Rayaldee® (calcifediol)

Policy # 00551
Original Effective Date: 04/19/2017
Current Effective Date: 05/11/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Rayaldee®‡ (calcifediol) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Rayaldee (calcifediol) will be considered when ALL of the following criteria are met:

- Patient has a diagnosis of secondary hyperparathyroidism; AND
- Patient is 18 years of age or older; AND
- Patient has stage 3 or 4 chronic kidney disease; AND
- Patient is NOT on dialysis; AND
- Patient's serum total 25-hydroxyvitamin D level is less than 30 ng/mL; AND
- Patient has tried and failed at least TWO generic products for the requested condition (e.g. calcitriol or vitamin D analogs such as doxercalciferol, paricalcitol)
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as **not medically necessary**** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Rayaldee (calcifediol) when the patient has NOT tried and failed at least TWO generic products for the requested condition (e.g. calcitriol or vitamin D analogs such as doxercalciferol, paricalcitol) to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Rayaldee (calcifediol) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Rayaldee is approved 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. Other therapies for this condition include calcitriol or vitamin D analogs, such as doxercalciferol capsules and injection (Hectorol®‡) and paricalcitol capsules and injection (Zemplar®‡). Each of these products has a different mechanism of action. Rayaldee is an analog of a naturally occurring prohormone of calcitriol and innate negative feedback pathways prevent excessive conversions of Rayaldee to calcitriol. Due to the slow rise in calcitriol, it is has been proposed that Rayaldee may result in lower rates of adverse events. However, there are no comparative data with Rayaldee and the other vitamin D analogs to prove whether or not the rates of adverse events differ. There is also no comparative data to prove that Rayaldee provides any clinical advantage as compared to the other options for treatment of secondary hyperparathyroidism. To note, other vitamin D analogs are approved for use in patients on dialysis, while Rayaldee is not recommended in that patient population.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Rayaldee is approved 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.

Rationale/Source

Rayaldee was evaluated in two identical, multicenter, randomized, double-blind, placebo controlled trials in patients with secondary hyperparathyroidism with stage 3 or 4 chronic kidney disease and serum total 25-hydroxyvitamin D level between 10 ng/mL and 30 ng/mL. The primary endpoint for

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these trials was at least a 30% reduction in plasma intact parathyroid hormone levels from baseline to the end of the trial. In the first study, 33% of patients receiving Rayaldee achieved the primary endpoint compared with 8% of patients receiving placebo (P<0.001). In the second study, 34% of patients receiving Rayaldee achieved the primary endpoint compared with 7% of patients receiving placebo (p<0.001).

The patient selection criteria presented in this policy takes into consideration the FDA approved indication of this drug as well as other therapeutic alternatives that currently exist for this condition. There have been no direct, head to head comparisons of Rayaldee to calcitriol or other vitamin D analogs to prove that Rayaldee has any clinical superiority over the existing products.

References

1. Rayaldee [package insert]. Opko Pharmaceuticals, LLC. Miami, Florida. Updated June 2016.
2. Rayaldee Drug Evaluation. Express Scripts. Updated August 2016.

Policy History

Original Effective Date: 04/19/2017
Current Effective Date: 05/11/2020

04/06/2017	Medical Policy Committee review
04/19/2017	Medical Policy Implementation Committee approval. New policy
04/05/2018	Medical Policy Committee review
04/18/2018	Medical Policy Implementation Committee approval. No change to coverage.
04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2021

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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