



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 3/15/18
LAST REVIEW DATE: 2/21/19
LAST CRITERIA REVISION DATE: 2/21/19
ARCHIVE DATE:

RAYALDEE® (calcifediol) extended-release oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "**Description**" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "**Criteria**" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

RAYALDEE® (calcifediol) extended-release oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Rayaldee (calcifediol) extended release is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a Nephrologist or Endocrinologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of secondary hyperparathyroidism defined as persistently elevated or progressively rising serum intact PTH that is above the upper limit of normal for the assay used
4. Serum total 25-hydroxyvitamin D levels are between 10-30 ng/mL
5. Stage 3 or 4 chronic kidney disease
6. Individual has failed, or intolerant to, or has a contraindication such that the individual is unable to use **ALL** the following preferred step therapy agents:
 - Calcitrol (generic for Rocaltrol)
 - Doxercalciferol (generic for Hectorol)
 - Paricalcitol (generic for Zemplar)
7. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
 - Serum calcium, phosphorus, albumin, 25-hydroxyvitamin D, and intact parathyroid hormone
 - A corrected serum calcium is < 9.8 mg/dL before initiation
8. Individual does not have Stage 5 chronic kidney disease or end-stage renal disease on dialysis

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Rayaldee (calcifediol) extended release is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a Nephrologist or Endocrinologist
2. Individual's condition has responded and not worsened while on therapy
 - Response is defined as:
 - Serum total 25-hydroxyvitamin D level is between 30-100 ng/mL
 - Intact PTH level is within the desired therapeutic range
 - Serum calcium (corrected for low albumin) is within the normal range
 - Serum phosphorus is < 5.5 mg/dL
3. Individual has been adherent with the medication



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4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
 - Significant adverse effect such as:
 - Severe hypercalcemia
 - Hypercalciuria
 - Hyperphosphatemia
5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Rayaldee (calcifediol ER) 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. It is not indicated for the treatment of secondary hyperparathyroidism in patients with stage 5 CKD or in patients with end-stage renal disease on dialysis.

Calcifediol is also known as calcidiol, 25-hydroxycholecalciferol or 25-hydroxyvitamin D3. Calcifediol is a prohormone of the active form of vitamin D3, calcitriol (or 1, 25-dihydroxyvitamin D3). Calcifediol is converted to calcitriol by cytochrome P450 27B1 (CYP27B1) (also called 1-alpha hydroxylase) 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 synthesis.

Secondary hyperparathyroidism is a complication of CKD that can result in considerable morbidity and mortality, including severe bone disease. It is associated with elevated levels of parathyroid hormone (PTH) and phosphorus, and decreased levels of calcium and vitamin D.

Rayaldee (calcifediol ER) has been shown to reduce intact parathyroid hormone (iPTH) levels and increase vitamin D levels.

The major factors responsible for stimulating parathyroid gland function in renal failure are hypocalcemia, diminished 1,25-dihydroxyvitamin D3 levels, and hyperphosphatemia. If physiologic abnormalities are uncorrected, renal bone disease will develop. This disorder can result in weakness, fractures, bone and muscle pain, and avascular necrosis, which most commonly occurs in those undergoing dialysis.

The management of secondary hyperparathyroidism in dialysis patients principally involves the administration of some combination of phosphate binders (either calcium- or non-calcium-containing binders), calcitriol or synthetic vitamin D analogs and a calcimimetic (cinacalcet, etelcalcetide).

Serum calcium, albumin, phosphate, 25-hydroxyvitamin D (25(OH)D), and intact PTH (iPTH) levels are measured initially and then on an ongoing basis.

RAYALDEE® (calcifediol) extended-release oral capsule (cont.)

Definitions:

Serum calcium correction for albumin:

Corrected calcium = serum calcium + 0.8 (4 – serum albumin)

Ex. Calcium 9.9 mg/dl; albumin 3.2 gm/dl

Corrected calcium = 9.9 + 0.8 (4 – 3.2)

Corrected calcium = 10.54 (10.5 mg/dl)

Stages of CKD:

Stage	GFR (mL/min/1.73 m ²)	
1	≥ 90	Normal kidney or high
2	60-89	Mildly reduced kidney function
3 A	45-59	Mild to moderately reduced kidney function
3 B	30-44	Moderate to severely reduced kidney function
4	15-29	Severely reduced kidney function
5	< 15 or on dialysis	End stage kidney failure (sometimes called established renal failure)
In the absence of evidence of kidney damage, neither Stage 1 nor Stage 2 fulfill the criteria for CKD		

Resources:

Royaldee (calcifediol) product information accessed 01-18-19 at DailyMed:

<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6a95effd-32a5-46b6-a30e-7f4f9bf8cc77>

Royaldee. Package Insert. Revised by manufacturer 6/2016. Accessed 01-16-18.

UpToDate: Management of secondary hyperparathyroidism in adult non-dialysis patients with chronic kidney disease. Current through Dec 2018. https://www.uptodate-com.mwu.idm.oclc.org/contents/management-of-secondary-hyperparathyroidism-in-adult-nondialysis-patients-with-chronic-kidney-disease?search=secondary%20hyperparathyroidism&source=search_result&selectedTitle=1~130&usage_type=default&display_rank=1

UpToDate: Primary hyperparathyroidism: Diagnosis, differential diagnosis, and evaluation. Current through Dec 2018. https://www.uptodate-com.mwu.idm.oclc.org/contents/primary-hyperparathyroidism-diagnosis-differential-diagnosis-and-evaluation?search=secondary%20hyperparathyroidism&source=search_result&selectedTitle=3~130&usage_type=default&display_rank=3



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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com. Call 866-325-1794 to check the status of a request. All requested data must be provided. Incomplete forms or forms without the chart notes will be returned. Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.

REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information			
Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information			
Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information		
Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information			
Medication Name:	Strength:	Dosage Form:	
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

Check if requesting **brand** only Check if requesting **generic**

Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review	
<input type="checkbox"/> Standard <input type="checkbox"/> Urgent. Sign here: _____	<input type="checkbox"/> Exigent (requires prescriber to include a written statement)

Clinical Information	
1. What is the diagnosis? Please specify below. ICD-10 Code: _____ Diagnosis Description: _____	
2. <input type="checkbox"/> Yes <input type="checkbox"/> No Was this medication started on a recent hospital discharge or emergency room visit?	
3. <input type="checkbox"/> Yes <input type="checkbox"/> No There is absence of ALL contraindications.	

4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. Are there any supporting labs or test results? Please specify below.

Date	Test	Value

Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature:	Date:
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Please note: Some medications may require completion of a drug-specific request form.

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