**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 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, can occur in patients treated with PIQRAY. Pneumonitis was reported in 1.8% of patients treated with PIQRAY.

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 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 for full instructions.

**The most common adverse reactions (all grades, incidence ≥20%)**
- Diarrhea (69%)
- Rash (52%)
- Nausea (45%)
- Fatigue (42%)
- Decreased appetite (36%)
- Stomatitis (30%)
- Vomiting (27%)
- Weight loss (27%)
- Alopecia (20%)
- Myalgia (20%)
- Fatigue (15%)
- Anemia (15%)
- Hyperglycemia (15%)
- Rash (15%)
- Hypertension (14%)
- Hypothyroidism (10%)
- Pericardial effusion (8%)
- Arthralgia (8%)
- Pruritus (8%)
- Weight decrease (8%)
- Urinary tract infection (8%)
- Pneumonia (8%)

**The most common laboratory abnormalities (all grades, incidence ≥20%)**
- Glucose increased (39%)
- Lymphocyte count decreased (36%)
- Lipase increased (35%)
- Calcium decreased (27%)
- Hemoglobin decreased (27%)
- Creatine increased (26%)
- Alanine aminotransferase (ALT) increased (24%)
- Aspartate aminotransferase (AST) increased (24%)
- Bilirubin increased (23%)
- Gamma-glutamyl transferase (GGT) increased (21%)
- Glucose decreased (21%)
- HbA1c increased (20%)
- Platelet count decreased (20%)
- Uric acid increased (19%)
- Glucose decreased (19%)
- Albumin decreased (19%)
- Potassium increased (18%)
- Potassium decreased (18%)
- Sodium increased (18%)
- Sodium decreased (18%)
- Hemoglobin decreased (17%)
- Creatinine increased (16%)
- Cholesterol increased (16%)
- Lipase decreased (16%)
- Calcium increased (16%)
- Bilirubin decreased (16%)
- Gamma-glutamyl transferase (GGT) decreased (16%)
- Creatine decreased (15%)
- Phosphorus increased (15%)
- Phosphorus decreased (15%)
- Sodium decreased (15%)
- Urea decreased (15%)
- Potassium increased (15%)
- Potassium decreased (15%)
- Sodium increased (15%)
- Calcium decreased (15%)
- Hemoglobin decreased (15%)
- Creatinine increased (15%)

**Please click here for full Prescribing Information.**
This tool is designed to provide information on the safety profile of PIQRAY® (alpelisib) tablets and guidance on dose modifications and management of selected adverse reactions (ARs). 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.

*Click the yellow buttons to view information relevant to your patients’ current situation.*

**If one of the following ARs occurs**

Find information about managing the following ARs associated with PIQRAY:

- SCARs or Rash
- Hyperglycemia
- Diarrhea
- Other toxicities

**What to expect before and during treatment**

Find out about monitoring and considerations for severe cutaneous adverse reactions (SCARs), hyperglycemia, and rash:

- **Before** treatment
- **During** treatment
Dosing and administration

PIQRAY is given in combination with fulvestrant\(^1,2\)

<table>
<thead>
<tr>
<th>PIQRAY</th>
<th>FULVESTRANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting dose: 300 mg daily (Two 150-mg tablets)</td>
<td>Recommended dose: 500 mg</td>
</tr>
<tr>
<td>Once-daily continuous oral dosing Should be swallowed whole and taken with food, at approximately the same time each day*</td>
<td>Administered on days 1, 15, and 29, and once monthly thereafter</td>
</tr>
</tbody>
</table>

Continue treatment until disease progression or unacceptable toxicity occurs.

*DOSAGE MODIFICATIONS:

- 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\(^1,2\)

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

Follow guidance in the dose modification and management recommendation tables to find out when you should reduce your patient’s dose. The management plan of each patient should be based on the individual benefit/risk assessment.

- Dose interruptions may be required prior to dose reductions\(^1\)
- The PIQRAY® (alpelisib) tablets dose may be reduced in increments of 50 mg\(^2\)
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY\(^1\)

\(^1\)Only one dose reduction is permitted for pancreatitis.

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

- PIQRAY approved doses\(^1\)
  - 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)

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.

