Clinical Policy: Leniolisib (Joenja)

Reference Number: CP.PHAR.597
Effective Date: 03.24.23
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Leniolisib (Joenja®) is a kinase inhibitor.

FDA Approved Indication(s)

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

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results, or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Joenja is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Activated Phosphoinositide 3-Kinase Delta Syndrome (must meet all)**:**

1. Diagnosis of APDS;
2. Prescribed by or in consultation with an immunologist;
3. Age ≥ 12 years;
4. Weight ≥ 45 kg;
5. Confirmed PI3Kδ genetic mutation of either the PIK3CD (APDS1) or PIK3R1 (APDS2) gene;
6. Documentation of at least one measurable nodal lesion on a computed tomography (CT) or magnetic resonance imaging (MRI) scan;
7. Evidence of clinical findings and manifestations compatible with APDS/PASLI (e.g., history of repeated oto-sino-pulmonary infections and/or organ dysfunctions) (*see Appendix D)*;
8. Dose does not exceed both of the following (a and b):
   a. 140 mg per day;
   b. 2 tablets per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Activated Phosphoinositide 3-Kinase Delta Syndrome (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Weight ≥ 45 kg;
3. Member is responding positively to therapy as evidenced by reduction in size of nodal lesions from baseline prior to initiating leniolisib;
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 140 mg per day;
   b. 2 tablets per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

APDS: activated phosphoinositide 3-kinase delta syndrome
CT: computed tomography
FDA: Food and Drug Administration
MRI: magnetic resonance imaging
PASLI: p110δ-activating mutation causing senescent T cells, lymphadenopathy and immunodeficiency
PI3Kδ: phosphoinositide 3-kinase delta

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Clinical findings and manifestations compatible with APDS/PASLI
  - Organ dysfunctions such as significant nonmalignant lymphoproliferation including bronchial and intestinal lymphoid hyperplasia and lymphadenopathy/splenomegaly/hepatomegaly
  - History of repeated oto-sino-pulmonary infections include bronchiectasis, upper respiratory tract infections, otitis media, sinusitis, pneumonia, bronchitis, chronic Epstein-Barr virus (EBV) and cytomegalovirus (CMV) viremia, and an increased risk of autoimmune disease including cytopenias

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
APDS	70 mg PO BID	140 mg/day

VI. Product Availability

Tablet: 70 mg

VII. References

1. Joenja Prescribing Information. Warren, NJ: Pharming Healthcare Inc.; May 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/217759s005lbl.pdf. Accessed August 5, 2025.

2. Rao VK, Webster S, Šedivá A, Plebani A, et al. A randomized, placebo-controlled phase 3 trial of the PI3Kδ inhibitor leniolisib for activated PI3Kδ syndrome. *Blood.* 2023 Mar 2;141(9):971-983. doi: 10.1182/blood.2022018546.
3. Coulter TI, Chandra A, Bacon CM, Babar J, et al. Clinical spectrum and features of activated phosphoinositide 3-kinase δ syndrome: A large patient cohort study. J Allergy Clin Immunol. 2017 Feb;139(2):597-606.e4. doi: 10.1016/j.jaci.2016.06.021.
4. Maccari ME, Abolhassani H, Aghamohammadi A, et al. Disease evolution and response to rapamycin in activated phosphoinositide 3-kinase δ syndrome: The European Society for Immunodeficiencies-Activated Phosphoinositide 3-Kinase δ Syndrome Registry. Front Immunol. 2018 Mar 16;9:543. doi: 10.3389/fimmu.2018.00543.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.11.22	11.22
RT4: drug is now FDA approved – criteria updated per FDA labeling: added minimum body weight dosing requirement; references reviewed and updated.	04.03.23	
4Q 2023 annual review: no significant changes; references reviewed and updated.	08.10.23	11.23
Extended initial approval duration from 3 months to 6 months to allow sufficient time for full clinical response to meet reauthorization criteria; extended continued therapy approval duration from 6 months to 12 months; references reviewed and updated.	11.06.23	02.24
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.30.24	11.24
4Q 2025 annual review: no significant changes; references reviewed and updated.	08.05.25	11.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.