# pexidartinib (Turalio™)

EOCCO POLICY

## Policy Type: PA/SP  Pharmacy Coverage Policy: EOCCO085

### Description

Pexidartinib (Turalio) is an oral kinase inhibitor FDA-approved 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.

### Length of Authorization

- Initial: Six months
- Renewal: 12 months

### Quantity limits

| Product Name | Dosage Form | Indication | Quantity Limit | DDID |
|---|---|---|---|---|
| pexidartinib (Turalio) | 200 mg capsule | Tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery | 120 capsules/30 days | 207496<br>207495 |

### Initial Evaluation

I. Pexidartinib (Turalio) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. The medication is prescribed by or in consultation with an oncologist or orthopedic surgeon; **AND**
   C. Member has a confirmed diagnosis of symptomatic tenosynovial giant cell tumor; **AND**
   D. A surgical/orthopedic oncologist or orthopedic surgeon has evaluated that the member is not a candidate for surgery; **AND**
   E. Member does not have preexisting increased serum transaminases such as ALT and AST or an indication of hepatotoxicity; **AND**
   F. The medication is used as a monotherapy

II. Pexidartinib (Turalio) is considered investigational when used for all other conditions, including but not limited to:
   A. Metastatic tenosynovial giant cell tumor (TGCT)
   B. Active cancer that requires therapy (e.g. surgical, chemotherapy, or radiation therapy)

C. Pexidartinib (Turalio) is used in combination with other tyrosine kinase inhibitors that also target colony-stimulating factor (CSF1) or the CSF1 receptor (CSF1R) (e.g., imatinib, nilotinib, sorafenib, or sunitinib)

## Renewal Evaluation

I. Pexidartinib (Turalio) may be considered for continuation of therapy when the following criteria below are met:
   A. Member has an absence of unacceptable toxicity from the medication; **AND**
   B. Clinical documentation showing symptomatic/disease improvement(s) including
      1. Stable or improved range of motion of affected joint; **OR**
      2. Stable or improved pain in affected joint; **OR**
      3. Stable or improved in stiffness of affected joint

## Supporting Evidence

I. Pexidartinib (Turalio) is FDA-approved 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.
II. Tenosynovial giant cell tumor is also referred to as giant cell tumor of the tendon sheath (GCTTS) or pigmented villonodular synovitis (PVNS).
III. Patients with recurrent and/or relapsed TGCT may typically undergo surgical interventions, however, if further surgery would result in significant morbidity or functional impairment, systemic therapy such as pexidartinib (Turalio) may be beneficial.
IV. Pexidartinib (Turalio) was studied in a clinical trial with two parts:
   - Part 1: A randomized, double-blind, multicenter, Phase 3 study (n=120) patients with symptomatic advanced TGCT for whom surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity. The primary efficacy outcome in Part 1 was overall response rate (ORR): 39% (24 of 61) with pexidartinib (Turalio) vs. 0% with placebo at week 25 ($p$<0.0001); 53% at data cutoff.
   - Part 2: An open-label, Phase 3 trial for patients (n=78; 30 from the placebo group) who completed the part 1, evaluating ORR of the patients on the crossover treatment. The primary efficacy outcome in Part 2 was ORR: 30% (9 of 30) at week 25; 53% (16 of 30) at data cutoff.
V. Pexidartinib (Turalio) has boxed warnings and REMS program for the risk of serious and potentially fatal liver injury and embryo-fetal toxicity.
VI. Common adverse events (>20%) in the clinical trial were: hair color change (67%), fatigue (54%), AST increase (39%), nausea (38%), ALT increase (28%), and dysgeusia (25%).
VII. Most common grade 3 or 4 adverse events occurring at a higher incidence in patients treated with pexidartinib (Turalio) were increases in liver enzymes. Hepatic adverse events were also the

most common cause of treatment interruption, dose reduction (38% combined), or treatment discontinuation (13%) in the pexidartinib (Turalio) group.

VIII. In the clinical trial (ENLIVEN), pexidartinib (Turalio) was used as a single-agent therapy.

## Investigational Uses

I. All condition(s) listed as investigational use
   A. These conditions are parts of the exclusion criteria from the ENLIVEN clinical trial. Safety and efficacy of pexidartinib (Turalio) for these conditions are not studied and unknown.

## References

1. Turalio [Prescribing Information]. Daiichi Sankyo, Inc. Basking Ridge, NJ. August 2019.
2. Tap WD, Gelderblom H, Palmerini E, et al. Pexidartinib versus placebo for advanced tenosynovial giant cell tumour (ENLIVEN): a randomised phase 3 trial. *Lancet*. 2019;394(10197):478-487. doi: 10.1016/S0140-6736(19)30764-0.
3. UpToDate, Inc. Treatment for tenosynovial giant cell tumor and other benign neoplasms affecting soft tissue and bone. UpToDate [database online]. Waltham, MA. Updated September 4, 2019. Available at: http://www.uptodate.com/home/index.html. Accessed September 10, 2019.
4. Scharschmidt, T. (2017). Tenosynovial Giant Cell Tumor - NORD (National Organization for Rare Disorders). [online] NORD (National Organization for Rare Disorders). Available at: https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor. Accessed 30 Sep. 2019.
5. National Comprehensive Cancer Network. NCCN Guidelines: Soft Tissue Sarcoma. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma_blocks.pdf. Updated August 16, 2019. Accessed September 3, 2019.
6. Cassier PA, Gelderblom H, Stacchiotti S, et al. Efficacy of imatinib mesylate for the treatment of locally advanced and/or metastatic tenosynovial giant cell tumor/pigmented villonodular synovitis. *Cancer*. 2012;118(6):1649-55. doi: 10.1002/cncr.26409.

## Policy Implementation/Update:

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| Date Created | September 2019 |
| Date Effective | November 2019 |
| Last Updated | |
| Last Reviewed | |

| Action and Summary of Changes | Date |
|---|---|
| Policy created | 09/2019 |