*FOR PATIENTS 2 YEARS AND OLDER WITH SEVERE MANIFESTATIONS OF **PIK3CA-RELATED OVERGROWTH SPECTRUM (PROS)** WHO REQUIRE SYSTEMIC THERAPY*

Patient Management Guide

This guide is designed to provide guidance on dose modifications and management of select adverse reactions (ARs) related to treatment with VIJOICE® (alpelisib) tablets. It does not cover all ARs associated with VIJOICE. The management strategies presented in this guide 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. Depending on severity, not all ARs may be managed.

INDICATION

VIJOICE® (alpelisib) tablets is indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy.

This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

VIJOICE is contraindicated in patients with severe hypersensitivity to alpelisib or any of its ingredients.

Severe Hypersensitivity. Severe hypersensitivity reactions, including anaphylaxis, angioedema, and anaphylactic shock, have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE. VIJOICE is not approved for use in the oncology setting. Permanently discontinue VIJOICE in the event of severe hypersensitivity.

Please click here for additional Important Safety Information.
Please click here for full Prescribing Information.

Vijoice® (alpelisib) tablets
50 mg | 125 mg | 200 mg

*The **FIRST** and **ONLY** FDA-approved treatment for pediatric and adult patients with PROS*

VIJOICE is the **FIRST** and **ONLY** FDA-approved treatment for pediatric and adult patients with PROS

VIJOICE shrunk overgrowth[1]

27%

10/37 (95% CI, 14-44)

OF PATIENTS EXPERIENCED A RESPONSE AT WEEK 24*,†

Response was determined by BICR.

Two additional patients experienced a response, but the response was not confirmed by BICR.[2]

Patients maintained response

70% of patients maintained response after 6 months

60% of patients maintained response after 12 months

The major efficacy outcome measure for the study was the proportion of patients with radiological response at Week 24, which was defined as a ≥20% reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions) confirmed by at least 1 subsequent imaging assessment, provided that none of the individual target lesions had a ≥20% increase from baseline, nontarget lesions had not progressed, and there were no new lesions.

In an exploratory analysis of the EPIK-P1 study,

Improvements in the most common PROS signs and symptoms were observed[2]

Percentage of patients with improvements at Week 24 in the most commonly reported signs and symptoms

- Pain: 90.9% (20/22)
- Vascular malformations: 78.9% (30/38)
- Fatigue: 76.2% (32/42)
- Limb asymmetry: 69.0% (20/29)
- Disseminated intravascular coagulation: 55.2% (16/29)

Improvement was defined based on CTCAE version 4.03 grade reduction or resolution of the event. Percentages were calculated based on the number of patients who reported the event at baseline.

Study information[1]

REAL-WORLD STUDY OF PROS

FDA approval was based on EPIK-P1, a single-arm clinical study.

Pediatric and adult patients (N=57) with PROS received VIJOICE® (alpelisib) tablets as part of a compassionate use program.

The efficacy of VIJOICE was evaluated in a total of 37 patients with at least 1 target lesion identified on imaging performed within 24 weeks prior to receipt of the first dose of VIJOICE.

Patients with CLOVES syndrome, MCAP or M-CM, KTS, FIL, and 2 patients with unspecified PROS conditions were included in the study.

A larger, phase 2, prospective study is ongoing.[3]

*Confirmed response as determined by BICR.
†Patients without any response assessment at Week 24 were considered nonresponders.
BICR, blinded independent central review; CTCAE, Common Terminology Criteria for Adverse Events; CLOVES, congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal; MCAP or M-CM, megalencephaly-capillary malformation; KTS, Klippel-Trenaunay syndrome; FIL, facial infiltrating lipomatosis.

IMPORTANT SAFETY INFORMATION (cont)

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), have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE. If signs or symptoms of SCARs occur, interrupt VIJOICE until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, permanently discontinue VIJOICE. If a SCAR is not confirmed, VIJOICE may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Please click here for additional Important Safety Information. Please click here for full Prescribing Information.

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What you will find in this guide:

SAFETY PROFILE

Safety profile in PROS

CONSIDERATIONS **BEFORE AND DURING** TREATMENT

Review your patient's medical history

Advise patients about potential serious ARs

Assess and optimize blood glucose

Review drug interactions and pharmacokinetics

DOSING AND ADMINISTRATION

Pediatric dosing

Adult dosing

STRATEGIES FOR MANAGING SELECT ARs

Rash and SCARs

Hyperglycemia

Pneumonitis

Diarrhea

Pancreatitis

Other ARs

IMPORTANT SAFETY INFORMATION (cont)

Hyperglycemia. Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) or fatal cases of ketoacidosis, has occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE® (alpelisib) tablets.

In the EPIK-P1 study, grade 1 or 2 hyperglycemia was reported in 12% of patients treated with VIJOICE.

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Safety profile

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Safety profile in PROS[1]

ARs and laboratory abnormalities occurring in all patients (N=57)		
AR (≥5% of patients)	**All grades (%)**	**Grades 3-4 (%)**
Diarrhea	16	0
Stomatitis[a]	16	0
Hyperglycemia	12	0
Eczema	7	0
Dry skin	7	0
Cellulitis	5	3.5
Alopecia	5	0
Headache	5	0
Laboratory abnormality (>20% of patients)[b]	**All grades (%)**	**Grades 3-4 (%)**
Chemistry		
Decreased calcium (corrected)	60	0
Decreased phosphate	59	5[e]
Increased glucose[c]	56	11[e]
Increased glycosylated hemoglobin (HbA1c)[d]	38[d]	NA[d]
Increased creatinine	31	0
Increased bilirubin	29	2[e]
Increased potassium	24	0
Hematology		
Decreased leukocyte	22	0
Decreased hemoglobin	20	6[e]
Decreased lymphocyte	20	0

The most commonly reported ARs were diarrhea (16%), stomatitis (16%), and hyperglycemia (12%)

- All ARs occurring in ≥10% of patients were mild to moderate (grade 1 or 2)
- Serious ARs occurred in 12% of patients who received VIJOICE® (alpelisib) tablets. Dehydration (n=2) and cellulitis (n=2) were the only serious ARs that occurred in multiple patients

No patients permanently discontinued treatment due to ARs

- 95% of all patients received VIJOICE for 6 months or longer
- 79% of all patients received VIJOICE for >12 months

Additional safety data

- 5% of patients required dose reductions due to ARs. Alopecia, memory impairment, and soft tissue infection were the only ARs that required dose reduction
- Dose interruption due to an AR occurred in 11% of patients. Vomiting (n=2) and dizziness (n=2) were the only ARs that required dose interruption in 2 or more patients

PEDIATRIC AND ADULT SAFETY PROFILES ›

Grading according to CTCAE version 4.03.
[a]Stomatitis, including stomatitis and aphthous ulcer.
[b]The denominator used to calculate the rate varied from 9 to 50 based on the number of patients with a baseline value and at least 1 posttreatment value.
[c]Glucose increase is an expected laboratory abnormality of PI3K inhibition.
[d]No CTCAE grade available. For HbA1c, baseline values increasing posttreatment to a value above the upper limit of the normal range (≥5.7%) are considered increased.
[e]No grade 4 laboratory abnormalities were reported.
NA, not available; PI3K, phosphatidylinositol-3 kinase.

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Pediatric and adult safety profiles[2]

ARs occurring in >10% of either pediatric or adult patients

AR	All grades (%)		Grades 3-4 (%)	
	Pediatric (n=39)	Adult (n=18)	Pediatric (n=39)	Adult (n=18)
Diarrhea	12.8	22.2	0	0
Vascular malformation	10.3	0	0	0
Aphthous ulcer	7.7	16.7	0	0
Inflammation	7.7	11.1	0	5.6
Hyperglycemia	5.1	27.8	0	0
Disseminated intravascular coagulation	5.1	16.7	0	5.6
Dry skin	2.6	16.7	0	0
Eczema	2.6	16.7	0	0
Cellulitis	2.6	11.1	2.6	5.6
Pain in extremity	2.6	11.1	0	5.6
Headache	0	16.7	0	0
Alopecia	0	16.7	0	0

Grading according to CTCAE version 4.03.

