HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VIJOICE safely and effectively. See full prescribing information for VIJOICE.

VIJOICE® (alpelisib) tablets, for oral use
Initial U.S. Approval: 2019

----------INDICATIONS AND USAGE----------
VIJOICE is a kinase inhibitor 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 a confirmatory trial(s). (1)

----------DOSAGE AND ADMINISTRATION----------
Recommended Dose:
- Pediatric patients (2 to less than 18 years of age): 50 mg taken orally once daily with food. (2.1)
- Adult patients: 250 mg taken orally once daily with food. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 50 mg, 125 mg, and 200 mg (3)

----------CONTRAINDICATIONS----------
Severe hypersensitivity to VIJOICE or to any of its ingredients. (4)

----------WARNINGS AND PRECAUTIONS----------
- Severe Hypersensitivity: Permanently discontinue VIJOICE. Promptly initiate appropriate treatment. (5.1)
- Severe Cutaneous Adverse Reactions (SCARs): VIJOICE can cause SCARs, including Stevens-Johnson syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS). Interrupt VIJOICE for signs or symptoms of SCARs. Permanently discontinue VIJOICE if SCARs are confirmed. (2.3, 5.2)
- Hyperglycemia: VIJOICE can cause severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar non-ketotic syndrome (HHNKS) or ketoacidosis. The safety of VIJOICE in patients with Type 1 or uncontrolled Type 2 diabetes has not been established. Before initiating treatment with VIJOICE, test fasting plasma glucose (FPG), HbA1c, and optimize blood glucose. After initiating treatment, monitor periodically. Initiate or optimize anti-hyperglycemic medications as clinically indicated. Interrupt, reduce dose, or discontinue VIJOICE if severe hyperglycemia occurs. (2.3, 5.3)
- Pneumonitis: VIJOICE can cause severe pneumonitis and interstitial lung disease. Monitor for clinical symptoms or radiological changes. Permanently discontinue VIJOICE if pneumonitis occurs. (2.3, 5.4)
- Diarrhea: VIJOICE can cause severe diarrhea, dehydration, and acute kidney injury. Interrupt, reduce dose, or permanently discontinue VIJOICE based on severity. (2.3, 5.5)
- Embryo-Fetal Toxicity: VIJOICE can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception. (5.6, 8.1, 8.3)

----------ADVERSE REACTIONS----------
Most common adverse reactions (Grades 1 to 4, incidence ≥ 10%) were diarrhea, stomatitis, and hyperglycemia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- CYP3A4 Inducers: Avoid coadministration of VIJOICE with a strong CYP3A4 inducer. (7.1)
- Breast Cancer Resistance Protein (BCRP) Inhibitors: Avoid the use of BCRP inhibitors in patients treated with VIJOICE. If unable to use alternative drugs, closely monitor for increased adverse reactions. (7.1)
- CYP2C9 Substrates: Closely monitor when VIJOICE is coadministered with CYP2C9 substrates where decreases in the plasma concentration of these drugs may reduce activity. (7.2)

----------USE IN SPECIFIC POPULATIONS----------
Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 4/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VIJOICE 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 a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Adult Patients

The recommended dosage of VIJOICE in adult patients is 250 mg orally, once daily, administered as recommended *[see Dosage and Administration (2.2)]* until disease progression or unacceptable toxicity.

Pediatric Patients (2 to less than 18 years of age)

The recommended initial dosage of VIJOICE in pediatric patients is 50 mg orally, once daily, administered as recommended *[see Dosage and Administration (2.2)]* until disease progression or unacceptable toxicity.

Consider a dose increase to 125 mg once daily in pediatric patients ≥ 6 years old for response optimization (clinical/radiological) after 24 weeks of treatment with VIJOICE at 50 mg once daily. When a pediatric patient turns 18 years old, consider a gradual dose increase up to 250 mg. Recommended dose increases by age group are listed in Table 1.

Table 1: Recommended Daily VIJOICE Dose Levels for Pediatric Patients (2 to less than 18 years of age)

Patient age (years)	Initial dose	Dose increase
2 to < 6	50 mg	Not applicable*
6 to < 18	50 mg	125 mg

*A recommended increased dose has not been established.

2.2 Administration

Take VIJOICE with food at approximately the same time each day.

No tablet should be used if it is broken, cracked, or otherwise damaged at the time of opening the blister pack.

Swallow VIJOICE tablets whole. Do not split or chew.

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.

Preparation and Administration for Patients Who Have Difficulty Swallowing Tablets

- For patients who are not able to swallow tablets, administer VIJOICE as an oral suspension with food *[see Clinical Pharmacology (12.3)]*.
    - Place VIJOICE tablets in a glass containing 2 to 4 ounces of water and let it stand for approximately 5 minutes. Make the suspension with water only.
    - Crush the tablets with a spoon and stir until an oral suspension is obtained.
    - Administer the oral suspension immediately after preparation. Discard the oral suspension if it is not administered within 60 minutes after preparation.
    - After administration of the oral suspension, add approximately 2 to 3 tablespoons of water to the same glass. Stir with the same spoon to re-suspend any remaining particles and administer the entire contents of the glass. Repeat if particles remain.

2.3 Dosage Modifications for Adverse Reactions

The recommended VIJOICE dose reductions for adverse reactions in adult and pediatric patients are listed in Table 2 and Table 3, respectively.

Table 2: VIJOICE Dosage Reduction Recommendations for Adverse Reactions in Adult Patients

VIJOICE dose level	Dose and schedule
First-dose reduction	125 mg once daily
Second-dose reduction	50 mg once daily

Table 3: VIJOICE Dosage Reduction Recommendations for Adverse Reactions in Pediatric Patients

Action	VIJOICE dose prior to dose reduction	
	125 mg once daily	50 mg once daily
Dose reduction	50 mg once daily	Not applicable

Discontinue VIJOICE in adults or pediatric patients who cannot tolerate 50 mg daily.

