KEEPING TRAQ WITH PIQRAY® (alpelisib) tablets

Cutaneous adverse reactions and hyperglycemia monitoring and consideration checklist

Using this checklist

This checklist is designed to provide guidance on cutaneous adverse reactions and hyperglycemia monitoring and considerations. **It does not cover all adverse reactions (ARs) associated with PIQRAY therapy, as there are other serious ARs to consider, including severe hypersensitivity, severe cutaneous adverse reactions (SCARs), pneumonitis, diarrhea, and embryo-fetal toxicity.** The information presented here does not constitute medical advice and is not intended to take the place of your own clinical judgment based on each patient's particular presentation.

Before treatment

- ☐ **Assess fasting plasma glucose (FPG) and HbA1c**[1]
- ☐ **Optimize blood glucose**[1]
  - 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)[2]
- ☐ **Assess patient's past medical history:**
  - 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[1]
  - Patients with a history of diabetes mellitus may require intensified diabetic treatment. Closely monitor patients with diabetes[1]
- ☐ **Consider prophylaxis with antihistamines prior to onset of rash**
  - Antihistamines administered prior to rash onset may decrease incidence and severity of rash based on SOLAR-1 trial[1]

Effects of prophylactic treatment, including antihistamines, prior to onset of rash in patients receiving PIQRAY + fulvestrant[1]

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	3.5%	4.2%

HbA1c, glycosylated hemoglobin.

SOLAR-1 Data

15 days (range: 5-517 days)[1]

Median time to first occurrence of grade ≥2 (FPG 160-250 mg/dL) **hyperglycemia**[1]

12 days (range: 2-220 days)[1,2]

Median time to first onset of grade 2 or 3 **rash**[1]

Indication

PIQRAY 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.

During treatment with PIQRAY

- ☐ **Test fasting glucose as recommended**[1]

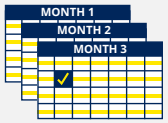
When monitoring fasting glucose, measure FPG or fasting blood glucose.

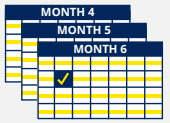
First 2 weeks: At least 1x per week[1]

After first 2 weeks: At least once every 4 weeks and as clinically indicated for the duration of treatment[1]

- ☐ **Test HbA1c**[1]

Once every 3 months and as clinically indicated for the duration of treatment[1]





- ☐ **Advise patients of the following signs and symptoms of hyperglycemia and to contact their health care provider immediately should they occur**[1]
  - Excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss[1]
- ☐ **Advise patients of the following signs and symptoms of SCARs and to contact their health care provider immediately should they occur**[1]
  - A prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash or lymphadenopathy[1]
- ☐ **Monitor for different forms of rash**[1]
  - 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[2]

If severe cutaneous adverse reactions (SCARs) or rash occur

- ☐ **If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCAR during treatment**
- ☐ **Refer to PIQRAY Prescribing Information and/or Patient Management Brochure for management recommendations and medication used for rash in the SOLAR-1 trial**

If hyperglycemia occurs

- ☐ **Adjust monitoring schedule**
  - Monitor fasting glucose as clinically indicated and **at least 2x per week** until fasting glucose decreases to normal levels[1]
- ☐ **Refer to PIQRAY Prescribing Information and/or Patient Management Brochure for management recommendations and medication used in the SOLAR-1 trial**

During treatment with antihyperglycemic medication

- ☐ **Adjust monitoring schedule**

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

After first 8 weeks
Monitor fasting glucose every 2 weeks and as clinically indicated[1]

Please see additional Important Safety Information on reverse. Please click here for full Prescribing Information.

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

Important Safety Information (cont)

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.

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. Piqray [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2020. **2.** Data on file. Novartis Pharmaceuticals Corp; 2018.

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