Fyarro™ (sirolimus albumin-bound)
(Intravenous)

Document Number: MH-0647

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Effective Date: 01/01/2023

I. Length of Authorization

Coverage is provided for six months and may be renewed.

II. Dosing Limits

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

- Fyarro 100 mg vial: 6 vials every 21 days

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

- 300 billable units (300 mg) on days 1 and 8 of every 21-day cycle

III. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

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

Universal Criteria

- Patient does not have a severe hypersensitivity to rapamycin derivatives (i.e., sirolimus, everolimus, temsirolimus, etc.); **AND**
- Patient will avoid concomitant therapy with any of the following:
  - Coadministration with P-gp inhibitors and/or strong CYP3A4 inhibitors (e.g., boceprevir, itraconazole, ketoconazole, etc.), if therapy is unavoidable, the patient will

be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

- Coadministration with combined P-gp inducers and/or strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's Wort, etc.), if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**
- Coadministration with grapefruit or grapefruit juice; **AND**

- Therapy will not be administered concurrently with live vaccines and close contact with individuals who have received live vaccines will be avoided; **AND**
- Patient does not have uncontrolled or symptomatic CNS metastases; **AND**
- Patient has had no prior treatment with or will not be used in combination with other mTOR inhibitors (i.e., sirolimus, everolimus, temsirolimus, etc.); **AND**
- Patient does not have lymphangioleiomyomatosis (LAM); **AND**

Perivascular Epithelioid Cell Tumor (PEComa) † Φ [1-4]

- Used as single agent therapy; **AND**
- Patient has locally advanced unresectable or metastatic disease

† FDA-labeled indication; ‡ Compendia approved indication(s); Φ Orphan Drug

IV. Renewal Criteria [1-3]

Coverage can be renewed based upon 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**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: stomatitis, myelosuppression, infections, hypokalemia and hyperglycemia, interstitial lung disease, hemorrhage, azoospermia/oligospermia, severe hypersensitivity reactions, etc.

V. Dosage/Administration [1]

Indication	Dose
PEComa	100 mg/m^2 administered intravenously on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drug *(Discontinue use on 07/01/2022)*
- J9331 – Injection, sirolimus protein-bound particles, 1 mg; 1 billable unit = 1 mg *(Effective 07/01/2022)*

- C9091 – Injection sirolimus protein-bound particles, 1 mg; 1 billable unit = 1 mg *(Discontinue use on 07/01/2022)*

NDC:

- Fyarro 100 mg of sirolimus injection, single-use vial: 80803-0153-xx

VII. References

1. Fyarro [package insert]. Pacific Palisades, CA; Aadi Bioscience Inc; December 2021. Accessed March 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) sirolimus-albumin bound. National Comprehensive Cancer Network, 2022. 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 2022.
3. Wagner AJ, Ravi V, Riedel RF, et al. nab-Sirolimus for Patients With Malignant Perivascular Epithelioid Cell Tumors. J Clin Oncol. 2021 Oct 12:JCO2101728. doi: 10.1200/JCO.21.01728. [Epub ahead of print].
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma Version 3.2021. National Comprehensive Cancer Network, 2021. 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 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
D49.2	Neoplasm of unspecified behavior of bone, soft tissue, and skin
Z85.831	Personal history of malignant neoplasm of soft tissue

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

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at:

https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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