Considerations before and during treatment

Vijoice®
(alpelisib) tablets
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Consider these steps before and during treatment:

1. REVIEW YOUR PATIENT'S MEDICAL HISTORY
2. ADVISE PATIENTS ABOUT POTENTIAL SERIOUS ARs
3. ASSESS AND OPTIMIZE BLOOD GLUCOSE
4. REVIEW DRUG INTERACTIONS AND PHARMACOKINETICS

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Before treatment:

Review your patient's medical history[1]

Severe hypersensitivity

Severe hypersensitivity reactions, including anaphylaxis, angioedema, and anaphylactic shock, have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE® (alpelisib) tablets.

VIJOICE is contraindicated in patients with severe hypersensitivity to alpelisib or any of its ingredients.

Diabetes

The safety of VIJOICE in patients with type 1 and uncontrolled type 2 diabetes has not been established.

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

Renal impairment

The effect of severe renal impairment (CrCl <30 mL/min) on the pharmacokinetics of alpelisib is unknown.

VIJOICE is not approved for use in the oncology setting.

CrCl, creatinine clearance.

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Before and during treatment:

Advise patients and their caregivers about potential serious ARs[1]

Advise your patients and their caregivers about the following serious ARs that have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE® (alpelisib) tablets. VIJOICE is not approved for use in the oncology setting.

Hyperglycemia

Signs and symptoms may include:

- Excessive thirst
- Urinating more often than usual or higher amount of urine than usual
- Increased appetite with weight loss

Diarrhea or colitis

Severe diarrhea can result in dehydration and, in some cases, acute kidney injury and colitis. Advise patients and their caregivers to start antidiarrheal treatment, increase oral fluids, and notify their health care professional (HCP) if diarrhea occurs while taking VIJOICE. Advise patients and their caregivers to notify their HCP immediately of any symptoms of colitis, such as abdominal pain and mucus or blood in stool, while taking VIJOICE.

Hypersensitivity

Signs and symptoms may include:

- Dyspnea
- Flushing
- Rash
- Fever
- Tachycardia

Tell your patients to notify their HCP if serious ARs occur while taking VIJOICE

SCARs

Signs and symptoms may include:

- A prodrome of fever
- Flu-like symptoms
- Mucosal lesions
- Progressive skin rash
- Lymphadenopathy

Noninfectious pneumonitis

Nonspecific respiratory signs and symptoms in patients in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations may include:

- Hypoxia
- Cough
- Dyspnea
- Interstitial infiltrates on radiologic exams

Embryo-fetal toxicity

Based on findings in animals and its mechanism of action, VIJOICE 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 VIJOICE 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 VIJOICE and for 1 week after the last dose.

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Before and during treatment:

Assess and optimize blood glucose[1]

Before treatment, test fasting plasma glucose (FPG) and HbA1c, and optimize blood glucose

Hyperglycemia is a serious AR associated with VIJOICE® (alpelisib) tablets. As a result, it is important to monitor your patient's fasting glucose levels (FPG or fasting blood glucose) with blood tests before and during treatment with VIJOICE.

After initiating treatment with VIJOICE, continue laboratory monitoring

Fasting glucose (FPG or fasting blood glucose)

During the first 2 weeks of treatment:

- At least once every week

After the first 2 weeks of treatment:

- At least once every 4 weeks, and as clinically indicated

HbA1c

Every 3 months and as clinically indicated

Keep in mind your patient's monitoring schedule will change if hyperglycemia occurs.

Monitor fasting glucose levels more frequently for the first few weeks during treatment with VIJOICE in patients with the following risk factors for hyperglycemia:

- Obesity (BMI ≥30)
- Elevated FPG
- HbA1c at the upper limit of normal or above
- Use of concomitant systemic corticosteroids
- Age ≥75 years

Blood glucose monitoring recommendations are based on hyperglycemia in the oncology setting.

VIJOICE is not approved for use in the oncology setting.

BMI, body mass index.

Vijoice® (alpelisib) tablets 50 mg | 125 mg | 200 mg

Before and during treatment:

Review drug interactions and pharmacokinetics[1]

Effect of other drugs on VIJOICE

CYP3A4 inducers

Avoid coadministration of VIJOICE® (alpelisib) tablets with strong CYP3A4 inducers. Alpelisib is metabolized by CYP3A4. Concomitant use of VIJOICE with a strong CYP3A4 inducer may decrease the concentration of VIJOICE, which may decrease the activity of alpelisib.