Tables 4, 5, 6, 7, 8, and 9 summarize recommendations for dose interruption, reduction, or discontinuation of VIJOICE in the management of specific adverse reactions.

Cutaneous Adverse Reactions

If a severe cutaneous adverse reaction (SCAR) is confirmed, permanently discontinue VIJOICE. Do not reintroduce VIJOICE in patients who have experienced previous SCAR during VIJOICE treatment *[see Warnings and Precautions (5.2)]*.

Table 4: Dosage Modification and Management for Rash and Severe Cutaneous Adverse Reactions (SCARs) *[see Warnings and Precautions (5.1, 5.2)]*

Grade[a,b]	Recommendation for adult and pediatric patients[c]
Grade 1 (< 10% body surface area (BSA) with active skin toxicity)	No VIJOICE dosage modification is required 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% to 30% BSA with active skin toxicity)	No VIJOICE dosage modification is required 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 (e.g., 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:

Grade[a,b]	Recommendation for adult and pediatric patients[c]
	• Patient was receiving antihistamines at the time of rash onset and antihistamine dose cannot be increased • Grade ≥ 3 rash recurs
Grade 4 (e.g., 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 Common Terminology Criteria for Adverse Events (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.	

Hyperglycemia

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. In patients with risk factors for hyperglycemia, monitor fasting glucose more closely and as clinically indicated *[see Warnings and Precautions (5.3)]*.

Table 5: Dosage Modification and Management for Hyperglycemia *[see Warnings and Precautions (5.3)]*

Fasting plasma glucose (FPG)/Fasting blood glucose values[a]	Recommendation for adult and pediatric patients
Dose modifications and management should only be based on fasting glucose values (FPG or fasting blood glucose).	
Grade 1 Fasting glucose > ULN - 160 mg/dL or > ULN - 8.9 mmol/L	No VIJOICE dosage modification is required. Initiate or intensify oral anti-hyperglycemic treatment[b].
Grade 2 Fasting glucose > 160 - 250 mg/dL or > 8.9 - 13.9 mmol/L	No VIJOICE dosage modification is required. Initiate or intensify oral anti-hyperglycemic treatment[b]. Adult Patients: • If fasting glucose does not decrease to ≤ 160 mg/dL or 8.9 mmol/L within 21 days under appropriate anti-hyperglycemic treatment[b], reduce VIJOICE dose by 1 dose level and follow fasting glucose value specific recommendations. Pediatric Patients: • If fasting glucose does not decrease to ≤ 160 mg/dL or 8.9 mmol/L within 21 days under appropriate anti-hyperglycemic 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 anti-hyperglycemic treatment[b] and consider additional anti-hyperglycemic medications for 1-2 days until hyperglycemia improves, as clinically indicated. Administer intravenous hydration and consider appropriate treatment (e.g., 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 anti-hyperglycemic 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 anti-hyperglycemic treatment, consultation with a physician with expertise in the treatment of hyperglycemia is recommended. • If fasting glucose does not decrease to ≤ 160 mg/dL or 8.9 mmol/L within 21 days following appropriate anti-hyperglycemic 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 anti-hyperglycemic 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 anti-hyperglycemic treatment, consultation with a physician with expertise in the treatment of 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 anti-hyperglycemic 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 anti-hyperglycemic treatment[b]. Administer intravenous hydration and consider appropriate treatment (e.g., intervention for electrolyte/ketoacidosis/hyperosmolar disturbances). Re-check fasting glucose within 24 hours and as clinically indicated. • If fasting glucose decreases to ≤ 500 mg/dL 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.
Abbreviation: ULN, upper limit of normal. [a]FPG/Fasting Blood Glucose/Grade levels reflect hyperglycemia grading according to Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03. [b]Initiate applicable anti-hyperglycemic medications, including metformin in adult and pediatric patients ≥ 10 years, 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 *[see Warnings and Precautions (5.3)]*.	

Pneumonitis

Table 6: Dosage Modification for Pneumonitis *[see Warnings and Precautions (5.4)]*

Grade[a]	**Recommendation for adult and pediatric patients**
Any Grade	• Interrupt VIJOICE if pneumonitis is suspected. • Permanently discontinue VIJOICE if pneumonitis is confirmed.
[a]Grading according to CTCAE Version 5.0.	

Diarrhea

In pediatric patients, consider consultation with a physician with experience in the treatment of gastrointestinal conditions.

Table 7: Dosage Modification and Management for Diarrhea *[see Warnings and Precautions (5.5)]*

Grade[a]	**Recommendation for adult and pediatric patients**
Grade 1	No VIJOICE dosage modification is required. Initiate appropriate medical therapy and monitor as clinically indicated.
Grade 2	Interrupt VIJOICE dose until improvement to Grade ≤ 1, then resume VIJOICE at the same dose level. Initiate or intensify appropriate medical therapy and monitor as clinically indicated.

	Adult Patients: • If diarrhea recurs at Grade ≥ 2, interrupt VIJOICE dose until improvement to Grade ≤ 1, then resume VIJOICE at the next lower dose level. Pediatric Patients: • If diarrhea recurs at Grade ≥ 2, interrupt VIJOICE dose until improvement to Grade ≤ 1, then resume VIJOICE at 50 mg.
Grade 3	Interrupt VIJOICE dose until improvement to Grade ≤ 1. Initiate or intensify appropriate medical therapy and monitor as clinically indicated. Adult Patients: • Once improved to Grade ≤ 1, then 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 diarrhea recurs at Grade ≥ 3, consider permanent discontinuation of VIJOICE.
Grade 4	Permanently discontinue VIJOICE.
[a]Grading according to CTCAE Version 5.0.	

