BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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INQOVI® (decitabine and cedazuridine) 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.**

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Criteria:

- **Criteria for initial therapy:** Inqovi (decitabine and cedazuridine) 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 18years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Myelodysplastic syndromes (MDS), including previously treated and untreated, *de novo* and secondary MDS of **any** of the following types: (See Definitions section)
        i. French-American-British subtype
        ii. Intermediate-1 International Prognostic Scoring System (IPSS) groups
        iii. Intermediate-2 IPSS groups
        iv. High-risk IPSS groups

     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. **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
     b. Eastern Cooperative Oncology Group (ECOG) Performance Score is 0-2

  5. Documented failure, contraindication per FDA-label, intolerance to **EITHER** of the following:
     a. Generic azacitidine
     b. Generic decitabine

  6. Will not be used as a replacement for intravenous decitabine within a cycle

  7. Individual does not have severe renal impairment (CrCl 15-29 mL/min) or end-stage renal disease (ESRD: CrCl <15 mL/min)

  8. Individual does not have moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal with any aspartate aminotransferase)

  9. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Inqovi (decitabine and cedazuridine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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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 progression
        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 adverse drug effects that may exclude continued use

5. Will not be used as a replacement for intravenous decitabine within a cycle

6. Individual does not have severe renal impairment (CrCl 15-29 mL/min) or end-stage renal disease (ESRD: CrCl <15 mL/min)

7. Individual does not have moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal with any aspartate aminotransferase)

8. There are no significant interacting drugs

Renewal duration: 12 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:

Inqovi (decitabine and cedazuridine) is a combination of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor that is indicated for treatment of adult patients with myelodysplastic syndromes (MDS), including previously treated and untreated, *de novo* and secondary MDS with the following French-American- British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System (IPSS) groups.

The product label stated that Inqovi (decitabine and cedazuridine) is not a substitute for an intravenous decitabine product within a cycle.

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The safety and efficacy of Inqovi (decitabine and cedazuridine) was evaluated in two open-label randomized studies. Patients were randomized to receive Inqovi (35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 in Cycle 1 and decitabine 20 mg/m intravenously on Days 1 through 5 in Cycle 2, or the reverse sequence, and then Inqovi (35 mg decitabine and 100 mg cedazuridine) orally once daily on Days 1 through 5 of each 28-day cycle in Cycles 3 and beyond until disease progression or unacceptable toxicity.

One study included 80 adult patients with MDS (IPSS Intermediate-1, IPSS Intermediate-2, or high-risk) or CMML. The other included 133 adult patients with MDS or CMML, including all French-American-British (FAB) classification criteria and IPSS Intermediate-1, Intermediate-2, or high-risk prognostic scores.

Efficacy was established on the basis of complete response (CR) and the rate of conversion from transfusion dependence to transfusion independence. CR was seen in 18-21%, patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 49-53% became independent of RBC and platelet transfusions during post-baseline period, and patients who were independent of both RBC and platelet transfusions at baseline, 63-64%) remained transfusion-independent during post-baseline period.

Definitions:

French American British (FAB) Classification:
Divides MDS in to five subtypes based on percentage of blasts in the bone marrow and the peripheral blood
It is used less frequently than the WHO classification system

FAB-type	% blasts in blood	% blasts in bone marrow
RA (Refractory Anemia)	< 1	< 5
RARS (Refractory Anemia with Ring Sideroblasts	< 1	< 5
RAEB (Refractory Anemia with Excess Blasts in Transmission) Note: Now called AML (acute myelogenous leukemia)	< 5	5 - 20
RAEB-t (Refractory Anemia with Excess Blasts in Transformation)	> 5	21 - 30
CMML (chronic myelomonocytic Leukemia)	> 5	5 - 20

International Prognostic Scoring System (IPSS) in myelodysplastic syndrome:

Survival and AML evolution					
	Score value				
Prognostic Variable	**0**	**0.5**	**1.0**	**1.5**	**2.0**
Bone Marrow Blast percentage	< 5	5-10		11-20	21-30
Karyotype	Good	Intermediate	Poor		
Cytopenias	0/1	2/3			

Prognosis			
Score	**IPSS Group**	**Median Survival (Years)**	**25% AML progression (years) in absence of therapy**
0	Low	5.7	9.4
0.5-1.0	Intermediate-1	3.5	3.3
1.5-2.0	Intermediate-2	1.1	1.1
> 2.5	High	0.4	0.2

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* Cytogenetic definitions:
Good = normal, -Y alone, del(5q) alone, del(20q) alone
Poor = complex (≥3 abnormalities) or chromosome 7 anomalies
Intermediate = other abnormalities (excludes karyotypes t(8;21), inv16, and 5(15;17)
Cytopenias: neutrophil count < 1,800mcL, platelets < 100,000 mcL, Hg < 10 g/dL

Revised international prognostic scoring system (IPSS-R) in myelodysplastic syndrome:

Prognostic variable	Score value						
	0	**0.5**	**1.0**	**1.5**	**2.0**	**3.0**	**4.0**
Cytogenetics*	Very good		Good		Intermediate	Poor	Very poor
Bone marrow blast (percent)	≤ 2		> 2 to < 5		5 to 10	> 10	
Hemoglobin (g/dL)	≥ 10		8 to < 10	<8			
Platelets (cells/microL)	≥ 100	50 to 100	< 50				
Absolute neutrophil count (cells/microL)	≥ 0.8	< 0.8					

This scoring system was applied to an initial group of 7012 patients with primary MDS by the French-American-British classification who had at least two months of stable blood counts, ≤ 30 percent bone marrow blasts and ≤19 percent peripheral blood blasts, and who were observed until progression to AML transformation or death (did not receive disease-modifying agents for MDS). Patients could be stratified into five groups with the following estimated overall survival and progression to AML.

Risk group	IPSS-R score	Median overall survival (years)	Median time to 25 percent AML evolution (years)
Very low	≤ 1.5	8.8	> 14.5
Low	> 1.5 to 3.0	5.3	10.8
Intermediate	> 3 to 4.5	3.0	3.2
High	> 4.5 to 6	1.6	1.4
Very high	> 6	0.8	0.7

The prognostic value of the IPSS-R was validated in an external cohort of 200 patients with MDS

AML: acute myeloid leukemia; MDS: myelodysplastic syndrome.
* Cytogenetic definitions:
Very good: -Y, del(11q).
Good: Normal, del(5q), del(12p), del(20q), double including del(5q).
Intermediate: del(7q), +8, +19, i(17q), any other single, double not including del(5q) or -7/del(7q), or independent clones.
Poor: -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities.
Very poor: Complex: > 3 abnormalities

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Resources:

Inqovi (decitabine and cedazuridine) oral product information, revised by Taiho Pharmaceutical Co., Ltd. 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

Dacogen (decitabine) injection product information, revised by Otsuka America Pharmaceutical, Inc. 06-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

Decitabine injection product information, revised by Mylan Institutional LLC 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

Onureg (azacitidine) oral product information, revised by Celgene Corporation 05-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

Azacitidine injection product information, revised by Mylan Institutional LLC. 09-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

Vidaza (azacitidine) injection product information, revised by Celgene Corporation 03-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 28, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myelodysplastic Syndromes Version 3.2021 – Updated January 03, 2021. Available at https://www.nccn.org. Accessed August 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 August 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.