

**Pharmacy Policy Bulletin: J-0506 Rayaldee (calcifediol) - Commercial and Healthcare Reform**

<b>Number:</b> J-0506	<b>Category:</b> Prior Authorization
<b>Line(s) of Business:</b> <input checked="" type="checkbox"/> Commercial <input checked="" type="checkbox"/> Healthcare Reform <input type="checkbox"/> Medicare	<b>Benefit(s):</b> <b>Commercial:</b> <b>Prior Authorization (1.):</b> 1. Other Managed Drugs = Yes w/ Prior Authorization  <b>Healthcare Reform:</b> Not Applicable
<b>Region(s):</b> <input checked="" type="checkbox"/> All <input type="checkbox"/> Delaware <input type="checkbox"/> New York <input type="checkbox"/> Pennsylvania <input type="checkbox"/> West Virginia	<b>Additional Restriction(s):</b> None
<b>Version:</b> J-0506-011	<b>Original Date:</b> 09/07/2016
<b>Effective Date:</b> 10/08/2025	<b>Review Date:</b> 09/17/2024

<b>Drugs Product(s):</b>	<ul style="list-style-type: none"> <li>• Rayaldee (calcifediol)</li> </ul>
<b>FDA-Approved Indication(s):</b>	<ul style="list-style-type: none"> <li>• Treatment of secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease (CKD) and serum total 25-hydroxyvitamin D levels of less than 30 ng/mL.</li> </ul>

<b>Background:</b>	<ul style="list-style-type: none"> <li>• Rayaldee is a self-administered, oral extended-release capsule. It is a vitamin D3 analog that is converted to calcitriol by 1-alpha hydroxylase enzyme, primarily in the kidney. Calcitriol binds to the vitamin D receptor in target tissues and activates vitamin D responsive pathways that result in increased intestinal absorption of calcium and phosphorus and reduced parathyroid hormone (PTH) synthesis.</li> <li>• CKD is defined as abnormalities in the kidney structure or function that are present for greater than 3-months and have implications on the patients health.</li> <li>• CKD is classified based on cause, glomerular filtration rate (GFR) category (G1-G5) and albuminuria category (A1-A3).</li> <li>• Diagnosis requires either a functional abnormality observed as a decreased GFR less than 60 or there must be one or more markers of kidney damage present. Markers of kidney damage may include albuminuria greater than or equal to 30 mg/g, urine sediment abnormalities, and history of kidney transplant.</li> <li>• The Kidney Disease Improving Global Outcomes 2024 guidelines recommend classifying CKD based on cause, GFR category, and albuminuria category.</li> <li>• Stages of CKD include:             <ul style="list-style-type: none"> <li>• G1: GFR greater than or equal to 90 mL/min/1.73 m<sup>2</sup></li> <li>• G2: GFR between 60-89 mL/min/1.73 m<sup>2</sup></li> <li>• G3a: GFR between 45-59 mL/min/1.73 m<sup>2</sup></li> <li>• G3b: GFR between 30-44 mL/min/1.73 m<sup>2</sup></li> <li>• G4: GFR between 15-29 mL/min/1.73 m<sup>2</sup></li> <li>• G5: GFR less than 15 mL/min/1.73 m<sup>2</sup> (or dialysis)</li> </ul> </li> </ul>
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- Complications of CKD may include changes in calcium and phosphate homeostasis as well as changes in bone mineral metabolism. These changes are often termed chronic kidney disease-Mineral Bone Disease (CKD-MBD). CKD-MBD is a mineral and bone disorder characterized by biochemical abnormalities (calcium, phosphate, parathyroid hormone, and vitamin D); abnormalities in bone turnover, mineralization, volume linear growth, or strength; and by extra skeletal calcification. Secondary hyperparathyroidism is defined as adaptive parathyroid gland hyperplasia and increased production of PTH. Serum calcium is the main factor for determining PTH release. Defects in the activation of vitamin D in the kidneys due to CKD lead to hypocalcemia and hyperphosphatemia and a compensatory increase in PTH production.
  - Additional medications utilized for the treatment of secondary hyperparathyroidism include calcitriol and paricalcitol.
  - Calcitriol is a vitamin D<sub>3</sub> analog indicated for the treatment of hypocalcemia and secondary hyperparathyroidism and resultant metabolic bone disease (renal osteodystrophy) in patients with CKD. Oral therapy is indicated for patients with stage 3 or 4 CKD while oral or intravenous therapy is indicated for those with stage 5 CKD.
  - Paricalcitol is a synthetic, biologically active analog of calcitriol indicated for the prevention and treatment of secondary hyperparathyroidism and resultant metabolic bone disease (renal osteodystrophy). Oral therapy is indicated for patients with stage 3 or 4 CKD while oral or intravenous therapy is indicated for those with stage 5 CKD.
- The 2017 CKD-MBD KDIGO guideline suggests not routinely using calcitriol and vitamin D analogs for patients with CKD G3a-G5 not on dialysis. They recommend nutritional vitamin D supplementation with cholecalciferol and ergocalciferol as an alternative to calcitriol and its analogs. For those whom serum PTH is progressively increasing or remains persistently elevated despite lifestyle intervention, calcitriol and vitamin D analogs may be used. It is reasonable to reserve these medications for G4-G5. In patients with G5 CKD it is recommended to use calcimimetics, calcitriol, or vitamin D analogs, or a combination of calcimimetics with calcitriol or vitamin D analogs.
- Prescribing considerations:
  - Serum calcium should be below 9.8 mg/dL before initiating treatment with Royaldee.
  - 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 (8.6-10.3 mg/dL) or serum 25-hydroxyvitamin D is consistently above 100 ng/mL.
  - Patients will need routine monitoring of laboratory parameters such as calcium, intact PTH, serum phosphorous and serum total 25-hydroxyvitamin D. Initial monitoring should occur 3-months after starting therapy and after changing the dose. Subsequent monitoring should occur every 6 to 12 months.
  - Royaldee is not indicated in patients with stage 5 chronic kidney disease or end-stage renal disease on dialysis.

