Clinical Policy Title:	Non-Calcium Phosphate Binders
Policy Number:	RxA.130
Drug(s) Applied:	Auryxia®, Renagel®, Velphoro®
Original Policy Date:	02/07/2020
Last Review Date:	01/17/2022
Line of Business Policy Applies to:	All lines of business

Background

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

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

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ferric citrate (Auryxia®)	Iron Deficiency Anemia	210 mg (1 tablet) orally three times daily with meals. Adjust dose as needed to achieve and maintain haemoglobin goal.	12 tablets/day
ferric citrate (Auryxia®)	Hyperphosphatemia	210 mg (2 tablets) orally three times daily with meals; titrate by 1 to 2 tabs/day at 1-week or longer intervals based on serum phosphorus level	12 tablets/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
sevelamer hydrochloride (Renagel®)	Hyperphosphatemia	Starting dose based on serum phosphorus level: >5.5 to <7.5 mg/dL: Renagel® 800 mg – 1 tab orally three times daily with meals; ≥7.5 to < 9 mg/dL: Renagel® 800 mg - 2 tabs orally three times daily with meals; ≥ 9 mg/dL: Renagel® 800 mg - 2 tabs orally three times daily with meals; Starting dose for patients switching from calcium acetate to Renagel® based on calcium acetate 667 mg/capsule dosing schedule:	13 gm/day
		Calcium acetate: 667 mg -1 cap orally three times: Renagel® 800 mg – 1 tab orally three times daily with meals; Calcium acetate: 667 mg - 2 caps orally three times: Renagel® 800 mg – 2 tabs orally three times daily with meals; Calcium acetate: 667 mg - 3 caps orally three times: Renagel® 800 mg - 3 tabs orally three times daily with meals;	
sucroferric oxyhydroxide (Velphoro®)	Hyperphosphatemia	500 mg orally three times daily with meals. Adjust by 500 mg (1 tablet) per day as needed until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. Titrate as often as weekly.	3,000 mg/day

Dosage Forms

- ferric citrate (Auryxia®): Tablets: 210 mg ferric iron (equivalent to 1 g ferric citrate)
- sevelamer hydrochloride (Renagel®): Tablets: 800 mg
- sucroferric oxyhydroxide (Velphoro®): Tablets, chewable: 500 mg iron

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. 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. Age ≥ 18 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 generic lanthanum or generic sevelamer carbonate at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed:
   a. Auryxia®: 12 tablets (2,520 mg ferric iron) per day;
   b. Renagel®: 13 g per day;
   c. Velphoro®: 3,000 mg (6 tablets) per day

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Iron deficiency Anemia (must meet all):

1. Request is for Auryxia®;
2. Diagnosis of iron deficiency anemia with CKD not on dialysis;
3. Failure of 4 weeks trial of at least one (1) alternative oral iron therapy (e.g., ferrous sulfate, ferrous fumarate, ferrous gluconate) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 12 tablets (2,520 mg ferric iron) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new does not exceed:
   a. Auryxia®: 12 tablets (2,520 mg ferric iron) per day;
   b. Renagel®: 13 g per day;
   c. Velphoro®: 3,000 mg (6 tablets) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CKD: chronic kidney disease
ESRD: end-stage renal disease
FDA: Food and Drug Administration
PTH: parathyroid hormone
BSA: body surface area

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
calcium acetate	**Hyperphosphatemia** 1334 mg (2 tablets or capsules) orally with each meal initially. The dosage may be gradually increased every 2 to 3 weeks to lower serum phosphate concentrations within the desired range	2000 mg/day total elemental calcium
lanthanum carbonate (Fosrenol®)	**Hyperphosphatemia** 1,500 mg orally 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 orally three times w/ meals 7.5 mg/dL: 1.6 g orally three times w/ meals Starting dose for pediatric patients (6 years and older) based on body surface area (BSA) ≥ 0.75 to < 1.2: 0.8 mg orally three times w/ meals ≥ 1.2: 1.6 g orally three times 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 orally three times: Renvela® 0.8 g orally three times w/ meals Calcium acetate 2 caps orally three times: Renvela® 1.6 g orally three times w/ meals Calcium acetate 3 caps orally three times: Renvela® 2.4 g	14 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	orally three times w/ meals	
ferrous sulfate, ferrous fumarate, ferrous gluconate	**Iron Deficiency Anemia** 60 mg elemental iron orally 1 to 3 times daily for 4 week	Varies