Pancreatitis

Table 8: Dosage Modification for Pancreatitis

Grade[a]	**Recommendation for adult and pediatric patients**
Grade 2	Interrupt VIJOICE dose until improvement to Grade < 2. Adult Patients: • Resume VIJOICE at the next lower dose level (only one 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 VIJOICE dose until improvement to Grade < 2. • Resume VIJOICE at the next lower dose level (only one 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.	

Other Adverse Reactions

Table 9: Dosage Modification and Management for Other Adverse Reactions (Excluding Rash and Severe Cutaneous Adverse Reactions, Hyperglycemia, Pneumonitis, Diarrhea, and Pancreatitis)

Grade[a]	**Recommendation for adult and pediatric patients**
Grade 1 or 2[b,c]	No VIJOICE dosage modification is required. Initiate appropriate medical therapy and monitor as clinically indicated[b,c].
Grade 3	Interrupt VIJOICE dose until improvement to Grade ≤ 1. Initiate or intensify appropriate medical therapy and monitor as clinically indicated.

	Adult Patients: • Once improved to Grade ≤ 1, then 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 adverse reaction recurs at Grade ≥ 3, consider permanent discontinuation of VIJOICE. • Consider consultation with a qualified physician with specific expertise in the field of the concerned adverse reaction.
Grade 4	Permanently discontinue VIJOICE.

[a]Grading according to CTCAE Version 5.0.
[b]For Grade 2 total bilirubin elevation in adult patients, interrupt VIJOICE dose 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 VIJOICE dose 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.

3 DOSAGE FORMS AND STRENGTHS

Tablets: 50 mg, 125 mg, and 200 mg alpelisib

50 mg: Light yellow, unscored, round and curved with beveled edges film-coated tablet, debossed with "C7" on one side and "NVR" on the other side.

125 mg: Dark yellow, unscored, ovaloid and curved with beveled edges film-coated tablet, debossed with "Y7" on one side and "NVR" on the other side.

200 mg: Pale yellow, unscored, ovaloid and curved with beveled edges film-coated tablet, debossed with "CL7" on one side and "NVR" on the other side.

4 CONTRAINDICATIONS

VIJOICE is contraindicated in patients with severe hypersensitivity to alpelisib or any of its ingredients *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Severe Hypersensitivity

Severe hypersensitivity reactions, including anaphylaxis 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 *[see Contraindications (4)]*.

5.2 Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions (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. VIJOICE is not approved for use in the oncology setting.

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, as described in Table 4 *[see Dosage and Administration (2.3)]*.

5.3 Hyperglycemia

Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar non-ketotic 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. VIJOICE is not approved for use in the oncology setting.

In the EPIK-P1 study, Grade 1 or 2 hyperglycemia was reported in 12% of patients treated with VIJOICE *[see Adverse Reactions (6.1)]*.

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 (BMI ≥ 30), elevated FPG, HbA1c at the upper limit of normal or above, use of concomitant systemic corticosteroids, or age ≥ 75 *[see Use in Specific Populations (8.5)]*.

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 anti-hyperglycemic 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 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.

Interrupt, reduce the dose, or permanently discontinue VIJOICE based on the severity as decribed in Table 5 *[see Dosage and Administration (2.3)]*.

5.4 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. VIJOICE is not approved for use in the oncology setting.

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 non-infectious pneumonitis in patients presenting with non-specific respiratory signs and symptoms, such as hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams and in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations.

Permanently discontinue VIJOICE in all patients with confirmed pneumonitis *[see Dosage and Administration (2.3)]*.

5.5 Diarrhea

Severe diarrhea, including cases resulting in dehydration and acute kidney injury, has 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.

In the EPIK-P1 study, 16% of patients experienced Grade 1 diarrhea during treatment with VIJOICE *[see Adverse Reactions (6.1)]*.

Interrupt, reduce the dose or permanently discontinue VIJOICE based on severity *[see Dosage and Administration (2.3)]*.

5.6 Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, VIJOICE can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, oral administration of alpelisib to pregnant animals during organogenesis caused adverse developmental outcomes, including embryo-fetal mortality (post-implantation loss), reduced fetal weights, and increased incidences of fetal malformations at doses that were approximately equivalent to the recommended pediatric and adult doses. 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 *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.1)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed elsewhere in the labeling:

- Severe Hypersensitivity *[see Warnings and Precautions (5.1)]*
- Severe Cutaneous Adverse Reactions *[see Warnings and Precautions (5.2)]*
- Hyperglycemia *[see Warnings and Precautions (5.3)]*
- Pneumonitis *[see Warnings and Precautions (5.4)]*
- Diarrhea *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of VIJOICE was evaluated in EPIK-P1 (NCT04285723), a single-arm clinical study in patients who were treated as part of an expanded access program for compassionate use. Fifty-seven patients 2 years of age and older with severe or life-threatening PIK3CA-Related Overgrowth Spectrum (PROS) received VIJOICE based on age at dosages ranging from 50 mg to 250 mg orally once daily *[see Clinical Studies (14)]*. Among patients who received VIJOICE, 95% were exposed for 6 months or longer and 79% were exposed for greater than one year.

The median age of patients who received VIJOICE was 14 years (range, 2 to 50); 58% were female; 12% were White and race was not reported for 88%.

Serious adverse reactions occurred in 12% of patients who received VIJOICE. Serious adverse reactions occurring in two or more patients included dehydration (n = 2) and cellulitis (n = 2).

