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Coverage Policy Number **IP0568**

Leniolisib

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for leniolisib (**Joenja**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Leniolisib (Joenja) is considered medically necessary when the following are met:

Activated phosphoinositide 3-kinase delta syndrome (APDS). Individual meets **ALL** of the following criteria:

A. Age 12 years or older
B. Weighs at least 45 kg
C. Documentation of activated phosphoinositide 3-kinase delta (PI3Kδ) with a pathogenic variant in *PIK3CD* and/or *PIK3R1* genes

D. Has at least one clinical manifestation consistent with APDS (for example, recurrent respiratory tract infections, bronchiectasis, chronic non-resolving infections with herpes group of viruses, chronic non-malignant lymphoproliferation, cytopenias, glomerulonephritis, immunodysregulation)
E. Medication is prescribed by, or in consultation with, an immunologist, gastroenterologist, hematologist, pulmonologist, an infectious disease physician who treats primary immune deficiencies or a physician who specializes in genetic disorders

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of leniolisib (Joenja) is considered medically necessary for activated phosphoinositide 3-kinase delta syndrome (APDS) when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 6 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Joenja, a kinase inhibitor, is indicated for the treatment of **activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS)** in adults and pediatric patients ≥12 years of age.[1]

Disease Overview
APDS is an ultra-rare, genetic, progressive primary immunodeficiency disorder.[2,3] It is estimated to occur in 1 to 2 people per one million. APDS is an autosomal dominant disease caused by variants in *PIK3CD* or *PIK3R1* genes, resulting in hyperactivation of the PI3Kδ pathway. APDS is characterized by both immune deficiency and dysregulation, which causes various clinical manifestations, such as recurrent sinopulmonary infections, recurrent herpesvirus infections, lymphadenopathy, hepatomegaly, splenomegaly, nodular lymphoid hyperplasia, autoimmunity, cytopenias, enteropathy, and bronchiectasis. APDS can lead to end-organ damage, malignancy, and early mortality. There are no other FDA-approved treatments for APDS. Current APDS management includes immunosuppressants, prophylactic antimicrobials, immunoglobulin replacement therapy, sirolimus, hematopoietic stem cell transplantation (HSCT), and surgery or procedures.

Clinical Efficacy
The efficacy of Joenja was evaluated in one Phase III, randomized, triple-blind, placebo-controlled, multicenter, pivotal study in 31 patients with APDS.[2] Eligible patients were 12 to 75 years of age, had pathogenic variants in *PIK3CD* or *PIK3R1* genes, had clinical findings consistent with APDS (e.g., history of repeated oto-sino-pulmonary infection and organ dysfunction), and more than one measurable lymph node on computed tomography or magnetic resonance imaging scan. The co-primary outcomes were differences from baseline in the index lymph node size and the percentage of naïve B cells in peripheral blood, which are measures of immune dysregulation and deficiency.[2] Both co-primary endpoints were met. Joenja significantly reduced lymphadenopathy and significantly increased the percentage of naïve B cells. Joenja also improved other outcome measures, such as spleen size, lymphocyte subsets, cytopenias, and immunoglobulin (Ig)M levels.

Although changes in health-related quality of life measures were not statistically significant, many patients reported increase in activity and energy levels. An ongoing open label extension study reported results in an interim analysis from 37 patients with least 5 years of Joenja exposure.[3,4] Joenja demonstrated a reduction in use of immunoglobulin replacement therapy and a decrease in the annualized yearly infection rate. Continued improvements in mean index lymph node size; mean immunoglobulin M (IgM) levels; and mean percentages of naïve B cells and transitional B cells were seen.

References

1. Joenja® tablets [prescribing information]. Warren. NJ: Pharming; March 2023.
2. Rao V, Webster S, Sediva A, et al. A randomized, placebo-controlled phase 3 trial of the PI3Kδ inhibitor leniolisib for activated PI3Kδ syndrome. *Blood*. 2023;141(9):971-983.
3. Data on File. Leniolisib Pre-approved Product Dossier. Based on AMCP guidelines for formulary submission. Pharming; received March 23, 2023.
4. Rao VK, et al. Interim safety and efficacy analysis of an ongoing long-term open-label extension study of leniolisib for patients with activated PI3K delta syndrome (APDS). Presented at: European Society for Immunodeficiencies (ESID) 20th Biennial Meeting; Gothenburg, Sweden; October 12-15, 2022.