Breast cancer resistance protein (BCRP) inhibitors

Avoid the use of BCRP inhibitors in patients treated with VIJOICE. If unable to use alternative drugs, when VIJOICE is used in combination with BCRP inhibitors, closely monitor for increased ARs. Alpelisib is transported by BCRP. Concomitant use of VIJOICE with a BCRP inhibitor may increase exposure of alpelisib, which may increase the risk of ARs.

Effect of VIJOICE on other drugs

CYP2C9 substrates

Closely monitor CYP2C9 substrates where minimal concentration changes of the CYP2C9 substrate may reduce activity when used concomitantly with VIJOICE. Alpelisib induces CYP2C9. Concomitant use of VIJOICE with CYP2C9 substrates may reduce exposure of these drugs, which may reduce activity.

Metabolism

Alpelisib is primarily metabolized by chemical and enzymatic hydrolysis and to a lesser extent by CYP3A4, in vitro.

Effect of food

A high-fat, high-calorie meal (985 calories with 58.1 g of fat) increased the AUC of alpelisib by 73% and C_{max} by 84%, and a low-fat, low-calorie meal (334 calories with 8.7 g of fat) increased the AUC of alpelisib by 77% and C_{max} by 145% following a single 300-mg dose of alpelisib.

AUC, area under the curve; C_{max}, maximum serum concentration.

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Dosing and administration

Vijoice®
(alpelisib) tablets
50 mg | 125 mg | 200 mg

VIJOICE is taken orally, once daily[1]

Recommended starting dose and dose modifications for pediatric patients (ages 2 to <18 years)

VIJOICE® (alpelisib) tablets is taken orally, once daily, with food, and at approximately the same time every day until disease progression or unacceptable toxicity occurs.

RECOMMENDED STARTING DOSE

50 mg qd (One 50-mg tablet)

For pediatric patients ≥6 years: Consider a **dose increase to 125 mg (one 125-mg tablet) for response optimization after 24 weeks** of treatment with VIJOICE.

Dose reduction back to 50 mg may be required if ARs occur. Discontinue VIJOICE in patients who cannot tolerate the 50-mg dose.

Available dosage for dose increase

125 mg qd (One 125-mg tablet)

For pediatric patients who turn 18 years: Consider a gradual dose increase up to 250 mg.

CLICK HERE FOR RECOMMENDED DOSE MODIFICATIONS AND MANAGEMENT FOR SELECT ARs

Additional information:

- **If a dose of VIJOICE is missed,** it can be taken with food within 9 hours after the time it is usually taken. After more than 9 hours, skip the dose for that day. The next day, take VIJOICE at the usual time
- **If the patient vomits after taking the dose,** advise the patient not to take an additional dose on that day and to resume the dosing schedule the next day at the usual time
- **If an AR occurs,** there are dose reduction and interruption guidelines for VIJOICE. Some patients may need to stop taking the drug

Patients who are able to swallow tablets should swallow VIJOICE tablets whole. Tablets should not be chewed or split prior to swallowing.

qd, once daily.

FOR PATIENTS WHO ARE UNABLE TO SWALLOW TABLETS

Vijoice® (alpelisib) tablets
50 mg | 125 mg | 200 mg

Patients who are unable to swallow tablets should take VIJOICE by following these steps[1]:

1. Place VIJOICE® (alpelisib) tablets or tablet in a glass containing 2 to 4 ounces of water, and let it stand for approximately 5 minutes. Make the suspension with water only.

2. Crush the tablet or tablets with a spoon, and stir until an oral suspension is obtained.

3. Administer the oral suspension immediately after preparation. Discard the oral suspension if it is not administered within 60 minutes after preparation.

4. After administration of the oral suspension, add approximately 2 to 3 tablespoons of water to the same glass. Stir with the same spoon to resuspend any remaining particles, and administer the entire contents of the glass. Repeat if particles remain.

LIQUIDS OTHER THAN WATER SHOULD NOT BE USED FOR MAKING THE ORAL SUSPENSION

VIJOICE is taken orally, once daily[1]

Recommended starting dose and dose modifications for adult patients (ages ≥18 years)

VIJOICE® (alpelisib) tablets is taken orally, once daily, with food, and at approximately the same time every day until disease progression or unacceptable toxicity occurs.

RECOMMENDED STARTING DOSE

250 mg qd (One 200-mg tablet + one 50-mg tablet)

Dose reductions may be required if an AR occurs.

