



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:

---

## 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.

**BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.**

---

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](http://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](mailto:Pharmacyprecert@azblue.com). **Incomplete forms or forms without the chart notes will be returned.**



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:

---

## INQOVI® (decitabine and cedazuridine) oral

---

### 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. Individual has failure, contraindication or intolerance to **EITHER** of the following:
    - a. Generic azacitidine
    - b. Generic decitabine
  5. Will not be used as a replacement for intravenous decitabine within a cycle
  6. Eastern Cooperative Oncology Group (ECOG) Performance Score is less than or equal to 2
  7. Individual does not have severe renal impairment (CLcr 15-29 mL/min) or end-stage renal disease (ESRD: CLcr <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)

**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:
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:



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:

---

## INQOVI® (decitabine and cedazuridine) oral

---

- i. Disease progressed while on Inqovi
  - 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. Hepatotoxicity
    - iii. Tumor lysis syndrome
    - iv. Renal toxicity
5. There are no significant interacting drugs

**Renewal duration:** 12 months

- Inqovi (decitabine and cedazuridine) 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:**

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.

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

**INQOVI® (decitabine and cedazuridine) oral**

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					
Prognostic Variable	Score value				
	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		

\* Cytogenetic definitions:

Good = normal, -Y alone, del(5q) alone, del(20q) alone

Poor = complex (≥3 abnormalities) or chromosome 7 anomalies

**INQOVI® (decitabine and cedazuridine) oral**

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					
<p>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.</p>							
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



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:

---

## INQOVI® (decitabine and cedazuridine) oral

---

### Resources:

Inqovi (decitabine and cedazuridine) product information, revised by manufacturer Taiho Pharmaceutical Co., Ltd. 07-2020, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 12, 2020.

Azacidine product information, revised by manufacturer Mylan Institutional LLC 09-2018, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 12, 2020.

Vidaza (azacitidine) product information, revised by manufacturer Celgene Corporation 03-2020, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 12, 2020.

Dacogen (decitabine) product information, revised by manufacturer Otsuka America Pharmaceutical, Inc. 06-2020, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 13, 2020.

Decitabine product information, revised by manufacturer Mylan Institutional LLC 07-2019, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 13, 2020.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Myelodysplastic Syndromes Version 1.2021 – Updated September 11, 2020 ; <https://www.nccn.org>. Accessed October 12, 2020.

Aster JC, Stone RM. Clinical manifestation and diagnosis of myelodysplastic syndromes (MDS). In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Accessed on October 12, 2020.

Estey EH, Sekeres MA. Overview of the management of myelodysplastic syndromes. In: UpToDate, Larson RA, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. <http://uptodate.com>. Accessed on 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.

---