VIJOICE® (alpelisib) tablets
ACCESS SUPPORT GUIDE

Clinical Considerations

Review the clinical considerations for VIJOICE in order to identify appropriate patients and communicate relevant information to your patients' health plans.

Review the Clinical Considerations for VIJOICE

Coverage Considerations

These questions provide your office some background knowledge on the steps to take when VIJOICE is prescribed and guide you through the coverage approval process.

Prior Authorization

Step therapy

Formulary Exception

Letter of Appeal

Letter of Medical Necessity

Support References

ICD-10 Codes

Resources

Help your eligible patients access the co-pay card.

Information about the co-pay card

Helping to support patients' access to VIJOICE

Novartis cannot guarantee insurance coverage or reimbursement for any patient. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the health care provider (HCP) to select the proper billing codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

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

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The indication and select study information in this resource can help support VIJOICE as an appropriate treatment choice for patients with PIK3CA-Related Overgrowth Spectrum (PROS)

Indication for VIJOICE:

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 in patients treated with VIJOICE. VIJOICE is not approved for use in the oncology setting. Permanently discontinue VIJOICE in the event of severe hypersensitivity.

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VIJOICE is the first and only FDA-approved treatment for patients with PROS

Select Information From EPIK-P1[1-3]

Description	FDA approval for VIJOICE was based on EPIK-P1, a single-arm clinical study. Pediatric patients aged 2 years and older and adult patients (N=57) with PROS received VIJOICE as part of a compassionate use program. The efficacy population (n=37), which was a subset of the full study population, included patients who had 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.
Response (primary end point)	VIJOICE shrunk overgrowth: 27% of patients (10/37) (95% CI, 14-44) experienced a response at Week 24 (confirmed response as determined by blinded independent central review [BICR]). Two additional patients experienced a response, but the response was not confirmed by BICR. Patients without any response assessment at Week 24 were considered nonresponders. Response was determined by BICR and defined as the proportion of patients achieving 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.
Duration of response (select secondary end point)	The median duration of response was not reached at Week 24. Duration of response was defined as the time from the first documented response to the date of the first documented disease progression or death due to any cause. Response was maintained after 6 months for 70% of patients; 60% of patients maintained response after 12 months.
Measurable target lesion volume (select secondary end point)	In an exploratory analysis of the EPIK-P1 study, VIJOICE led to broad overgrowth reduction: 74.2% of patients (23/31) experienced any reduction in the sum of target lesion volume. The analysis included patients who had a radiological investigation at Week 24 (n=31). Not all patients with lesion volume reduction were confirmed with a subsequent imaging assessment.
Patient functionality (select secondary end point)	In an exploratory analysis of the EPIK-P1 study, approximately 30% of patients (14/47) treated with VIJOICE experienced functional improvements at Week 24. Performance status was recorded at baseline for 47 patients (33 pediatric patients; 14 adult patients) using ECOG, Karnofsky, and Lansky assessments. For the ECOG scale, improvement is defined as a decrease by at least 1 point and worsening is defined as an increase by at least 1 point. For the Karnofsky and Lansky scales, improvement is defined as an increase by at least 20 points and worsening is defined as a decrease by at least 20 points.
PROS signs and symptoms (select secondary end point)	In an exploratory analysis of the EPIK-P1 study, improvements in the most common PROS signs and symptoms were observed, including in pain, vascular malformations, fatigue, limb asymmetry, and disseminated intravascular coagulation. Improvements in signs and symptoms were seen as early as Week 12.

FDA, US Food and Drug Administration; 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; ECOG, Eastern Cooperative Oncology Group.

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 or systemic corticosteroids, or oral antihistamine treatment.

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VIJOICE Coverage Considerations

Q1 At what specialty pharmacy can my patient get their prescription filled?

A There is an open specialty pharmacy network for VIJOICE, which means your patient can get it filled at the specialty pharmacy of their choice. However, the patient's insurance may require them to use a specific pharmacy.

Q2 How are severe manifestations of PROS defined?

A Payers may allow prescriber attestation that the disease manifestations are severe. This includes, but is not limited to, vascular malformations, gastrointestinal bleeding, scoliosis, epilepsy, or excessive tissue growth.

Q3 What are the PA requirements for VIJOICE?

