BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**9/20/2018**
LAST REVIEW DATE:	**8/19/2021**
LAST CRITERIA REVISION DATE:	**8/19/2021**
ARCHIVE DATE:	

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

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.**

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

Criteria:

- **Criteria for initial therapy:** Tretinoin (all-trans retinoic acid [ATRAC]) is considered ***medically necessary*** and will be approved when **ALL** of 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. 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 t(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 or 2A

  4. Individual has failure, contraindication or intolerance to:
     a. Anthracycline chemotherapy (such as daunorubicin or idarubicin)

  5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Negative pregnancy test in a woman of childbearing potential

  6. There are **NO** contraindications.
     a. Contraindications include:
        i. Hypersensitivity to tretinoin, any of its components, or other retinoids

  7. There are no significant interacting drugs

  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** of the following criteria are met:

  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 responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

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

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other 4 adverse drug effects that may exclude continued use
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. Retinoic acid-APL syndrome
        ii. Rapidly evolving leukocytosis
        iii. Pseudotumor cerebri
        iv. Thrombosis (venous and arterial)
        v. Respiratory compromise – pleural effusion, pulmonary edema, respiratory insufficiency
        vi. Hepatotoxicity

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

6. There are no significant interacting drugs

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 a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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

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 Glenmaek Pharmaceuticals, Inc. 01-2016. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 3.2021 – Updated March 02,2021. Available at https://www.nccn.org. Accessed on June 28, 2021.

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.