decitabine/cedazuridine (Inqovi™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO202

Description

Decitabine/cedazuridine (Inqovi) is an orally administered combination of DNA methylation inhibitor and cytidine deaminase inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
decitabine/cedazuridine (Inqovi)	35/100 mg tablet	Myelodysplastic Syndrome (MDS); Chronic myelomonocytic leukemia (CMML); Acute myeloid leukemia (AML)	5 tablets/28 days

Initial Evaluation

I. **Decitabine/cedazuridine (Inqovi)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   C. Decitabine/cedazuridine (Inqovi) will not be used in combination with any other oncology therapy, except in combination with venetoclax in the setting of acute myeloid leukemia; **AND**
   D. Member has a diagnosis of **Myelodysplastic syndrome (MDS)**; **AND**
      I. Provider attests that member's bone marrow blast count is less than (<) 20%; **AND**
      II. Member has one of the following French-American-British (FAB) subtypes of **myelodysplastic syndrome (MDS)**:
         a. Refractory anemia; **OR**
         b. Refractory anemia with ringed sideroblasts; **OR**
         c. Refractory anemia with excess blasts; **OR**
         d. Chronic myelomonocytic leukemia (CMML); **AND**
      III. Documentation of the members International Prognostic Score (IPSS) denoting whether the member has intermediate or high risk (e.g. IPSS Intermediate-1; Intermediate-2, or high risk); **AND**
      IV. Treatment with IV azacitidine (Vidaza) OR IV decitabine (Dacogen) has been ineffective, contraindicated, or not tolerated; **OR**
   E. Request is for induction therapy for a member with newly diagnosed **acute myeloid leukemia (AML)**; **AND**

1. Member has not previously progressed on, or after, treatment with another chemotherapy regimen indicated for the treatment of AML (e.g., azacitidine, venetoclax, decitabine, cladribine, daunorubicin); **AND**
2. Member is not a candidate for intensive induction therapy, defined by the following:
   i. Age ≥75 years old; **OR**
   ii. Provider attests that the member has comorbidities that preclude intensive induction chemotherapy (e.g., baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2 or greater, severe cardiac or pulmonary disease, hepatic impairment with bilirubin >1.5 times the upper limit of normal, or creatine clearance <30 mL/min); **AND**
3. Provider attestation that decitabine/cedazuridine (Inqovi) will be used in combination with oral venetoclax.

II. Decitabine/cedazuridine (Inqovi) is considered investigational when used for all other conditions, including but not limited to:
   A. Acute myeloid leukemia (AML) in the relapsed and/or refractory setting
   B. Lower risk myelodysplastic syndrome (e.g. IPSS low; IPSS-R Very low, low; WPSS very low, low)
   C. Refractory anemia with del(5q) abnormality
   D. Chronic myelogenous leukemia (CML)
   E. Acute lymphoblastic leukemia (ALL)
   F. Multiple myeloma (MM)
   G. Ovarian cancer

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited response to treatment defined by complete or partial response to treatment, disease stabilization, or achieving transfusion independence; **AND**
IV. Decitabine/cedazuridine (Inqovi) will not be used in combination with any other oncology therapy except for venetoclax in the setting of acute myeloid leukemia.

Supporting Evidence

I. Decitabine/cedazuridine (Inqovi) is FDA-approved for use in patients aged 18 years and older. Decitabine/cedazuridine (Inqovi) is a combination of DNA methylation inhibitor and cytidine deaminase inhibitor, indicated for the treatment of MDS, including previously treated and

untreated, de novo and secondary MDS, and CMML. Decitabine/cedazuridine (Inqovi) is also FDA-approved for the treatment (in combination with venetoclax) of newly diagnosed acute myeloid leukemia in adults ≥75 years of age, or with comorbidities that preclude use of intensive induction chemotherapy.

