Clinical Policy: Sirolimus Protein-Bound Particles (Fyarro), Topical Gel (Hyftor)

Reference Number: PA.CP.PHAR.574
Effective Date: 01/2023
Last Review Date: 01/2024

Revision Log

Description
Sirolimus protein-bound particles (Fyarro™) and topical gel (Hyftor™) are mammalian target of rapamycin (mTOR) inhibitors.

FDA Approved Indication(s)
Fyarro is indicated for the treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa).

Hyftor is indicated for the treatment of facial angiofibroma associated with tuberous sclerosis in adults and pediatric patients 6 years of age and older.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Fyarro and Hyftor are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Perivascular Epithelioid Cell Tumor (PEComa) (must meet all)**:**

1. Diagnosis of locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa);
2. Request is for Fyarro;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Use as a single agent;
6. Member does not have PEComa type lymphangioleiomyomatosis;
7. Request meets one of the following (a or b):
   a. Dose does not exceed 100 mg/m² IV on Days 1 and 8 of each 21 day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Facial Angiofibroma Associated with Tuberous Sclerosis (must meet all)**:**

1. Diagnosis of facial angiofibroma associated with tuberous sclerosis;
2. Request is for Hyftor;
3. Prescribed by or in consultation with an oncologist, neurologist, or dermatologist;
4. Age ≥ 6 years;
5. Dose does not exceed one of the following (a or b):
   a. Age 6 to 11 years: 600 mg (2 cm);

b. Age ≥ 12 years: 800 mg (2.5 cm).

Approval duration: 3 months

C. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Perivascular Epithelioid Cell Tumor (PEComa) (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Request is for Fyarro;
3. Member is responding positively to therapy;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. Both of the following (i and ii):
      i. New dose does not exceed 100 mg/m² IV on Days 1 and 8 of each 21 day cycle;
      ii. Dose is at least 45 mg/m² IV on Days 1 and 8 of each 21 day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Facial Angiofibroma Associated with Tuberous Sclerosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Request is for Hyftor;
3. Member is responding positively to therapy as evidenced by, including but not limited to, a reduction in the size and/or redness of facial angiofibroma;
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Age 6 to 11 years: 600 mg (2 cm);
   b. Age ≥ 12 years: 800 mg (2.5 cm).

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
PEComa: perivascular epithelioid cell tumor

Appendix B: Therapeutic Alternatives

Not Applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): History of severe hypersensitivity to sirolimus, other rapamycin derivatives, or albumin.
- Boxed warning(s): None reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Sirolimus protein-bound particles (Fyarro)	Locally advanced unresectable or metastatic malignant PEComa	100 mg/m² administered as an IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity	100 mg/m² administered as an IV infusion over 30 minutes on Days 1 and 8 of each 21-day cycle
Sirolimus topical gel (Hyftor)	Facial angiofibroma associated with tuberous sclerosis	Apply to the skin of the face affected with angiofibroma twice daily	Age 6 to 11 years: 600 mg (2 cm) Age ≥ 12 years: 800 mg (2.5 cm)

VI. Product Availability

Drug Name	Availability
Sirolimus protein-bound particles (Fyarro)	Lyophilized powder for infusion: 100 mg of sirolimus formulated as albumin-bound particles in single-dose vial for reconstitution
Sirolimus topical gel (Hyftor)	Topical gel, 0.2%: 2 mg of sirolimus per gram

VII. References

1. Fyarro Prescribing Information. Pacific Palisades, CA. Aadi Bioscience, Inc; November 2021. Available at

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213312Orig1s000Corrected_lbl.pdf. Accessed November 13, 2023.
2. Hyftor Prescribing Information. Bathesda, MD. Nobelpharma America, LLC; March 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/213478s000lbl.pdf. Accessed November 13, 2023.
3. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed November 13, 2023.
4. ClinicalTrials.gov. A Phase 2 Study of ABI-009 in Patients with Advanced Malignant PEComa (AMPECT). Available at https://www.clinicaltrials.gov/ct2/show/NCT02494570. Accessed November 13, 2023.
5. Bissler JJ, McCormack FX, Young LR et al. Sirolimus for Angiomyolipoma in Tuberous Sclerosis complex or Lymphangioleiomyomatosis. The New England Journal of Medicine. 2008; 358:140-51.
6. Wagner AJ, Malinowska-Kolodziej I, Morgan JA et al. Clinical Activity of mTOR Inhibition with Sirolimus in Malignant Perivascular Epithelioid Cell Tumors: Targeting the Pathogenic Activation of mTORC1 in Tumors. Journal of Clinical Oncology. 2010; DOI: 10.1200/JCO.2009.25.2981.
7. Wataya-Kaneda M, Ohno Y, Fujita Y, et al. Sirolimus Gel Treatment vs Placebo for Facial Angiofibromas in Patients With Tuberous Sclerosis Complex: A Randomized Clinical Trial. JAMA Dermatol. 2018 Jul 1;154(7):781-788.
8. Northrup H, Aronow ME, Bebin EM, et al. International Tuberous Sclerosis Complex Consensus Group. Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations. Pediatr Neurol. 2021 Oct;123:50-66.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9331	Injection, sirolimus protein-bound particles (Fyarro), 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024