BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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TURALIO™ (pexidartinib)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Turalio (pexidartinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist Orthopedist, or Orthopedic Surgeon

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Treatment of non-metastatic, symptomatic tenosynovial giant cell tumor (either pigmented villonodular synovitis (PVNS) or giant cell tumor of tendon sheath (GCT-TS)) associated with severe morbidity or functional limitations and is not amenable to improvement with surgery

     b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Liver function tests including AST, ALT, total bilirubin, direct bilirubin, ALP, and gamma-glutamyl transferase (GGT) as required by the Risk Evaluation and Mitigation Strategy (REMS) [Note: This is waved if it is verified that Provider, Patient, and Pharmacy are enrolled in the REMS]
     b. Negative pregnancy test in a woman of child bearing potential
     c. Baseline range of motion of affected joint by goniometer
     d. Baseline worst pain of at least 4 based on scale of 0-10, with 10 representing "pain as bad as you can imagine" **OR** worst stiffness of at least 4 based on a scale of 0-10, with 10 representing "stiffness as bad as you can imagine"

  5. Individual is on a stable analgesic regimen for at least 2 months

  6. There are no significant drug interactions
     a. Will not be used with other medications known to cause hepatotoxicity
     b. Will not be used with strong CYP3A4 inducers
     c. Will not be used with proton pump inhibitors (e.g., dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, or rabeprazole)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Turalio (pexidartinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Orthopedist, or Orthopedic Surgeon

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2. Individual's condition responded while on therapy
    a. Response is defined as **TWO** of the following:
        i. No evidence of disease progression
        ii. Improvement in range of motion of affected joint
        iii. Improvement in pain in affected joint **OR** improvement in stiffness of affected joint over baseline

3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Hepatotoxicity

5. Patient dose is at least 200 mg twice daily

6. There are no significant interacting drugs
    a. Will not be used with other medications known to cause hepatotoxicity
    b. Will not be used with strong CYP3A4 inducers
    c. Will not be used with proton pump inhibitors (e.g., dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, or rabeprazole)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

Description:

Turalio (pexidartinib) is a small molecular kinase inhibitor indicated 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. Turalio (pexidartinib) is available only through a restricted program called the *Turalio* Risk Evaluation and Mitigation Strategy (REMS) Program.

TGCT, also known as pigmented villonodular synovitis (PVNS) and giant cell tumor of tendon sheath (GCT-TS), is a rare proliferative lesion of synovial tissue. It is characterized by hypervascular proliferative synovium containing multinucleated giant cells, macrophages, and hemosiderin. The multinucleated cells express features of osteoclasts. Progressive nodular disease near or in the joints limits function and may destroy adjacent bone. TGCT usually involves a single joint; commonly, the knee and foot synovial structures are affected, while involvement of the shoulder, wrist/hand, elbow, and hip is less common. TGCT occurs in two forms: a diffuse form

that involves the entire synovium and a more common localized form that involves a discrete section of the synovium. The local and diffuse forms occur intra-articularly throughout the body. The diffuse form can be extra-articular and in rare circumstances can metastasize. Historically, surgery with adjuvant radiation in some cases has been the mainstay of treatment, but the diffuse type of disease has a high rate of recurrence. The majority of nonmalignant proliferative soft tissue and bone lesions are of modest clinical consequence. However, some locally aggressive proliferative lesions, despite their nonmalignant nature, can cause significant morbidity and, in some cases, mortality.

Expression of the colony-stimulating factor 1 (*CSF1*) gene is elevated in most TGCTs with subsequent elevated CSF1 levels and increased interaction with its CSF1 receptor (CSF1R). Overexpression of CSF1 causes immune infiltration within the tumor.

Pexidartinib targets colony stimulating factor 1 receptor (CSF1R), KIT proto-oncogene receptor tyrosine kinase (KIT), and FMS-like tyrosine kinase 3 (FLT3) harboring an internal tandem duplication (ITD) mutation. Overexpression of the CSF1R ligand promotes cell proliferation and accumulation in the synovium. In vitro, pexidartinib inhibited proliferation of cell lines dependent on CSF1R and ligand-induced autophosphorylation of CSF1R. Pexidartinib also inhibited the proliferation of a CSF1R dependent cell line in vivo

Definitions:

Symptomatic Disease:

One of the following:

Worst pain of at least 4 at any time during the week preceding initiation (based on scale of 0 to 10, with 10 representing "pain as bad as you can imagine")

Worst stiffness of at least 4 at any time during the week preceding initiation (based on a scale of 0 to 10, with 10 representing "stiffness as bad as you can imagine")

Goniometer:

A device used to measure the range of motion around a joint in the body

Risk Evaluation and Mitigation Strategy (REMS) Program

A REMS program requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks.

Because of the risk of hepatotoxicity, Turalio (pexidartinib) is only available through a restricted REMS program

Requirements of the Turalio (pexidartinib) REMS Program include the following:

- Prescribers must be certified with the program by enrolling and completing training
  - Prescribers are educated on the following:
    - Approved indication
    - Risk of serious and potentially fatal liver injury associated with the use

  - Need for liver monitoring at baseline and periodically during treatment with dose modifications as described in the Prescribing Information
  - Need to counsel patients about the risk of serious and potentially fatal liver injury, liver monitoring at baseline and periodically during treatment and to report signs and/or symptoms of liver injury to the prescriber during therapy
- Patients must complete and sign an enrollment form for inclusion in a patient registry
- Pharmacies must be certified with the program and must only dispense to patients who are authorized to receive Turalio (pexidartinib)

Resources:

Turalio (pexidartinib) product information, revised by Daiichi Sankyo, Inc. 04-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 28, 2021.

DeLaney TF. Treatment for tenosynovial giant cell tumor and other benign neoplasms affecting soft tissue and bone. In: UpToDate, Maki R, Shah S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on June 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 2.2021 – Updated April 28, 2021. Available at https://www.nccn.org. Accessed on June 28, 2021.

ClinicalTrials.gov NCT02371369: Phase 3 study of pexidartinib for pigmented villonodular synovitis (PVNS) or giant cell tumor of the tendon sheath (GCT-TS), ENLIVEN study; Last Updated January 23, 2019. Available from: http://clinicaltrials.gov. Accessed on August 10, 2019. Re-reviewed on June 28, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.