MDS

II. Myelodysplastic syndrome is a heterogeneous disease involving ineffective, dysplastic hematopoiesis leading to cytopenias, bleeding, infections, and in one-third of patients ultimately progressing to acute AML. CMML is a related hematopoietic condition involving peripheral blood monocytosis. MDS may be classified in to seven subtypes as per French-British-American (FAB) system. Decitabine/cedazuridine (Inqovi) received FDA-approved for four of the seven subtypes, namely: refractory anemia; refractory anemia with ringed sideroblasts; refractory anemia with excess blasts; and CMML**.** Additionally, approval of decitabine/cedazuridine (Inqovi) was limited to intermediate-1 (Int-1), Int-2, and high-risk MDS according to the IPSS classification.

III. Based on symptoms at presentation (fatigue, bone pain, frequent infections, and bleeding), MDS may be misdiagnosed as other conditions such as anemia, HIV infection, autoimmune disorder or osteomyelitis. Proper diagnosis and treatment of MDS requires histochemical and cytogenetic studies; therefore, decitabine/cedazuridine (Inqovi) must be prescribed by, or in consultation with an oncologist or hematologist.

IV. The only FDA-approved therapies for Int-1, Int-2, and high-risk MDS and CMML are IV administered hypomethylating agents (HMA): azacitidine (Vidaza) and decitabine (Dacogen). Lenalidomide (Revlimid) oral capsule also has FDA approval for treatment of MDS; however, use of this drug is limited to transfusion-dependent anemia in low-risk MDS with 5q deletion. Decitabine/cedazuridine (Inqovi) tablet is the first oral HMA and provides the advantage of self-administration for patients. Decitabine/cedazuridine (Inqovi) may be considered an alternative first-line therapy option for MDS and CMML treatment.

V. Regimens involving combination of IV administered HMA (azacitidine and decitabine) with other agents such has ruxolitinib (Jakafi), and venetoclax (Venclexta) have been studied and recommended by NCCN guidelines in the settings of MDS, CMML, and AML. Limited low quality clinical data are also available with respect to combinations of IV HMA with lenalidomide (Revlimid), vorinostat (Zolinza), phenylbutyrate or valproic acid. However, efficacy and safety of decitabine/cedazuridine (Inqovi) in combination with other drugs for the treatment of MDS and CMML has not been studied and remains unknown. Treatment of newly diagnosed AML with decitabine/cedazuridine (Inqovi) is FDA-approved when used in combination with oral venetoclax. Combination therapy of chemotherapy and/or other oncology medications outside of the labeled indication has not been sufficiently studied.

VI. Decitabine/cedazuridine (Inqovi) was studied in two (Phase 2 ASTX727-1-B trial, and Phase 3 ASCERTAIN), open-label, randomized, crossover trials in 222 patients with Int-1 or Int-2 or high risk MDS or CMML. Patients with de novo or secondary MDS or CMML were included. Additional inclusion criteria consisted of absence of secondary hematological malignancy and a bone marrow blast count of ≤ 20% (of note, a bone marrow blast count of >20% is a parameter used

in differential diagnosis of AML versus MDS). One prior cycle of decitabine or azacitidine was allowed, but no other chemotherapy within two weeks before randomization was permitted.

VII. The primary efficacy outcome was pharmacokinetic (PK) measurement of five-day exposure of oral decitabine/cedazuridine (Inqovi) vs IV decitabine, using area under the curve (AUC) during first two cycles of treatment. Decitabine/cedazuridine (Inqovi) showed comparable PK data to that of IV decitabine during cycles one and two of the treatment. For Phase 3 (ASCERTAIN) study, five-day oral/IV decitabine exposure was 98.9% (90% CI; 92.7, 105.6). Additionally, overall response rates (ORR) were reported in 60% patients across all cohorts during Phase 2 trial, with 21% patients exhibiting complete response (CR) to decitabine/cedazuridine (Inqovi).

VIII. Safety data was pooled from both studies. Reported treatment emergent adverse events (TEAE) were similar between oral and IV decitabine patient populations with neutropenia, thrombocytopenia, leukopenia, anemia, pneumonia, and sepsis as the most common. Gastro-intestinal (GI) adverse reactions were comparable between oral and IV formulations of decitabine. Thirteen (6.1%) deaths were reported during treatment period, among which, 11 (5.2%) were associated to adverse events. Overall, 30-day mortality rate was 0.5%.

