LOUISIANA BLUE

pexidartinib (Turalio™)

Policy # 00696
Original Effective Date: 01/08/2020
Current Effective Date: 02/10/2025

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 pexidartinib (Turalio™)‡ for the treatment of tenosynovial giant cell tumor to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for pexidartinib (Turalio) will be considered when the following criteria are met:

- Patient has a diagnosis of tenosynovial giant cell tumor (TGCT); AND
- Tumor is not amenable to improvement with surgery; AND
- Patient is experiencing severe morbidity or functional limitations due to the tumor.

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 pexidartinib (Turalio) when patient selection criteria are not met to be **investigational.***

Background/Overview

Turalio is the first FDA-approved systemic treatment for symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery. It is a kinase inhibitor that targets colony stimulating factor 1 (CSF1) receptor as well as other tyrosine kinase proteins to combat the cell proliferation and accumulation promoted by CSF1. Turalio should be administered as 250 mg by mouth twice daily with a low-fat meal and should be continued until disease progression or unacceptable toxicity. Due to the risk of serious and potentially fatal liver injury, Turalio carries a black box warning and is only available through a Risk Evaluation and Mitigation Strategy (REMS) program. This program requires prescribers, patients, and pharmacies to be certified in order to prescribe, access, or dispense the drug.

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TGCTs are rare, benign tumors of the synovium, bursae, and tendon sheath. These non-cancerous tumors cause thickening and overgrowth of the affected tissues, leading to pain, swelling, and reduced mobility. This disease is caused by a chromosomal translocation that causes CSF1 overexpression which leads to macrophage recruitment and inflammation. TGCT may be either localized or diffuse. The localized type typically presents as a well circumscribed, small lesion affecting the digits or occasionally larger joints. Diffuse TGCT, also known as pigmented villonodular synovitis, is a more locally aggressive form and involves a poorly circumscribed, widespread tumor affecting the entire joint. In most cases of diffuse TGCT, only one joint is involved. Onset is typically gradual with pain and swelling as the primary symptoms. There may be a sense of "locking" or "catching" of the joint. Due to these nonspecific symptoms, there is usually a significant delay in the time to diagnosis. TGCT is rarely malignant, but is associated with significant morbidity, functional limitation, and reduced quality of life.

The mainstay of treatment for TGCT is surgery to remove the tumor. Localized TGCT has a good prognosis with surgical excision, but it may occasionally recur. Treatment of diffuse TGCT is more complex, and complete resection of the affected synovium may not always be possible. Untreated or recurrent disease can lead to damage and degeneration of the affected joint. Diffuse TGCTs have a high recurrence rate after surgery of up to 50%, often with multiple recurrences. Although no other medications are FDA-approved for TGCT, imatinib has been evaluated in a small, single-arm, open-label, retrospective study in 29 patients. After a median follow-up time of 10.8 months, 1 patient achieved a complete response and four patients achieved a partial response (ORR 19%). The National Comprehensive Cancer Network (NCCN) Guidelines for Soft Tissue Sarcoma briefly mention TGCT and recommend Turalio with category 1 evidence for TGCT and imatinib with category 2A evidence.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Turalio was approved in August 2019 for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

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.

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The efficacy of Turalio was evaluated in ENLIVEN, a double-blind, randomized, placebo-controlled, multicenter trial in 120 patients with symptomatic TGCT for whom surgical removal of the tumor would be associated with worsening functional limitation or severe morbidity. Eligible patients were required to have measurable disease as determined by the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Patients were randomized (1:1) to placebo or Turalio 400 mg in the morning and 600 mg in the evening for 2 weeks followed by 400 mg twice daily. Treatment continued until unacceptable toxicity or disease progression. The major efficacy outcome measure was overall response rate (ORR) at week 25 using the RECIST criteria. Patients in the placebo arm were offered Turalio at week 25 beginning with a 400 mg twice daily dose. There was a statistically significant improvement in ORR in patients randomized to Turalio (38%) compared to placebo (0%).

The efficacy of Turalio 250 mg orally twice daily administered with a low-fat meal has been established based on studies of Turalio 400 mg orally twice daily administered on an empty stomach and additional pharmacokinetic data that indicated there is no clinically significant difference in the relative exposure between the two dosages.

References

1. Turalio [package insert]. Daiichi Sankyo Inc. Basking Ridge, NJ. Updated August 2019.
2. Turalio Drug Evaluation. Express Scripts. Updated August 2019.
3. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology Soft Tissue Sarcoma Version 4.2019. Updated September 2019.

Policy History

Original Effective Date: 01/08/2020
Current Effective Date: 02/10/2025

01/03/2020	Medical Policy Committee review
01/08/2020	Medical Policy Implementation Committee approval. New policy.
01/07/2021	Medical Policy Committee review
01/13/2021	Medical Policy Implementation Committee approval. No change to coverage.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. No change to coverage.
01/05/2023	Medical Policy Committee review
01/11/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/04/2024	Medical Policy Committee review
01/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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01/02/2025 Medical Policy Committee review
01/08/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 01/2026

*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.

**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.

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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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