BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

TRETINOIN (all-trans retinoic acid [ATRAC]) oral capsule

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Tretinoin (all-trans retinoic acid [ATRAC]) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Hematologist.

  2. Individual is 1 year of age or older.

  3. Individual has a confirmed diagnosis of **ONE** of the following:
     a. For induction of remission of patients with acute promyelocytic leukemia (APL), French-American-British (FAB) classification M3 (including the M3 variant), characterized by the presence of the (15;17) translocation and/or the presence of the PML/RARα gene

b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Documented failure, contraindication per FDA label or intolerance to, or not a candidate for anthracycline chemotherapy (such as daunorubicin or idarubicin)

5. The individual is undergoing induction of remission and Tretinoin will not be used for consolidation or maintenance.

6. The individual has received and completed **a baseline** Negative pregnancy test in a woman of childbearing potential before initiation of treatment and with continued monitoring as clinically appropriate.

7. There is **NO** FDA-label contraindication of hypersensitivity to tretinoin, any of its components, or other retinoids.

8. Individual is not using any vitamin A product.

Initial approval duration: 3 months

- **Criteria for continuation of coverage (renewal request):** Tretinoin (all-trans retinoic acid [ATRAC]) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist or Hematologist.

2. Individual's condition has responded while on therapy with response defined as:
   a. No evidence of disease progression
   b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual is undergoing induction of remission and Tretinoin will not be used for consolidation or maintenance.

4. Individual has not developed any adverse drug effects that may exclude continued use such as:
   a. Retinoic acid-APL syndrome
   b. Rapidly evolving leukocytosis
   c. Pseudotumor cerebri
   d. Thrombosis (venous and arterial)
   e. Respiratory compromise – pleural effusion, pulmonary edema, respiratory insufficiency
   f. Hepatotoxicity

5. There is evidence for pregnancy testing and contraception counseling monthly throughout the period of treatment in a woman of childbearing potential.

6. Individual is not using any vitamin A product.

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Renewal duration: 6 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Tretinoin (all-trans retinoic acid [ATRAC]) capsules are indicated for the induction of remission in patients with acute promyelocytic leukemia (APL), French-American-British (FAB) classification M3 (including the M3 variant), characterized by the presence of the t(15;17) translocation and/or the presence of the PML/RARα gene who are refractory to, or who have relapsed from, anthracycline chemotherapy, or for whom anthracycline based chemotherapy is contraindicated. Tretinoin is for the induction of remission only. The optimal consolidation or maintenance regimens have not been defined, but all patients should receive an accepted form of remission consolidation and/or maintenance therapy for APL after completion of induction therapy with tretinoin.

In general therapy with tretinoin should be discontinued 30 days after achievement of complete remission or after 90 days of treatment, whichever occurs first. Initiation of therapy with tretinoin may be based on the morphological diagnosis of acute promyelocytic leukemia. Confirmation of the diagnosis of APL should be sought by detection of the t(15;17) genetic marker by cytogenetic studies. If these are negative, PML/RARα fusion should be sought using molecular diagnostic techniques. The response rate of other AML subtypes to tretinoin has not been demonstrated; therefore, patients who lack the genetic marker should be considered for alternative treatment. Tretinoin appears to bind to one or more nuclear receptors and it decreases proliferation and induces differentiation of APL cells; initially it produces maturation of primitive promyelocytes and repopulates the marrow and peripheral blood with normal hematopoietic cells to achieve complete remission. Chemically, tretinoin, USP is all-*trans* retinoic acid and is related to retinol (Vitamin A).

FDA Indication: Tretinoin capsules are indicated for the induction of remission in patients with acute promyelocytic leukemia (APL), French-American-British (FAB) classification M3 (including the M3 variant), characterized by the presence of the t(15;17) translocation and/or the presence of the PML/RAR-alpha gene who are refractory to, or who have relapsed from, anthracycline chemotherapy, or for whom anthracycline-based chemotherapy is contraindicated. Tretinoin is for the induction of remission only. The optimal consolidation or maintenance regimens have not been defined, but all patients should receive an accepted form of remission consolidation and/or maintenance therapy for APL after completion of induction therapy with tretinoin.

Resources:

Tretinoin (all-trans retinoic acid [ATRAC]) product information, revised by Teva Pharmaceuticals USA, Inc. 12-2015. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 06, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 2.2022 – Updated June 14, 2022. Available at https://www.nccn.org. Accessed August 06, 2022.

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

ORIGINAL EFFECTIVE DATE: 09/20/2018 | ARCHIVE DATE: | LAST REVIEW DATE: 08/18/2022 | LAST CRITERIA REVISION DATE: 08/18/2022

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