# Clinical Policy: Fluorouracil Cream (Tolak)

Reference Number: PA.CP.PMN.165
Effective Date: 10/2018
Last Review Date: 10/2025

**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 usetopical 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®) | Actinic Keratosis:<br>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 21, 2025.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 21, 2025.
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 |
|---|---|
| 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 |
| 4Q 2025 annual review: no significant changes; references reviewed and updated. | 10/2025 |