Joenja (leniolisib) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
11/1/2023	11/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Joenja® (leniolisib) Tablets	Treatment of activated phosphoinositide 3-kinase delta (PI3K-delta) syndrome (APDS) in adult and pediatric patients 12 years of age and older		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Primary Immunodeficiencies	Primary immunodeficiencies (PIDs) are a group of inborn error disorders that cause immune dysfunction and manifest with increased susceptibility to infections. Many PIDs are monogenic diseases. To date, mutations in more than 300 genes have been shown to cause various PIDs. Activated phosphoinositide 3-kinase delta syndrome (APDS) is a PID that results from pathogenic variant mutations in either the PIK3CD gene (APDS1) or the PIK3R1 gene (APDS2). Both genes are important for the growth, survival and function of lymphocytes.(2,3,4,6) Definitive diagnosis is made through genetic testing, which Pharming Healthcare Inc offers at no-charge (including counseling) for individuals who are suspected to carry a pathogenic variant in PIK3CD or PIK3R1. Patients may present in childhood or later in life with severe, persistent and recurrent bacterial and viral infections, lymphadenopathy, delayed growth, and/or hepato- or splenomegaly. Additionally, patients may present with signs of autoimmune or inflammatory conditions, such as anemia, thrombocytopenia, colitis, glomerulonephritis, etc.(5,7)
Efficacy	Joenja (leniolisib) is an oral selective PI3K-delta inhibitor. In cell-based assays, Joenja inhibited the signaling pathways that lead to the dysregulation of B and T cells.(1) The efficacy of Joenja was evaluated in the placebo-controlled portion of Study 2201 (NCT02435173), a 12-week blinded, randomized, placebo-controlled study in adult and pediatric patients 12 years of age and older with confirmed APDS-associated genetic PI3K-delta 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). 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 and the normalization of immunophenotype as measured by the percentage of naïve B cells out of total B cells. Findings showed that leniolisib met the coprimary endpoints demonstrating a statistically significant reduction in index lymph node size (p=.006) and normalization of immunodeficiency (as evidenced by an increased proportion of naïve B cells from baseline; p=.002), compared with placebo.(1,6)

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Safety(1)	Joenja (leniolisib) has no boxed warnings or contraindications.

REFERENCES

Number	Reference
1	Joenja prescribing information. Pharming Technologies BV. March 2023.
2	Singh A, Joshi V, Jindal AK, et al. An Updated Review on Activated PI3 Kinase Delta Syndrome (APDS). Genes Dis. 2020 Mar;7(1):67-74.
3	Michalovich D, Nejentsev S. Activated PI3 Kinase Delta Syndrome: From Genetics to Therapy. Front Immunol. 2018 Feb;9:369.
4	Ewertowska M, Grzesk E, Urbanczyk A, et al. Activated Phosphoinositide 3-Kinase Delta Syndrome 1 and 2 (APDS 1 and APDS 2): Similarities and Differences Based on Clinical Presentation in Two Boys. Allergy Asthma Clin Immunol. 2020 Apr;16:22.
5	Oh J. Activated Phosphoinositide 3-Kinase Delta Syndrome (APDS). National Organization of Rare Diseases (NORD). Last updated: April 2023. Available at: https://rarediseases.org/rare-diseases/activated-phosphoinositide-3-kinase-delta-syndrome-apds/
6	Rao VK, Webster S, Sediva A, et al. A Randomized, Placebo-Controlled Phase 3 Trial of the PI3K-delta Inhibitor Leniolisib for Activated PI3K-delta Syndrome. Blood. 2023 Mar;141(9):971-983.
7	International Patient Organization for Primary Immunodeficiencies (IPOPI). Primary Immunodeficiencies: APDS - Activated PI3K Delta Syndrome. 2020. Available at: http://www.immunodeficiencyuk.org/static/media/up/IPOPIADPS.pdf

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Joenja	leniolisib phosphate tab	70 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Joenja	leniolisib phosphate tab	70 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Joenja	leniolisib phosphate tab	70 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Joenja	leniolisib phosphate tab	70 MG	Medicaid

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Joenja

      1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**

   B. BOTH of the following:
      1. The patient has a diagnosis of activated phosphoinositide 3-kinase (PI3K) delta syndrome (APDS) **AND**
      2. The patient has a variant in either PIK3CD or PIK3R1 **AND**
2. If the patient has an FDA approved indication, then ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested agent **AND**
3. The patient's weight is 45 kg or greater **AND**
4. The prescriber has assessed the patient's baseline (prior to therapy with the requested agent) lymphoproliferation (nodal and/or extranodal) and immunophenotype (as measured by the percentage of naive B cells out of total B cells) **AND**
5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, immunologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of Approval: 3 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND**
2. The patient has had clinical benefit with the requested agent (e.g., improvement in lymphoproliferation, normalization of immunophenotype) **AND**
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, immunologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
4. The patient does NOT have any FDA labeled contraindications to the requested agent

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Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval:** Initial 3 months; Renewal 12 months

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