UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Fyarro Utilization Management Medical Policy
- Fyarro® (sirolimus protein-bound particles [albumin bound] intravenous infusion – Aadi Bioscience)

REVIEW DATE: 01/29/2025

OVERVIEW

Fyarro, a mammalian target of rapamycin (mTOR) inhibitor, is indicated for the treatment of locally advanced unresectable or metastatic **malignant perivascular epithelioid cell tumor (PEComa)** in adults.[1]

Disease Overview

PEComas are rare mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular cells.[2,3] Most PEComas are benign; however, malignant PEComa is locally aggressive or metastatic.[2] Malignant PEComa is a type of soft tissue sarcoma with a ≤ 1:1,000,000 annual incidence. The most frequent sites are renal, uterine, and gastrointestinal; more females than males are affected. Some patients with PEComas have responded to mTOR inhibitors (sirolimus, everolimus, or temsirolimus), although these data are limited to case reports and retrospective analyses.

Guidelines

National Comprehensive Cancer Network (NCCN) guidelines address Fyarro:

- **Soft Tissue Sarcoma**: NCCN guidelines (version 4.2024 – November 21, 2024), recommend Fyarro as the "Preferred" regimen for malignant PEComa for locally advanced unresectable or metastatic disease (category 2A).[3] "Other recommended regimens" include sirolimus, everolimus, and temsirolimus (category 2A for all).
- **Uterine Neoplasm**: NCCN guidelines (version 1.2025 – December 16, 2024) recommend Fyarro as "Useful in Certain Circumstances" for first-line, second-line, or subsequent therapy as clinically appropriate if not previously used in advanced, recurrent/metastatic, or inoperable disease; however, this recommendation only applies to PEComa (category 2A).[4]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Fyarro. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Fyarro as well as the monitoring required for adverse events and long-term efficacy, approval requires Fyarro to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fyarro is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Perivascular Epithelioid Cell Tumor (PEComa), Malignant.** Approve for 1 year the patient meets ALL of the following (A, B, and C):
   Note: Examples of possible sites of PEComa include, but are not limited to, the gastrointestinal tract, kidneys, and uterus.
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient has locally advanced unresectable disease; OR
      ii. Patient has metastatic disease; AND
   C) Fyarro is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 100 mg/m^2 given intravenously on Days 1 and 8 of each 21-day cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Fyarro is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Fyarro® intravenous infusion [prescribing information]. Morristown. NJ: Aadi Bioscience; December 2024.
2. Wagner AJ, Ravi V, Riedel RF, et al. *nab*-Sirolimus for patients with malignant perivascular epithelioid cell tumors. *J Clin Oncol*. 2021 Nov 20;39(33):3660-3670.
3. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 4.2024 – November 21, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 24, 2025.
4. The NCCN Uterine Neoplasm Clinical Practice Guidelines in Oncology (version 1.2025 – December 16, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on January 24, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/17/2024
Annual Revision	No criteria changes.	01/29/2025