Available dosages for dose reductions

125 mg qd (One 125-mg tablet)

50 mg qd (One 50-mg tablet)

Discontinue VIJOICE in patients who cannot tolerate the 50-mg dose.

CLICK HERE FOR RECOMMENDED DOSE MODIFICATIONS AND MANAGEMENT FOR SELECT ARs

Additional information:

- **If a dose of VIJOICE is missed,** it can be taken with food within 9 hours after the time it is usually taken. After more than 9 hours, skip the dose for that day. The next day, take VIJOICE at the usual time
- **If the patient vomits after taking the dose,** advise the patient not to take an additional dose on that day and to resume the dosing schedule the next day at the usual time
- **If an AR occurs,** there are dose reduction and interruption guidelines for VIJOICE. Some patients may need to stop taking the drug

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LIQUIDS OTHER THAN WATER SHOULD NOT BE USED FOR MAKING THE ORAL SUSPENSION

Strategies for managing select ARs

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Select an AR for management recommendations:

RASH AND SCARs

HYPERGLYCEMIA

PNEUMONITIS

DIARRHEA

PANCREATITIS

OTHER ARs

Vijoice® (alpelisib) tablets 50 mg | 125 mg | 200 mg

Dosage modifications and management for rash and SCARs[1]

Grade[a,b]	Recommendations for adult and pediatric patients[c]
Grade 1 **(<10% BSA with active skin toxicity)**	• No dosage modification is required for VIJOICE® (alpelisib) tablets unless the etiology is determined to be SCAR • Initiate topical corticosteroid treatment • Consider adding oral antihistamine to manage symptoms • If active rash is not improved within 28 days of appropriate treatment, add a low-dose, systemic corticosteroid • If the etiology is determined to be SCAR, permanently discontinue VIJOICE
Grade 2 **(10%-30% BSA with active skin toxicity)**	• No dosage modification is required for VIJOICE unless the etiology is determined to be SCAR • Initiate or intensify topical corticosteroid and oral antihistamine treatment • Consider low-dose, systemic corticosteroid treatment • If rash improves to grade ≤1 within 10 days, systemic corticosteroid may be discontinued • If the etiology is determined to be SCAR, permanently discontinue VIJOICE
Grade 3 **(eg, severe rash not responsive to medical management)** **(>30% BSA with active skin toxicity)**	• Interrupt VIJOICE and initiate or intensify topical/systemic corticosteroid and oral antihistamine treatment • If the etiology is determined to be SCAR, permanently discontinue VIJOICE • For rashes other than SCAR  **Adult patients:** Upon improvement to grade ≤1, resume VIJOICE at the next lower dose level.  **Pediatric patients:** Upon improvement to grade ≤1, either resume VIJOICE at 50 mg while continuing oral antihistamine treatment or permanently discontinue VIJOICE. Permanently discontinue VIJOICE if: • Patient was receiving antihistamines at the time of rash onset and the dose of the antihistamine cannot be increased • Grade ≥3 rash recurs
Grade 4 **(eg, severe bullous, blistering, or exfoliating skin conditions)** **(any % BSA associated with extensive superinfection, with IV antibiotics indicated; life-threatening consequences)**	Permanently discontinue VIJOICE.

[a]Grading according to CTCAE version 5.0.
[b]For all grades of rash, consider consultation with a dermatologist.
[c]Antihistamines administered prior to rash onset may decrease incidence and severity of rash.
BSA, body surface area; IV, intravenous.

Dosage modifications and management for hyperglycemia[1]

If a patient experiences hyperglycemia, adjust their monitoring schedule

Monitor fasting glucose as clinically indicated and at least twice weekly until fasting glucose decreases to normal levels.

