 1 week after the last dose. Refer to the full Prescribing Information of fulvestrant for pregnancy and contraception information.

The most common adverse reactions (all grades, incidence ≥20%) were diarrhea (58%), rash (52%), nausea (45%), fatigue (42%), decreased appetite (36%), stomatitis (30%), vomiting (27%), weight decreased (27%), and alopecia (20%). The most common grade 3/4 adverse reactions (incidence ≥2%) were rash (20%), diarrhea (7%), fatigue (5%), weight decreased (3.9%), nausea (2.5%), stomatitis (2.5%), and mucosal inflammation (2.1%).

The most common laboratory abnormalities (all grades, incidence ≥20%) were glucose increased (79%), creatinine increased (67%), lymphocyte count decreased (52%), gamma-glutamyl transferase (GGT) increased (52%), alanine aminotransferase (ALT) increased (44%), hemoglobin decreased (42%), lipase increased (42%), calcium decreased (27%), glucose decreased (26%), and activated partial thromboplastin time (aPTT) prolonged (21%). The most common grade 3/4 laboratory abnormalities (incidence ≥5%) were glucose increased (39%), GGT increased (11%), lymphocyte count decreased (8%), lipase increased (7%), and potassium decreased (6%).

Please click here for full Prescribing Information.

References: 1. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature.* 2012;490(7418):61-70. **2.** Tolaney S, Toi M, Neven P, et al. Presented at: 2019 American Association for Cancer Research (AACR) Annual Meeting; March 29-April 3, 2019; Atlanta, GA. **3.** Di Leo A, Johnston S, Seok Lee K, et al. *Lancet Oncol.* 2018;19(1):87-100. **4.** Moynahan ME, Chen D, He W, et al. *Br J Cancer.* 2017;116(6):726-730. **5.** Piqray [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2020. **6.** André F, Ciruelos E, Rubovszky G, et al. Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. *N Engl J Med.* 2019;380(20):1929-1940. **7.** Data on file. Novartis Pharmaceuticals Corp; 2018. **8.** OncologyPRO. https://oncologypro.esmo.org/Oncology-in-Practice/Palliative-and-Supportive-care/Multikinase-Inhibitor-Related-Skin-Toxicity/Healthcare-Professionals/Symptoms-and-Grading/Skin-Changes/Maculopapular-Rash. Accessed September 27, 2019. **9.** Goncalves MD, Hopkins BD, Cantley LC. Phosphatidylinositol 3-kinase, growth disorders, and cancer. *N Engl J Med.* 2018;379(21):2052-2062.

PIQRAY®
(alpelisib) tablets
50 mg • 150 mg • 200 mg

NOVARTIS

PIQRAY®
(alpelisib) tablets
50 mg · 150 mg · 200 mg

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

9/20

PIQ-1233475