A PA is the main utilization management requirement health plans have in place for VIJOICE. In this scenario, the prescribing health care provider (HCP) will need to provide additional clinical information and therapeutic rationale for the prescribed medication before the health plan will process the prescription or reimburse the claim. PA forms should be completed and submitted to the plan by your office and are usually located on the health plan's website or may be submitted electronically. Some plans may require that a Letter of Medical Necessity accompany submissions of Appeals or Formulary Exception Requests.

PA criteria vary from plan to plan; however, the following criteria are commonly found across large payer types and may be required before covering VIJOICE. Depending on the plan's criteria, these criteria should be considered when submitting a PA request form.

VIJOICE Coverage Considerations (cont)

Q3 What are the PA requirements for VIJOICE? (cont)

Standard requirements for a PA request include:

- Documented diagnosis of PROS
- Documentation that the patient is 2 years of age and older
- Attestation the patient requires systemic therapy
- Documentation of severe clinical manifestations of PROS

Note that there have been denials due to inadequate proof of severity, so it is important to list all the clinical manifestations that the patient is facing when submitting the PA.

Documentation of a PIK3CA mutation as confirmed by genetic testing

Q: What do I need to know about the genetic testing for VIJOICE?

While some plans require evidence of a PIK3CA mutation, this may not always be feasible to obtain.[4,5]

- Due to the mosaic nature of PIK3CA mutations in PROS, genomic testing may not always reveal the presence of a PIK3CA mutation
- Per the 2013 National Institutes of Health workshop on recommended clinical diagnostic criteria for PROS, the failure to detect a somatic PIK3CA mutation does not preclude diagnosis
- Detection of a PIK3CA mutation depends on the degree of overgrowth, as well as the distribution and amount of detectable mutation in the tissue
- Technical limitations, sample availability, and difficulties with interpreting the results may impact the decision to test
- There may be difficulty in getting an appointment with a geneticist
- For coverage of genetic testing if the patient does not have a PIK3CA mutation but still meets the diagnostic criteria for PROS, you may need to appeal and provide additional information to the health plan, when feasible. One published case report summarizes alpelisib efficacy in a patient with PROS who had no documented PIK3CA mutation

The VIJOICE indication statement does not include a genetic testing requirement; however, the insurance plan may require genetic testing.

VIJOICE Coverage Considerations (cont)

Q3 What are the PA requirements for VIJOICE? (cont)

Examples of spectrum features and isolated features include, but are not limited to[4]:

Spectrum features

- Overgrowth: adipose, muscle, nerve, skeletal
- Epidermal nevus
- Vascular malformations: capillary, venous, arteriovenous, lymphatic

Isolated features

- Large, isolated lymphatic malformation
- Truncal adipose overgrowth
- Benign lichenoid keratoses
- Epidermal nevus
- Seborrheic keratoses
- HME (bilateral)/DMEG /focal cortical dysplasia type II
- Isolated macrodactyly or overgrown, splayed feet/hands, overgrown limbs

Prescribed dosage[1]

Recommended initial dose of VIJOICE

Adult patients	Pediatric patients (2 to <18 years of age)
250 MG ONCE DAILY*	50 MG ONCE DAILY†

- HCPs may consider a dose increase to 125 mg once daily in pediatric patients ≥6 years of age for response optimization (clinical/radiological) after 24 weeks of treatment with VIJOICE at 50 mg once daily. When a pediatric patient turns 18 years of age, consider a gradual dose increase up to 250 mg
- For patients unable to swallow tablets, HCPs may consider an oral suspension (using tablets or oral granules) or administration via feeding tube

If the patient is currently receiving treatment with VIJOICE, include information on how the patient is responding to treatment and/or if the patient is able to decrease supportive therapies, such as pain medications, antiepileptics, antiinfectives, and antithrombotics[6]

Some plans may have specific requirements regarding response to therapy for reauthorization requests, so it is important to ensure you are providing specific details on patient response.

*For adult patients, dose can be administered as VIJOICE tablets or VIJOICE oral granules at the second-dose reduction (50 mg once daily).
†For pediatric patients, dose can be administered as VIJOICE tablets or VIJOICE oral granules.

IMPORTANT SAFETY INFORMATION (cont)

Hyperglycemia (cont). 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.

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VIJOICE Coverage Considerations (cont)

Q4 How does the office properly prepare the requirements for the PA request?