During treatment with antihyperglycemic medication, adjust monitoring schedule

- 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 an HCP with expertise in treating hyperglycemia, and counsel patients on lifestyle changes

Metformin was used in select patients in the EPIK-P1 study to manage hyperglycemia[2]

HYPERGLYCEMIA MANAGEMENT
RECOMMENDATIONS CONTINUED ON NEXT PAGE

Dosage modifications and management for hyperglycemia (cont)[1]

FPG/fasting blood glucose values[a]	Recommendations for adult and pediatric patients
Dose modifications and management should be based only on fasting glucose values (FPG or fasting blood glucose)	
Grade 1 **Fasting glucose >ULN-160 mg/dL or >ULN-8.9 mmol/L**	• No dosage modification is required for VIJOICE® (alpelisib) tablets • Initiate or intensify oral antihyperglycemic treatment[b]
Grade 2 **Fasting glucose >160-250 mg/dL or >8.9-13.9 mmol/L**	• No dosage modification is required for VIJOICE • Initiate or intensify oral antihyperglycemic treatment[b]  **Adult patients:** If fasting glucose does not decrease to ≤160 mg/L or 8.9 mmol/L within 21 days under appropriate antihyperglycemic treatment,[b] reduce the dose of VIJOICE by 1 dose level and follow fasting glucose value-specific recommendations.  **Pediatric patients:** If fasting glucose does not decrease to ≤160 mg/L or 8.9 mmol/L within 21 days under appropriate antihyperglycemic treatment,[b] interrupt VIJOICE until improvement to grade ≤1, then resume VIJOICE at 50 mg and follow fasting glucose value-specific recommendations.
Grade 3 **Fasting glucose >250-500 mg/dL or >13.9-27.8 mmol/L**	• Interrupt VIJOICE • Initiate or intensify oral antihyperglycemic treatment[b] and consider additional antihyperglycemic medications for 1 to 2 days until hyperglycemia improves, as clinically indicated • Administer IV hydration and consider appropriate treatment (eg, intervention for electrolyte/ketoacidosis/hyperosmolar disturbances)  **Adult patients:** • If fasting glucose decreases to ≤160 mg/dL or 8.9 mmol/L within 3 to 5 days under appropriate antihyperglycemic treatment, resume VIJOICE at 1 lower dose level • If fasting glucose does not decrease to ≤160 mg/dL or 8.9 mmol/L within 3 to 5 days under appropriate antihyperglycemic treatment, consultation with an HCP with expertise in treating hyperglycemia is recommended • If fasting glucose does not decrease to ≤160 mg/dL or 8.9 mmol/L within 21 days following appropriate antihyperglycemic treatment,[b] permanently discontinue VIJOICE  **Pediatric patients:** • If fasting glucose decreases to ≤160 mg/dL or 8.9 mmol/L within 3 to 5 days under appropriate antihyperglycemic treatment, resume VIJOICE at 50 mg • If fasting glucose does not decrease to ≤160 mg/dL or 8.9 mmol/L within 3 to 5 days under appropriate antihyperglycemic treatment, consultation with an HCP with expertise in treating hyperglycemia is recommended to determine if treatment with VIJOICE should be resumed or permanently discontinued • If fasting glucose does not decrease to ≤160 mg/dL or 8.9 mmol/L within 21 days following appropriate antihyperglycemic treatment,[b] permanently discontinue VIJOICE • If hyperglycemia recurs at grade ≥3, consider permanent discontinuation of VIJOICE
Grade 4 **Fasting glucose >500 mg/dL or >27.8 mmol/L**	• Interrupt VIJOICE • Initiate or intensify appropriate oral antihyperglycemic treatment[b] • Administer IV hydration and consider appropriate treatment (eg, intervention for electrolyte/ketoacidosis/hyperosmolar disturbances) • Recheck fasting glucose within 24 hours and as clinically indicated – If fasting glucose decreases to ≤500 mg/dL or 27.8 mmol/L, follow fasting glucose value-specific recommendations for grade 3 – If fasting glucose is confirmed at >500 mg/dL or 27.8 mmol/L, permanently discontinue VIJOICE

[a]FPG/fasting blood glucose/grade levels reflect hyperglycemia grading according to CTCAE version 4.03.
[b]Initiate applicable antihyperglycemic medications, including metformin in adult and pediatric patients ≥10 years, sodium-glucose transport protein 2 (SGLT2) inhibitors or insulin sensitizers (such as thiazolidinediones or dipeptidyl peptidase-4 inhibitors) in adult patients, and review respective prescribing information for dosing and dose titration recommendations, including local hyperglycemic treatment guidelines.
ULN, upper limit of normal.

Dosage modifications for pneumonitis[1]

Grade[a]	Recommendations for adult and pediatric patients
Any grade	• Interrupt VIJOICE® (alpelisib) tablets if pneumonitis is suspected • Permanently discontinue VIJOICE if pneumonitis is confirmed

[a]Grading according to CTCAE version 5.0.

