Managing your patient on PIQRAY

Strategies for managing hyperglycemia, rash, 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 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.

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, were reported 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

More than doubled the response rate\(^\text{5,6}\)

Overall response rate (ORR) in patients with a PIK3CA mutation who had measurable disease\(^\text{5,6}\)

<table>
<thead>
<tr>
<th>ORR, %</th>
<th>(95%) CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.7%</td>
<td>(27.4–44.7)</td>
</tr>
<tr>
<td>16.2%</td>
<td>(10.4–23.5)</td>
</tr>
</tbody>
</table>

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](http://www.fda.gov/CompanionDiagnostics).

*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 PIK3CA mutation whose disease had progressed or recurred on or after Al-based treatment (N=572). In the PIK3CA mutation cohort (n=341), patients were randomized 1:1 to receive PIQRAY\(^\text{®}\) (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.

Al, 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 Reactions: Severe cutaneous reactions, including Stevens-Johnson syndrome (SJS) and erythema multiforme (EM) were reported in patients treated with PIQRAY. SJS and EM were reported in 0.4% and 1.1% of patients, respectively. Do not initiate PIQRAY treatment in patients with a history of SJS, EM, or toxic epidermal necrolysis (TEN). If signs or symptoms of severe cutaneous reactions occur, interrupt PIQRAY until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended.

Severe Cutaneous Reactions (cont): If SJS, TEN, or EM is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous severe cutaneous reactions during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antimetabolite treatment.

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

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.

Severe Cutaneous Reactions (cont): If SJS, TEN, or EM is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous severe cutaneous reactions during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antimetabolite treatment.

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

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**Tumor shrinkage observed in 3 out of 4 patients with a PIK3CA mutation**

Best percentage change in tumor size in patients with a PIK3CA mutation

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 from baseline in sum of diameters per investigator assessment in the PIK3CA mutant cohort

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

- 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)\(^a\)

**Safety profile**

Serious ARs associated with PIQRAY include severe hypersensitivity, severe cutaneous reactions, hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.\(^5\)

| ARs occurring in >20% of the total population\(^a\) |
|------------------|------------------|------------------|------------------|------------------|
| **AR** | **PIQRAY + fulvestrant (n=284)** | **Placebo + fulvestrant (n=287)** |
| **Gastrointestinal disorders** | | | | |
| Diarrhea | 58 | 7\(^*\) | 16 | 0.3\(^*\) |
| Nausea | 45 | 2.5\(^*\) | 22 | 0.3\(^*\) |
| Stomatitis\(^b\) | 30 | 6 | 6 | 0\(^*\) |
| Vomiting | 27 | 0.7\(^*\) | 10 | 0.3\(^*\) |
| **General disorders and administration site conditions** | | | | |
| Fatigue\(^c\) | 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\(^d\) | 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**

<table>
<thead>
<tr>
<th>Laboratory abnormality</th>
<th><strong>PIQRAY + fulvestrant (n=284)</strong></th>
<th><strong>Placebo + fulvestrant (n=287)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematological parameters</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocyte count decreased</td>
<td>52</td>
<td>8</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>42</td>
<td>4.2(^*)</td>
</tr>
<tr>
<td><strong>Biochemical parameters</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose increased(^e)</td>
<td>79</td>
<td>39</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>67</td>
<td>2.8(^*)</td>
</tr>
<tr>
<td>Gamma Glutamyl Transferase (GGT) increased</td>
<td>52</td>
<td>11</td>
</tr>
<tr>
<td>Alanine Aminotransferase (ALT) increased</td>
<td>44</td>
<td>3.5</td>
</tr>
<tr>
<td>Lipase increased</td>
<td>42</td>
<td>7</td>
</tr>
</tbody>
</table>

\(^*\)Glucose increase is an expected laboratory abnormality of PI3K inhibition.

\(^a\)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\(^a\).

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

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

Please see additional Important Safety Information throughout and on pages 12-13. Please click here for full Prescribing Information.
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Glucose increase, including hyperglycemia, is an expected, on-target effect of PI3K inhibition. ¹

- 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.
- Glucose increased (all grades) was reported in 79% of patients treated with PIQRAY + fulvestrant.

