Clinical Policy: Non-Calcium Phosphate Binders

Reference Number: CP.PMN.04
Effective Date: 11.15.17
Last Review Date: 02.24
Line of Business: Commercial, HIM*, Medicaid

Revision Log

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

Description

The following are non-calcium containing phosphate binders requiring prior authorization: ferric citrate (Auryxia®), lanthanum carbonate (Fosrenol®), sevelamer carbonate (Renvela®), sevelamer hydrochloride (Renagel®), and sucroferric oxyhydroxide (Velphoro®).

_____

***For Health Insurance Marketplace (HIM),** if request is through pharmacy benefit, Auryxia and Renagel are non-formulary and should not be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Non-calcium containing phosphate binders (Auryxia, Fosrenol, Renvela, Renagel, and Velphoro) are indicated for the control of serum phosphorus levels in patients with chronic kidney disease (CKD) on dialysis or with end stage renal disease (ESRD).

Auryxia is also indicated for the treatment of iron deficiency anemia in adult patients with CKD not on dialysis.

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 Auryxia, Fosrenol, Renvela, Renagel, and Velphoro are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hyperphosphatemia (must meet all)**:**

1. Diagnosis of hyperphosphatemia associated with CKD or ESRD;
2. Prescribed by or in consultation with a nephrologist, or member is on dialysis;
3. Member meets one of the following (a or b):
   a. Auryxia, Fosrenol, Renagel, Velphoro: Age ≥ 18 years;
   b. Renvela: Age ≥ 6 years;
4. Member meets one of the following (a, b, c, or d):
   a. Failure (e.g., serum phosphorus > 5.5 mg/dL) of a 4-week trial of calcium acetate at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Hypercalcemia as evidenced by recent (within the previous 30 days) corrected total serum calcium level > 10.2 mg/dL;
   c. Plasma parathyroid hormone (PTH) levels < 150 pg/mL on 2 consecutive measurements in the past 180 days;

d. History of severe vascular and/or soft-tissue calcifications;

5. For Auryxia, Renagel, or Velphoro: Failure (e.g., serum phosphorus > 5.5 mg/dL) of a 4-week trial of Fosrenol (generic is preferred) or Renvela (generic is preferred) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for Fosrenol and Renvela*
6. For Fosrenol, member must use generic lanthanum carbonate, unless contraindicated or clinically significant adverse effects are experienced;
7. For Renvela, member must use generic sevelamer carbonate, unless contraindicated or clinically significant adverse effects are experienced;
8. For Renagel, member must use generic sevelamer hydrochloride, unless contraindicated or clinically significant adverse effects are experienced;
9. Dose does not exceed any of the following (a, b, c, d, or e):
   a. Auryxia: 2,520 mg ferric iron (12 tablets) per day;
   b. Fosrenol: 4,500 mg per day;
   c. Renagel: 13 g per day;
   d. Renvela: 14 g per day;
   e. Velphoro: 3,000 mg (6 tablets) per day.

Approval duration:
Medicaid – 12 months
HIM – 12 months for Fosrenol, Renvela, and Velphoro *(refer to HIM.PA.103 for Auryxia and Renagel*)
Commercial – 12 months or duration of request, whichever is less

B. Iron Deficiency Anemia (must meet all)**:**

1. Request is for Auryxia;
2. Diagnosis of iron deficiency anemia with CKD;
3. Member is not on dialysis;
4. Failure of a 4-week, adherent trial of alternative oral iron therapy (e.g., ferrous sulfate, ferrous fumarate, ferrous gluconate), unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 2,520 mg ferric iron (12 tablets) per day.

Approval duration:
Medicaid – 12 months
HIM – *refer to HIM.PA.103 for Auryxia*
Commercial – 12 months or duration of request, whichever is less

C. 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

A. All Indications in Section I (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 (e.g., reduction in serum phosphorus from pretreatment level; maintenance of serum phosphorus level ≤ 5.5 mg/dL; increased hemoglobin);
3. For Fosrenol, member must use generic lanthanum carbonate, unless contraindicated or clinically significant adverse effects are experienced;
4. For Renvela, member must use generic sevelamer carbonate, unless contraindicated or clinically significant adverse effects are experienced;
5. For Renagel, member must use generic sevelamer hydrochloride, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, new does not exceed any of the following (a, b, c, d, or e):
   a. Auryxia: 2,520 mg ferric iron (12 tablets) per day;
   b. Fosrenol: 4,500 mg per day;
   c. Renagel: 13 g per day;
   d. Renvela: 14 g per day;
   e. Velphoro: 3,000 mg (6 tablets) per day.