Please click here for Indication and full Important Safety Information. Please click here for full Prescribing Information.
Serious ARs associated with PIQRAY® (alpelisib) tablets include severe hypersensitivity, severe cutaneous adverse reactions (SCARs), hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.¹

### Serious and common ARs

<table>
<thead>
<tr>
<th>ARs</th>
<th>PIQRAY + fulvestrant (n=284)</th>
<th>Placebo + fulvestrant (n=287)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades (%)</td>
<td>Grade 3-4 (%)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>58</td>
<td>7*</td>
</tr>
<tr>
<td>Nausea</td>
<td>45</td>
<td>2.5*</td>
</tr>
<tr>
<td>Stomatitisa</td>
<td>30</td>
<td>2.5*</td>
</tr>
<tr>
<td>Vomiting</td>
<td>27</td>
<td>0.7*</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigueb</td>
<td>42</td>
<td>5*</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight decreased</td>
<td>27</td>
<td>3.9*</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>36</td>
<td>0.7*</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rashc</td>
<td>52</td>
<td>20*</td>
</tr>
</tbody>
</table>

*No grade 4 ARs were reported.

¹Including stomatitis, aphthous ulcer, mouth ulceration.

³Including fatigue, asthenia.

⁴Including rash, rash maculopapular, rash macular, rash generalized, rash papular, rash pruritic.

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**Laboratory abnormalities**

Serious ARs associated with PIQRAY® (alpelisib) tablets include severe hypersensitivity, severe cutaneous adverse reactions (SCARs), hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.¹

<table>
<thead>
<tr>
<th>ARs</th>
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<th>Placebo + fulvestrant (n=287)</th>
</tr>
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<tbody>
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<td>Laboratory abnormalities</td>
<td>All grades (%)</td>
<td>Grade 3-4 (%)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>58</td>
<td>7*</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>45</td>
<td>2.5*</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>30</td>
<td>2.5*</td>
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<td>Rash</td>
<td>27</td>
<td>0.7*</td>
</tr>
</tbody>
</table>

Please click here for Indication and full Important Safety Information. Please click here for full Prescribing Information.
Serious ARs associated with PIQRAY® (alpelisib) tablets include severe hypersensitivity, severe cutaneous adverse reactions (SCARs), hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.  

**Serious and common ARs**

Laboratory abnormalities occurring in >30% of the total population¹

<table>
<thead>
<tr>
<th>Laboratory abnormality</th>
<th>PIQRAY + fulvestrant (n=284)</th>
<th>Placebo + fulvestrant (n=287)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All grades (%)</td>
<td>Grade 3-4 (%)</td>
</tr>
<tr>
<td>Hematological parameters</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>Biochemical parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose increased*</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.

¹No 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 ARs¹
- Dose reductions due to ARs occurred in 55% of patients receiving PIQRAY and fulvestrant¹
- 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%)¹

The most common ARs leading to treatment discontinuation of PIQRAY in patients receiving PIQRAY + fulvestrant were¹:

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

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
Severe cutaneous adverse reactions (SCARs) in SOLAR-1 and postmarketing setting

- In the SOLAR-1 study, 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.

Rash in SOLAR-1

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

Median time to first onset of grade 2 or 3 rash

12 days (range: 2-220 days)
If a severe cutaneous adverse reaction (SCAR) is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment.

---

**Manage your patient’s**

**Grade 1 SCARs or rash**

<10% body surface area [BSA] with active skin toxicity

**Dose modification and management recommendation**

**Initial dose modification**

No PIQRAY dose adjustment

*If the etiology is SCAR*, permanently discontinue PIQRAY

**Administer medical management**

Initiate topical corticosteroid treatment

Consider adding oral antihistamine to manage symptoms

*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.

**Click the buttons to view other grades**

**Grade 2**

10%-30% BSA with active skin toxicity

**Grade 3**

e.g., severe rash not responsive to medical management

>30% BSA with active skin toxicity

**Grade 4**

e.g., severe bullous, blistering, or exfoliating skin conditions

Any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences
If a severe cutaneous adverse reaction (SCAR) is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment.

