Clinical Policy: Calcifediol (Rayaldee)

Reference Number: CP.PMN.76
Effective Date: 11.01.16
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Calcifediol (Rayaldee®) 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® 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. Prescribed by or in consultation with a nephrologist or endocrinologist;
3. Age ≥ 18 years;
4. Member has stage 3 or 4 CKD defined by eGFR of 15-59 mL/min;
5. Current (within the last 30 days) serum total 25-hydroxyvitamin D level is less than 30 ng/mL;
6. Failure of ergocalciferol or cholecalciferol, at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
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 normal levels;
8. Rayaldee is not prescribed concurrently with other vitamin D derivatives/analogs (e.g., calcitriol, doxercalciferol);
9. Dose does not exceed any of the following (a and b):
   a. 60 mcg per day;
   b. 2 capsules per day.

Approval duration:
Medicaid/HIM – 6 months

Commercial – 6 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.

II. Continued Therapy

A. Secondary Hyperparathyroidism (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 (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. Rayaldee is not prescribed concurrently with other vitamin D derivatives/analogs (e.g., calcitriol, doxercalciferol);
4. If request is for a dose increase, new dose does not exceed any of the following (a and b):
   a. 60 mcg per day;
   b. 2 capsules per day.

Approval duration:
Medicaid/HIM – 12 months
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
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.

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

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 m^2
- Stage 3: eGFR between 30-59 mL/min/1.73 m^2
- Stage 4: eGFR between 15-29 mL/min/1.73 m^2
- Stage 5: eGFR less than 15 mL/min/1.73 m^2 (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 capsule: 30 mcg

VII. References

1. Rayaldee Prescribing Information. Miami, FL: Opko Pharmaceuticals, LLC. January 2024. http://www.rayaldee.com/. Accessed May 10, 2024.
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. 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.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 10, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
3Q 2022 annual review: no significant changes; adjusted Commercial authorization duration from “Length of Benefit” to “12 months or duration of request, whichever is less”; references reviewed and updated.	05.17.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2023 annual review: to align with previously P&T-approved policies for other agents FDA-approved for secondary hyperparathyroidism – added specialist prescriber requirement, added requirement for no concomitant use with other vitamin D derivatives/analogs, and shortened initial approval duration to 6 months instead of 12 months; references reviewed and updated.	04.19.23	08.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.10.24	08.24

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.