Your Novartis Access and Reimbursement Field Team may be able to provide you with PA requirements for specific plans and pharmacy benefit managers.

It is crucial when completing the PA request to include all requested information on the PA form. When a PA request is denied, whether for incomplete information or a different reason, an appeal will need to include additional support for why the medication is clinically necessary for the patient. An appeal should also be submitted in the time frame specified by the patient's insurance; failing to do so may delay initation of therapy. See page 11 for additional details on appeals.

Additional information to include about the patient and physician:

- The patient's name, policy number, ID number, group number, and date of birth
- The prescribing physician's name, specialty, and NPI number
- The phone numbers for the prescribing physician and patient if the health plan requires any additional information
- Signature from the prescribing physician
- Specific ICD-10 codes (please see page 14 for more details)

IMPORTANT SAFETY INFORMATION (cont)

Hyperglycemia (cont). 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.

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VIJOICE Coverage Considerations (cont)

Q5 What can I do if my patient's plan requires step therapy in addition to a PA?

Step Therapy

Some plans may also apply step therapy for VIJOICE in addition to a PA. You may need to submit additional information with your request.

Step therapy, or fail-first, is a management tool sometimes included in a PA that requires a trial of one or more preferred medications before a nonpreferred medication is covered.[7]

Some plans might have a requirement for prior use of another therapy (eg, sirolimus) before VIJOICE is covered. Sirolimus is not FDA approved for the treatment of PROS. When submitting your request, it will be important to note that VIJOICE is the only FDA-approved therapy for PROS. If the patient has tried and failed other agents, be sure to include that information. Some plans may require a Letter of Medical Necessity to be submitted with the step therapy request if the patient has not tried and failed the plan's preferred medications.[7]

VIJOICE Coverage Considerations (cont)

Q6 What can I do if my patient's formulary excludes coverage for VIJOICE?

Formulary exclusion

Health plans usually offer 2 basic types of formularies - open and closed.[7]

Open
An open formulary pharmacy benefit provides coverage at the point of sale for all medications covered under the prescription benefit, even those not listed on the formulary. Formulary Exclusion denials usually do not occur under an open formulary.

Closed
However, under a closed formulary pharmacy benefit, only the drugs listed on the formulary are covered at the point of sale. Nonformulary medications can only be obtained via a formulary exception process.

Some plans may have VIJOICE as formulary excluded. You can request coverage for VIJOICE even if it is formulary excluded. A formulary exception request form prepared by the prescribing physician should be submitted to the patient's health plan as part of this process. A plan may require that a Letter of Medical Necessity be included when requesting coverage for a formulary-excluded drug.

In addition to the information listed in the PA request form checklist, consider including the following items in a formulary exception request form:

Formulary Exception Request Form Checklist

- Be sure to provide as much information on the form as possible. Incomplete information can lead to a denial
- Clearly state the rationale for prescribing VIJOICE if it is not on formulary and why the formulary agents are not appropriate. Possible reasons include:
  - VIJOICE is the only FDA-approved therapy for PROS
  - The patient has had prior therapeutic failure on formulary agent
  - Formulary alternatives are not appropriate for this patient
- Include a Letter of Medical Necessity

VIJOICE Coverage Considerations (cont)

Q7 The request for VIJOICE was denied. What are the possible denial reasons?

Refer to the denial letter to confirm the specific denial reason. Possible denial reasons (not comprehensive) include:

- Incomplete information
- Lack of documentation of PIK3CA mutation
- Inadequate proof of disease severity
- Inadequate proof of improvement while on VIJOICE (for patients currently on therapy)
- Lack of trial of preferred agent

When you are filing an appeal, ensure that you are addressing the specific denial reason

VIJOICE Coverage Considerations (cont)

Q8 What can I do if a health plan denies the PA request or coverage for VIJOICE?

Letter of Appeal

When a patient's health insurance plan denies the HCP's request for PA or coverage for VIJOICE, they may submit an appeal. When submitting an appeal to a patient's health insurance plan, including an **Appeal Letter** can help explain the rationale and clinical decision-making behind prescribing VIJOICE.

Below are some tips that may be helpful when appealing a coverage denial.