Dosage interruption of VIJOICE due to an adverse reaction occurred in 11% of patients. Adverse reactions which required dosage interruption in two or more patients included dizziness (n = 2) and vomiting (n = 2). Dose reductions of VIJOICE due to an adverse reaction occurred in 5% of patients. Adverse reactions which required dose reduction included alopecia, memory impairment, and soft tissue infection.

The most common adverse reactions (≥ 10%) were diarrhea, stomatitis, and hyperglycemia. The most common Grade 3 or 4 laboratory abnormalities (≥ 2%) were increased glucose, decreased hemoglobin, decreased phosphate, increased bilirubin, decreased sodium, and decreased platelets.

Adverse reactions and laboratory abnormalities are listed in Table 10 and Table 11, respectively.

Table 10: Adverse Reactions (≥ 5%) in Patients with PROS Who Received VIJOICE in EPIK-P1

Adverse reactions	**VIJOICE N = 57**	
	All Grades (%)	**Grade 3 or 4 (%)**
Gastrointestinal disorders		
Diarrhea	16	0
Stomatitis[a]	16	0
Metabolism and nutrition disorders		
Hyperglycemia	12	0
Skin and subcutaneous tissue disorders		
Eczema	7	0
Dry skin	7	0
Alopecia	5	0
Nervous system disorders		
Headache	5	0

Adverse reactions	VIJOICE N = 57	
	All Grades (%)	Grade 3 or 4 (%)
Infections and infestations		
Cellulitis	5	3.5

Grading according to CTCAE Version 4.03.
[a]Stomatitis: including stomatitis and aphthous ulcer.

Clinically relevant adverse reactions in < 5% of patients who received VIJOICE included nausea, vomiting, dehydration, and mucosal dryness.

Table 11: Laboratory Abnormalities Worsening from Baseline in ≥ 10% of Patients with PROS Who Received VIJOICE in EPIK-P1

Laboratory abnormality	VIJOICE[a] N = 57	
	All Grades %	Grade 3 or 4 %
Chemistry		
Decreased calcium (corrected)	60	0
Decreased phosphate	59	5[b]
Increased glucose[c]	56	11[b]
Increased glycosylated hemoglobin (HbA1c)[d]	38[d]	N/A[d]
Increased creatinine	31	0
Increased bilirubin	29	2[b]
Increased potassium	24	0
Increased triglycerides	19	0
Decreased magnesium	18	0
Increased aspartate aminotransferase (AST)	17	0
Increased cholesterol	13	0
Decreased albumin	13	0
Decreased sodium	12	2[b]
Decreased potassium	12	0
Increased gamma glutamyl transferase (GGT)	11	0
Increased alanine aminotransferase (ALT)	10	0
Hematology		
Decreased leukocyte	22	0
Decreased hemoglobin	20	6[b]
Decreased lymphocyte	20	0
Decreased neutrophil	19	0
Increased lymphocyte	17	0
Decreased platelets	14	2[b]

Grading according to CTCAE Version 4.03.
Abbreviation: N/A, not available.

Laboratory abnormality	VIJOICE[a] N = 57	
	All Grades %	Grade 3 or 4 %

[a]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 one post-treatment value.
[b]No Grade 4 laboratory abnormalities were reported.
[c]Glucose increase is an expected laboratory abnormality of PI3K inhibition.
[d]No CTCAE grade available. For HbA1c, baseline values increasing post-treatment to a value above the upper limit of the normal range (≥ 5.7%) are considered increased.

6.2 Postmarketing Experience and Other Spontaneous Adverse Reaction Reports

The following adverse reactions have been identified with VIJOICE use in patients with PROS in an expanded access program for compassionate use. Because these reactions are reported from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Metabolism and nutrition disorders: Decreased appetite.

Skin and subcutaneous tissue disorders: Pruritus, rash (including rash maculo-papular, rash erythematous, rash papular, and rash pruritic), acne (including dermatitis acneiform).

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on VIJOICE

CYP3A4 Inducers

Avoid coadministration of VIJOICE with strong CYP3A4 inducers.

Alpelisib is metabolized by CYP3A4. Concomitant use of VIJOICE with a strong CYP3A4 inducer may decrease alpelisib concentration *[see Clinical Pharmacology (12.3)]*, which may decrease alpelisib activity.

Breast Cancer Resistance Protein Inhibitors (BCRP)

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 adverse reactions.

Alpelisib is transported by BCRP. Concomitant use of VIJOICE with a BCRP inhibitor may increase alpelisib exposure *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions.

7.2 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 *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on animal data and mechanism of action, VIJOICE can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available data in pregnant women to inform the drug-associated risk. In animal reproduction studies, oral administration of alpelisib to pregnant rats and rabbits during organogenesis caused adverse developmental outcomes, including embryo-fetal mortality (post-implantation loss), reduced fetal weights, and increased incidences of fetal malformations at doses described below *(see Data)*. Advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. However, the estimated background risk of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies in the U.S. general population.

Data

Animal Data

In embryo-fetal development studies in rats and rabbits, pregnant animals received oral doses of alpelisib during the period of organogenesis. In the rat study, animals were dosed at 3, 10, or 30 mg/kg/day from gestation day 6 to 17; and in the rabbit study, animals were dosed at 3, 15, 25, and 30 mg/kg/day from gestation day 7 to 20.

In rats, oral administration of alpelisib resulted in maternal toxicity (body weight loss, low food consumption) and no viable fetuses (post-implantation loss) at 30 mg/kg/day (approximately 3.6 to 1.2 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA). At a dose of 10 mg/kg/day (approximately 1.2 to 0.4 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA), toxicities included reduced fetal weight and increased incidences of skeletal malformations (bent scapula and thickened or bent long bones) and fetal variations (enlarged brain ventricle, decreased bone ossification).

