Clinical Policy: Fluorouracil Cream (Tolak)

Reference Number: CP.PMN.165
Effective Date: 12.01.18
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Fluorouracil (Tolak® Cream, 4%) is a nucleoside metabolic inhibitor.

FDA Approved Indication(s)

Tolak is indicated for the topical treatment of actinic keratosis lesions of the face, ears, and/or scalp.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results, or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Tolak is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Actinic Keratosis (must meet all)**:**

1. Diagnosis of actinic keratosis of the face, ears, or scalp;
2. Member must use fluorouracil 5% topical cream, unless contraindicated or clinically significant adverse effects are experienced;†
   †For Illinois HIM requests, the step therapy requirement above does not apply as of 1/1/2026 per IL HB 5395
3. Dose does not exceed once daily application.

Approval duration: 4 weeks

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Actinic Keratosis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Tolak therapy for the current requested use has not exceeded 4 weeks;
4. If request is for a dose increase, new dose does not exceed once daily application.

Approval duration: Up to 4 weeks total per treatment course

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DPD: dihydropyrimidine dehydrogenase deficiency
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fluorouracil 5% topical cream (Efudex®)	Actinic Keratosis: Apply to lesions topically BID for 2 to 6 weeks	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindications: dihydropyrimidine dehydrogenase (DPD) deficiency, pregnancy
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Actinic keratosis lesions	Apply topically QD for 4 weeks in an amount sufficient to cover the lesions with a thin film, massaging uniformly into the skin	As specified

VI. Product Availability

Topical cream (4%): 40 g

VII. References

1. Tolak Prescribing Information. Sanford, Florida. Hill Dermaceuticals, Inc.; September 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=59de2709-00b8-4f0a-867c-f0dfeb947192. Accessed July 13, 2026.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2026. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 22, 2026.
3. Jansen MHE, Kessels JPHM, Nelemans PJ, et al. Randomized trial of four treatment approaches for actinic keratosis. N Engl J Med. 2019 Mar 7;380(10):935-946.
4. Eisen DB, Asgari MM, Bennet DD, et al. Guidelines of care for the management of actinic keratosis. J Am Acad Dermatol. 2021 Oct; 85(4): e209-e233.
5. Kandolf L, Peris K, Malvehy J, et al.; European Association of Dermato-Oncology, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists. European consensus-based interdisciplinary guideline for diagnosis, treatment, and prevention of actinic keratoses, epithelial UV-induced dysplasia and field cancerization on behalf of European Association of Dermato-Oncology, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists. J Eur Acad Dermatol Venereol. 2024 Jun;38(6):1024-1047. doi: 10.1111/jdv.19897.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; revised from "failure" of fluorouracil 5% cream to "member must use" language since both Tolak and this product are the same active ingredient and vehicle; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.20.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.18.23	11.23
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.19.24	11.24
4Q 2025 annual review: no significant changes; added step therapy bypass for IL HIM per IL HB 5395; references reviewed and updated.	07.10.25	11.25
4Q 2026 annual review: no significant changes; added ICHRA line of business; references reviewed and updated.	07.13.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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