BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/15/18**
SECTION: DRUGS	**LAST REVIEW DATE: 3/15/18**
	LAST CRITERIA REVISION DATE:
	ARCHIVE DATE:

CARAC® (fluorouracil) and FLUOROURACIL cream 0.5%
EFUDEX® (fluorouracil) cream 5%
FLUOROPLEX® (fluorouracil) cream 1%

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Carac, Efudex, Fluoroplex, Fluorouracil

Medication class:
- Dermatologicals, Antineoplastic or Premalignant Lesion Agents – Topical

FDA-approved indication(s):
- **0.5%, 1%, 2%, 5% strengths**: multiple actinic (solar) keratoses
- **5% strength**: superficial basal cell carcinomas when conventional methods are impractical (eg, due to multiple lesions or difficult treatment sites)

Limitations of use:
- Establish diagnosis of superficial basal cell carcinoma prior to treatment (use has not been proven effective in other types of basal cell carcinomas); surgery is preferred with isolated, easily accessible basal cell carcinomas because success with such lesions is almost 100% and the success rate with fluorouracil cream and solution is approximately 93%.

Recommended Dose:

Actinic or solar keratoses
- **0.5% and 4% cream**: Apply once a day to the skin where actinic keratosis lesions appear, using enough to cover the entire area with a thin film. Apply for up to 4 weeks as tolerated.
- **1% cream**: Apply sufficient medication to cover the entire face or other affected areas twice daily. A treatment period of 2 to 6 weeks is usually required. Increased frequency of application and a longer period of administration with fluorouracil cream may be required on areas other than the head and neck. When the inflammatory reaction reaches the erosion, ulceration, and necrosis stages, the use of the drug should be terminated. Responses may sometimes occur in areas that appear clinically normal. These may be sites of subclinical actinic (solar) keratosis that the medication is affecting.
- **5% cream and 2% and 5% solutions**: Apply cream or solution twice daily in an amount sufficient to cover the lesions.
- When fluorouracil is applied to a lesion, a response occurs with the following sequence: erythema, usually followed by vesiculation, desquamation, erosion, and reepithelialization. The usual duration of therapy is from 2 to 4 weeks. Medication should be continued until the inflammatory response reaches the erosion stage, at which time use of the drug should be terminated.
- Complete healing of the lesions may not be evident for 1 to 2 months following cessation of fluorouracil therapy.

Superficial basal cell carcinomas
- **5% strengths**: Apply cream or solution twice daily in an amount sufficient to cover the lesions. Treatment should be continued for at least 3 to 6 weeks. Therapy may be required for as long as 10 to 12 weeks before the lesions are obliterated. As in any neoplastic condition, the patient should be followed for a reasonable period of time to determine if a cure has been obtained.

Available Dosage Forms:
- **Carac**: Cream, 0.5%
- **Efudex**: Cream, 5%

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EFUDEX® (fluorouracil) cream 5%
FLUOROPLEX® (fluorouracil) cream 1% (cont.)

- **Fluoroplex**: Cream, 1%
- **Fluorouracil**: Solution, 2% and 5%

Warnings and Precautions:

- *Local skin reactions*: When applied to a lesion, erythema followed by vesiculation, desquamation, erosion and reepithelialization occurs. Local reactions and alterations in skin appearance may persist for several weeks after discontinuation. Bruising, burning, crusting, dryness, edema, irritation, pain, pruritus, scaling, scarring, soreness, stinging, and ulceration may commonly result from topical therapy. Increased absorption through ulcerated or inflamed skin is possible.
- *Dihydropyrimidine dehydrogenase enzyme deficiency*: Individuals lacking DPD enzyme activity may exhibit severe toxicity with topical fluorouracil. Life-threatening systemic toxicity has been reported with the topical use of fluorouracil in a patient with DPD enzyme deficiency; signs/symptoms included bloody diarrhea, stomatitis, esophagus, stomach, and small bowel inflammation, severe abdominal pain, vomiting, chills, fever, erythematous skin rash, neutropenia, and thrombocytopenia. It is unknown if patients with profound DPD enzyme deficiency would develop systemic toxicity with lower concentrations of topical fluorouracil. Discontinue if signs of DPD deficiency develop.
- *Appropriate use*: Avoid topical application to mucous membranes due to potential for local inflammation and ulceration; cases of miscarriage and a birth defect (ventricular septal defect) have been reported when fluorouracil was applied to mucous membrane areas during pregnancy. The use of occlusive dressings with topical preparations may increase the severity of inflammation in nearby skin areas (a porous gauze dressing may be applied for cosmetic reasons without increase in reaction). Avoid eyelids, eyes, and periocular area when applying (corneal and conjunctival disorders have occurred with topical fluorouracil). Wash hands well following application; if ocular exposure occurs, flush with large amounts of water.
- *Benzyl alcohol and derivatives*: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (99 mg/kg/day or more) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension and cardiovascular collapse; some data suggests that benzoate displaces bilirubin from protein binding sites, avoid or use dosage forms containing benzyl alcohol with caution in neonates. See manufacturer's labeling.
- *Peanut oil*: Some dosage forms contain peanut oil.
- *Hypersensitivity*: May be associated with delayed-type hypersensitivity reactions, including allergic contact dermatitis. Severe pruritus or eczema (at the application site or at a distant site) may be indicative of hypersensitivity. Patch testing may not be useful in the evaluation of these reactions. Discontinue immediately for signs of hypersensitivity.
- *Photosensitivity*: Topical fluorouracil is associated with photosensitivity, including severe sunburn. Avoid prolonged exposure to sunlight or ultraviolet irradiation during treatment; reaction intensity may be increased.

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Criteria:

- **Criteria for initial therapy:** Carac and Fluorouracil cream 0.5%, Efudex cream 5%, and Fluoroplex cream 1% is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a Dermatologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     - Multiple actinic (solar) keratoses
     - For Efudex 5% cream: Superficial basal cell carcinomas when conventional methods are impractical (eg, due to multiple lesions or difficult treatment sites)

  4. **For Actinic keratosis:** Individual has failure, contraindication or intolerance to **BOTH** Tolak 4% cream and 2% fluorouracil solution
     For Superficial basal cell carcinomas: Individual has failure, contraindication or intolerance to generic fluorouracil cream 5%

  5. There are **NO** contraindications.
     - Contraindications include:
       - Hypersensitivity to fluorouracil or any component of the formulation
       - Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency
       - Women who are or may become pregnant

  Initial approval duration: 2 months

- **Criteria for continuation of coverage (renewal request):** Carac and Fluorouracil cream 0.5%, Efudex cream 5%, and Fluoroplex cream 1% is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a Dermatologist

  2. The indication for use is one that requires a longer duration as patient has not reached the erosion stage or additional dosage due to high number of lesions

  3. 1-2 months as passed since the last treatment with fluorouracil therapy as complete healing takes that much time

  4. Individual has been adherent with the medication

  5. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use

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- Contraindications or adverse effect:
  - Signs and symptoms may include:
  - Bloody diarrhea, stomatitis, severe abdominal pain, vomiting etc. indicating DPD enzyme deficiency

6. There are no significant interacting drugs

Renewal duration: 3 months

Resources:

Carac. Package Insert. Revised by manufacturer 5/2017. Accessed 2/9/18.

Efudex. Package Insert. Revised by manufacturer 5/2017. Accessed 2/9/18.

Fluoroplex. Package Insert. Revised by manufacturer 7/2017. Accessed 2/9/18.

Fluorouracil. Package Insert. Revised by manufacturer 2/2018. Accessed 2/9/18.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.