IX. Decitabine/cedazuridine (Inqovi) has not been compared with IV azacitidine (Vidaza) or IV decitabine (Dacogen) in head-to-head clinical trials. The majority of the safety and efficacy data for hypomethylating agents in the MDS treatment space are rooted in the trials for the IV therapies. Approval of decitabine/cedazuridine (Inqovi) was based off of comparative pharmacokinetic exposure to decitabine between oral and IV formulations. Although this trial showed comparable efficacy and safety, there is lack of data to show superiority of the oral decitabine/cedazuridine (Inqovi) over IV decitabine (Dacogen). Weighing the safety, efficacy, cost, and clinical experience, IV therapies are considered standard and appropriate high-value treatment options for MDS and CMML and are preferred over decitabine/cedazuridine (Inqovi).

AML

X. Decitabine/cedazuridine (Inqovi) was FDA-approved for treatment (in combination with venetoclax) of newly diagnosed acute myeloid leukemia (AML) in adults ≥75 years of age, or with comorbidities that preclude use of intensive induction chemotherapy. The National Comprehensive Cancer Network (NCCN) guidelines have been updated to provide a category 2A recommendation for treatment with decitabine/cedazuridine (Inqovi) as other recommended treatment for newly diagnosed patients with AML who are not candidates for intensive induction therapy.

- AML with IDH1 mutation: preferred: azacitadine and venetoclax, azacitidine and ivosidenib (category 1) or decitabine and venetoclax (category 2A). Other recommended: ivosidenib or oral decitabine and cedazuridine and venetoclax (Inqovi) (category 2A). Useful in certain circumstances: low-dose cytarabine (LDAC) and venetoclax, azacitidine or decitabine, or olutasidenib (category 2A).
- AML without IDH1 mutation: azacitadine and venetoclax (category 1), or azacitidine and ivosidenib (category 2A). Other recommended: oral decitabine and cedazuridine (Inqovi) and venetoclax, or cladribine and LDAC and venetoclax (category 2B). Useful in certain circumstances: LDAC and venetoclax, azacitidine or decitabine, LDAC and

glasdegib, LDAC, gilteritinib +/- azacitidine, enasidenib +/- azacitadine, or gemtuzumab ozogamicin (category 2A).

XI. Decitabine/cedazuridine (Inqovi) was studied in a Phase 1 and 2 open-label, multicenter, non-randomized interventional study (ASTX727). In the pivotal Phase 2b portion of the study, decitabine/cedazuridine (Inqovi) was used in combination with oral venetoclax for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy (n=101). The median age was 78 years old. Most patients were male (60%), had an ECOG status of 1 (51%), had an intermediate cytogenetic risk classification according to the European Leukemia Net (ELN) 2017 criteria (65%), had a TP53 mutation (17%), and had one reason for ineligibility to receive intensive induction therapy (81%). The primary efficacy endpoint was complete response (CR), and key secondary endpoints were CR with partial hematologic recovery, and overall survival. In Phase 2b, CR was achieved in 47% of the patients (95% CI, 36-57), and either a CR or CR with incomplete hematologic recovery was observed in 63% (95% CI, 53-73). Median overall survival was 15.5 months (95% CI, 7.6-could not be estimated). Results from the ASTX727 study are low quality. Phase 1 and 2 trials lack the scale of larger, Phase 3 randomized control trials, as evidenced by the small sample size of ASTX727 with lack of placebo control and an active comparator to preferred therapies. The benefit of decitabine/cedazuridine (Inqovi) used in the relapsed/refractory setting, as monotherapy, and in comparison to no treatment and standard of care remains unknown. CR is a surrogate marker that does not correlate with clinically significant outcomes, such as effects on morbidity or mortality. However, OS is a validated endpoint in AML and endpoint results were similar to that of guideline preferred regimens in this space, however, ASTX727-2b lacked the Phase 3, randomized, and placebo-controlled settings of the confirmatory trials for preferred treatments in this space. The most common adverse events (≥20%) in the ASTX727-2b study were anemia (30%), neutropenia (26%), febrile neutropenia (26%), decreased platelet count (25%), thrombocytopenia (20%), and decreased neutrophil count (20%). Treatment led to dose interruption in 69 (68%), dose discontinuation in 9 (9%), dose reduction in 14(14%) and death in 16 (16%) of patients. The safety of decitabine/cedazuridine (Inqovi) for AML was similar to that of its other FDA approved indication, MDS. When indirectly compared, decitabine/cedazuridine (Inqovi) does not have safety concerns relating to hepatoxicity, injection-site reactions, tumor lysis syndrome, and nephrotoxicity when indirectly compared to azacitidine, and has a similar overall safety profile when indirectly compared to decitabine. However, there are no head-head trials comparing decitabine/cedazuridine (Inqovi) to preferred treatments for newly diagnosed AML. Balancing safety and efficacy results, there is low confidence that decitabine/cedazuridine (Inqovi) provides a clinically objective and/or meaningful benefit relative to comparable treatment options.