HbA1c

Duration of treatment

Once every 3 months and as clinically indicated.²

SOLAR-1

15 days (range: 5-517 days).³

Median time to first occurrence of grade ≥2 FPG 160-250 mg/dL hyperglycemia.⁴

Median time to improvement* of grade ≥2 hyperglycemia (n=153) was 8 days (range: 2-65 days).³

³ Improvement by at least 1 grade from time of first event.

Assess FPG and HbA1c

- 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)³
- HbA1c, glycosylated hemoglobin.

Optimize blood glucose

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- HbA1c, glycosylated hemoglobin.

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.
- Patients with a history of diabetes mellitus may require intensified diabetic treatment. Closely monitor patients with diabetes.

Monitor for hyperglycemia throughout your patient’s treatment

- The only laboratory monitoring needed for patients on PIQRAY is for FPG and HbA1c.

FPG and/or fasting blood glucose

If monitoring blood glucose levels instead of FPG after treatment initiation, patients should measure fasting blood glucose levels.

First 2 weeks

At least 1x per week.

After first 2 weeks

At least once every 4 weeks and as clinically indicated for the duration of treatment.

If hyperglycemia occurs

Hyyperglycemia was generally manageable and reversible. ²

- In the SOLAR-1 trial, 87% (163/187) of patients with hyperglycemia were managed with antihyperglycemic medication.²
- 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).²
- 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.²

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

Glucose modification

- First 8 weeks:
  - Follow FPG value-specific recommendations for grade 3.
  - If FPG is confirmed at >500 mg/dL:
    - Permanently discontinue PIQRAY.

- After first 8 weeks:
  - Monitor FPG or fasting blood glucose every 2 weeks and as clinically indicated.

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

Adjunct monitoring schedule

If a patient experiences hyperglycemia

Monitor FPG or fasting blood glucose as clinically indicated and at least 2x per week until blood glucose or FPG decreases to normal levels.⁴

Consider consultation with a health care provider with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.⁴

Adjusting doses

- Reduce dose by 1 level and follow FPG value-specific recommendations.
- Reduce to at lower dose level.
- Follow FPG value-specific recommendations for grade 3.
- Permanently discontinue.

Other laboratory monitoring

LFTs, complete blood count, and urinalysis are recommended as clinically appropriate.

Duration of treatment with antihyperglycemic medication

If FPG does not decrease to ≤160 mg/dL within 21 days under appropriate antihyperglycemic treatment:

- Resume at 1 lower dose level.
- Follow FPG value-specific recommendations for grade 3.
- Permanently discontinue.

During treatment with antihyperglycemic medication

First 8 weeks

Monitor FPG or fasting blood glucose at least 1x per week.⁴

After first 8 weeks

Monitor FPG or fasting blood glucose every 2 weeks and as clinically indicated.

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LFTs, complete blood count, and urinalysis are recommended as clinically appropriate.

Other laboratory monitoring

CTCAE, Common Terminology Criteria for Adverse Events; UCN, upper limit of normal.

² FPG blood glucose grade reflects hyperglycemia grading according to CTCAE version 4.03.
³ Initiate appropriate 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.
⁴ 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.
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Other insulin sensitizers such as thiazolidinediones or DPP-4 inhibitors can also be used as antihyperglycemic treatment.
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.
- Maculopapular rash was reported as one of the most common types of rash.

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

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

Assess patient’s past medical history

- Do not initiate PIQRAY treatment in patients with a history of Stevens-Johnson syndrome (SJS), erythema multiforme (EM), or toxic epidermal necrolysis (TEN).

SOLAR-1

12 days (range: 2-220 days)

- Median time to first onset of grade 2 or 3 rash.

Examples of maculopapular rash

(photos are not from the SOLAR-1 trial)

- Flat, red area covered with small confluent bumps.