In a pilot embryo-fetal development study in rabbits, a dose of 30 mg/kg/day (approximately 7 to 2.2 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients based on BSA) resulted in no viable fetuses (post-implantation loss). Doses ≥ 15 mg/kg/day (approximately 3.5 to 1.1 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA) resulted in increased embryo-fetal deaths, reduced fetal weights, and malformations, mostly related to the tail and head.

8.2 Lactation

Risk Summary

There are no data on the presence of alpelisib in human milk, its effects on milk production, or the breastfed child. Because of the potential for serious adverse reactions in the breastfed child, advise lactating women to not breastfeed during treatment with VIJOICE and for 1 week after the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify the pregnancy status in females of reproductive potential prior to initiating VIJOICE.

Contraception

Females

VIJOICE can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with VIJOICE and for 1 week after the last dose.

Males

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.

Infertility

Based on findings from animal studies, VIJOICE may impair fertility in males and females of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of VIJOICE have been established in pediatric patients 2 to less than 18 years of age with PROS based on results from a single-arm clinical study of VIJOICE (EPIK-P1) that enrolled 39 pediatric patients: 11 patients aged 2 to 5 years, 12 patients aged 6 to 11 years, and 16 patients aged 12 to less than 18 years of age *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

The safety and effectiveness of VIJOICE in pediatric patients below the age of 2 years have not been established.

Although there were no new safety signals observed in pediatric patients, there is insufficient data to determine whether VIJOICE has an adverse impact on growth and development in pediatric patients with PROS. Based on the animal toxicity data (described below), regular monitoring of growth and development in pediatric patients treated with VIJOICE is recommended.

Animal Toxicity Data

In a 4-week general toxicology study, rats administered alpelisib had growth plate thickening and decreased trabeculae of the knee joint, dentin thinning, and degenerative odontoblasts at the dose of 30 mg/kg/day (approximately 2.8 to 1.2 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA). Dentin thinning/irregular dentin was also observed in the 13-week toxicology study in rats at the high dose of 20 mg/kg/day (approximately 2 to 0.8 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA).

8.5 Geriatric Use

There were no adult patients aged 65 years of age or older who received VIJOICE in EPIK-P1.

10 OVERDOSAGE

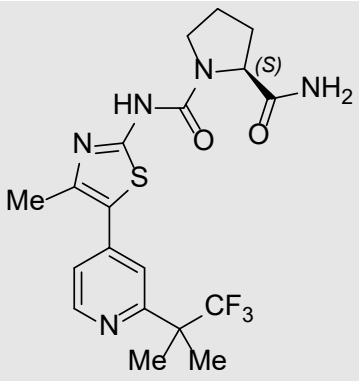
There is limited experience of overdose with alpelisib in clinical trials.

In cases where accidental overdosage of alpelisib was reported in the clinical studies, the adverse reactions associated with the overdose were consistent with the known safety profile of alpelisib and included hyperglycemia, nausea, asthenia, and rash.

Initiate general symptomatic and supportive measures in all cases of overdosage where necessary. There is no known antidote for VIJOICE.

11 DESCRIPTION

VIJOICE (alpelisib) is a kinase inhibitor. The chemical name of alpelisib is (2S)-N1-[4-Methyl-5-[2-(2,2,2-trifluoro-1,1-dimethylethyl)-4-pyridinyl]-2-thiazolyl]-1,2-pyrrolidinedicarboxamide. Alpelisib is a white to almost white powder. The molecular formula for alpelisib is $C_{19}H_{22}F_3N_5O_2S$ and the relative molecular mass is 441.47 g/mol. The chemical structure of alpelisib is shown below:



VIJOICE film-coated tablets are supplied for oral administration with three strengths that contain 50 mg, 125 mg and 200 mg of alpelisib. The tablets also contain hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, and sodium starch glycolate. The film-coating contains hypromellose, iron oxide red (applicable only to 50 mg and 200 mg strengths), iron oxide yellow, macrogol/polyethylene glycol (PEG) 4000, talc, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Alpelisib is an inhibitor of phosphatidylinositol-3-kinase (PI3K) with inhibitory activity predominantly against PI3Kα. Gain-of-function mutations in the gene encoding the catalytic α-subunit of PI3K (PIK3CA) lead to activation of PI3Kα and Akt-signaling, cellular transformation and the generation of tumors in in vitro and in vivo models.

Activating mutations in PIK3CA have been found to induce a spectrum of overgrowths and malformations comprising a wide group of clinically recognizable disorders commonly known as PROS.

In an inducible mouse model of Congenital Lipomatous Overgrowth, Vascular Malformations, Epidermal Nevi, Scoliosis/Skeletal and Spinal syndrome (CLOVES), a phenotype of PROS, alpelisib inhibition of the PI3K pathway resulted in the prevention or improvement of organ abnormalities associated with the disease, depending on when alpelisib treatment was started. These findings were reversed after withdrawal of alpelisib.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of VIJOICE have not been characterized.

Cardiac Electrophysiology

At a dose of 300 mg, alpelisib does not prolong the QT interval to any clinically relevant extent in the oncology setting. VIJOICE is not approved for use in the oncology setting.

12.3 Pharmacokinetics

The pharmacokinetics of alpelisib has been studied in healthy subjects and adult patients with solid tumors and are presented as mean (% CV) under fed conditions unless otherwise specified. Steady-state alpelisib maximum plasma concentration (C_{max}) and area under the curve (AUC) increased proportionally over the dose range of 30 mg (0.6 times the lowest approved recommended dosage) to 450 mg (1.8 times the highest approved recommended dosage) under fed conditions. The mean accumulation of alpelisib is 1.3 to 1.5 and steady-state plasma concentrations are reached within 3 days following daily dosage.

