Clinical Policy: Decitabine/Cedazuridine (Inqovi)

Reference Number: CP.PHAR.479
Effective Date: 07.07.20
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Decitabine/cedazuridine (Inqovi®) is a combination of decitabine, a nucleoside metabolic inhibitor, and cedazuridine, a cytidine deaminase inhibitor.

FDA Approved Indication(s)

Inqovi 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 groups.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Inqovi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Myelodysplastic Syndromes (must meet all)**:**

1. Diagnosis of MDS;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member must use decitabine (Dacogen®), unless one of the following (a or b):
   a. Decitabine (Dacogen) is contraindicated or clinically significant adverse effects are experienced;
   b. Request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix D)*;

   **Prior authorization may be required for decitabine*
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 35 mg decitabine/100 mg cedazuridine (1 tablet) per day on Days 1 through 5 of each 28-day cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months

Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Myelodysplastic Syndromes (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Inqovi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 35 mg decitabine/100 mg cedazuridine (1 tablet) per day on Days 1 through 5 of each 28-day cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CMML: chronic myelomonocytic leukemia	MDS: myelodysplastic syndrome
FDA: Food and Drug Administration	NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
decitabine (Dacogen®)	MDS Three day regimen: 15 mg/m^2 by IV infusion every 8 hours for 3 days. Repeat cycle every 6 weeks. Five day regimen: 20 mg/m^2 by IV infusion repeated daily for 5 days. Repeat cycle every 4 weeks.	See regimens

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: States with Regulations against Redirections in Certain Oncology Settings

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
LA	Yes	For stage 4 advanced, metastatic cancer or associated conditions. Exception if "clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	**Applies to HIM requests only** For stage 4 metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes	For advanced metastatic cancer and associated conditions
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MDS	1 tablet (35 mg decitabine/100 mg cedazuridine) PO QD on Days 1 through 5 of each 28-day cycle for a minimum of 4 cycles until disease progression or unacceptable toxicity. A complete or partial response may take longer than 4 cycles.	1 tablet (35 mg decitabine/100 mg cedazuridine)/day

VI. Product Availability

Tablet: 35 mg decitabine/100 mg cedazuridine

VII. References

1. Inqovi Prescribing Information. Princeton, NJ: Otsuka Pharmaceutical Co., Ltd.; July 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212576s000lbl.pdf. Accessed February 14, 2022.
2. Dacogen Prescribing Information. Rockville, MD: Otsuka America Pharmaceuticals, Inc.; June 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021790s025lbl.pdf. Accessed February 14, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 14, 2022.
4. National Comprehensive Cancer Network Myelodysplastic Syndromes Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed February 14, 2022.
5. Garcia-Manero G, Griffiths EA, Steensma DP, et al. Oral cedazuridine/decitabine: a phase 2, pharmacokinetic/pharmacodynamic, randomized, crossover study in MDS and CMML [published online ahead of print, 2020 Apr 13]. Blood. 2020;blood.2019004143. doi:10.1182/blood.2019004143
6. Garcia-Manero G, McCloskey J, Griffiths EA, 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 (Supplement_1).

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	04.07.20	05.20
Drug is now FDA approved - criteria updated per FDA labeling: MDS criteria collapsed given complexity of disease state/treatment guidelines and expert feedback; AML and MF criteria deleted pending NCCN Inqovi recommendations; references reviewed and updated.	08.18.20	11.20
2Q 2021 annual review: revised medical justification language to state 'member must use'; revised reference to HIM off-label use policy from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	01.14.21	05.21
2Q 2022 annual review: modified commercial approval duration from length of benefit to "12 months or duration of request, whichever is less"; for decitabine redirection added by-passing of redirection if state regulations do not allow step therapy in certain oncology settings; references reviewed and updated.	02.14.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional

organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.