BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/19/2020
LAST REVIEW DATE:
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

ONUREG® (azacitidine) oral

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.**

ONUREG® (azacitidine) oral

Criteria:

- **Criteria for initial therapy:** Onureg (azacitidine) 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
  2. Individual is 18 years of age or older
  3. A confirmed diagnosis of **ONE** of the following:
     a. Continued treatment of acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy

     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. Eastern Cooperative Oncology Group (ECOG) Performance Status score is less than or equal to 2
  5. Will not be a substitute for intravenous or subcutaneous azacitidine
  6. Will not be used to treat myelodysplastic syndromes (MDS)
  7. Will not be used in moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal)

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Onureg (azacitidine) 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
  2. Individual's condition has not worsened while on therapy.
     a. Worsening is defined as:
        i. Disease progressed while on Onureg
        ii. There is no evidence of efficacy, disease stability and/or improvement
  3. Individual has been adherent with the medication
  4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
     a. Adverse effect such as:
        i. Myelosuppression

ii. Interstitial lung disease
iii. Tumor lysis syndrome Sweet's syndrome (acute febrile neutrophilic dermatosis)
iv. Necrotizing fasciitis
v. Differential syndrome

5. There are no significant interacting drugs

Renewal duration: 12 months

- Onureg (azacitidine) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any one or more of the following criteria are met:
  1. Lack of final approval from the Food and Drug Administration;
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes;
  3. Insufficient evidence to support improvement of the net health outcome;
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; **or**
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, but are not limited to:
  - Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration.

Description:

Onureg (azacitidine) is a nucleoside metabolic inhibitor indicated for continued treatment of adult patients with acute myeloid leukemia (AML) who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

Azacitidine is a pyrimidine nucleoside analog of cytidine that inhibits DNA/RNA methyltransferases. Azacitidine is incorporated into DNA and RNA following cellular uptake and enzymatic biotransformation to nucleotide triphosphates.

Treatment of AML is determined by the ability or fitness of the individual for intensive anti-leukemic therapy based upon the patient's performance status and physiologic function from comorbid conditions. For most medically-fit patients who undergo intensive induction therapy for AML, the goal of treatment is to achieve long-term-survival with the possibility of cure. Medically-unfit but not frail patients that are unlikely to tolerate intensive anti-leukemic therapy, the goal of treatment is to achieve a remission, improve quality of life, and/or prolong life. Frail AML patients are those patients whose debility or comorbid conditions do not permit treatments that modify the disease course as the potential for harms from intensive therapy outweighs the benefits. The goals of managing these patients is to relive symptoms and improve quality of life through supportive care measures.

Medically-unfit but not frail patients are not candidates for intensive anti-leukemic therapy. Hypomethylating agents (HMA) such as azacitidine or decitabine are the mainstays of treatment; usually combined with the B-cell

lymphoma-2 (BCL2) inhibitor venetoclax rather than use of HMA or BCL2 agents as monotherapy. For patients with an actionable mutation such as an isocitrate dehydrogenase (IDH 1 or IDH2) mutation, use of an IDH inhibitor (ivosidenib for IDH1 mutation or enasidenib for IDH2 mutation) is an alternative to HMA-based therapy. Low dose cytarabine (LoDAC) can be used when the patient is not eligible for an HMA and who does not have an actionable mutation or an available target agent.

Definitions:

Response definitions:

Based on blood counts, transfusion needs, and relief of symptoms

- **Complete response (CR)**
  - Normalization of the complete blood count (CBC), including absolute neutrophil count (ANC) ≥1000/microL and platelets ≥100,000/microL, transfusion-independence, and relief of AML-related symptoms
- **CR with incomplete hematologic recovery (CRi)**
  - Transfusion-independent and meets above criteria for CR, but without complete platelet recovery (usually) or ANC recovery
- **Partial response (PR)**
  - Improvements in CBC, but not to levels that define CR/Cri with ongoing transfusion needs and/or inadequate symptom relief
- **Refractory disease**
  - No meaningful improvement in CBC, ongoing transfusion needs, and/or inadequate symptom relief

Resources:

Onureg (azacitidine) (chemical name) product information, revised by manufacturer Celgene Corporation 09-2020, at DailyMed http://dailymed.nlm.nih.gov. Accessed October 12, 2020.

Larsen RA. Acute myeloid leukemia: Management of medically-unfit adults. In: UpToDate, Lowenberg B, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on October 12, 2020.

Kolitz JE. Overview of acute myeloid leukemia in adults. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on October 14, 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 4.2020 – Updated September 28, 2020 ; https://www.nccn.org. Accessed October 12, 2020.

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.