



Medication Policy Manual

Policy No: dru197

Topic: Folutyn®, pralatrexate

Date of Origin: January 15, 2010

Committee Approval Date: July 14, 2017

Next Review Date: July 2018

Effective Date: August 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Pralatrexate (Folutyn), an analogue of methotrexate, is a chemotherapy medication used in the treatment of a rare form of cancer (peripheral T-cell lymphoma). It is administered via an intravenous infusion.

Policy/Criteria

- I. Most contracts require prior authorization approval of pralatrexate (Folotyn) prior to coverage. Pralatrexate (Folotyn) may be considered medically when criteria A and B below are met.
 - A. A diagnosis of peripheral T-Cell lymphoma (PTCL).

AND

 - B. At least one prior therapy for PTCL has been ineffective or not tolerated (see *Appendix 1* for therapy options).

- II. Administration, Quantity Limitations, and Authorization Period
 - A. OmedaRx does not consider pralatrexate (Folotyn) to be a self-administered medication.
 - B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

- III. Pralatrexate (Folotyn) is considered investigational when used for all other conditions, including but not limited to:
 - A. Cutaneous T Cell Lymphoma (CTCL)
 - B. Hodgkin Lymphoma
 - C. Malignant Pleural Mesothelioma
 - D. Non-Hodgkin Lymphomas
 - E. Non-Small Cell Lung Cancer (NSCLC)

Position Statement

- Pralatrexate (Folotyn), a methotrexate analog, is used in the treatment of peripheral T-cell lymphoma (PTCL). Its efficacy in this condition is based on tumor response assessments. Clinical benefit, such as improvement in survival, has not been demonstrated.
- Pralatrexate (Folotyn) was studied in patients who had at least one prior medication therapy for their PTCL.
- National Comprehensive Cancer Network (NCCN) guidelines list several options for the treatment of PTCL. There are no studies comparing pralatrexate (Folotyn) with any of these other options.
- Pralatrexate (Folotyn) is administered as an intravenous push once weekly for 6 weeks in 7-week cycles. Supplementation of vitamin B12 and folic acid is given with pralatrexate (Folotyn) to minimize hematologic toxicity.
- Pralatrexate (Folotyn) is being studied in a variety of other cancers; however, there is insufficient evidence supporting its safety and efficacy in these other conditions at this time.

Clinical Efficacy

- The efficacy of pralatrexate (Folotyn) is based on a single, unreliable study that used response criteria as its primary outcome. ^[1]
 - * The single-arm trial studied 111 patients with relapsed or refractory PTCL.
 - * Efficacy was based on the overall response rates defined as the sum of the complete response rate, unconfirmed complete response rate, and partial response rate.
 - * The median number of prior systemic therapies was 3 (range 1 to 12).
- Pralatrexate (Folotyn) has not been shown to improve clinical outcomes such as progression-free survival or overall survival.
- Pralatrexate (Folotyn) has not been compared with any other therapy for PTCL. ^[2]
- National Comprehensive Cancer Network (NCCN) T-cell lymphomas guideline lists several potential options for the treatment of PTCL (see *Appendix 1*), including pralatrexate (Folotyn). ^[3] All of these options are listed as NCCN category 2A recommendations meaning the quality of evidence is low but there was consensus among oncologists on the panel for inclusion on the guideline.
- Pralatrexate (Folotyn) is being studied in the treatment of several additional conditions including other types of non-Hodgkin's lymphomas, non-small cell lung cancer (NSCLC) and mesothelioma. There is also interest in using pralatrexate (Folotyn) as a front-line therapy for patients with PTCL.
 - * Results from most of the non-Hodgkin's lymphoma studies (other than PTCL) have not been reported in peer-reviewed literature. ^[4]
 - * In a small, published trial pralatrexate (Folotyn) demonstrated some activity in patients with NSCLC based on objective response rates. ^[5] A second, published trial comparing pralatrexate (Folotyn) and erlotinib (Tarceva) used overall survival as a primary endpoint. No statistical difference was reported; however, the trial was not adequately powered to detect a difference between interventions so results are not meaningful. ^[6] Larger, well-controlled studies are needed to establish the safety and efficacy of pralatrexate (Folotyn) in NSCLC.
 - * A single small trial failed to demonstrate any benefit from single-agent pralatrexate (Folotyn) in patients with malignant pleural mesothelioma. ^[7]
 - * When used as a front-line therapy, the addition of pralatrexate (Folotyn) to conventional chemotherapy (i.e. cyclophosphamide, doxorubicin, vincristine, prednisone), did not improve outcomes compared to historical data using chemotherapy alone. ^[8]

OmedaRx performs independent analyses of oncology medications. The OmedaRx analysis and coverage policy may differ from NCCN guidelines.