- ☐ Review the reason for the denial from the denial letter.
  - If information was missing from the original request that may have led to the denial, include that information in the appeal
- ☐ Provide clinically relevant and patient-specific information to address the denial reason
- ☐ Include your clinical rationale for prescribing VIJOICE supported by medical history
- ☐ Refer to the FDA approval of VIJOICE and any additional supporting publications to support your rationale for prescribing
- ☐ Discuss the potential consequences of a denial for the patient
- ☐ Provide a copy of the patient's record with details on the patient's condition (diagnosis/diagnoses) and the severity of disease for which VIJOICE is being/will be used
- ☐ Document the previous therapies used, dates used, and reasons for discontinuation (if applicable)
- ☐ Include a Letter of Medical Necessity if required by the patient's health plan

See page 15 to download the sample Letter of Appeal

- If an initial appeal is denied, there may be multiple levels of appeal
- If the first- and second-level appeals are denied, additional adjudication may include review by an independent noninsurance-affiliated external review board or hearing; if this is a second- or third-level appeal, include the letter of denial and medical notes in response to the denial

IMPORTANT SAFETY INFORMATION (cont)

Pneumonitis. 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.

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VIJOICE Coverage Considerations (cont)

Q9 What should I do if my patient's plan requires that a Letter of Medical Necessity be included with my request?

Letter of Medical Necessity (LMN)

An LMN is a critical component of appealing a coverage denial, or requesting a formulary exception. A plan may require an LMN in other situations as well. The LMN is the prescribing physician's opportunity to present the rationale for why VIJOICE is clinically necessary for the patient. It is important to note that an LMN should be concise while making as strong an argument as possible.

In addition to the information listed in the PA Request form checklist, consider including the following items in the LMN.

Common clinical evidence required for LMNs include:

1. Patient's history, including the patient's diagnosis with PROS, severity of disease, and manifestations that may require systemic therapy
2. Information about the current treatment(s) being used for the patient's condition (if applicable) and how the patient is doing clinically while taking the current treatment(s)
3. Clinically relevant and patient-specific information that makes VIJOICE an appropriate therapy for the patient
4. Clinical rationale for why other treatments are not appropriate, if applicable

See page 15 to download the sample Letter of Medical Necessity

VIJOICE Coverage Considerations (cont)

Q10 What other information may be valuable to include with my coverage request?

Support References

Please refer to the below information to support VIJOICE treatment, which may be included in a PA request form or an appeals letter, an LMN, or a formulary exception request form to further support coverage for the patient.

Support	Link to Reference
• Additional information on the EPIK-P1 and EPIK-P2 Trials	Canaud G, Lopez Gutierrez JC, Irvine AD, et al. Alpelisib for treatment of patients with PIK3CA-related overgrowth spectrum (PROS). *Genet Med.* 2023;25(12):100969. doi:10.1016/j.gim.2023.100969
Rationale for a positive PIK3CA test IS NOT required to confirm a PROS diagnosis[1,5]	
• The FDA-approved indication for VIJOICE does not include the requirement of a PIK3CA mutation • One published case report summarizes alpelisib efficacy in a patient with PROS who had no documented PIK3CA mutation	Prescribing Information (PI) for VIJOICE Raghavendran P, Albers SE, Phillips JD, Zarnegar-Lumley S, Borst AJ. Clinical response to PI3K-α inhibition in a cohort of children and adults with PIK3CA-related overgrowth spectrum disorders. *J Vasc Anom (Phila).* 2022;3(1):e038. doi:10.1097/jova.0000000000000038
Support for VIJOICE if plan requires step through another therapy[1]	
• The VIJOICE PI does not require failure of any agents prior to VIJOICE utilization • VIJOICE is the only FDA-approved therapy for PROS	VIJOICE PI

VIJOICE Coverage Considerations (cont)

Q11 What is the appropriate ICD-10 code for PROS disorders to include on the VIJOICE PA form?

ICD-10 Coding Information

The coding information provided may assist you in completing the health plan's forms for VIJOICE, may not represent all possible codes, and is for informational purposes only. The determination of appropriate codes for a health form should be based on the treating HCP's clinical judgment.

There are no ICD-10 site codes specifically for PROS disorders. Below are examples of diagnostic codes that may be used to describe PROS in certain clinical situations. There may be other diagnostic codes that are appropriate as well.