Absorption

The median time to reach peak plasma concentration (T_{max}) ranged between 2.0 to 4.0 hours.

Effect of food

A high-fat high-calorie meal (985 calories with 58.1 g of fat) increased alpelisib AUC by 73% and C_{max} by 84%, and a low-fat low-calorie meal (334 calories with 8.7 g of fat) increased alpelisib AUC by 77% and C_{max} by 145% following a single alpelisib dose of 300 mg. No clinically relevant differences in alpelisib AUC were observed between low-fat low-calorie and high-fat high-calorie meals.

Distribution

The apparent volume of distribution of alpelisib at steady-state is 114 L (46%). Protein binding of alpelisib is 89% and is independent of concentration.

Elimination

The half-life of alpelisib is predicted to be 8 to 9 hours. The clearance of alpelisib is 9.2 L/hr (21%) under fed conditions.

Metabolism

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

Excretion

Following a single oral dose of 400 mg (1.6 times the highest approved recommended dosage) radiolabeled alpelisib under fasted condition, 81% of the administered dose was recovered in feces (36% unchanged) and 14% (2% unchanged) in urine. CYP3A4-mediated metabolites (12%) and glucuronides amounted to approximately 15% of the dose.

Specific Populations

No clinically significant differences in the pharmacokinetics of alpelisib were predicted based on age (21 to 87 years), sex, race/ethnicity (Japanese or Caucasian), body weight (37 to 181 kg), mild to moderate renal impairment (CLcr 30 to < 90 mL/min based on the Cockcroft-Gault formula), or mild to severe hepatic impairment (Child-Pugh Class A, B, and C). The effect of severe renal impairment (CLcr < 30 mL/min) on the pharmacokinetics of alpelisib is unknown.

Pediatric Patients

The pharmacokinetics of VIJOICE in pediatric patients have not been evaluated.

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Acid Reducing Agents: No clinically significant differences in the pharmacokinetics of alpelisib were observed when used concomitantly with ranitidine (H2 receptor antagonist) and administered with food as directed.

Concomitant use of ranitidine decreased alpelisib AUC approximately 30% and C_{max} by 51% with a single 300 mg oral dose (1.2 times the highest approved recommended dosage) of alpelisib under the fasted state. In the presence of a low-fat low-calorie meal, AUC was decreased by 21% and C_{max} by 36% with ranitidine.

CYP3A4 Substrates: No clinically significant differences in pharmacokinetics of everolimus (a substrate of CYP3A4 and P-gp) were observed when used concurrently with alpelisib.

In Vitro Studies

Effect of Alpelisib on CYP Enzymes: Alpelisib inhibits CYP3A4 in a time-dependent manner and induces CYP2B6, CYP2C9 and CYP3A4.

Effect of Transporter on Alpelisib: Alpelisib is a substrate of BCRP.

Effect of Alpelisib on Transporters: Alpelisib is an inhibitor of P-gp. Alpelisib has a low potential to inhibit BCRP, MRP2, BSEP, OATP1B1, OATP1B3, OCT1, OAT1, OAT3, OCT2, MATE1, and MATE2K at clinically relevant concentrations.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with alpelisib.

Alpelisib was not mutagenic in an in vitro bacterial reverse mutation (Ames) assay, or aneugenic or clastogenic in human cell micronucleus and chromosome aberration tests in vitro. Alpelisib was not genotoxic in an in vivo rat micronucleus test.

In a fertility and early embryonic development study in rats, female animals were administered alpelisib doses of 3, 10, and 20 mg/kg/day orally. Animals were dosed for 4-weeks prior to pairing, during the mating period, and up to Gestation Day 6. At the dose of 20 mg/kg/day, alpelisib increased pre- and post-implantation losses, leading to reduced numbers of implantation sites and live embryos. These findings were observed at doses approximately 2.4 to 0.8 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on body surface areas (BSA). In a repeated-dose toxicity study in rats, adverse effects in female reproductive organs included vaginal atrophy and estrous cycle variations in rats at doses ≥ 6 mg/kg/day (approximately 0.7 to 0.2 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA). In a male fertility study, alpelisib administered orally at doses of 3, 10 and 20 mg/kg/day for up to 99 days (10-weeks prior to pairing, during mating period and continuing during post-pairing) to male rats, resulted in reduced weights of seminal vesicles and prostate, which correlated with atrophy and/or reduced secretion in prostate and seminal vesicles at ≥ 10 mg/kg/day (approximately 1.2 to 0.4 times the initial recommended doses of 50 mg and 250 mg in pediatric and adult patients, respectively, based on BSA). No adverse effects on male fertility parameters were observed at doses up to 20 mg/kg/day.

14 CLINICAL STUDIES

The efficacy of VIJOICE was assessed in EPIK-P1 (NCT04285723), a single-arm clinical study in patients who were treated as part of an expanded access program for compassionate use which enrolled patients across seven sites in five countries (France, Spain, US, Ireland and Australia). Eligible patients 2 years of age and older with PIK3CA-Related Overgrowth Spectrum (PROS) who received VIJOICE had clinical manifestations of PROS that were assessed by the treating physician as severe or life-threatening and necessitating systemic treatment and had documented evidence of mutation in the PIK3CA gene as determined by a local laboratory. Patients received VIJOICE at dosages based on age ranging from 50 mg to 250 mg orally once daily.

