UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2305-3
Program	Prior Authorization/Medical Necessity
Medication	Joenja® (leniolisib)
P&T Approval Date	5/2023, 5/2024, 5/2025
Effective Date	8/1/2025

1. Background:

Joenja (leniolisib) is a kinase inhibitor indicated for the treatment activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) in adult and pediatric patients 12 years of age and older.[1]

APDS is a rare primary immunodeficiency caused by variations in the genes encoding subunits of the PI3Kδ enzyme complex and PI3Kδ hyperactivity. PI3Kδ hyperactivity results in altered development of B and T-cell which can lead to severe lymphoproliferation, recurrent infections, autoimmune disorders, and malignancies. APDS can be characterized by a variety of symptoms, including recurrent respiratory tract infections (e.g., pneumonia, otitis media, rhinosinusitis), recurrent herpesvirus infections (e.g., Epstein Barr virus, cytomegalovirus, herpes simplex virus), lymphoproliferation (e.g., lymphadenopathy, hepatosplenomegaly), autoimmune cytopenia and glomerulonephritis, and neurodevelopmental delay. A definitive diagnosis can be made through genetic testing. Current standard of care includes antimicrobial prophylaxis (e.g., trimethoprim/sulfamethoxazole, azithromycin), immunoglobulin replacement therapy (IRT), immunosuppressive therapy (e.g., glucocorticoids, rituximab), and hematopoietic stem cell transplant (HSCT).[4]

2. Coverage Criteria[a]:

A. Initial Authorization

1. **Joenja** will be approved based upon **all** of the following criteria:

   a. Diagnosis of activated phosphoinositide 3-kinase delta syndrome (APDS)

   -AND-

   b. Diagnosis has been confirmed by the presence of an APDS-associated genetic variant in either PIK3CD or PIK3R1.

   -AND-

   c. Documentation of other clinical findings and manifestations consistent with APDS (e.g., recurrent respiratory tract infections, recurrent herpesvirus infections, lymphadenopathy, hepatosplenomegaly, autoimmune cytopenias)

   -AND-

   d. Patient has a history of trial and failure, intolerance or contraindication to current

standard of care for APDS (e.g., antimicrobial prophylaxis, immunoglobulin replacement therapy, immunosuppressive therapy)

-AND-

e. Prescribed by **one** of the following:

1) Hematologist
2) Immunologist

-AND-

f. **Both** of the following:

1) Patient is 12 years of age or older

-AND-

2) Patient weighs greater than or equal to 45 kg

Authorization will be issued for 12 months.

B. Reauthorization

1. **Joenja** will be approved based on **all** the following criterion:

a. Documentation of positive clinical response to Joenja therapy (e.g., reduced lymph node size, increased naïve B-cell percentage, decreased frequency or severity of infections, decreased frequency of hospitalizations)

-AND-

b. Prescribed by **one** of the following:

1) Hematologist
2) Immunologist

-AND-

c. Patient weighs greater than or equal to 45 kg

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.

- Supply limits may be in place.

4. Reference:

1. Joenja [package insert]. Foster City, CA: Pharming Technologies, Inc.; March 2023.
2. Rao VK, Webster S, Šedivá 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. Singh A, Joshi V, Jindal AK, Mathew B, Rawat A. An updated review on activated PI3 kinase delta syndrome (APDS). Genes Dis. 2019 Oct 14;7(1):67-74.
4. Vanselow S, Wahn V, Schuetz C. Activated PI3Kδ syndrome - reviewing challenges in diagnosis and treatment. Front Immunol. 2023 Jul 20;14:1208567.

Program	Prior Authorization/Medical Necessity - Joenja (leniolisib)
Change Control	
5/2023	New program.
5/2024	Annual review. Updated initial authorization duration to 12 months. Updated references.
5/2025	Annual review with no changes to coverage criteria. Updated references.