Code[8]	Description[8]
Q04.3	Other reduction deformities of brain
Q04.5	Megalencephaly
Q04.8	Other specified congenital malformations of brain
Q27.8	Other specified congenital malformations of peripheral vascular system
Q74.0	Other congenital malformations of upper limb(s), including shoulder girdle
Q74.2	Other congenital malformations of lower limb(s), including pelvic girdle
Q87.2	Congenital malformation syndromes predominantly involving limbs
Q87.3	Congenital malformation syndromes involving early overgrowth
Q87.8	Other specified congenital malformation syndromes, not elsewhere classified
Q89.9	Congenital malformation, unspecified

Sample Letters

These sample letters can be used if the health plan requires further documentation to support the HCP's clinical decision. Novartis cannot provide any assistance to your office in completing or submitting forms or letters related to coverage requests.

Sample Letters of Appeal and Medical Necessity can be downloaded through the links below. Each letter may be submitted with a copy of the patient's relevant medical records.

Click here to access the sample Letter of Appeal.

Click here to access the sample Letter of Medical Necessity.

Consider including the following documentation, if applicable, to support an appeal for VIJOICE:

- Medical records
- Other clinical information (eg, clinical study data from the PI for VIJOICE)
- Your response to previous denial letters (if filing a second- or third-level appeal)

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 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 or systemic 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.

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 of, or permanently discontinue VIJOICE based on severity.

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IMPORTANT SAFETY INFORMATION (cont)

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%).

The following additional adverse reactions and laboratory abnormality have been identified following administration of VIJOICE: hypersensitivity, lipase increased, dermatitis, and abdominal pain.

Please click here for full Prescribing Information.

Resources and support programs are available for your eligible patients

Universal Co-pay Program

Patients may be eligible for immediate co-pay savings on their next prescription of VIJOICE.

- Eligible patients with private insurance may pay as little as $0 per month
- Novartis will pay the remaining co-pay, up to $15,000 per calendar year, per product*

*Limitations apply. This offer is only available to patients with private insurance. The program is not available for patients who are enrolled in Medicare, Medicaid, or any other federal or state health care program. Novartis reserves the right to rescind, revoke, or amend this program without notice. For full Terms and Conditions, visit Copay.NovartisOncology.com or call 1-877-577-7756.

Encourage your patients to find out if they are eligible to enroll in the Universal Co-pay Program by visiting Copay.NovartisOncology.com or calling 1-877-577-7756.

IMPORTANT SAFETY INFORMATION (cont)

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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NOVARTIS

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

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080

Re: Appeal of Denial of VIJOICE® (alpelisib) tablets ([XX] mg)

[Date]
[Health Plan Name]
ATTN: [Department]
[Medical/Pharmacy Director Name]
[Health Plan Address]
[City, State Zip code]

[Patient's Name]
[Date of Birth]
[Policy ID/Group #]
[Date of Service]

Re: Appeal of Denial of VIJOICE®(alpelisib) tablets ([XX] mg)

To Whom it May Concern:

I am writing to request reconsideration of your denial of coverage for VIJOICE, which I have prescribed for the patient referenced above. I have read and acknowledged your policy for VIJOICE. I understand you are denying coverage for ‹patient's name› because:

- ‹reason for the denial›
- ‹further reason(s) for the denial, if applicable›

However, I believe the treatment with VIJOICE is reasonable, appropriate, and medically necessary for my patient, based on my clinical experience, the patient's condition, and their medical history.

Clinical Information to Support Appeal

[Patient's name] is [a/an] [age]-year-old [male/female] patient who has been diagnosed with PIK3CA-Related Overgrowth Spectrum (PROS) as of [date]. [She/He] has been in my care since [date]. This patient requires systemic therapy for severe manifestations of PROS, which include [brief description or list of severe manifestations]. [Include supporting information as requested by the plan in their denial letter and any clinical attributes of VIJOICE that are relevant to the patient.]

