

Clinical Policy: Fluorouracil Cream (Tolak)

Reference Number: PA.CP.PMN.165

Effective Date: 10/2018

Last Review Date: 10/2024

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 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 PA Health & Wellness[®] 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 ketatosis lesions on the face, ears and/or scalp;
2. Member must use topical fluorouracil 5% topical cream, unless contraindicated or clinically significant adverse effects are experienced.
3. Dose does not exceed once daily application.

Approval duration: 4 weeks

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Actinic Keratosis (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
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. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.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 policy – PA.CP.PMN.53 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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fluorouracil 5% topical cream (Efudex®)	<u>Actinic Keratosis:</u> Apply to lesions topically BID for 2 to 6 weeks	Not applicable

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 Warnings: 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.; August 2022. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=59de2709-00b8-4f0a-867c-f0dfeb947192> Accessed July 19, 2024.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed August 15, 2024.
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, Malveyh 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
Policy created.	10/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: References reviewed and updated.	08/2020
4Q 2021 annual review: no significant changes; references reviewed and updated.	10/2021
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.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: no significant changes; references reviewed and updated.	10/2024