Approval duration:
Medicaid – 12 months
HIM – 12 months for Fosrenol, Renvela, and Velphoro *(refer to HIM.PA.103 for Auryxia and Renagel*)
Commercial – 12 months or duration of request, whichever is less

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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CKD: chronic kidney disease
ESRD: end-stage renal disease
FDA: Food and Drug Administration
PTH: parathyroid hormone

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
calcium acetate	**Hyperphosphatemia** 2 capsules PO TID with meals; titrate to phosphorus < 6 mg/dL and calcium < 9.5 mg/dL	1,500 mg/day total elemental calcium
lanthanum (Fosrenol®)	**Hyperphosphatemia** 1,500 mg PO daily in divided doses; titrate by 750 mg/day every 2 to 3 weeks based on serum phosphorus level	4,500 mg/day
sevelamer carbonate (Renvela®)	**Hyperphosphatemia** *Starting dose for adult dialysis patients based on serum phosphorus level* If serum phosphorus is: > 5.5 to < 7.5 mg/dL: 0.8 g PO TID w/ meals ≥ 7.5 mg/dL: 1.6 g PO TID w/ meals *Starting dose for pediatric patients (6 years and older) based on body surface area (BSA)*	14 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	≥ 0.75 to < 1.2: 0.8 g PO TID w/ meals ≥ 1.2: 1.6 g PO TID w/ meals *Starting dose for patients switching from calcium acetate to Renvela based on calcium acetate 667 mg/capsule dosing schedule* • Calcium acetate 1 cap PO TID: Renvela 0.8 g PO TID w/ meals • Calcium acetate 2 caps PO TID: Renvela 1.6 g PO TID w/ meals • Calcium acetate 3 caps PO TID: Renvela 2.4 g PO TID w/ meals	
ferrous sulfate, ferrous fumarate, ferrous gluconate	**Iron Deficiency Anemia** 100 to 200 mg elemental iron PO daily in 2 to 3 divided doses (or daily with extended release tablets)	Varies

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

- Contraindication(s):
  - Auryxia: iron overload syndromes (e.g., hemochromatosis)
  - Fosrenol: bowel obstruction, ileus, and fecal impaction
  - Renagel: bowel obstruction; known hypersensitivity to sevelamer hydrochloride or to any of the excipients
  - Renvela: bowel obstruction; known hypersensitivity to sevelamer carbonate, sevelamer hydrochloride, or to any of the excipients
  - Velphoro: none reported
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
ferric citrate (Auryxia)	Iron deficiency anemia	1 tablet PO TID with meals. Adjust dose as needed to achieve and maintain hemoglobin goal.	12 tablets/day
	Hyper-phosphatemia	2 tablets PO TID with meals; titrate by 1 to 2 tabs/day at 1-week or longer intervals based on serum phosphorus level	12 tablets/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
lanthanum (Fosrenol)	Hyper-phosphatemia	1,500 mg PO daily in divided doses; titrate by 750 mg/day every 2 to 3 weeks based on serum phosphorus level	4,500 mg/day
sevelamer carbonate (Renvela)	Hyper-phosphatemia	*Starting dose for adult dialysis patients based on serum phosphorus level* If serum phosphorus is: > 5.5 to < 7.5 mg/dL: 0.8 g PO TID w/ meals ≥ 7.5 mg/dL: 1.6 g PO TID w/ meals *Starting dose for pediatric patients (6 years and older) based on body surface area (BSA)* ≥ 0.75 to < 1.2: 0.8 g PO TID w/ meals ≥ 1.2: 1.6 g PO TID w/ meals *Starting dose for patients switching from calcium acetate to Renvela based on calcium acetate 667 mg/tablet dosing schedule* • Calcium acetate 1 tablet PO TID: Renvela 0.8 g PO TID w/ meals • Calcium acetate 2 tablets PO TID: Renvela 1.6 g PO TID w/ meals • Calcium acetate 3 tablets PO TID: Renvela 2.4 g PO TID w/ meals	14 g/day
sevelamer hydrochloride (Renagel)	Hyper-phosphatemia	*Starting dose based on serum phosphorus level* • > 5.5 to < 7.5 mg/dL: Renagel 800 mg - 1 tab PO TID; 400 mg - 2 tabs PO TID w/meals • ≥ 7.5 to < 9 mg/dL: Renagel 800 mg - 2 tabs PO TID; 400 mg - 3 tabs PO TID w/meals • ≥ 9 mg/dL: Renagel 800 mg - 2 tabs PO TID; 400 mg - 4 tabs PO TID w/meals *Starting dose for patients switching from calcium acetate to Renagel based on calcium acetate 667 mg/tablet dosing schedule*	13 g/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		• Calcium acetate 1 tablet PO TID: Renagel 800 mg - 1 tab PO TID; 400 mg - 2 tabs PO TID • Calcium acetate 2 tablets PO TID: Renagel 800 mg - 2 tabs PO TID; 400 mg - 3 tabs PO TID • Calcium acetate 3 tablets PO TID: Renagel 800 mg - 3 tabs PO TID; 400 mg - 5 tabs PO TID	
sucroferric oxyhydroxide (Velphoro)	Hyper-phosphatemia	500 mg PO TID with meals	3,000 mg/day

