leniolisib (Joenja®)

Policy # 00856
Original Effective Date: 12/11/2023
Current Effective Date: 12/11/2023

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 the use of leniolisib (Joenja®)‡ for the treatment of activated phosphoinositide 3-kinase delta syndrome to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for leniolisib (Joenja) will be considered when the following criteria are met:

- Initial
    - Patient is ≥12 years of age; AND
    - Patient weighs ≥45 kg; AND
    - Patient has a diagnosis of activated phosphoinositide 3-kinase (PI3K) delta syndrome (APDS)/p110 delta-activating mutation causing senescent T cells, lymphadenopathy, and immunodeficiency (PASLI); AND
    - Diagnosis has been verified by genetic testing revealing mutations in the *PIK3CD* or *PIK3R1* genes; AND
    - Patient has at least one clinical sign or symptom associated with APDS. Examples of signs or symptoms associated with APDS include recurrent oto-sino-pulmonary infections, recurrent herpesvirus infections, lymphadenopathy, hepatomegaly, splenomegaly, nodular lymphoid hyperplasia, autoimmunity, cytopenias, enteropathy, bronchiectasis, and organ dysfunction; AND
      *(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.)*
    - Joenja will not be used in combination with an immunosuppressive medication.

*(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.)*

- Continuation
  - Patient has received an initial authorization for Joenja; AND
  - Joenja will not be used in combination with an immunosuppressive medication; AND
    *(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.)*
  - Patient is NOT receiving concurrent immunosuppressive medication; AND
  - Patient has experienced a positive clinical response Joenja as evidenced by improvement in the symptoms of APDS. Examples of positive responses in the signs and symptoms of APDS include reduction of lymph node size, spleen size, immunoglobulin replacement therapy use, infection rate, or immunoglobulin M (IgM) levels.
    *(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 leniolisib (Joenja) when the patient does not have at least one clinical sign or symptom associated with APDS or when it will be used in combination with an immunosuppressive medication to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of leniolisib (Joenja) when the patient has not experienced a positive clinical response to Joenja to be **not medically necessary.****

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 leniolisib (Joenja) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

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Background/Overview

Joenja is a kinase inhibitor indicated for the treatment of the ultra-rare condition activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) and is thought to work by blocking the active binding site of PI3Kδ to inhibit the signaling pathways that cause dysregulation of B and T cells. It should be administered by mouth twice daily, approximately 12 hours apart with or without food. There is no recommended dosage for patients weighing less than 45 kg. Additionally, Joenja is known to cause embryofetal toxicity and thus pregnancy status of patients of reproductive potential should be verified before initiating treatment with Joenja.

APDS is an ultra-rare, genetic, progressive primary immunodeficiency disorder that was first described in 2013. It is thought to occur in 1 to 2 people per million. APDS is an autosomal dominant disease caused by mutations in the PI3Kδ catalytic subunit delta (PIK3CD) or PI3Kδ regulatory subunit 1 (*PIK3R1*) genes. This leads to hyperactivation of the PI3Kδ pathway which affects immune system activity. In patients with APDS, immune cell production speeds up, resulting in underdeveloped cells with lessened activity. Patients have a deficiency of white blood cells, particularly certain types of B cells and T cells. 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. The condition can lead to end-organ damage, malignancy (lymphoma), and early mortality. Prior to the approval of Joenja, therapy for APDS involved managing the various manifestations of the disease using immunosuppressants (e.g., corticosteroids, rituximab, and sirolimus), prophylactic antibiotics, surgery, immunoglobulin replacement therapy, or hematopoietic stem cell transplantation.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Joenja was approved in March 2023 for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older.

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 federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Jeonja was evaluated in the placebo-controlled portion of Study 2201, a 12-week blinded, randomized, placebo-controlled study in adult and pediatric patients 12 years of age and older with confirmed APDS-associated genetic PI3Kδ mutation with a documented variant in either PIK3CD or PIK3R1. Patients had nodal and/or extranodal lymphoproliferation, as measured by index nodal lesion selected by the Cheson methodology on CT or MRI and clinical findings and manifestations compatible with APDS (e.g., history of repeated oto-sino-pulmonary infections, organ dysfunction). Immunosuppressive medications or PI3Kδ inhibitors (selective or non-selective) were prohibited within 6 weeks of baseline and throughout the study. In addition, patients who had previous or concurrent B cell depleters (e.g., rituximab) within 6 months of baseline were excluded from the study, unless absolute B lymphocytes in the blood were normal. B cell depleters were prohibited throughout the study.

Thirty-one patients were randomized 2:1 to receive either Joenja 70 mg (n=21) or placebo (n=10) twice a day for 12 weeks. The co-primary efficacy endpoints were improvement in lymphoproliferation as measured by a change from baseline in lymphadenopathy measured by the log10-transformed sum of product diameters (SPD) and the normalization of immunophenotype as measured by the percentage of naïve B cells out of total B cells. Both co-primary endpoints demonstrated a statistically significant improvement in the Joenja group compared to the placebo group. The LS Mean change from baseline in the log10-transformed SPD was -0.27 in the Joenja group and -0.02 in the placebo group. The change in percentage of naïve B cells from baseline was 37.39% in the Joenja group and 0.09% in the placebo group.

References

1. Joenja [package insert]. Pharming Healthcare, Inc. Warren, NJ. Updated March 2023

Policy History

Original Effective Date: 12/11/2023
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11/02/2023 Medical Policy Committee review

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11/08/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 11/2024

*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: 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 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.