Dosage modifications and management for diarrhea or colitis[1]

Grade[a]	Recommendations for adult and pediatric patients
Grade 1	• No dosage modification is required for VIJOICE® (alpelisib) tablets • Initiate appropriate medical therapy, and monitor as clinically indicated
Grade 2	• Interrupt the dose of VIJOICE until improvement to grade ≤1, then resume VIJOICE at the same dose level • Initiate or intensify appropriate medical therapy, and monitor as clinically indicated[b]  **Adult patients:** • For recurrent grade ≥2, interrupt the dose of VIJOICE until improvement to grade ≤1, then resume VIJOICE at the next lower dose level  **Pediatric patients:** • For recurrent grade ≥2, interrupt the dose of VIJOICE until improvement to grade ≤1, then resume VIJOICE at 50 mg
Grade 3	• Interrupt the dose of VIJOICE until improvement to grade ≤1 • Initiate or intensify appropriate medical therapy, and monitor as clinically indicated[b]  **Adult patients:** • Once improved to grade ≤1, resume VIJOICE at the next lower dose level  **Pediatric patients:** • Once improved to grade ≤1, either resume VIJOICE at 50 mg or permanently discontinue VIJOICE • For recurrent grade ≥3, consider permanent discontinuation of VIJOICE
Grade 4	Permanently discontinue VIJOICE.

[a]Grading according to CTCAE version 5.0.
[b]For grade 2 and 3 colitis, consider additional treatment, such as enteric-acting and/or systemic steroids.

Dosage modifications for pancreatitis[1]

Grade[a]	Recommendations for adult and pediatric patients
Grade 2	Interrupt the dose of VIJOICE® (alpelisib) tablets until improvement to grade <2.  **Adult patients:** • Resume VIJOICE at the next lower dose level (only 1 dose reduction is permitted) • If pancreatitis recurs, permanently discontinue VIJOICE  **Pediatric patients:** • Resume VIJOICE at 50 mg • If pancreatitis recurs, permanently discontinue VIJOICE
Grade 3	 **Adult patients:** • Interrupt the dose of VIJOICE until improvement to grade <2 • Resume VIJOICE at the next lower dose level (only 1 dose reduction is permitted) • If pancreatitis recurs, permanently discontinue VIJOICE  **Pediatric patients:** • Permanently discontinue VIJOICE
Grade 4	Permanently discontinue VIJOICE.

[a]Grading according to CTCAE version 5.0.

Dosage modifications and management for other ARs[1]

(excluding rash and SCARs, hyperglycemia, pneumonitis, diarrhea or colitis, and pancreatitis)

Grade[a]	Recommendations for adult and pediatric patients
Grade 1 or 2[b,c]	• No dosage modification is required for VIJOICE® (alpelisib) tablets • Initiate appropriate medical therapy, and monitor as clinically indicated[b,c]
Grade 3	• Interrupt the dose of VIJOICE until improvement to grade ≤1 • Initiate or intensify appropriate medical therapy, and monitor as clinically indicated  **Adult patients:** • Once improved to grade ≤1, resume VIJOICE at the next lower dose level  **Pediatric patients:** • Once improved to grade ≤1, either resume VIJOICE at 50 mg or permanently discontinue VIJOICE • If an AR recurs at grade ≥3, consider permanent discontinuation of VIJOICE • Consider consultation with a qualified HCP with specific expertise in the field of the concerned AR
Grade 4	Permanently discontinue VIJOICE.

[a]Grading according to CTCAE version 5.0.
[b]For grade 2 total bilirubin elevation in adult patients, interrupt the dose of VIJOICE until improvement to grade ≤1. If improvement occurs in ≤14 days, resume at the same dose level. If improvement occurs in >14 days, resume VIJOICE at the next lower dose level.
[c]For grade 2 total bilirubin elevation in pediatric patients, interrupt the dose of VIJOICE until improvement to grade ≤1. If improvement occurs in ≤14 days, resume at the same dose level. If improvement occurs in >14 days, resume VIJOICE at 50 mg.

Indication and Important Safety Information

INDICATION

VIJOICE® (alpelisib) tablets is indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA-Related Overgrowth Spectrum (PROS) who require systemic therapy.