The efficacy of VIJOICE was evaluated in a total of 37 patients with at least one target lesion identified on imaging performed within 24 weeks prior to receipt of the first dose of VIJOICE. The median age of patients was 14 years (range: 2 to 38); 22% of patients were 2 to 5 years, 22% were 6 to 11 years, 27% were 12 to less than 18 years of age, and 30% were ≥ 18 years; 57% were female, 11% were White and race was not reported for 89%. Ninety-two percent of patients had congenital overgrowth and 8% had early childhood-onset. Patients had heterogeneous manifestations of PROS, including CLOVES, (81%), Megalencephaly-Capillary Malformation Polymicrogyria (MCAP; 8%), Klippel-Trenaunay

Syndrome (KTS; 2.7%), Facial Infiltrating Lipomatosis (FIL; 8%), and Other (5%). Five percent (5%) of patients had concurrent manifestations of CLOVES and MCAP.

The major efficacy outcome measure for the study was the proportion of patients with radiological response at Week 24 as determined by blinded independent central review (BICR), defined as a ≥ 20% reduction from baseline in the sum of measurable target lesion volume (1 to 3 lesions) confirmed by at least one subsequent imaging assessment, in the absence of a ≥ 20% increase from baseline in any target lesion, progression of non-target lesions, or appearance of a new lesion. An additional efficacy outcome measure was duration of response, defined as the time from the first documented response to the date of the first documented disease progression or death due to any cause.

Efficacy results are presented in Table 12.

Table 12: Efficacy Results at Week 24 in EPIK-P1

Efficacy parameters	**All patients N = 37**
Response rate[a,b]	
Responders, n (%) 95% CI	10 (27) (14, 44)
Duration of response (DOR)	
Median in months (range)	NR (0.9+, 42.9+)
% ≥ 6 months	70
% ≥ 12 months	60

Abbreviation: +: censored observation.
[a]Confirmed response as determined by blinded independent central review (BICR).
[b]Patients without any response assessment at Week 24 were considered non-responders.

16 HOW SUPPLIED/STORAGE AND HANDLING

VIJOICE (alpelisib) 50 mg, 125 mg, and 200 mg film-coated tablets are available in blister packs based on daily dose as described in Table 13.

Table 13: VIJOICE Daily Dose Blister Packs

Daily dose	**Each child-resistant carton contains**	**Each blister pack contains**	**NDC**
50 mg daily dose	One 28-day supply blister pack	28 tablets; 50 mg alpelisib per tablet	NDC 0078-1021-84
125 mg daily dose	One 28-day supply blister pack	28 tablets; 125 mg alpelisib per tablet	NDC 0078-1028-84
250 mg daily dose	**Two** 14-day supply blister packs (56 tablets total)	14 tablets: 200 mg alpelisib per tablet, and 14 tablets: 50 mg alpelisib per tablet	NDC 0078-1035-02

Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient and their caregivers to read the FDA-approved patient labeling (Patient Information).

Severe Hypersensitivity

Inform patients and their caregivers of the signs and symptoms of hypersensitivity. Advise patients and their caregivers to contact their healthcare provider immediately for signs and symptoms of hypersensitivity *[see Warnings and Precautions (5.1)]*.

Severe Cutaneous Adverse Reactions

Inform patients and their caregivers of the signs and symptoms of severe cutaneous adverse reactions (SCARs). Advise patients and their caregivers to contact their healthcare provider immediately for signs and symptoms of SCARs (e.g., a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy) *[see Warnings and Precautions (5.2)]*.

Hyperglycemia

Advise patients and their caregivers of the possibility of developing hyperglycemia and the need to monitor fasting glucose periodically during therapy. Advise patients and their caregivers of the signs and symptoms of hyperglycemia (e.g., excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss) *[see Warnings and Precautions (5.3)]*.

Pneumonitis

Inform patients and their caregivers of the possibility of developing pneumonitis and to immediately report new or worsening respiratory symptoms *[see Warnings and Precautions (5.4)]*.

Diarrhea

Advise patients and their caregivers that VIJOICE may cause diarrhea, which may be severe in some cases. Inform patients and their caregivers to start anti-diarrheal treatment, increase oral fluids, and notify their healthcare provider if diarrhea occurs while taking VIJOICE *[see Warnings and Precautions (5.5)]*.

Alopecia

Advise patients and caregivers that VIJOICE may cause alopecia *[see Adverse Reactions (6.1)]*.

Embryo-Fetal Toxicity

- Inform pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.6) and Use in Specific Populations (8.1)]*.
- Advise females of reproductive potential to use effective contraception during treatment with VIJOICE and for 1 week after the last dose *[see Use in Specific Populations (8.3)]*.
- 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 *[see Use in Specific Populations (8.3)]*.

Lactation

Advise women not to breastfeed during treatment with VIJOICE and for 1 week after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise males and females of reproductive potential that VIJOICE may impair fertility *[see Use in Specific Populations (8.3)]*.

Drug Interactions

Advise patients and their caregivers to inform their healthcare providers of all concomitant medications, herbal and dietary supplements *[see Drug Interactions (7.1, 7.2)]*.

Dosing

Instruct patients and their caregivers of the following:

- Take VIJOICE with food at approximately the same time each day *[see Dosage and Administration (2.2)]*.
- Swallow the tablets whole (tablets should not be chewed or split prior to swallowing) *[see Dosage and Administration (2.2)]*.
- For patients unable to swallow, advise how to prepare an oral suspension *[see Dosage and Administration (2.2)]*.

- 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. Instruct patients not to take 2 doses to make up for a missed dose *[see Dosage and Administration (2.2)]*.
- If vomiting occurs after taking the dose of VIJOICE, they should not take an additional dose on that day and should resume the usual dosing schedule the next day at the usual time *[see Dosage and Administration (2.2)]*.

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Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936

PATIENT INFORMATION
VIJOICE® (vi' joiz)
(alpelisib)
tablets

What is VIJOICE?

