PRIOR AUTHORIZATION POLICY

POLICY: Immune Disorder - Joenja Prior Authorization Policy
- Joenja® (leniolisib tablets – Pharming)

REVIEW DATE: 03/29/2023; selected revision 04/12/2023

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Joenja. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Joenja as well as the monitoring required for adverse events and long-term efficacy, approval requires Joenja to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Joenja® (leniolisib tablets (Pharming)**

is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Activated phosphoinositide 3-kinase delta syndrome (APDS).** Approve for the duration noted if the patient meets the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets all of the following criteria (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient weighs ≥ 45 kg; AND
     - **iii.** Patient has a genetic phosphoinositide 3-kinase delta (PI3Kδ) mutation with a variant in *PIK3CD* and/or *PIK3R1* genes; AND

iv. Patient has at least one clinical finding or manifestation consistent with APDS; AND
Note: Examples of clinical findings or manifestations of APDS include recurrent sinopulmonary infections, recurrent herpesvirus infections, lymphadenopathy, hepatomegaly, splenomegaly, nodular lymphoid hyperplasia, autoimmunity, cytopenias, enteropathy, bronchiectasis, and organ dysfunction.

v. The medication is prescribed by or in consultation with an immunologist, pulmonologist, gastroenterologist, hematologist, or an infectious diseases physician who treats patients with primary immune deficiencies.

B) Patient is currently receiving Joenja. Approve for 1 year if the patient meets all of the following criteria (i, ii, iii, iv, and v):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy should be considered under criterion A (Initial Therapy).

ii. Patient is ≥ 12 years of age; AND

iii. Patient weighs ≥ 45 kg; AND

iv. Patient has a genetic phosphoinositide 3-kinase delta (PI3Kδ) mutation with a variant in *PIK3CD* and/or *PIK3R1* genes; AND

v. Patient has had a positive clinical response in the signs and manifestations of APDS.
Note: Examples of positive clinical response in the signs and manifestations of APDS include reduction of: lymph node size, spleen size, immunoglobulin replacement therapy use, infection rate, or immunoglobulin M (IgM) levels.

CONDITIONS NOT COVERED

- **Joenja® (leniolisib tablets (Pharming)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	03/29/2023
Selected Revision	**Activated phosphoinositide 3-kinase delta syndrome (APDS).** The following specialists were removed from the list of specialists: allergist and otolaryngologist (ear, nose, and throat [ENT] physician) and the following specialists were added: gastroenterologist or hematologist for initial therapy. The criteria was separated into initial therapy with an approval duration of 6 months and continuation of therapy with an approval duration of 12 months. For patients currently receiving Joenja, the following criteria were added: patient has been established on therapy for at least 6 months along with a note to refer to initial therapy criteria if the patient has not been on therapy for at least 6 months or is restarting therapy; patient is ≥ 12 years of age; patient weighs ≥ 45 kg; patient has a genetic phosphoinositide 3-kinase delta (PI3Kδ) mutation with a variant in *PIK3CD* and/or *PIK3R1* genes; AND patient has had a positive clinical response in the signs and manifestations of APDS with a note including examples of signs and manifestations of APDS.	04/12/2023