This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

VIJOICE is contraindicated in patients with severe hypersensitivity to alpelisib or any of its ingredients.

Severe Hypersensitivity. Severe hypersensitivity reactions, including anaphylaxis, angioedema, and anaphylactic shock, have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE. VIJOICE is not approved for use in the oncology setting. Permanently discontinue VIJOICE 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), have occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE. If signs or symptoms of SCARs occur, interrupt VIJOICE until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended. If a SCAR is confirmed, permanently discontinue VIJOICE. If a SCAR is not confirmed, VIJOICE may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Hyperglycemia. Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) or fatal cases of ketoacidosis, has occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE.

In the EPIK-P1 study, grade 1 or 2 hyperglycemia was reported in 12% of patients treated with VIJOICE.

Before initiating treatment with VIJOICE, test fasting plasma glucose (FPG), HbA1c, and optimize blood glucose. After initiating treatment with VIJOICE, 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. Monitor fasting glucose more frequently for the first few weeks during treatment with VIJOICE in patients with risk factors for hyperglycemia, such as obesity (body mass index ≥30), elevated FPG, HbA1c at the upper limit of normal or above, use of concomitant systemic corticosteroids, or age ≥75.

If a patient experiences hyperglycemia after initiating treatment with VIJOICE, monitor fasting glucose as clinically indicated and at least twice weekly until fasting glucose decreases to normal levels. During treatment with antihyperglycemic 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 provider with expertise in the treatment of hyperglycemia, and counsel patients on lifestyle changes.

Vijoice® (alpelisib) tablets
50 mg | 125 mg | 200 mg

Please click here for full Prescribing Information.

Indication and Important Safety Information (cont)

The safety of VIJOICE® (alpelisib) tablets in patients with type 1 and uncontrolled type 2 diabetes has not been established. Patients with a history of diabetes mellitus may require intensified hyperglycemic treatment. Closely monitor patients with diabetes.

Interrupt, reduce the dose of, or permanently discontinue VIJOICE based on severity.

Pneumonitis. Severe pneumonitis, including acute interstitial pneumonitis and interstitial lung disease, has occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE.

In patients who have new or worsening respiratory symptoms or are suspected to have developed pneumonitis, interrupt VIJOICE 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 examinations and in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations.

Permanently discontinue VIJOICE in all patients with confirmed pneumonitis.

Diarrhea or Colitis. Severe diarrhea, resulting in dehydration, and, in some cases, acute kidney injury and colitis, has occurred in adult patients treated with alpelisib in the oncology setting and may occur in patients treated with VIJOICE. In the EPIK-P1 study, 16% of patients experienced grade 1 diarrhea during treatment with VIJOICE. Monitor patients for diarrhea and additional symptoms of colitis, such as abdominal pain and mucus or blood in the stool. Interrupt, reduce the dose of, or permanently discontinue VIJOICE based on the severity of diarrhea or colitis.

Embryo-Fetal Toxicity. Based on findings in animals and its mechanism of action, VIJOICE 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 VIJOICE 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 VIJOICE and for 1 week after the last dose.

The most common adverse reactions (all grades, incidence ≥10%) were diarrhea (16%), stomatitis (16%), and hyperglycemia (12%).

The most common laboratory abnormalities (all grades, incidence ≥20%) were decreased calcium (corrected) (60%), decreased phosphate (59%), increased glucose (56%), increased HbA1c (38%), increased creatinine (31%), increased bilirubin (29%), increased potassium (24%), decreased leukocyte (22%), decreased lymphocyte (20%), and decreased hemoglobin (20%).

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For more information, visit VIJOICE-HCP.com

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*The **FIRST** and **ONLY** FDA-approved treatment for pediatric and adult patients with PROS*

References: 1. Vijoice [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. Novartis Pharmaceuticals Corp; 2021. **3.** Study assessing the efficacy, safety and PK of alpelisib (BYL719) in pediatric and adult patients with PIK3CA-related Overgrowth Spectrum (EPIK-P2). ClinicalTrials.gov identifier: NCT04589650. https://clinicaltrials.gov/ct2/show/NCT04589650. Updated September 7, 2022. Accessed November 23, 2022.

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

NOVARTIS

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