VIJOICE is a prescription medicine used to treat adults and children 2 years of age and older with severe phosphatidylinositol-3-kinase catalytic subunit alpha (PIK3CA)-Related Overgrowth Spectrum (PROS).

It is not known if VIJOICE is safe and effective in children below 2 years of age.

Do not take VIJOICE if you have had a severe allergic reaction to alpelisib or are allergic to any of the ingredients in VIJOICE.

- See the end of this Patient Information leaflet for a complete list of the ingredients in VIJOICE.
- See "What are the possible side effects of VIJOICE?" for signs and symptoms of severe allergic reactions.

Before you take VIJOICE, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of diabetes.
- have a history of skin rash, redness of skin, blistering of the lips, eyes or mouth, or skin peeling.
- are pregnant or plan to become pregnant. VIJOICE can harm your unborn baby.

  Females who are able to become pregnant:
  - Your healthcare provider will check to see if you are pregnant before you start treatment with VIJOICE.
  - You should use effective birth control during treatment with VIJOICE and for 1 week after the last dose. Talk to your healthcare provider about birth control methods that may be right for you during this time.
  - If you become pregnant or think you are pregnant, tell your healthcare provider right away.

  Males with female partners who are able to become pregnant should use condoms and effective birth control during treatment with VIJOICE and for 1 week after the last dose. If your female partner becomes pregnant, tell your healthcare provider right away.
- are breastfeeding or plan to breastfeed. It is not known if VIJOICE passes into your breast milk. Do not breastfeed during treatment with VIJOICE and for 1 week after the last dose.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. VIJOICE and other medicines may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take VIJOICE?

- Take VIJOICE exactly as your healthcare provider tells you.
- Do not change your dose or stop taking VIJOICE unless your healthcare provider tells you.
- Take VIJOICE 1 time each day, at about the same time each day.
- Take VIJOICE with food.
- Swallow VIJOICE tablets whole. Do not split or chew the tablets.
- Do not take VIJOICE tablets that are broken, cracked or that look damaged at the time of opening the blister pack.
- If you cannot swallow tablets, you can take VIJOICE mixed with water (suspension) as follows:
  - Place VIJOICE tablets into a glass that contains 2 to 4 ounces of water and let it stand for about 5 minutes. **Use water only.**
  - Crush the tablets with a spoon and stir to dissolve. The liquid will be cloudy and you may see tablet pieces.
  - **Swallow the mixture right away.**
  - Next, add about 2 to 3 tablespoons of water to the same glass and stir with the same spoon. Then swallow the entire contents of the glass to ensure the entire dose is consumed. Repeat this step if necessary.
  - Throw away any of the VIJOICE that is not taken within 60 minutes after it is prepared.
- If you miss a dose of VIJOICE, you may still take it with food up to 9 hours after the time you usually take it. If it has been more than 9 hours after you usually take your dose, skip the dose for that day. The next day, take the dose at your usual time. Do not take 2 doses to make up for a missed dose.
- If you vomit after taking a dose of VIJOICE, do not take another dose on that day. Take your next dose at your usual time.
- If you take too much VIJOICE, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of VIJOICE?

VIJOICE may cause serious side effects, including:

- **Severe allergic reactions.** Tell your healthcare provider or get medical help right away if you have trouble breathing, flushing, rash, fever, or fast heart rate during treatment with VIJOICE.
- **Severe skin reactions.** Tell your healthcare provider or get medical help right away if you get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever.
- **High blood sugar levels (hyperglycemia).** Hyperglycemia is common with VIJOICE and can be severe. Your healthcare provider will monitor your sugar levels before you start and during treatment with VIJOICE. Your healthcare provider may monitor your sugar levels more often if you have a history of diabetes. Tell your healthcare provider right away if you develop symptoms of hyperglycemia, including:
  - excessive thirst
  - dry mouth
  - more frequent urination than usual or a higher amount of urine than normal
  - increased appetite with weight loss
  - confusion
  - nausea
  - vomiting
  - fruity odor on breath
  - difficulty breathing
  - dry or flushed skin
- **Lung problems (pneumonitis).** Tell your healthcare provider right away if you develop new or worsening symptoms of lung problems, including:
  - shortness of breath or trouble breathing
  - cough
  - chest pain
- **Diarrhea.** Diarrhea is common with VIJOICE and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney injury. Tell your healthcare provider right away if you develop diarrhea during treatment with VIJOICE. Your healthcare provider may tell you to drink more fluids or take medicines to treat diarrhea.

Your healthcare provider may tell you to decrease your dose, temporarily stop your treatment, or completely stop your treatment with VIJOICE if you get certain serious side effects.

The most common side effects of VIJOICE include:

- diarrhea
- high blood sugar
- dry skin
- mouth sores (stomatitis)
- headache
- hair loss (alopecia)

VIJOICE may affect fertility in males and in females who are able to become pregnant. Talk to your healthcare provider if this is a concern for you. These are not all of the possible side effects of VIJOICE.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store VIJOICE?

- Store VIJOICE at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F).

Keep VIJOICE and all medicines out of the reach of children.

General information about the safe and effective use of VIJOICE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use VIJOICE for a condition for which it was not prescribed. Do not give VIJOICE to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about VIJOICE that is written for health professionals.

What are the ingredients in VIJOICE?

Active ingredient: alpelisib

Inactive ingredients: hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, and sodium starch glycolate. The film-coating contains hypromellose, iron oxide red (applicable only to 50 mg and 200 mg strengths), iron oxide yellow, macrogol/polyethylene glycol (PEG) 4000, talc, and titanium dioxide.

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For more information, go to www.VIJOICE.com or call 1-888-VIJOICE (1-888-845-6423).

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: April 2022