BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TURALIO™ (pexidartinib)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Turalio (pexidartinib) is considered ***medically necessary*** and will be approved when **ALL** 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. Individual has 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. The individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual 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 childbearing potential
    c. 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. Individual does not have severe hepatic impairment (total bilirubin greater than 3 to 10 times ULN and any AST).

7. Individual is not using **ANY** of the following interacting drugs:
    a. Strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, others)
    b. 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** the following criteria are met **(samples are not considered for continuation of therapy**):

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.

2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
    a. No evidence of disease progression
    b. Improvement in range of motion of affected joint
    c. 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 evidence of severe hepatic impairment (total bilirubin greater than 3 to 10 times ULN and any AST) that may exclude continued use.

5. Individual's dose is at least 200 mg twice daily.

6. Individual is not using any of the following interacting drugs:
    a. Strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, others)

b. 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 Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

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

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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. 07-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 07, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma Version 2.2022 – Updated May 17, 2022. Available at https://www.nccn.org. Accessed August 07, 2022.

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.