BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

PALSONIFY™ (paltusotine) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Palsonify (paltusotine) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **acromegaly** in an individual who has had an inadequate response to surgery and/or for whom surgery is not an option

4. Individual has an insulin-like growth factor 1 (IGF-1) level that supports the diagnosis of acromegaly

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** the following:
    a. Sandostatin LAR (octreotide acetate) injection
    b. Somatuline Depot (lanreotide) injection
    c. Mycapssa (octreotide acetate) oral
    d. Maximally tolerated bromocriptine or cabergoline

7. Individual will not use Palsonify (paltusotine) concurrently with any octreotide product or lanreotide

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Palsonify (paltusotine) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual has documentation of positive clinical response to therapy defined as **ALL** of the following:
    a. No evidence of disease progression
    b. Achieved and maintains normalization of growth hormone and IGF-I levels for age and gender (must use the same laboratory assay that was used at baseline measurement, laboratory reference range must be provided)

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Acute cholecystitis
    b. Cholelithiasis
    c. Pancreatitis

6. Individual will not use Palsonify (paltusotine) concurrently with any octreotide product or lanreotide

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

PHARMACY COVERAGE GUIDELINE

PALSONIFY™ (paltusotine) oral
Generic Equivalent (if available)

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Palsonify (paltusotine) 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. Paltusotine is a nonpeptide somatostatin receptor agonist.

Similar to the natural hormone somatostatin, paltusotine suppresses growth hormone (GH) and insulin-like growth factor-1 (IGF-1) secretion. Paltusotine exerts its pharmacological activity via selective agonism at somatostatin receptor 2 (SSTR2) and exhibits little or no affinity for other somatostatin receptor subtypes

Acromegaly is a disease characterized by excessive release of GH. Increased levels of GH stimulate an increase in hepatic production of IGF-1. Excess IGF-1 causes increased growth of bones and soft-tissues while excess GH can cause other conditions such as diabetes mellitus, hypertension, and an increase in cardiovascular risk. Both serum GH concentrations and IGF-1 concentrations are increased in virtually all patients with acromegaly.

The goals of therapy in patients with acromegaly are to lower the serum IGF-1 concentration to within the normal range for the patient's age and gender and to lower the serum GH concentration to < 1 mcg/L. The Endocrine Society guidelines suggest that an age-normalized serum IGF-1 and a random GH < 1 mcg/L should both be therapeutic goals, as they correlate with control of acromegaly.

First-generation long-acting somatostatin injectable analog (e.g., lanreotide, octreotide) are considered first-line therapy in patients with persistent disease despite surgical resection or in whom surgery is not appropriate.

Alternative agents are suggested for patients with mild disease postoperatively.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Palsonify (paltusotine) product information, revised by Crinetics Pharmaceuticals, Inc. 09-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 20, 2025.

Melmed S, Katznelson L. Treatment of acromegaly. In: UpToDate, Snyder PJ, Martin KA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2025. Topic last updated April 28, 2023. Accessed October 21, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04837040: A Randomized, Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Paltusotine in Subjects With Acromegaly Treated With Long-acting Somatostatin Receptor Ligands (PATHFNDR-1). Available from: http://clinicaltrials.gov. Last update posted June 12, 2025. Last verified June 2025. Accessed October 21, 2025.

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ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT05192382: A Randomized, Controlled, Multicenter Study to Evaluate the Safety and Efficacy of Paltusotine in Subjects With Non-pharmacologically Treated Acromegaly (PATHFNDR-2). Available from: http://clinicaltrials.gov. Last update posted June 12, 2025. Last verified June 2025. Accessed October 21, 2025.

Gadelha MR, Gordon MB, Doknic M, et al.: ACROBAT Edge: Safety and Efficacy of Switching Injected SRLs to Oral Paltusotine in Patients With Acromegaly. J Clin Endocrin & Metab 2023, 108, e148–e159 https://doi.org/10.1210/clinem/dgac643. Accessed October 21, 2025.

Gadelha MR, Casagrande A, Strasburger CJ, et al.: Acromegaly Disease Control Maintained After Switching From Injected Somatostatin Receptor Ligands to Oral Paltusotine. J Clin Endocrin & Metab 2025, 110, 228–237 https://doi.org/10.1210/clinem/dgae385. Accessed October 21, 2025.