VI. Product Availability

Drug Name	Availability
ferric citrate (Auryxia)	Tablet: 210 mg ferric iron (equivalent to 1 g ferric citrate)
lanthanum (Fosrenol)	Chewable tablets: 500 mg, 750 mg, 1,000 mg Oral powder: 750 mg, 1,000 mg
sevelamer carbonate (Renvela)	Tablet: 800 mg Oral powder, packet: 0.8 g, 2.4 g
sevelamer hydrochloride (Renagel)	Tablets: 400 mg, 800 mg
sucroferric oxyhydroxide (Velphoro)	Chewable tablet: 500 mg

VII. References

1. Auryxia Prescribing Information. Boston, MA: Keryx Biopharmaceuticals, Inc.; March 2021. Available at: https://www.auryxia.com/. Accessed October 20, 2023.
2. Renagel Prescribing Information. Cambridge, MA: Genzyme Corporation; March 2023. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5e30120b-f2bf-43a0-86b2-44ae996dc681. Accessed October 20, 2023.
3. Velphoro Prescribing Information. Waltham, MA: Fresenius Medical Care North America; February 2020. Available at: https://www.velphorohcp.com. Accessed October 20, 2023.
4. Fosrenol Prescribing Information. Lexington, MA: Shire US, Inc.; May 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021468s026,204734s008lbl.pdf. Accessed October 20, 2023.
5. Renvela Prescribing Information. Cambridge, MA: Genzyme Corporation; June 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022127Orig1s021lbl.pdf. Accessed October 20, 2023.
6. Sevelamer hydrochloride 400 mg tablets Prescribing Information. Mahwaj, NJ: Glenmark Pharmaceuticals Inc.; June 2020. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=2cd6512f-0edd-4a30-a4fa-aa996038633c. Accessed October 20, 2023.

7. National Kidney Foundation. KDOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. *Am J Kidney Dis.* 42:S1-S202, 2003 (suppl 3).
8. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. Clinical practice guideline for anemia in chronic kidney disease. *Kidney Inter*. Supp. 2012; 2(4):279-335. doi:10.1038/kisup.2012.39
9. Kidney Disease: Improving Global Outcomes (KDIGO) CKD–MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD–MBD). *Kidney Inter.* 2017; 92(1):26-36.
10. Clinical Pharmacology [database online]. Elsevier, Inc.; 2022. Updated Periodically. Available at https://www.clinicalkey.com/pharmacology/. Accessed October 26, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; moved examples of positive response from appendix to criterion 2 in section IIA; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: no significant changes; consolidated HIM-specific Velphoro policy with this one (HIM.PA.SP30 will be retired); revised Commercial approval duration from Length of Benefit to 12 months or duration of request, whichever is less; references reviewed and updated.	11.09.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.19.22	
1Q 2023 annual review: for Fosrenol, Renvela, and Renagel requests added requirement that member must use generic; references reviewed and updated.	10.26.22	02.23
1Q 2024 annual review: no significant changes; for iron deficiency anemia separated requirement that member is not on dialysis for added clarity; references reviewed and updated.	10.20.23	02.24

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.