STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Fyarro (sirolimus protein-bound particles)
PAM–059

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	04/01/2022
Revision Number:	1	**Last Rev Date:**	07/21/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/19/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/21/2023

Overview

Medication:[1]	sirolimus protein-bound particles (albumin-bound)
Brand Name:	Fyarro™
Pharmacologic Category:	mechanistic target of rapamycin kinase (mTOR) inhibitor
FDA-Approved Indication(s):	Treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa)
How Supplied:	Single-dose vial containing 100 mg of sirolimus as a lyophilized powder
Dosage and Administration:	Intravenous (IV) infusion: 100 mg/m^2 on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity
Benefit Category:	Medical

Descriptive Narrative

Soft tissue sarcomas (STS) are a heterogeneous group of rare tumors that arise from mesenchymal cells, such as muscle, adipose, fibrous, cartilage, nerve, and vascular tissue. STS arise most frequently in the limbs (particularly the lower extremity), followed by the abdominal cavity/retroperitoneum, the trunk/thoracic region, and the head and neck. There are many histologic subtypes of STS with distinct clinical profiles, molecular alterations, treatment responses, and prognoses.

In patients with STS, the specific organs that are affected by recurrent and metastatic disease vary by histology. For most soft tissue sarcomas (with the exception of gastrointestinal stromal tumors), the lungs are the primary site of metastatic disease. However, certain STS subtypes can disseminate to the bones, liver, paraspinal soft tissues, retroperitoneum, and regional lymph nodes. [2]

Guidelines

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[3]

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Soft Tissue Sarcoma (Version 2.2023 – April 25, 2023).[4]

NCCN Guidelines® Recommendation(s) for sirolimus protein-bound (Fyarro™) in soft tissue sarcoma
(1) Malignant perivascular epithelioid cell tumor PEComa*, for locally advanced unresectable or metastatic disease A. Albumin-bound sirolimus (Fyarro™): Category 2A, preferred regimen

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale[5]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themself, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient and determine appropriate treatment and prognosis.

GRADE	ECOG PERFORMANCE STATUS [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Fyarro™ is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa); **AND**
2. Member is 18 years of age or older; **AND**
3. Member has an Eastern Cooperative Oncology Group (ECOG) Performance Status score of 0 or 1; **AND**
4. Member does **NOT** have lymphangioleiomyomatosis; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling.

Fyarro™ is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	100 mg/m^2 on days 1 and 8 of each 21-day cycle	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9331	Injection, sirolimus protein-bound particles, 1 mg

ICD-10	Description
C49.4 – C49.9	Malignant neoplasm of connective and soft tissue of abdomen

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
80803-0153-50	Aadi Bioscience, Inc. (80803)	1 mg	1	EA	100

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Fyarro™ prescribing information (12/2021). Aadi Bioscience, Inc.: Pacific Palisades, CA. Available at www.fyarrohcp.com. Accessed May 16, 2023.

[2] George S, Razak AA. Overview of the initial treatment of metastatic soft tissue sarcoma. Shah S, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 7, 2023.

[3] National Comprehensive Cancer Network (NCCN). Development and Update of Guidelines. Available online at www.nccn.org. Accessed January 19, 2023.

[4] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma (v.2.2023 – April 25, 2023). Accessed July 5, 2023. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version of the guidelines, go online to NCCN.org.

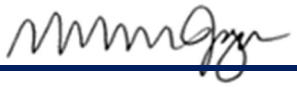
[5] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee