Clinical Policy Title:	calcifediol
Policy Number:	RxA.273
Drug(s) Applied:	Rayaldee®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All Line of Business

Background

Rayaldee® is a vitamin D3 analog indicated for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease (CKD) and serum total 25-hydroxyvitamin D levels less than 30 ng/mL.

Limitation(s) of use: Rayaldee® is not indicated in patients with stage 5 CKD or end-stage renal disease on dialysis.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
calcifediol (Rayaldee®)	Secondary hyperparathyroidism	Initial: 30 mcg PO once daily at bedtime. Serum calcium should be below 9.8 mg/dL before initiating. Increase the dose to 60 mcg once daily after 3 months if intact PTH is above the treatment goal. Additionally, ensure serum calcium is below 9.8 mg/dL, phosphorus is below 5.5 mg/dL and 25-hydroxyvitamin D is below 100 ng/mL before increasing the dose. Suspend dosing if intact PTH is persistently abnormally low, serum calcium is consistently above the normal range or serum 25-hydroxyvitamin D is consistently above 100 ng/mL.	60 mcg per day

Dosage Forms

- Extended-release capsules: 30 mcg

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.

I. Initial Approval Criteria

A. Secondary Hyperparathyroidism (must meet all)**:**

1. Diagnosis of secondary hyperparathyroidism;
2. Age ≥ 18 years;
3. Member has stage 3 or 4 CKD defined by eGFR of 15-59 mL/min;
4. Current (within the last 30 days) serum total 25-hydroxyvitamin D level is less than 30 ng/mL;
5. Serum total calcium is below 9.8 mg/dL prior to initiating therapy;
6. Failure of ergocalciferol or cholecalciferol, at up to maximally indicated doses, unless both are contraindicated, or clinically significant adverse effects are experienced;
7. Lab results over the previous 3-6 months show trending increase in iPTH level or current (within the last 30 days) labs show iPTH above the normal levels;
8. Dose does not exceed 60 mcg per day (2 capsules per day).

Approval Duration

Commercial: 12 months

Medicaid: 12 months

II. Continued Therapy Approval

A. Secondary Hyperparathyroidism (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (suspend dosing if intact PTH is persistently abnormally low, serum calcium is consistently above the normal range or serum 25-hydroxyvitamin D is consistently above 100 ng/mL);
3. If request is for a dose increase, new dose does not 60 mcg per day (2 capsules per day).

Approval Duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

CKD: chronic kidney disease

FDA: Food and Drug Administration

eGFR: estimated glomerular filtration rate

iPTH: intact parathyroid hormone

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

cholecalciferol (Vitamin D3)	1,000 international units (IU) PO daily	1,000 IU/day
ergocalciferol (Calcidol®, Drisdol®)	50,000 IU PO once weekly for 8 weeks; repeat for another 8 weeks if 25-hydroxy vitamin D levels are less than 30 nanograms/mL	50,000 IU/week

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):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

The stages of CKD are as follows:

- Stage 1: eGFR at least 90 mL/min/1.73 m^2
- Stage 2: eGFR between 60-89 mL/min/1.73 m2
- Stage 3: eGFR between 30-59 mL/min/1.73 m2
- Stage 4: eGFR between 15-29 mL/min/1.73 m2
- Stage 5: eGFR less than 15 mL/min/1.73 m2 (or dialysis)

Reference

1. Rayaldee® Prescribing Information. Miami, FL: Opko Pharmaceuticals, LLC. December 01, 2019. Available at: https://Rayaldee®.com/. Accessed February 03, 2021.
2. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67:2089. Accessed February 03, 2021.
3. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; 39: S1. Accessed February 03, 2021.
4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD–MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease—Mineral and Bone Disorder (CKD–MBD). Available at: https://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf. Accessed February 03, 2021.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed February 03, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated references	04/29/2020	05/20/2020

Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, or documentation supports that member is currently receiving Cabometyx or Cometriq for a covered indication and has received this medication for at least 30 days;	05/08/2020	05/20/2020
Policy was reviewed: 1. Clinical policy title table was updated. 2. Drug(s) applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Dosing information was updated for indication. 5. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 6. References were reviewed and updated. 7. Background updated to: Rayaldee® is a vitamin D3 analog indicated for the treatment of secondary hyperparathyroidism in adult patients with stage 3 or 4 chronic kidney disease (CKD) and serum total 25-hydroxyvitamin D levels less than 30 ng/mL. 8. Updated dosing regmine to: Initial: 30 mcg PO once daily at bedtime. Serum calcium should be below 9.8 mg/dL before initiating. Increase the dose to 60 mcg once daily after 3 months if intact PTH is above the treatment goal. Additionally, ensure serum calcium is below 9.8 mg/dL,	02/03/2021	03/09/2021

phosphorus is below 5.5 mg/dL and 25-hydroxyvitamin D is below 100 ng/mL before increasing the dose. Suspend dosing if intact PTH is persistently abnormally low, serum calcium is consistently above the normal range or serum 25-hydroxyvitamin D is consistently above 100 ng/mL. 9. Initial Approval Criteria updated to include: Serum total calcium is below 9.8 mg/dL prior to initiating therapy.		