Safety [2]

- The most common adverse effects reported with pralatrexate (Folotyn) include mucositis, thrombocytopenia, nausea, and fatigue.
- Folate and vitamin B₁₂ supplementation are recommended to reduce treatment-related hematologic toxicity and mucositis.
- Dose modifications are recommended for severe mucositis, neutropenia and thrombocytopenia, and liver enzyme elevations.
- Other medications that are primarily eliminated by the kidneys (e.g. trimethoprim/sulfa, NSAIDs) may interfere with pralatrexate secretion, thereby delaying its clearance.

Dosing Considerations [2]

- Pralatrexate (Folotyn) is given as an intravenous push over 3 to 5 minutes at a dose of 30 mg/m².
- It is given once weekly for 6 weeks in 7-week cycles until disease progression or unacceptable toxicity.
- Folic acid and vitamin B₁₂ are given concomitantly with pralatrexate (Folotyn) to limit its toxicity.

Appendix 1: Systemic Treatment Options for PTCL [3] a,b

First-line Therapy

- CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
- CHOP followed by IVE (ifosfamide, etoposide, epirubicin) alternating with methotrexate
- EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
- HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine

Second-line Therapy

<i>Transplant candidates</i>	<i>Non-transplant candidates</i>
<ul style="list-style-type: none"> • <i>Single agents:</i> <ul style="list-style-type: none"> ○ Belinostat (Beleodaq) ○ Bendamustine ○ Brentuximab vedotin (Adcetris) for CD30+ PTCL ○ Gemcitabine ○ Lenalidomide (Revlimid) ○ Pralatrexate (Folotyn) ○ Romidepsin (Istodax) • <i>Combination regimens:</i> <ul style="list-style-type: none"> ○ DHAP (dexamethasone, cisplatin, cytarabine) ○ ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ○ GDP (gemcitabine, dexamethasone, cisplatin) ○ GVD [gemcitabine, vinorelbine, liposomal doxorubicin (Doxil)] ○ GemOx (gemcitabine, oxaliplatin) ○ ICE (ifosfamide, carboplatin, etoposide) 	<ul style="list-style-type: none"> • <i>Single agents/regimens:</i> <ul style="list-style-type: none"> ○ Alemtuzumab (Campath) ○ Belinostat (Beleodaq) ○ Bendamustine ○ Bortezomib (Velcade) [category 2B] ○ Brentuximab vedotin (Adcetris) for CD30+ PTCL ○ Cyclosporine ○ Gemcitabine ○ Lenalidomide (Revlimid) ○ Pralatrexate (Folotyn) ○ Radiation therapy ○ Romidepsin (Istodax)

^a PTCL subtypes included: PTCL not otherwise specified (NOS), angioimmunoblastic T-cell lymphoma (AITL), anaplastic large cell lymphoma (ALCL), and enteropathy-associated T-cell lymphoma (EATL)

^b All therapies listed above are NCCN category 2A recommendations (lower quality evidence but uniform consensus among panel) unless otherwise indicated.

Cross References

Adcetris®, brentuximab, Medication Policy Manual, Policy No. 264

Beleodaq®, belinostat, Medication Policy Manual, Policy No. 362

Istodax®, romidepsin, Medication Policy Manual, Policy No. 198

Codes	Number	Description
HCPCS	J9307	Injection, pralatrexate, 1 mg

References

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- Advani, RH, Ansell, SM, Lechowicz, MJ, et al. A phase II study of cyclophosphamide, etoposide, vincristine and prednisone (CEOP) Alternating with Pralatrexate (P) as front line therapy for patients with peripheral T-cell lymphoma (PTCL): final results from the T-cell consortium trial. *British journal of haematology*. 2016 Feb;172(4):535-44. PMID: 26627450

Revision Date	Revision Summary
7/14/2017	No criteria changes with this annual review
9/9/2016	No criteria changes with this annual update.