

POLICY NUMBER UM_1308	SUBJECT Folotyn™ (pralatrexate)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATE REVIEWED 04/05/17, 04/06/18, 04/05/19	APPROVAL DATE April 10, 2019	EFFECTIVE DATE April 10, 2019	REVISION DATES (latest version listed last) 04/10/19	
PRIMARY BUSINESS OWNER: APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Oncology	

I. PURPOSE

To define and describe the accepted indications for Folotyn (pralatrexate) usage in the treatment of cancer.

II. DEFINITIONS

Folotyn (pralatrexate): is a novel 10-deazaaminopterin antifolate, structurally similar to methotrexate. It is a competitive inhibitor of dihydrofolate reductase. Compared to other antifolates, pralatrexate was designed to have a greater affinity for the reduced folate carrier and folylpolyglutamyl synthetase, enhancing intracellular accumulation and polyglutamylation in tumor cells.

Folotyn (pralatrexate) is FDA approved for the treatment of patients with relapsed or refractory peripheral T-cell lymphoma. Pralatrexate is the first agent to receive FDA-approval for the treatment of this rare, often aggressive, form of non-Hodgkin's lymphoma.

Folotyn (pralatrexate) is available in 20 mg and 40 mg vials.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Folotyn (pralatrexate) may be considered medically necessary when any of the following selection criteria is met:

1. Peripheral T-Cell Lymphoma (PTCL)

- a. The member has relapse or refractory PTCL (i.e. angioimmunoblastic T-cell lymphoma, peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, enteropathy-associated T-cell lymphoma, or monomorphic epitheliotropic intestinal T-cell lymphoma) **AND**
- b. Folotyn (pralatrexate) is being used as second line or subsequent therapy.

2. Primary Cutaneous Lymphomas

- a. The member has Mycosis Fungoides/Sezary Syndrome and Folotyn (pralatrexate) is being used as primary treatment.

Exclusion Criteria: Folutyn (pralatrexate) is not considered medically necessary when any of the following selection criteria is met:

1. Folutyn (pralatrexate) is being used after disease progression with the same regimen.
2. Concurrent use with other anti-cancer therapy.
3. Dosing exceeds single dose limit of Folutyn (pralatrexate) 30 mg/m².
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Folutyn (pralatrexate) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 30 mg/m² IV once weekly for 6 weeks in 7-week cycles until disease progression or unacceptable toxicity. To reduce the incidence and severity of adverse reactions, patients should receive folic acid and vitamin B12 supplementation. Folic acid 1-1.25 mg PO daily should begin 10 days prior to the first dose of pralatrexate and continue during the full course of therapy, until 30 days after the last dose of pralatrexate. Vitamin B12 1000 mcg IM should begin within 10 weeks prior to the first dose of pralatrexate and should be repeated every 8–10 weeks during therapy. Subsequent vitamin B12 injections may be given the same day as pralatrexate.
2. **Dosage Adjustments:**
 - a. Tumor lysis syndrome: Anticipate, monitor, and treat promptly.
 - b. Dermatologic reactions: Reactions, including fatal reactions, have occurred and may be progressive and increase in severity with further treatment. Monitor closely and omit and/or reduce dose or discontinue Folutyn.
 - c. Renal impairment, mild to moderate: Adjustment not necessary.
 - d. Renal impairment, estimated GFR (eGFR) 15 to less than 30 mL/min/1.73 m²: Initial, 15 mg/m².
 - e. Renal impairment, eGFR 15 to less than 30 mL/min/1.73 m²: Recovery from toxicity, reinstate therapy at 10 mg/m² for mucositis grade 2 recurrence or any grade 3 event; for platelets less than 50,000/mcL for 2 weeks; for recurrence or 2 weeks of absolute neutrophil count (ANC) 500 to 1000/mcL with fever or ANC less than 500/mcL; for any other grade 3 toxicity. Otherwise, if continuing therapy, may continue at prior dose.
 - f. Geriatric: Use caution in dose selection for patients 65 years of age or older.
 - g. Dialysis, ESRD: Avoid use unless potential benefits outweigh risks.
 - h. Absolute neutrophil count (ANC) 500 to 1000/mcL for 1 week and no fever: Omit dose and restart with prior dose when ANC is 1000/mcL or higher.
 - i. ANC 500 to 1000/mcL with fever or ANC less than 500/mcL for 1 week: Omit dose and give granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) support and restart with prior dose and G-CSF or GM-CSF support when ANC is 1000/mcL or higher.

- j. ANC 500 to 1000/mcL with fever or ANC less than 500/mcL for 2 weeks or recurrence: Omit dose and give G-CSF or GM-CSF support. Restart at 20 mg/m², or if eGFR is 15 to less than 30 mL/min/1.73 m² restart at 10 mg/m², with G-CSF or GM-CSF support when ANC is 1000/mcL or higher.
- k. ANC 500 to 1000/mcL with fever or ANC less than 500/mcL for 3 weeks or second recurrence: Stop therapy.
- l. Mucositis, grade 2: Omit dose. Upon recovery to grade 1 or less continue at prior dose.
- m. Mucositis, grade 2 recurrence or grade 3: Omit dose and upon recovery to grade 1 or less, continue at 20 mg/m² or if eGFR is 15 to less than 30 mL/min/1.73 m², restart at 10 mg/m².
- n. Mucositis, grade 4: Stop therapy.
- o. Other treatment-related toxicities, grade 3: Omit dose and upon recovery to grade 2 or less, continue at 20 mg/m² or if eGFR is 15 to less than 30 mL/min/1.73 m², restart at 10 mg/m².
- p. Other treatment-related toxicities, grade 4: Stop therapy.
- q. Platelet count less than 50,000/mcL for 1 week: Omit dose and continue prior dose when platelet count is 50,000/mcL or higher.
- r. Platelet count less than 50,000/mcL for 2 weeks: Omit dose and restart when platelet count is 50,000/mcL or higher at 20 mg/m² or if eGFR is 15 to less than 30 mL/min/1.73 m², restart at 10 mg/m².
- s. Platelet count less than 50,000/mcL for 3 weeks: Stop therapy.

3. **Monitoring**

- a. Objective evidence of clinical improvement in peripheral T-cell lymphoma is indicative of efficacy.
- b. CBC; baseline and weekly (including differential).
- c. Liver function tests; prior to the start of doses 1 and 4 of each cycle.
- d. Renal function tests; prior to the start of doses 1 and 4 of each cycle.
- e. Serum chemistry tests; prior to the start of doses 1 and 4 of each cycle.
- f. Signs and symptoms of tumor lysis syndrome in at risk patients.
- g. Mucositis at baseline and weekly.

V. **APPROVAL AUTHORITY**

1. Review – UM Department
2. Final Approval – UM Committee

VI. **ATTACHMENTS**

VII. **REFERENCES**

1. Folutyn PI prescribing information. Allos Therapeutics, Inc. Westminster, CO 2018.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.

4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.