Dose modification and management recommendation:

**Initial dose modification**
- No PIQRAY dose adjustment

**If the etiology is SCAR,** permanently discontinue PIQRAY

**Administer medical management**
- Initiate or intensify topical corticosteroid and oral antihistamine treatment
- Consider low-dose systemic corticosteroid treatment

*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.
If an AR occurs

If a severe cutaneous adverse reaction (SCAR) is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment.1

Manage your patient’s

**Grade 3 SCARs or rash**1†

- eg, severe rash not responsive to medical management
- >30% BSA with active skin toxicity

---

Dose modification and management recommendation1†:

**Initial dose modification**

- **If the etiology is not SCAR,** interrupt PIQRAY
- **If the etiology is SCAR,** permanently discontinue PIQRAY

**Administer medical management**

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

**Monitor and implement** as clinically appropriate

- **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

*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.

---

Click the buttons to view other grades

**Grade 1**<10% body surface area BSA with active skin toxicity

**Grade 2**10%-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

---

Management recommendations for SCARs or rash

Monitoring for different forms of SCARs or rash

Medications used to manage rash in SOLAR-1

Understanding dose modifications

---

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
If a severe cutaneous adverse reaction (SCAR) is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment.1

### Dose modification and management recommendation1**:

| 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 |

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

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

**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

**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).
Current PIQRAY patient

If an AR occurs

[SCARs or Rash] [Hyperglycemia] [Diarrhea] [Other toxicities]

Review dose modification and management table for severe cutaneous adverse reactions (SCARs) and rash prior to reviewing this page

♦ Examples of medication used to manage rash in the SOLAR-1 trial\(^{3,a}\)

**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.

♦ In the SOLAR-1 study

![92% (141/153)]

of patients who experienced rash had resolution of rash\(^1\)

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
If an AR occurs

Review dose modification and management table for severe cutaneous adverse reactions (SCARs) and rash prior to reviewing this page

**Certain ARs may require dose modifications**\(^1,2\)

This information will help you understand how to adjust your patient's dose if an AR occurs.

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

Follow guidance in the dose modification and management recommendation table to find out when you should adjust your patient's dose. The management plan of each patient should be based on the individual benefit/risk assessment.

- Dose interruptions may be required prior to dose reductions\(^1\)
- The PIQRAY® (alpelisib) tablets dose may be reduced in increments of 50 mg\(^*\)
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY\(^1\)

\(^*\)Only one dose reduction is permitted for pancreatitis.
Hyperglycemia was reported in 65% of patients. Grade 3 and 4 was reported in 33% and 3.9% of patients, respectively. Ketoacidosis was reported in 0.7% of patients.1

In the SOLAR-1 trial, hyperglycemia was generally manageable and reversible.¹

87% (163/187) of patients with hyperglycemia were managed with antihyperglycemic medication.¹
• Most patients (76%, 142/187) reported use of metformin as a single agent or in combination with other antihyperglycemic medication* (ie, insulin, DPP-4 inhibitors, and sulfonylureas)¹

FPG, fasting plasma glucose.
*The maximum dose of metformin allowed in SOLAR-1 was 2000 mg per day.

15 days (range: 5-517 days)¹

The median time to first occurrence of grade ≥2 (FPG 160-250 mg/dL) hyperglycemia was 15 days.¹

Median time to improvement† of grade ≥2 hyperglycemia (n=153) was 8 days (range: 2-65 days).¹

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

Based on the severity of the hyperglycemia, PIQRAY may require dose interruption, reduction, or discontinuation.

Click the buttons to learn more about hyperglycemia with PIQRAY.

Management recommendations for hyperglycemia
Adjust monitoring schedule if hyperglycemia occurs
Hyperglycemia management with metformin in SOLAR-1
Understanding dose modifications

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
Dose modifications and management should only be based on fasting glucose values (FPG or fasting blood glucose)\(^1\)

**Grade 1 hyperglycemia**

*Fasting glucose >ULN-160 mg/dL*

Manage your patient's

**Initial dose modification**

No PIQRAY\(^®\) (alpelisib) tablets dose adjustment

**Administer medical management**

Initiate or intensify antihyperglycemic treatment\(^a\)

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

\(^a\)Initiate applicable antihyperglycemic medications, including metformin and insulin sensitizers (such as thiazolidinediones or dipeptidyl peptidase-4 [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.

Click the buttons to view other grades

- **Grade 2**
  - Fasting glucose >160-250 mg/dL

- **Grade 3**
  - >250-500 mg/dL

- **Grade 4**
  - >500 mg/dL
If an AR occurs

**Hyperglycemia**

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

**Dose modification and management recommendation**:  

**Initial dose modification**

- No PIQRAY® (alpelisib) tablets dose adjustment
- **Administer medical management**
  - Initiate or further intensify antihyperglycemic treatment
  - Monitor and implement as clinically appropriate

**If fasting glucose does not decrease to ≤160 mg/dL within 21 days under appropriate antihyperglycemic treatment:**  
Reduction dose by 1 level and follow fasting glucose value-specific recommendations

*FPG/fasting blood glucose/grade levels reflect hyperglycemia grading according to CTCAE version 4.03.

*Initiate applicable antihyperglycemic medications, including metformin and insulin sensitizers (such as thiazolidinediones or dipeptidyl peptidase-4 [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.

**Grade 1**  
Fasting glucose >ULN-160 mg/dL

**Grade 3**  
>250-500 mg/dL

**Grade 4**  
>500 mg/dL

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
### Dose modifications and management should only be based on fasting glucose values (FPG or fasting blood glucose)

**Manage your patient’s Grade 3 hyperglycemia***

>250-500 mg/dL

#### Dose modification and management recommendation¹:

**Initial dose modification**
- Interrupt PIQRAY® (alpelisib) tablets

**Administer medical management**
- Initiate or intensify oral antihyperglycemic treatment and consider additional antihyperglycemic medications for 1-2 days until hyperglycemia improves
- Administer IV hydration and consider appropriate treatment including intervention for electrolyte/ketoacidosis/hyperosmolar disturbances

**Monitor and implement** as clinically appropriate

- **If fasting glucose decreases to ≤160 mg/dL within 3 to 5 days under appropriate antihyperglycemic treatment**: Resume PIQRAY at 1 lower dose level.
- **If fasting glucose does not decrease to ≤160 mg/dL within 3 to 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**: Permanently discontinue PIQRAY treatment.

---

**Grade 1**
- Fasting glucose >ULN-160 mg/dL

**Grade 2**
- Fasting glucose >160-250 mg/dL

**Grade 4**
- >500 mg/dL

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*FPG/fasting blood glucose/grade levels reflect hyperglycemia grading according to CTCAE version 4.03.

¹Initiate 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.

²As 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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**Management recommendations for hyperglycemia**

- Adjust monitoring schedule if hyperglycemia occurs
- Hyperglycemia management with metformin in SOLAR-1
- Understanding dose modifications

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Please click here for Indication and full Important Safety Information. 
Please click here for full Prescribing Information.
If an AR occurs

Hyperglycemia

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

<table>
<thead>
<tr>
<th>Grade 4 hyperglycemia*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500 mg/dL</td>
</tr>
</tbody>
</table>

Initial dose modification

Interrupt PIQRAY® (alpelisib) tablets

Administer medical management

- Initiate or intensify appropriate antihyperglycemic treatment
- Administer IV hydration and consider appropriate treatment including intervention for electrolyte/ketoacidosis/hyperosmolar disturbances

Monitor and implement as clinically appropriate

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 (>250-500 mg/dL). Click here to view grade 3 hyperglycemia dose modification and management recommendations

- If fasting glucose is confirmed at >500 mg/dL:
  - Permanently discontinue

*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.
If a patient experiences hyperglycemia:

Monitor fasting glucose (FPG or fasting blood glucose) as clinically indicated and **at least 2x per week** until fasting glucose decreases to normal levels.³

Consider consultation with a health care provider with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.³

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

During treatment with antihyperglycemic medication:

**First 8 weeks**
Monitor fasting glucose at least 1x per week.³

**After first 8 weeks**
Monitor fasting glucose every 2 weeks and as clinically indicated.³
In SOLAR-1, metformin was recommended with the following guidance if hyperglycemia occurred:

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.
Certain ARs may require dose modifications\textsuperscript{1,2}

This information will help you understand how to appropriately adjust your patient’s dose if an AR occurs.