[Additional information that may be supportive of the appeal should be included if not previously provided in the initial request, where applicable:

Clinical considerations for diagnosis of PROS may include, but are not limited to, the following:

- Congenital or early childhood onset
- Sporadic and mosaic overgrowth
- Spectrum features
  - Overgrowth: adipose, muscle, nerve, skeletal
  - Epidermal nevus
  - Vascular malformations: capillary, venous, arteriovenous, lymphatic
- Isolated features
  - Large, isolated lymphatic malformation
  - Truncal adipose overgrowth
  - Benign lichenoid keratoses
  - Seborrheic keratoses
  - Hemimegalencephaly (HME) bilateral/dysplastic megalencephaly (DMEG)/focal cortical dysplasia type II
  - Isolated macrodactyly or overgrown, splayed feet/hands, overgrown limbs
  - Epidermal nevus
- Documentation of PIK3CA genetic testing results
- Specific symptoms, complications, and supportive care treatment that the patient is experiencing/receiving
- Laboratory, imaging, or other study results
- Impact of PROS on patient functioning
- Prior PROS-related surgeries
- Trial and failure of any other medications, if applicable
- Reasons why plan formulary alternatives are not appropriate for the patient
- Patient is currently receiving treatment with VIJOICE and is responding favorably to treatment]

Summary

Based on my professional experience, VIJOICE is appropriate, medically necessary, and supported by the patient's individual medical history. A copy of the denial letter is included along with medical notes in response to the denial. If you have any further questions about this matter, please contact me at [physician's phone number] or via email at [physician's email]. Thank you for your time and consideration.

Sincerely,

[Physician's Signature, Name, and NPI number if applicable]

Enclosed:

[List and attach additional documents, which may include a denial letter, Letter of Medical Necessity, copies of original request, prescribing information, clinical notes/medical records, or PIK3CA genetic testing.]

Re: Letter of Medical Necessity for VIJOICE® (alpelisib) tablets ([XX] mg)

[Date]
[Health Plan Name]
ATTN: [Department]
[Medical/Pharmacy Director Name]
[Health Plan Address]
[City, State Zip code]

[Patient's Name]
[Date of Birth]
[Case ID Number›]
[Date of Service]

Re: Letter of Medical Necessity for VIJOICE® (alpelisib) tablets ([XX] mg)

To Whom it May Concern:

I am writing this letter on behalf of [patient's name] to request coverage for VIJOICE for the treatment of PIK3CA-Related Overgrowth Spectrum (PROS). VIJOICE is indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PROS who require systemic therapy. This letter provides the clinical rationale and relevant information about the patient's medical history and prior treatment.

Medical History

[Please include overview of disease course of the patient, including history and severity of disease, any symptoms, and hospitalizations. If there have been changes in disease activity or patient assessment of condition, include that information as well›.

[Previous Treatments]

‹Trial and failure of other medications, if applicable, including start/stop dates›
‹Reasons for discontinuation of previous therapies, including documentation of inadequate response and/or intolerable adverse events›
‹Prior PROS-related surgeries›

Clinical Rationale

My patient requires systemic therapy for severe manifestations of PROS, which include [brief description or list of severe manifestations].

[Additional information that may be supportive of the request that would be appropriate to include (where applicable):

Clinical considerations for diagnosis of PROS may include, but are not limited to, the following:

- Congenital or early childhood onset
- Sporadic and mosaic overgrowth
- Spectrum features
  - Overgrowth: adipose, muscle, nerve, skeletal
  - Epidermal nevus
  - Vascular malformations: capillary, venous, arteriovenous, lymphatic
- Isolated features
  - Large, isolated lymphatic malformation
  - Truncal adipose overgrowth
  - Benign lichenoid keratoses
  - Seborrheic keratoses
  - Hemimegalencephaly (HME) bilateral/dysplastic megalencephaly (DMEG)/focal cortical dysplasia type II
  - Isolated macrodactyly or overgrown, splayed feet/hands, overgrown limbs
  - Epidermal nevus
- Documentation of PIK3CA genetic testing results
- Specific symptoms, complications, and supportive care treatment that the patient is experiencing/receiving
- Laboratory, imaging, or other study results
- Impact of PROS on patient functioning
- Reasons why plan formulary alternatives are not appropriate for the patient
- Patient is currently receiving treatment with VIJOICE and is responding favorably to treatment]

[Provide clinical rationale for why your patient will benefit from VIJOICE over plan formulary alternatives]

Based on my professional experience, VIJOICE is appropriate, medically necessary, and supported by the patient's individual medical history. Attached are relevant test results and medical records to support my rationale. If you have any additional questions, please contact me at [physician's phone number] or via email at [physician's email]. Thank you for your time and consideration.

Sincerely,

[Physician's Signature, Name, and NPI number if applicable]

Enclosed:

[List and attach additional documents, which may include a denial letter, copies of original request, prescribing information, clinical notes/medical records, or PIK3CA genetic testing.]