## Approval Criteria

### I. Initial Authorization

When a benefit, coverage of Royaldee may be approved when all of the following criteria are met **(A. through E.)**:

- A.** The member is 18 years of age or older.
- B.** The member has a diagnosis of secondary hyperparathyroidism (ICD-10: E21.1, N25.81).

- C. The member has a diagnosis of stage 3 or 4 chronic kidney disease (ICD-10 codes: N18.3, N18.31, N18.32, N18.4).
- D. The prescriber provides clinical documentation of both of the following laboratory values (**1. and 2.**):
  - 1. Serum total 25-hydroxyvitamin D level is < 30 ng/mL
  - 2. Serum calcium is < 9.8 mg/dL
- E. The member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following plan-preferred products (**1. or 2.**):
  - 1. calcitriol
  - 2. paricalcitol

**II. Reauthorization**

When a benefit, reauthorization of Rayaldee may be approved when all of the following criteria are met (**A. and B.**):

- A. The prescriber attests that the member has experienced positive clinical response to therapy.
- B. The prescriber provides clinical documentation of both of the following laboratory values (**1. and 2.**):
  - 1. Serum total 25-hydroxyvitamin D level is < 100 ng/mL
  - 2. Serum calcium is < 9.8 mg/dL

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

**Limitations of Coverage**

- I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
- II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

**Authorization Duration**

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

**Automatic Approval Criteria**

None.

**References:**

- 1. Rayaldee [package insert]. Miami, FL., OPKO Pharmaceuticals, LLC.; January 2024.
- 2. UpToDate (database online). Management of Secondary Hyperparathyroidism and Mineral Metabolism Abnormalities in Dialysis Patients, Waltham, MA; Wolters Kluwer, Inc; 2020.
- 3. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2020.
- 4. Ketteler M, et al. Executive Summary of the 2017 KDIGO Chronic Kidney Disease—Mineral and Bone Disorder (CKD-MBD) Guideline Update: What’s Changed and Why It Matters. Kidney International. 2017;92:26-36.

5. Habas E, Eledrisi M, Khan F, Elzouki A. Secondary Hyperparathyroidism in Chronic Kidney Disease: Pathophysiology and Management. Cureus. 2021;13(7).

*Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.*

*The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.*