

## **Clinical Policy: Calcifediol (Rayaldee)**

Reference Number: CP.PMN.76

Effective Date: 11.01.16

Last Review Date: 08.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Calcifediol (Rayaldee<sup>™</sup>) is a prohormone of the active form of vitamin D3 (calcitriol).

### **FDA Approved Indication(s)**

Rayaldee is 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.

### **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<sup>®</sup> that Rayaldee is **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

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

1. Diagnosis of secondary hyperparathyroidism;
2. Age  $\geq$  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. Failure of ergocalciferol or cholecalciferol, at up to maximally indicated doses, unless both are contraindicated or clinically significant adverse effects are experienced;
6. 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;
7. Dose does not exceed 60 mcg (2 capsules) per day.

##### **Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – Length of Benefit

##### **B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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 (2 capsules) per day.

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less);** or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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

eGFR: estimated glomerular filtration rate

FDA: Food and Drug Administration

iPTH: intact 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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
cholecalciferol (Vitamin D3)	1,000 international units (IU) PO daily	1,000 IU/day
ergocalciferol	50,000 IU PO once weekly for 8 weeks; repeat for another 8 weeks if 25-hydroxy	50,000 IU/week

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(Calcidol <sup>®</sup> , Drisdol <sup>®</sup> )	vitamin D levels are less than 30 nanograms/mL	

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: General Information*

The stages of CKD are as follows:

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

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Secondary hyperparathyroidism	30 mcg PO once daily at bedtime. 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.	60 mcg per day

**VI. Product Availability**

Extended-release capsules: 30 mcg

**VII. References**

1. Rayaldee Prescribing Information. Miami, FL: Opko Pharmaceuticals, LLC. December 2019. <http://www.rayaldee.com/>. Accessed May 10, 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.
3. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39:S1.
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). <http://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf>. Accessed May 10, 2021.

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5. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Journal of the International Society of Nephrology 2013; 3 (1). Available at: [https://kdigo.org/wp-content/uploads/2017/02/KDIGO\\_2012\\_CKD\\_GL.pdf](https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf). Accessed May 10, 2021.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 10, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Updated template and references.	08.01.17	11.17
3Q 2018 annual review: policies combined for Medicaid and Commercial; no significant changes from previously approved corporate policy; added iPTH lab requirement for initial approval and iPTH, calcium/vitamin D level monitoring for continued approval to Commercial policy; references reviewed and updated.	03.27.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.10.19	08.19
3Q 2020 annual review: added HIM line of business; references reviewed and updated.	04.27.20	08.20
3Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	05.10.21	08.21

**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.

## CLINICAL POLICY

### Calcifediol

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.

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**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.

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