Starting dose

300 mg once daily
(Two 150-mg tablets)

First dose reduction

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

Second dose reduction

200 mg once daily
(One 200-mg tablet)

Follow guidance in the dose modification and management recommendation table to find out when you should adjust your patient’s dose. The management plan of each patient should be based on the individual benefit/risk assessment.

- Dose interruptions may be required prior to dose reductions\textsuperscript{1}
- The PIQRAY\textsuperscript{®} (alpelisib) tablets dose may be reduced in increments of 50 mg\textsuperscript{*}
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY\textsuperscript{1}

\*Only one dose reduction is permitted for pancreatitis.
Diarrhea in SOLAR-1

- Severe diarrhea, including dehydration and acute kidney injury, can occur\(^1\)
- In the SOLAR-1 trial, most patients (58%) experienced diarrhea during treatment with PIQRAY\(^\circledR\) (alpelisib) tablets\(^1\)
  - Grade 3 diarrhea occurred in 7% (n=19) of patients\(^1\)
  - No grade 4 diarrhea events were reported\(^1\)

Median time to first onset of grade 2 or 3 diarrhea

46 days (range: 1-442 days)\(^1\)

- In the 164 patients who experienced diarrhea, anti-diarrheal medications (eg, loperamide) were required to manage symptoms in 63% (104/164) of these patients\(^1\)

Based on the severity of the diarrhea, PIQRAY may require dose interruption, reduction, or discontinuation.

Click the buttons to learn more about diarrhea with PIQRAY.

Management recommendations for diarrhea

Understanding dose modifications
Dose modification and management recommendation¹:

Modify dose

No PIQRAY® (alpelisib) tablets dose adjustment

Administer medical management and monitor as clinically indicated

Initiate appropriate medical therapy and monitor as clinically indicated

*Grading according to CTCAE version 5.0.

Grade 1 diarrhea*: (Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline)

Click the buttons to view other grades

Grade 2

Grade 3 and 4
If an AR occurs

Grade 2 diarrhea*

(Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL)

Dose modification and management recommendation¹:

Modify dose

Interrupt PIQRAY® (alpelisib) tablets dose until recovery to grade ≤1, then resume PIQRAY at same dose level

Administer medical management and monitor as clinically indicated

Initiate or intensify appropriate medical therapy and monitor as clinically indicated

*Grading according to CTCAE version 5.0.

Click the buttons to view other grades

Grade 1

Grade 3 and 4

Management recommendations for diarrhea

Understanding dose modifications

Download this educational brochure for your patients
Contact Novartis

Please click here for Indication and full Important Safety Information.
Please click here for full Prescribing Information.
If an AR occurs

**Grade 2**

Modify dose

Interrupt PIQRAY® (alpelisib) tablets dose until recovery to grade ≤1, then resume PIQRAY at the next lower dose level

Administer medical management and monitor as clinically indicated

Initiate or intensify appropriate medical therapy and monitor as clinically indicated

**Grade 3**

(Decrease of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL)

and **Grade 4**

(Life-threatening consequences; urgent intervention indicated)

Diarrhea*

*Dose modification and management recommendation1:

Click the buttons to view other grades

Grade 1

Grade 2

*Grading according to CTCAE version 5.0.
Certain ARs may require dose modifications¹,²

This information will help you understand how to adjust your patient’s dose if an AR occurs.

Starting dose

300 mg once daily
(Two 150-mg tablets)

First dose reduction

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

Second dose reduction

200 mg once daily
(One 200-mg tablet)

Follow guidance in the dose modification and management recommendation table to find out when you should adjust your patient’s dose. The management plan of each patient should be based on the individual benefit/risk assessment.

- Dose interruptions may be required prior to dose reductions¹
- The PIQRAY® (alpelisib) tablets dose may be reduced in increments of 50 mg**
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY¹

*Only one dose reduction is permitted for pancreatitis.
Current PIQRAY patient

If an AR occurs

Other toxicities include ARs in PIQRAY® (alpelisib) tablets safety profile excluding hyperglycemia, rash, and diarrhea. Click here to view PIQRAY’s safety profile.

Click the buttons to view other grades

Grade 1 or 2 other toxicities*

Dose modification and management recommendation¹:

Modify dose

No PIQRAY dose adjustment\(^{a,b}\)

Administer medical management and monitor as clinically indicated

Initiate appropriate medical therapy and monitor as clinically indicated

*Grading according to CTCAE version 5.0.