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

Initial dose modification

- No PIQRAY dose adjustment

Administer medical management

- Initiate topical corticosteroid treatment
- Consider adding oral antihistamine to manage symptoms

Monitor and implement as clinically appropriate

- Consider low-dose systemic corticosteroid treatment

- Initiate or intensify topical/systemic corticosteroid and oral antihistamine treatment

- 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

- Permanently discontinue PIQRAY

- Initiate or intensify topical/systemic corticosteroid and oral antihistamine treatment
- Consider low-dose systemic corticosteroid treatment
- Consider adding oral antihistamine to manage symptoms
- Initiate topical corticosteroid treatment

Assess grade

- Grade 1 (%10 body surface area [BSA] with active skin toxicity)
- Grade 2 (10%-30% BSA with active skin toxicity)
- Grade 3 (eg, severe rash not responsive to medical management) (>30% BSA with active skin toxicity)
- Grade 4 (eg, severe bullous, blistering, or exfoliating skin conditions) (any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences)

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

- *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

- Diagnosis 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.

Rash monitoring + management

- If rash occurs

- Please see Important Safety Information throughout and on pages 12-13.
- Please click here for full Prescribing Information.
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. 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).1

Dose modifications and management for diarrhea²

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

*Grading according to CTCAE version 5.0.

Dose modifications and management for other toxicities⁵

<table>
<thead>
<tr>
<th>Grade¹</th>
<th>Modify dose</th>
<th>Administer medical management and monitor as clinically indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grades 1 or 2</td>
<td>No PIQRAY dose adjustment</td>
<td>Initiate appropriate medical therapy and monitor as clinically indicated¹⁴</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Interrupt PIQRAY dose until recovery to grade ≤1, then resume PIQRAY at the next lower dose level</td>
<td></td>
</tr>
<tr>
<td>Grade 4</td>
<td>Permanently discontinue PIQRAY</td>
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</tbody>
</table>

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

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

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

**Dosing and administration**

**PIQRAY is given in combination with fulvestrant⁶**

**FULVESTRANT**

**Recommended dose:** 500 mg

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<table>
<thead>
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<tbody>
<tr>
<td>First dose reduction</td>
<td>Second dose reduction</td>
</tr>
<tr>
<td>300 mg once daily (Two 150-mg tablets)</td>
<td>200 mg once daily (One 200-mg tablet)</td>
</tr>
<tr>
<td>250 mg once daily (One 200-mg tablet + one 50-mg tablet)</td>
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</tbody>
</table>

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 modifications³**

- Dose interruptions may be required prior to dose reductions³
- The PIQRAY dose may be reduced in increments of 50 mg⁵†
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY³

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)

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

200 mg (One 200-mg tablet once daily)

NDC 0078-0708-02

NDC 0078-0715-02

NDC 0078-0701-84

Please refer to the full prescribing information of fulvestrant for dose modification guidelines and for other relevant safety information.

Please see additional important safety information throughout and on pages 12-13. Please click here for full prescribing information.

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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, were reported 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 reactions.

Severe Cutaneous Reactions: Severe cutaneous reactions, including Stevens-Johnson syndrome (SJS) and erythema multiforme (EM) were reported in patients treated with PIQRAY. SJS and EM were reported in 0.4% and 1.1% of patients, respectively. Do not initiate PIQRAY treatment in patients with a history of SJS, EM, or toxic epidermal necrolysis (TEN). If signs or symptoms of severe cutaneous reactions occur, interrupt PIQRAY until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If SJS, TEN, or EM is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous severe cutaneous reactions 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 severe cutaneous reactions (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, or progressive skin rash).

Hyperglycemia: Severe hyperglycemia, including ketoacidosis, has been reported in patients treated with PIQRAY. Severe 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 was 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 FPG, Hba1c, and optimize blood glucose. After initiating treatment with PIQRAY, monitor blood glucose and/or FPG at least once every week for the first 2 weeks, then at least once every 4 weeks, and as clinically indicated. If a patient experiences hyperglycemia after initiating treatment with PIQRAY, monitor blood glucose and/or FPG as clinically indicated, and at least twice weekly until blood glucose or FPG decreases to normal levels. During treatment with anti-diabetic medication, continue monitoring blood glucose or FPG at least once a week for 8 weeks after PIQRAY discontinuation and clinically indicated. Monitor Hba1c every 3 months and as clinically indicated. If a patient has a history of diabetes mellitus or is a healthcare 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, has been reported 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 non-infectious pneumonitis in patients presenting with non-specific 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, occurred 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 anti-diarrheal 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 female patients to use effective contraception at least 4 months before starting 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 (77%), sodium 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%), and lipase increased (7%), and potassium decreased (6%).

Please click here for full Prescribing Information.