XII. Decitabine/cedazuridine (Inqovi) was FDA-approved for use in previously untreated AML. ASTX727 also excluded participants who were previously on a hypomethylating agent (azacitidine or decitabine), or venetoclax, including prior treatment for myelodysplastic syndrome (MDS). There is insufficient evidence to support the use of decitabine/cedazuridine (Inqovi) in patients who have previously progressed on, or after, treatment with another

chemotherapy regimen indicated for the treatment of AML (e.g., azacitidine, venetoclax, decitabine, cladribine, daunorubicin).

XIII. Study ASTX727 included patients who were not eligible for intensive induction therapy. There are no universally accepted guidelines to determine criteria for patients who are ineligible for intensive induction therapy, and NCCN guidelines do not provide specific criteria either. However, NCCN does recommend that determining factors should include ECOG performance status, cardiac, pulmonary, hepatic, and renal function, comorbidity burden, frailty/cognitive status, and/or ability to tolerate prolonged myelosuppression and hospitalization. Study ASTX727 specifically included patients who are at least 75 years old, who have severe cardiac, and/or pulmonary disorder, who have severe renal and/or hepatic impairment, and who have an Eastern Cooperative Oncology Group (ECOG) Performance Status of at least 2. NCCN provides a separate treatment course for patients who are good candidates for intensive induction therapy. Therefore, treatment of decitabine/cedazuridine (Inqovi) in combination with venetoclax for AML should be reserved for those who are ineligible for intensive induction therapy.

XIV. The pivotal ASTX727-2b study evaluated decitabine/cedazuridine (Inqovi) in combination with oral venetoclax for treatment of newly diagnosed AML. Decitabine/cedazuridine (Inqovi) was FDA-approved for use in combination with venetoclax. There is insufficient evidence to support the use of decitabine/cedazuridine (Inqovi) as monotherapy.

Investigational or Not Medically Necessary Uses

I. Decitabine/cedazuridine (Inqovi) has not been sufficiently studied for safety and efficacy for any other condition to date.

** The Moda Split Fill program is a physician-centric, patient engagement program intended to provide enhanced patient and physician support while accomplishing the goals of minimizing waste and avoiding incremental healthcare costs due to medication intolerance and unexpected change or termination of therapy regimen. Under the Split Fill program, the identified medications are programmed for fills of up to a 14 or 15-day supply for the duration of the first three months (86 or 90 days) of therapy. This program affords additional interactions with a specialty pharmacist, allowing more frequent assessments of side effects and barriers to adherence. Each fill is administered at half of the member cost-share, thereby reducing the economic burden if they must discontinue therapy mid-month.*