¹For 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.

²For 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.

Click here for Indication and full Important Safety Information. Please click here for full Prescribing Information.
Other toxicities include ARs in PIQRAY® (alpelisib) tablets safety profile excluding hyperglycemia, rash, and diarrhea. Click here to view PIQRAY's safety profile.

Dose modification and management recommendation¹:

Modify dose

Interrupt PIQRAY dose until recovery to grade ≤1, then resume PIQRAY at the next lower dose level

*Grading according to CTCAE version 5.0.

Click the buttons to view other grades

Grade 1 or 2

Grade 4

Based on the severity of the AR, PIQRAY may require dose interruption, reduction, or discontinuation.
If an AR occurs

Other toxicities include ARs in PIQRAY® (alpelisib) tablets safety profile excluding hyperglycemia, rash, and diarrhea. Click here to view PIQRAY's safety profile.

Dose modification and management recommendation¹:

Modify dose
Permanently discontinue PIQRAY

*Grading according to CTCAE version 5.0.

Click the buttons to view other grades

Grade 1 or 2
Grade 3

Based on the severity of the AR, PIQRAY may require dose interruption, reduction, or discontinuation.

Management recommendations for other toxicities

Understanding dose modifications

Please click here for Indication and full Important Safety Information. Please click here for full Prescribing Information.
Certain ARs may require dose modifications\(^1,2\)

This information will help you understand how to appropriately adjust your patient’s dose if an AR occurs.

Starting dose

- **300 mg once daily**
  - (Two 150-mg tablets)

First dose reduction

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

Second dose reduction

- **200 mg once daily**
  - (One 200-mg tablet)

Follow guidance in the dose modification and management recommendation table to find out when you should adjust your patient’s dose. The management plan of each patient should be based on the individual benefit/risk assessment.

- Dose interruptions may be required prior to dose reductions\(^1\)
- The PIQRAY\(^\circledR\) (alpelisib) tablets dose may be reduced in increments of 50 mg\(^*\)
- If further dose reduction below 200 mg/d is required, discontinue PIQRAY\(^1\)

\(*Only one dose reduction is permitted for pancreatitis.*
Assess patient’s history of diabetes

• 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.

It’s important to be aware of underlying health conditions your patient may have, including diabetes, before starting treatment with PIQRAY.
Assess FPG and HbA1c¹

Optimize blood glucose levels¹

• 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

Hyperglycemia is a serious and common adverse reaction (AR) associated with PIQRAY® (alpelisib) tablets. It is important to monitor your patient’s fasting glucose levels (FPG or fasting blood glucose) with blood tests during treatment with PIQRAY. Remind patients they should be fasting (not eating or drinking anything) overnight for 8 to 12 hours prior to their glucose test. Keep in mind your patient’s monitoring schedule will change if hyperglycemia occurs.¹³

FPG, fasting plasma glucose; HbA1c, hemoglobin A1c.
New PIQRAY patient - Hyperglycemia and rash considerations

Before treatment

Assess history of diabetes
Assess and optimize blood glucose
How hyperglycemia occurs
Prophylaxis prior to rash onset

Glucose increase, including hyperglycemia, is an expected, on-target effect of PI3K inhibition\(^1,4\)

- Hyperglycemia was reported in 65% of patients treated with PIQRAY\(^\circledR\) (alpelisib) tablets. Grade 3 and grade 4 hyperglycemia was reported in 33% and 3.9% of patients, respectively\(^1\)
- Glucose increased (all grades) was reported in 79% of patients treated with PIQRAY + fulvestrant\(^1\)

Normal PI3K signaling\(^5-7\)

PI3K inhibition\(^7,8\)

Glucose increase, including hyperglycemia, is an expected, on-target effect of PI3K inhibition\(^1,4\)

- Hyperglycemia was reported in 65% of patients treated with PIQRAY\(^\circledR\) (alpelisib) tablets. Grade 3 and grade 4 hyperglycemia was reported in 33% and 3.9% of patients, respectively\(^1\)
- Glucose increased (all grades) was reported in 79% of patients treated with PIQRAY + fulvestrant\(^1\)
Antihistamines administered prior to rash onset may decrease incidence and severity of rash based on the SOLAR-1 trial¹

