BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/15/18**
SECTION: DRUGS	**LAST REVIEW DATE: 3/15/18**
	LAST CRITERIA REVISION DATE:
	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.

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.)

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 chronic kidney disease 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 (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 D 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 occur 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 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.

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)	
G1	$\geq$ 90	Normal kidney or high
G2	60-89	Mildly reduced kidney function

G3 A	45-59	Mild to moderately reduced kidney function
G3 B	30-44	Moderate to severely reduced kidney function
G4	15-29	Severely reduced kidney function
G5	< 15 or on dialysis	End stage kidney failure (sometimes called established renal failure)
In the absence of evidence of kidney damage, neither G1 nor G2 fulfill the criteria for CKD		

Rayaldee (calcifediol) extended-release

Medication class:
Vitamin D Analog

FDA-approved indication(s):
- A vitamin D_3 analog indicated for the treatment of secondary hyperparathyroidism in adults with stage 3 or 4 chronic kidney disease and serum total 25-hydroxyvitamin D levels less than 30 ng/mL

Limitations of use:
- Not indicated in patients with stage 5 chronic kidney disease or end-stage renal disease on dialysis

Recommended Dose:
- Initial dose:
  - 30 mcg once daily at bedtime
  - Serum calcium should be < 9.8 mg/dL before initiating treatment
  - Increase the dose to 60 mcg once daily after 3 months if:
    - Intact parathyroid hormone (PTH) is above the treatment goal
    - Serum calcium is < 9.8 mg/dL
    - Serum phosphorus is < 5.5 mg/dL
    - Serum total 25-hydroxyvitamin D is < 100 ng/mL
- Maintenance dose should target:
  - 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
- 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

Maximum dosage
- No established maximum dose for the approved indication found in product labeling

Available Dosage Forms:
- Extended-release 30 mcg capsules

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

Warnings and Precautions:

- *Hypercalcemia:* Excessive administration of vitamin D compounds, including Rayaldee, can cause hypercalcemia and hypercalciuria. Severe hypercalcemia due to substantial overdosage of vitamin D and its metabolites may require emergency attention. Patients should be informed about the symptoms of elevated calcium.
- *Digitalis toxicity:* Potentiated by hypercalcemia of any cause. Monitor serum calcium and signs and symptoms of digitalis toxicity more frequently when initiating or adjusting the dose of Rayaldee.
- *Adynamic Bone Disease:* Monitor for abnormally low levels of intact PTH levels when using Rayaldee, and adjust dose if needed.
- The safety and efficacy of RAYALDEE in the treatment of secondary hyperparathyroidism in patients with stage 2 or stage 5 chronic kidney disease and patients with end-stage renal disease on dialysis have not been established

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 **ALL** the following:
     - Secondary hyperparathyroidism defined as a progressively rising serum intact PTH that is above the upper limit of normal for the assay used
     - Adult with stage 3 or 4 chronic kidney disease
     - Serum total 25-hydroxyvitamin D levels < 30 ng/mL
     - Corrected serum calcium is < 9.8 mg/dL before initiation

  4. Individual has failure, contraindication or intolerance to **ALL** the following preferred step therapy agents:
     - Calcitrol (generic for Rocaltrol)
     - Doxercalciferol (generic for Hectorol)
     - Paricalcitol (generic for Zemplar)

  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

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

- 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

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effect such as:
     - Severe hypercalcemia

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

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

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

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

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ 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

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

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:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

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