References

1. Steensma DP, Baer MR, Slack JL, Buckstein R, Godley LA, Garcia-Manero G, et al. Multicenter study of decitabine administered daily for 5 days every 4 weeks to adults with myelodysplastic syndromes: the alternative dosing for outpatient treatment (ADOPT) trial. J Clin Oncol. 2009;27(23):3842–3848.
2. Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Solé F, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood. 2012;120(12):2454–2465.
3. Garcia-Manero G. Myelodysplastic syndromes: 2015 update on diagnosis, risk-stratification, and management. Am J Hematol. 2015;90(9):832–841.
4. Garcia-Manero G, Griffiths EA, Steensma DP, et al. Oral cedazuridine/decitabine for MDS and CMML: a phase 2 pharmacokinetic/pharmacodynamic randomized crossover study. *Blood*. 2020;136(6):674-683. doi:10.1182/blood.2019004143.

5. Garcia-Manero G, McCloskey J, Griffiths EA, Yee KWL, et al. Pharmacokinetic exposure equivalence and preliminary efficacy and safety from a randomized cross over phase 3 study (ASCERTAIN study) of an oral hypomethylating agent ASTX727 (cedazuridine/decitabine) compared to IV decitabine. *Blood.* 2019, 134 (S1), conference abstract.
6. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al (eds.). SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. Bethesda, MD. 05 September 2019.
7. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz M, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–2405.
8. Parikh SA and Tefferi A. Chronic myelomonocytic leukemia: 2012 update on diagnosis, risk stratification, and management. Am J Hematol. 2012; 87: 611–619.
9. Decitabine and cedazuridine (Inqovi) [Prescribing Information]. Taiho Pharmaceutical Co., Ltd; Princeton NJ. July 2020.
10. National Comprehensive Cancer Network (NCCN) guidelines for myelodysplastic syndromes, V 1.2021; 09/2020.
11. Roboz GJ, Zeidan AM, Mannis GN, et al. All-Oral Treatment of Newly Diagnosed Acute Myeloid Leukemia. N Engl J Med. 2026;394(21):2107-2116. doi:10.1056/NEJMoa2510223
12. National Comprehensive Cancer Network (NCCN) guidelines for Acute Myeloid Leukemia, V 5.2026; 07/2026.
13. Food and Drug Administration. FDA approves oral combination of decitabine and cedazuridine tablets with venetoclax for newly diagnosed acute myeloid leukemia. Updated May 13, 2026. Accessed July 16, 2026. FDA approves oral combination of decitabine and cedazuridine tablets with venetoclax for newly diagnosed acute myeloid leukemia | FDA

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy

Policy Name Disease state	Policy Name Disease state
venetoclax (Venclexta)	Newly diagnosed acute myeloid leukemia (AML)
	Chronic lymphocytic leukemia (CLL); Small lymphocytic lymphoma (SLL)
IDH inhibitors	Acute myeloid leukemia, newly diagnosed
	Acute myeloid leukemia, relapsed/refractory
	Cholangiocarcinoma, advanced/ metastatic
	Myelodysplastic syndromes, relapsed/refractory
	Grade 2 IDH-mutant diffuse glioma (i.e., oligodendroglioma or astrocytoma)
glasdegib (DAURISMO)	Newly diagnosed acute myeloid leukemia (AML)
acalabrutinib (Calquence) Policy	Mantle cell lymphoma (previously treated)
	Chronic lymphocytic leukemia (CLL)
	Small lymphocytic lymphoma (SLL)
zanubrutinib (Brukinsa) Policy	Mantle cell lymphoma
	Waldenström macroglobulinemia
	Chronic lymphocytic leukemia/Small lymphocytic lymphoma
	Relapsed or refractory marginal zone lymphoma in adults who have received at least one anti-CD20-based regimen
duvelisib (Copiktra) Policy	Relapsed/refractory chronic lymphocytic leukemia (CLL)

	Relapsed/refractory small lymphocytic lymphoma (SLL)
idelalisib (Zydelig) Policy	Relapsed Chronic Lymphocytic Leukemia (CLL)

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated to include expanded indication for newly diagnosed AML. Added related policies table.	8/2026
Policy created	11/2020