- Consider prophylaxis with antihistamines prior to onset of rash¹
  - A subgroup of 86 patients received prophylaxis, including antihistamines (eg, cetirizine), prior to onset of rash¹
  - In these patients, rash was reported less frequently than in the overall population as shown in the table below

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients receiving prophylactic treatment prior to onset of rash (n=86)</th>
<th>Overall population (n=284)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All grades rash</td>
<td>27%</td>
<td>54%</td>
</tr>
<tr>
<td>Grade 3 rash</td>
<td>12%</td>
<td>20%</td>
</tr>
<tr>
<td>Rash leading to permanent discontinuation of PIQRAY</td>
<td>3.5%</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

Rash is a common AR associated with PIQRAY® (alpelisib) tablets. It is important to monitor for different forms of rash during treatment with PIQRAY, including rash, rash maculopapular, rash macular, rash generalized, rash papular, and rash pruritic.

Order a PIQRAY patient starter kit

The PIQRAY patient starter kit includes the printed patient brochure along with supportive tools and resources, like an antihistamine sample to help your patient manage rash. Contact a Novartis representative to learn more.
The only laboratory monitoring needed for patients on PIQRAY is fasting glucose (FPG or fasting blood glucose) and HbA1c

• Advise patients of signs and symptoms of hyperglycemia and to contact their health care provider immediately should they occur
  — Signs and symptoms include excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss

Fasting glucose
When monitoring fasting glucose, measure FPG or fasting blood glucose

**First 2 weeks of treatment**
Monitor fasting glucose at least 1x per week

**After first 2 weeks of treatment**
Monitor fasting glucose at least once every 4 weeks and as clinically indicated for the duration of treatment

HbA1c

**Duration of treatment**
Monitor HbA1c once every 3 months and as clinically indicated for the duration of treatment

Hyperglycemia is a serious and common adverse reaction (AR) associated with PIQRAY® (alpelisib) tablets. It is important to monitor your patient’s fasting glucose levels (FPG or fasting blood glucose) with blood tests during treatment with PIQRAY. Keep in mind your patient’s monitoring schedule will change if hyperglycemia occurs.

FPG, fasting blood glucose; HbA1c, hemoglobin A1c.
If hyperglycemia occurs, adjust monitoring schedule

- If a patient experiences hyperglycemia, monitor fasting glucose (FPG or fasting blood glucose) as clinically indicated and at least 2x per week until fasting glucose decreases to normal levels\(^1\)
  
  - HbA1c monitoring can continue once every 3 months and as clinically indicated for the duration of treatment\(^1\)

- Consider consultation with a health care provider with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes\(^1\)

Click here to learn about hyperglycemia in the SOLAR-1 trial and dose modifications and management recommendations

HbA1c, hemoglobin A1c.
During treatment with antihyperglycemic medication, adjust monitoring schedule

First 8 weeks of treatment with antihyperglycemic medication
Monitor fasting glucose (FPG or fasting blood glucose) at least 1x per week\(^1\)

After first 8 weeks of treatment with antihyperglycemic medication
Monitor fasting glucose every 2 weeks and as clinically indicated\(^1\)

Once your patient is being treated with antihyperglycemic medication (eg, metformin and other insulin sensitizers such as thiazolidinediones or dipeptidyl peptidase-4 inhibitors), follow the above adjusted monitoring recommendations.
Advise patients of signs and symptoms of severe cutaneous adverse reactions (SCARs) and to contact their health care provider immediately should they occur\(^1\)

- Signs and symptoms include a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy\(^1\)

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\(^1\)
- Maculopapular rash was reported as one of the most common types of rash\(^3\)

Examples of maculopapular rash\(^9\)

*(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).

Click here to learn about rash in the SOLAR-1 trial and dose modification and management recommendations.

Please click here for Indication and full Important Safety Information. Please click here for full Prescribing Information.
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 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.

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 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 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 (39%), albumin decreased (27%), and calcium decreased (27%). The most common grade 3/4 abnormalities (incidence ≥20%) were 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 ≥20%) 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.