Clinical Policy Title:	pexidartinib
Policy Number:	RxA.511
Drug(s) Applied:	Turalio®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2021
Line of Business Policy Applies to:	All lines of business

Background

Pexidartinib (Turalio®) is a 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pexidartinib (Turalio®)	TGCT	400 mg orally twice daily on an empty stomach (at least one hour before or two hours after a meal or snack) until disease progression or unacceptable toxicity. For mild to severe renal impairment (creatinine clearance [CrCl] 15 to 89 mL/min estimated by Cockcroft-Gault using actual body weight) recommended dosage is 200 mg in the morning and 400 mg in the evening.	800 mg/day

Dosage Forms

- Capsule: 200 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Tenosynovial Giant Cell Tumor (must meet all)**:**

1. Diagnosis of TGCT (also known as giant cell tumor of the tendon sheath [GCT-TS] or

pigmentedvillonodular synovitis [PVNS]);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is associated with severe morbidity or functional limitations and is not amenable to improvement with surgery;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration
Commercial: 6 months
Medicaid: 6 months

B. Histiocytic Neoplasms (off-label) (must meet all)**:**
1. Diagnosis of any of the following (a, b or c) along with colony stimulating factor 1 receptor (CSF1R) mutation:
   a. Langerhans cell histiocytosis;
   b. Erdheim-Chester disease;
   c. Rosai-Dorfman disease;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for first-line or subsequent therapy as single agent.
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b): *
   a. New dose does not exceed 800 mg (4 capsules) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

CSF1R: colony stimulating factor 1 Receptor
FDA: Food and Drug Administration
GCT-TS: giant cell tumor of the tendon sheath
PVNS: pigmented villonodular synovitis
TGCT: tenosynovial giant cell tumor

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - Hepatotoxicity
    - Turalio® is available only through a restricted program called the Turalio® Risk Evaluation and Mitigation Strategy (REMS) Program (additional information available at: www.TuralioREMS.com).
    - Turalio® can cause serious and potentially fatal liver injury.
    - Monitor liver tests prior to initiation of Turalio® and at specified intervals during treatment. Withhold and dose reduce or permanently discontinue Turalio® based on severity of hepatotoxicity.

APPENDIX D: General Information

- Pexidartinib is a small molecule tyrosine kinase inhibitor that 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.
- Turalio® may cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use an effective non-hormonal method of contraception.

References

1. Turalio® Prescribing Information. Basking Ridge, NJ: Daiichi Sankyo Inc.; April 2020. Available at: https://dsi.com/prescribing-information-portlet/getPIContent?productName=Turalio&inline=true. Accessed September 21, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed September 21, 2021.
3. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed September 21, 2021.
4. National Comprehensive Cancer Network. Histiocytic Neoplasms Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/histiocytic_neoplasms.pdf. Accessed September 21, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title Table was updated. 2. Line of business policy applies was	09/16/2020	12/07/2020

updated to All lines of business. 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Initial Approval criteria: Commercial approval duration was updated from member's Length of Benefit to 6 months. 5. Continued Approval criteria: Commercial approval duration were updated to 12 months. 6. APPENDIX D: General Information was updated to include the risk during pregnancy. 7. References was reviewed and updated. 8. Updated indication: pexidartinib (Turalio®) is a 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.		
Policy was reviewed: 1. Dosing information was updated to include Dosing Regimen for “mild to severe renal impairment”. 2. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3. Initial Approval Approval I.B for Off label indication ”Histiocytic Neoplasms” was added. 4. Continued Therapy Approval II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 5. References were reviewed and updated.	9/21/2021	12/07/2021