



Louisiana

alpelisib (Vioice®)

Policy # 00803

Original Effective Date: 09/12/2022

Current Effective Date: 09/09/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider alpelisib (Vioice®)[‡] for the treatment of *PIK3CA*-Related Overgrowth Spectrum to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility will be considered for alpelisib (Vioice) when the following criteria are met:

- Patient has a diagnosis of *PIK3CA*-Related Overgrowth Spectrum (PROS); AND
- Patient is ≥ 2 years of age; AND
- Patient has at least one severe clinical manifestation of PROS, as determined by the prescriber. Note that examples of severe clinical manifestations include excessive tissue growth, blood vessel malformations, scoliosis, vascular tumors, cardiac or renal manifestations, and those that require systemic treatment; AND
- Patient has a *PIK3CA* mutation as confirmed by documentation of genetic testing.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of alpelisib (Vioice) when the patient selection criteria are not met to be **investigational**.*

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Background/Overview

Vioice is a kinase inhibitor that works by inhibiting the PIK3 pathway and is the first treatment to be approved by the Food and Drug Administration (FDA) for the treatment of *PIK3CA*-related overgrowth spectrum (PROS). The recommended dose is based on age and ranges from 50 mg orally once daily to 250 mg orally once daily. The active ingredient in Vioice, alpelisib, is the same active ingredient in Piqray®, which is indicated for specific forms of advanced or metastatic breast cancer with a *PIK3CA* mutation. However, Piqray is typically dosed as 300 mg orally once daily with dose reductions allowed to 250 mg or 200 mg once daily for adverse reactions. With the exception of the dosing and indication, there is no significant difference between these two products.

PROS is an umbrella term for a heterogeneous group of diseases caused by mutations in the *PIK3CA* gene that includes a range of clinical findings and disorders. The prevalence rate is unknown, but some resources estimate it to be 14 people per million. The diagnosis is often suspected by clinical features of the syndrome and can be confirmed with genetic testing of the *PIK3CA* gene. Testing generally requires a biopsy of tissue with the greatest likelihood of having a detectable mutation. PROS is separated into different clinical syndromes based on the organs and tissues involved (e.g., congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal [CLOVES] syndrome, megalencephaly-capillary malformation [MCAP] syndrome, Klippel-Trenaunay syndrome [KTS], and others). The core features are congenital or early-childhood onset of segmental/focal overgrowth, predominantly affecting the brain, limbs, trunk, and face, all usually in an asymmetric distribution. PROS-related complications can include hemorrhages, embolisms, vascular or lymphatic anomalies, congenital neurological complications, developmental delays, and others. Management of the condition includes treatment of the various manifestations, such as surgery, debulking, orthopedic care, neurosurgical intervention, pain management, laser, therapy, sclerotherapy. Oral sirolimus is sometimes used off-label, but data are limited with sirolimus in this population.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Vioice was approved in April 2022 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.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Vioice was assessed in EPIK-P1, 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. Eligible patients 2 years of age and older with PROS who received Vioice 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. Patients received Vioice at dosages based on age ranging from 50 mg to 250 mg orally once daily. 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 Vioice) were included in the study. The median age of patients was 14 years (range: 2 to 38) and they had heterogenous manifestations of PROS.

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, defined as a $\geq 20\%$ 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 $\geq 20\%$ increase from baseline in any target lesion, progression of non-target lesions, or appearance of a new lesion. At Week 24, 10 patients (27%) were considered responders (95% CI: 14, 44).

References

1. Vioice [package insert]. Novartis Pharmaceuticals Corporation. East Hanover, NJ. Updated April 2022.
2. Piqrax [package insert]. Novartis Pharmaceuticals Corporation, East Hanover, NJ. Updated May 2022.

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08/04/2022 Medical Policy Committee review

08/10/2022 Medical Policy Implementation Committee approval. New Policy.

08/03/2023 Medical Policy Committee review

08/09/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

08/01/2024 Medical Policy Committee review

08/14/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

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****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

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