CENTENE® Corporation

Clinical Policy: Bardoxolone Methyl (RTA 402)

Reference Number: CP.PHAR.560
Effective Date: PDUFA Date: TBD
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Bardoxolone methyl (RTA 402®/™) is a nuclear factor erythroid 2-related factor 2 (Nrf2) activator.

FDA Approved Indication(s) [Pending]

RTA 402 is indicated for the treatment of chronic kidney disease (CKD) caused by Alport syndrome.

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 RTA 402 is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Chronic Kidney Disease of Alport Syndrome (must meet all)**:**

1. Diagnosis of Alport syndrome confirmed by one of the following (a, b, or c):*
   a. Genetic testing with variants in the *COL4A3*, *COL4A4*, or *COL4A5* genes;
   b. Kidney biopsy with one of the following (i or ii):
      i. Electron microscopy results show abnormalities of the glomerular basement membrane that are consistent with Alport syndrome;
      ii. Immunohistochemical staining confirms low to no levels of type IV collagen alpha-3, alpha-4, or alpha-5 chains;
   c. Skin biopsy with immunohistochemical staining confirms low to no levels of type IV collagen alpha-5 chains;
2. Member has CKD with an estimated glomerular filtration rate (eGFR) of 30-90 mL/min/1.73 m^2;
3. Member has a urinary albumin to creatinine ratio (UACR) of ≤ 3,500 mg/g;
4. Prescribed by or in consultation with a nephrologist;
5. Age ≥ 12 years;*
6. RTA 402 is prescribed in combination with an angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) (*see Appendix B for examples*), unless clinically significant adverse effects are experienced or all are contraindicated;

7. Member has not had a kidney transplant;
8. Dose does not exceed 30 mg per day.*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Chronic Kidney Disease of Alport Syndrome (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by stabilization or improvement in the member's baseline eGFR;
3. Member has not had a kidney transplant;
4. If request is for a dose increase, new dose does not exceed 30 mg per day.*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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;

B. Member has had a kidney transplant.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACE: angiotensin converting enzyme
ARB: angiotensin receptor blocker
CKD: chronic kidney disease
eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
GBM: glomerular basement membrane
Nrf2: nuclear factor erythroid 2-related factor 2
UACR: urinary albumin to creatinine ratio

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
ramipril	Initiate dosing with 1-2 mg/m^2 PO per day, titrate by 1-2 mg/m^2/day every 3 months	6 mg/m^2/day
lisinopril	Initiate dosing with 4-8 mg/m^2 PO per day, titrate by 4-8 mg/m^2/day every 3 months	24 mg/m^2/day
enalapril	Initiate dosing with 2-4 mg/m^2 PO per day, titrate by 2-4 mg/m^2/day every 3 months	12 mg/m^2/day
trandolapril	Initiate dosing with 0.5-1 mg/m^2 PO per day, titrate by 0.5-1 mg/m^2/day every 3 months	3 mg/m^2/day
losartan	Initiate dosing with 12.5 mg/m^2 PO per day, double dose every 3 months	50 mg/m^2/day
candesartan	Initiate dosing with 6.25 mg/m^2 PO per day, double dose every 3 months	25 mg/m^2/day
irbesartan	Initiate dosing with 37.5 mg/m^2 PO per day, double dose every 3 months	150 mg/m^2/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
telmisartan	Initiate dosing with 10 mg/m^2 PO per day, double dose every 3 months	40 mg/m^2/day
valsartan	Initiate dosing with 18.75 mg/m^2 PO per day, double dose every 3 months	75 mg/m^2/day

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 [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
CKD of Alport syndrome*	5-30 mg PO once daily*	30 mg/day*

VI. Product Availability [Pending]

Oral capsules: strengths pending*

VII. References

1. ClinicalTrials.gov. NCT03019185. A Phase 2/3 trial of the efficacy and safety of bardoxolone methyl in patients with Alport syndrome – CARDINAL.
2. ClinicalTrials.gov. NCT03749447. An extended access program for bardoxolone methyl in patients with CKD (EAGLE).
3. Kashtan CE, Gross O. Clinical practice recommendations for the diagnosis and management of Alport syndrome in children, adolescents, and young adults – an update for 2020. Pediatr Nephrol 2021;36:711-9.
4. Kashtan CE, Ding J, Gregory M, et al. Clinical practice recommendations for the treatment of Alport syndrome: a statement of the Alport Syndrome Research Collaborative. Pediatr Nephrol 2013;28:5-11.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.19.21	11.21
4Q 2022 annual review: no significant changes; in February 2022 the FDA issued a Complete Response Letter for this drug and the status of a BLA resubmission is unknown; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.24.22	11.22

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.