

paltusotine (Palsonify™)

Policy # 00958

Original Effective Date: 04/01/2026

Current Effective Date: 04/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 paltusotine (Palsonify™)† to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for paltusotine (Palsonify) will be considered when the patient selection criteria are met:

- Patient has a diagnosis of acromegaly; AND
- Diagnosis has been confirmed by ONE of the following:
 - Serum GH level greater than 1 ng/mL after a 2-hour OGTT at time of diagnosis; OR
 - Elevated serum IGF-1 (above the age and gender adjusted normal range per the reporting laboratory) at diagnosis; AND
- Patient is 18 years of age or older; AND
- Patient has had an inadequate response to surgery and/or surgery is not an option; AND
- Patient has failed therapy with a somatostatin analogue (e.g., octreotide [Sandostatin LAR®], lanreotide [Somatuline Depot®], pasireotide [Signifor LAR®]) unless there is clinical evidence or patient history that suggests the alternative somatostatin analogues are ineffective or will call and adverse reaction to the patient.

*(Note: This specific patient selection 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 paltusotine (Palsonify) when the patient has not failed therapy with a somatostatin analogue (e.g., octreotide [Sandostatin LAR], lanreotide [Somatuline Depot], pasireotide [Signifor LAR]) 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 paltusotine (Palsonify) when the patient selection criteria are not met (with the exception of the criterion denoted above as **not medically necessary****) to be **investigational**.*

Background/Overview

Palsonify is an oral, once-daily selective somatostatin receptor agonist indicated for the treatment of acromegaly in adults who have had an inadequate response to surgery and/or for whom surgery is not an option. Palsonify is structurally similar to the endogenous hormone somatostatin and suppresses growth hormone (GH) and insulin-like growth factor-1 (IGF-1) secretion through selective agonism of the somatostatin receptor subtype 2, with minimal activity at other somatostatin receptor subtypes. The recommended initial dose is 40 mg taken orally once daily, with titration up to a maximum dose of 60 mg once daily based on IGF-1 levels assessed 2 to 4 weeks after treatment initiation. Palsonify is available as 20 mg and 30 mg tablets and should be administered with water on an empty stomach, at least one hour before or six hours after a meal.

Acromegaly is a rare, chronic endocrine disorder caused by prolonged excess secretion of growth hormone (GH), most commonly due to a benign pituitary somatotroph adenoma, resulting in elevated insulin-like growth factor-1 (IGF-1) levels. The disease is characterized by gradual onset and progressive somatic changes, including enlargement of the hands and feet, soft-tissue swelling, arthralgia, hyperhidrosis, glucose intolerance or diabetes mellitus, hypertension, and cardiovascular and respiratory complications, which contribute to increased morbidity and mortality if inadequately controlled. Diagnosis is based on biochemical evidence of elevated age-adjusted IGF-1 levels with lack of GH suppression, supported by imaging to identify pituitary adenomas. Surgical resection of the pituitary tumor is generally considered first-line therapy; however, many patients have residual or recurrent disease or are not surgical candidates, necessitating long-term medical management. Current guidelines recommend somatostatin analogs as first-line medical therapy in patients with persistent disease following surgery or when surgery is not feasible, with treatment goals focused on normalization of IGF-1 and GH levels, control of symptoms, reduction of tumor-related complications, and improvement in quality of life. FDA-approved medical options for acromegaly include injectable somatostatin analogs such as octreotide long-acting release (Sandostatin LAR), lanreotide depot (Somatuline Depot), and pasireotide long-acting release (Signifor LAR); the oral somatostatin analog octreotide capsules (Mycapssa-for patients previously responsive to injectable therapy); growth hormone receptor antagonists; and dopamine agonists for select patients.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Palsonify was approved in September 2025 and is indicated for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The clinical efficacy of Palsonify for the treatment of acromegaly was evaluated in two randomized, double-blind, placebo-controlled, multinational Phase III pivotal trials, PATHFINDER-1 and PATHFINDER-2. PATHFINDER-1 enrolled adults with confirmed acromegaly who were previously controlled on stable doses of long-acting injectable somatostatin analogs (octreotide long-acting release or lanreotide depot) and assessed maintenance of biochemical control after switching to oral Palsonify or placebo over a 36-week treatment period. The primary endpoint was the proportion of patients who maintained insulin-like growth factor-1 (IGF-1) levels less than or equal to one times the upper limit of normal (ULN) at Weeks 34 and 36. In PATHFINDER-1 (n = 58), a significantly greater proportion of patients receiving Palsonify maintained biochemical control compared with placebo (83.3% vs 3.6%; $P < 0.0001$), with fewer patients requiring rescue therapy (3% vs 61%) and a higher proportion maintaining growth hormone (GH) levels < 1 ng/mL (87.0% vs 27.8%). PATHFINDER-2 evaluated adults with active acromegaly who were medically untreated, including treatment-naïve patients and those undergoing washout from prior somatostatin analog therapy, over a 24-week treatment period. The primary endpoint was the proportion of patients achieving IGF-1 levels ≤ 1 times the ULN at Weeks 22 and 24. In PATHFINDER-2 (n = 111), significantly more patients treated with Palsonify achieved biochemical control compared with placebo (55.6% vs 5.3%; $P < 0.0001$), with greater GH suppression (57.4% vs 17.5% achieving GH < 1 ng/mL), fewer patients requiring rescue medication (2% vs 23%), and significant improvement in acromegaly symptom scores. Across both studies, Palsonify demonstrated rapid onset of effect within 2 to 4 weeks and sustained biochemical control throughout the randomized treatment periods.

References

1. Palsonify [package insert]. Crinetics Pharmaceuticals, Inc. San Diego, California. Updated September 2025.
2. Palsonify Drug Evaluation. Express Scripts. Updated October 2025.

Policy History

Original Effective Date: 04/01/2026

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03/05/2026 Medical Policy Committee review

03/11/2026 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 03/2027

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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 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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.