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):
  - Auryxia®: iron overload syndromes (e.g., hemochromatosis);
  - Renagel®: bowel obstruction; known hypersensitivity to sevelamer hydrochloride or to any of the excipients;
  - Velphoro®: none reported.

- Boxed Warning(s):
  - None reported.

*Contraindications listed reflect direct statements made in manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

APPENDIX D: General Information

- Examples of positive response to therapy:
  - Reduction in serum phosphorus from pretreatment level
  - Maintenance of serum phosphorus level < 5.5 mg/dL, increased hemoglobin
- Serious cases of dysphagia, bowel obstruction, bleeding gastrointestinal ulcers, colitis, ulceration, necrosis, and perforation have been associated with sevelamer use, some requiring hospitalization and surgery.

References

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10. Locatelli F, Nissenson AR, Barrett BJ, et al. Clinical practice guidelines for anemia in chronic kidney disease: problems and solutions. A position statement from Kidney Disease: Improving Global Outcomes (Kdigo). Kidney Int. 2008;74(10):1237-1240. Available at: https://pubmed.ncbi.nlm.nih.gov/18596731/. Accessed on November 26, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Line of Business Policy Applies to was updated to “All lines of business”. 2. Dose strength of Renagel® was updated. 3. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 4. APPENDIX B language updated to ‘’Below are suggested therapeutic alternatives….’’. 5. Reference was reviewed and updated	1/19/2021	03/09/2021
Policy was reviewed: 1. Clinical policy sections: Drug(s) Applied, Background, Dosing Information, Dosage forms, Initial and Continued Approval Criteria (I.A. and II.A) , Appendix C, was updated to remove information about Fosrenol®, Renvela® as they no longer require Prior Authorization. 2. Background: Updated information	11/26/2021	01/17/2022

regarding indication chronic kidney disease (CKD) from Non-calcium containing phosphate binders (Auryxia®, 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) to Non-calcium containing phosphate binders (Auryxia®, Renagel®, and Velphoro®) are indicated for the control of serum phosphorus levels in patients with chronic kidney disease (CKD) on dialysis. 3. Dosing Information, Dosing Regimen, Velphoro®: Updated to include maintenance dosing information for indication Hyperphosphatemia. 4. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 5. Initial Approval Criteria, 1.B.3: Updated trial and failure criteria from 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 to Failure of 4 weeks for at least one (1) alternative oral iron therapy (e.g., ferrous sulfate, ferrous fumarate, ferrous gluconate) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced. 6. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 7. Appendix A: Updated to include abbreviation BSA. 8. Appendix B, Dosing Regimen, calcium acetate: Updated dosing information from 2 capsules PO TID with meals;		

titrate to phosphorus < 6 mg/dL and calcium < 9.5 mg/dL to 1334 mg (2 tablets or capsules) orally with each meal initially. The dosage may be gradually increased every 2 to 3 weeks to lower serum phosphate concentrations within the desired range for indication Hyperphosphatemia. 9. Appendix B, Maximum Dose, calcium acetate: Updated maximum dose information from 1,500 mg/day total elemental calcium to 2000 mg/day total elemental calcium for indication Hyperphosphatemia. 10. Appendix B, Dosing Regimen, ferrous sulfate, ferrous fumarate, ferrous gluconate: Updated dosing information from 100 to 200 mg elemental iron PO daily in 2 to 3 divided doses (or daily with extended release tablets) to 60 mg elemental iron orally 1 to 3 times daily for 4 week for indication Iron Deficiency Anemia. 11. Disclaimer about contraindications," Contraindications listed reflect statements made in the manufacturer's package insert.." was added to Appendix C. 12. References were reviewed and updated.		