Turalio® (pexidartinib)
(Oral)

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I. Length of Authorization

- Coverage will be provided for 6 months and may be renewed

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Turalio 125 mg capsules: 4 capsules per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- 500 mg per day

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient does not have any pre-existing active liver or biliary tract disease; **AND**
- Patient and prescriber are enrolled in and meet the conditions of the Turalio Risk Evaluation and Mitigation Strategy (REMS) Program; **AND**
- Used as single agent therapy; **AND**
- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.); **AND**
  - Coadministration with moderate or strong CYP3A inhibitors (e.g., fluconazole, itraconazole, grapefruit juice, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with UGT inhibitors (e.g., probenecid, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
- Coadministration with proton-pump inhibitors (pantoprazole, lansoprazole, esomeprazole, etc.); **AND**

Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (TGCT) † Φ [1-3]

- Patient has a histologically confirmed diagnosis of TGCT [also referred to as giant cell tumor of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)]

Histiocytic Neoplasms ‡ [2,5]

- Used for disease with colony stimulating factor 1 receptor (CSF 1R) mutation target; **AND**
- Patient has one of the following sub-types of disease:
  - Langerhans Cell Histiocytosis (LCH); **AND**
    - Used for multisystem disease with symptomatic or impending organ dysfunction or critical organ involvement; **OR**
    - Used for single-system lung disease; **OR**
    - Patient has multifocal single system bone disease not responsive to treatment with a bisphosphonate; **OR**
    - Patient has CNS lesions; **OR**
    - Used for relapsed or refractory disease; **OR**
  - Erdheim-Chester Disease; **AND**
    - Patient has symptomatic disease; **OR**
    - Used for relapsed or refractory disease; **OR**
  - Rosai-Dorfman Disease; **AND**
    - Patient has symptomatic disease that is multifocal or unresectable unifocal; **OR**
    - Used for relapsed or refractory disease

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hepatotoxicity, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease, decrease in size of tumor or tumor spread, or improvement in patient symptoms and/or functional status; **AND**

- Patient does not have any of the following signs of hepatotoxicity:
  - Increased ALT and/or AST >3 times the upper limit of normal; **OR**
  - Increase in both alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) >2 times the upper limit of normal; **OR**
  - Increased total bilirubin above the upper limit of normal

V. Dosage/Administration [1]

Indication	Dose
All Indications	Administer 250 mg orally twice daily with a low-fat meal (approximately 11 to 14 grams of total fat) until disease progression or unacceptable toxicity. ***NOTE:*** Avoid taking TURALIO with a high-fat meal (approximately 55 to 65 grams of total fat), which increases pexidartinib concentrations and may increase the risk of adverse reactions, including hepatotoxicity.
Note: Patients requiring dose reductions due to adverse reactions from Turalio should permanently discontinue therapy if they are unable to tolerate 125 mg twice daily after stepped taper.	

VI. Billing Code/Availability Information

HCPCS Code(s):

- J8999: Prescription drug, oral, chemotherapeutic, nos
- C9399 – Unclassified drugs or biologicals

NDC:

- Turalio 125 mg capsules: 65597-0407-xx

VII. References

1. Turalio [package insert]. Basking Ridge, NJ; Daiichi Sankyo, Inc.; November 2023. Accessed March 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for pexidartinib. National Comprehensive Cancer Network, 2024. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2024.
3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma 3.2023. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed March 2024.

4. Tap WD, Gelderblom H, Palmerini E, et al; ENLIVEN investigators. Pexidartinib versus placebo for advanced tenosynovial giant cell tumour (ENLIVEN): a randomised phase 3 trial. Lancet. 2019 Jun 19. Doi: 10.1016/S0140-6736(19)30764-0. [Epub ahead of print]
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Histiocytic Neoplasms 1.2024. National Comprehensive Cancer Network, 2024. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc." To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed March 2024.
6. Durham BH, Lopez-Rodrigo E, Picarsic J, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. Nat Med 2019;25:1839-1842.
7. Abeykoon JP, Lasho TL, Dasari S, et al; Mayo Clinic-University of Alabama at Birmingham Histiocytosis Working Group. Sustained, complete response to pexidartinib in a patient with CSF1R-mutated Erdheim-Chester disease. Am J Hematol. 2022 Mar 1;97(3):293-302. doi: 10.1002/ajh.26441. Epub 2022 Jan 3. PMID: 34978715; PMCID: PMC9536810.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C96.0	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
C96.5	Multifocal and unisystemic Langerhans-cell histiocytosis
C96.6	Unifocal Langerhans-cell histiocytosis
C96.9	Malignant neoplasm of lymphoid, hematopoietic and related tissue, unspecified
C96.Z	Other specified malignant neoplasms of lymphoid, hematopoietic and related tissue
D76.3	Other histiocytosis syndromes
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-

2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC