Clinical Policy Title:	decitabine/cedazuridine
Policy Number:	RxA.645
Drug(s) Applied:	Inqovi®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
decitabine/cedazuridine (Inqovi®)	MDS, CMML	35 mg decitabine and 100 mg cedazuridine orally once daily on an empty stomach 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	35 mg decitabine and 100 mg cedazuridine days 1 through 5 of each 28-day cycle

Dosage Forms

- Tablets: 35 mg decitabine and 100 mg cedazuridine

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia (must meet all):

1. Diagnosis of MDS or CMML;

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Maximum dose does not exceed 175 mg decitabine and 500 mg cedazuridine for 28 days.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (i.e., no evidence of unacceptable toxicity or disease progression);
3. If request is for a dose increase, maximum dose does not exceed 175 mg decitabine and 500 mg cedazuridine for 28 days.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CMML: chronic myelomonocytic leukemia
FDA: Food and Drug Administration
IPSS: International Prognostic Scoring System
MDS: myelodysplastic syndromes
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Jakafi®	5 mg orally twice a day for a 28-day cycle.	5 mg orally twice a day for a 28-day cycle.
imatinib (Gleevec®)	400 mg/day orally	800 mg/day orally
Reblozyl®	1 mg/kg once every 3 weeks by subcutaneous injection	1.75 mg/kg subcutaneously every 3 weeks
decitabine (Dacogen®)	Three Day Regimen: Administer Dacogen® at a dose of 15 mg/m^2 by continuous intravenous infusion over 3 hours repeated every 8 hours for 3 days. Repeat cycle every 6 weeks. Five Day Regimen: Administer Dacogen® at a dose of 20 mg/m^2 by continuous intravenous infusion over	3-day regimen: 15 mg/m^2 intravenous every 8 hours for 3 days repeated every 6 weeks. 5-day regimen: 20 mg/m^2 intravenous daily on days 1, 2, 3, 4, and 5 repeated every 4 weeks.

	1 hour repeated daily for 5 days. Repeat cycle every 4 weeks.	
azacitidine (Vidaza®)	The recommended starting dose for the first treatment cycle, for all patients regardless of baseline hematology values, is Vidaza® 75 mg/m^2 daily for 7 days to be administered by subcutaneous injection or intravenous infusion. Repeat cycles every 4 weeks. After 2 cycles, may increase dose to 100 mg/m^2	Intravenous or subcutaneous dosing: 100 mg/m^2 daily for 7 days per cycle. Oral dosing: 300 mg daily for 14 days per cycle.

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Myelosuppression: Fatal and serious myelosuppression and infectious complications can occur. Obtain complete blood cell counts prior to initiation of Inqovi®, prior to each cycle, and as clinically indicated to monitor for response and toxicity. Delay the next cycle and resume at the same or reduced dose as recommended.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception.
- The National Comprehensive Cancer Network (NCCN) Myelodysplastic Syndromes Guidelines have not been updated to include Inqovi®.

References

1. Inqovi® tablets, for oral use prescribing information (per FDA). Princeton, NJ: Otsuka Pharmaceutical Co., Ltd., July 2020. Available at: https://www.inqovi.com/. Accessed July 08, 2021.
2. Decitabine/cedazuridine. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 08, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Accessed with subscription at: http://www.nccn.org. Accessed July 08, 2021.
4. National Comprehensive Cancer Network Guidelines. Myelodysplastic Syndromes Version 3.2021. Available at: http://www.nccn.org. Accessed July 08, 2021.
5. Reblozyl® prescribing information (per FDA) April 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761136orig2lbl.pdf. Accessed July 08, 2021.
6. M.D. Anderson Cancer Center. Phase i Study of Ruxolitinib for Patients with Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS). clinicaltrials.gov; 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT01895842. Accessed July 08, 2021.

7. Clinical Pharmacology [database online] powered by Clinical Key. Accessed with subscription at: http://www.clinicalkey.com. Accessed July 08, 2021.
8. Vidaza® prescribing information (per FDA) March 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3495a71a-cc04-4776-851f-f185956f32af. Accessed July 08, 2021.
9. Dacogen® prescribing information (per FDA) June 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=deb4a13c-855b-4372-9778-6e81da598df6. Accessed July 08, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	08/27/2020	09/14/2020
Policy was reviewed: 1) Dosing Information dosing regimen and maximum dose were updated to remove “One (1) tablet”. 2) Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3) Initial Approval Criteria I.A.4 was updated to include “Maximum dose does not exceed 175 mg decitabine and 500 mg cedazuridine for 28 days.”. 4) Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 5) Continued Therapy Approval Criteria II.A.3 was updated to include “If request is for a dose increase, maximum dose does not exceed 175 mg decitabine and 500 mg cedazuridine for 28 days.”. 6) Therapeutic Alternatives verbiage was rephrased to "Below are suggested	07/08/2021	09/14/2021

therapeutic alternatives based on clinical guidance..". 7) Appendix B: Therapeutic Alternatives was updated from bullet-list format to table format. 8) Appendix B: Therapeutic Alternatives was updated to remove non-indicated drug "Inrebic (fedratinib)". 9) Appendix B: Therapeutic Alternatives was updated to include alternative drugs decitabine (Dacogen®) and azacitidine (Vidaza®) in addition to their respective dosing regimens and maximum doses. 10) Appendix B: Therapeutic Alternatives was updated to include specific dosing regimens and maximum doses for previously listed alternative drugs Jakafi®, imatinib (Gleevec®), and Reblozyl®. 11) Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 12) Appendix D was updated to include "Myelosuppression: Fatal and serious myelosuppression…" and "Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients…". 13) References were reviewed and updated.		