Joenja®
leniolisib

The first and only precision therapy that targets the underlying immune defect in patients with APDS[1-3]

APDS, activated PI3Kδ syndrome.

Indications and Usage

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

Select Safety Information

Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja targets the underlying immune defect of APDS and helps normalize the hyperactive PI3Kδ pathway[1,2,4]

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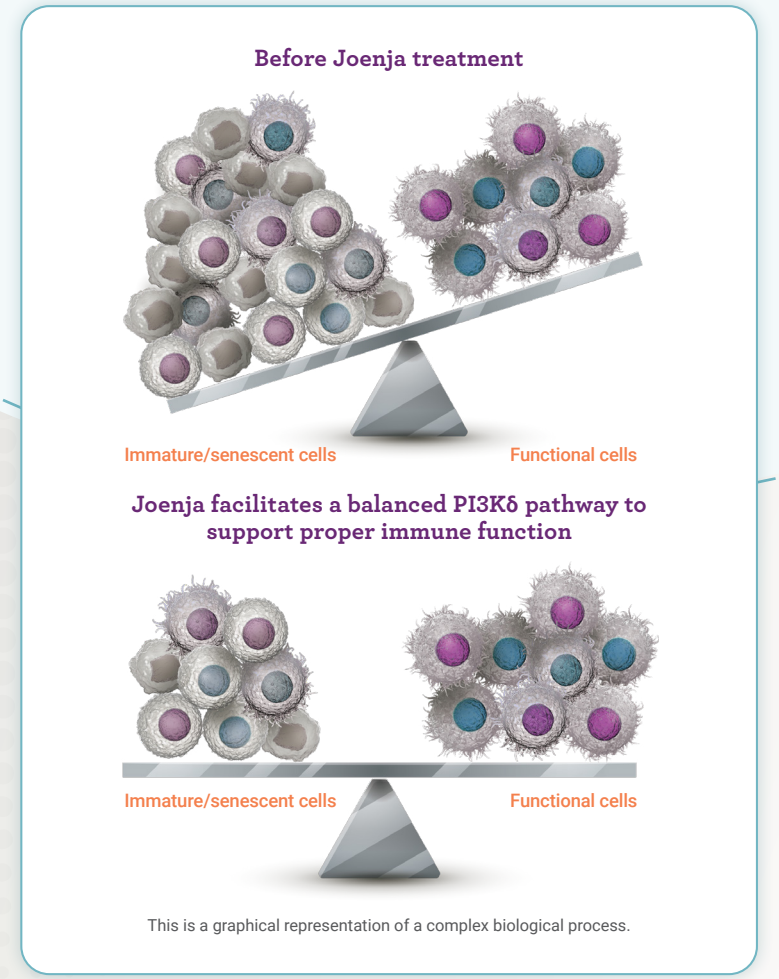
As a precision therapy, Joenja addresses both immune deficiency and immune dysregulation in patients with APDS



This is a graphical representation of a complex biological process.

Joenja is an **immune modulator that targets the overactive PI3Kδ pathway** to correct the underlying immune defect and help normalize the PI3Kδ pathway

Select Safety Information

JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja is supported by robust clinical trial data

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Trial Overview[1,2,5,6]

Part 1: Dose-Finding Study, 12 weeks | N=6

- Nonrandomized, open-label, dose-finding study in 6 patients with APDS; dose range was 10 mg, 30 mg, and 70 mg BID for 4 weeks at each dose
  - Oral dose of 70 mg BID selected for Part 2

Part 2: Efficacy and Safety Evaluation, randomized period | 12 weeks | N=31

- Randomized, triple-blinded (patient, caregiver, investigator), placebo-controlled, fixed-dose study of 70 mg BID
- Co-primary efficacy end points (improvement in lymphoproliferation and normalization of immunophenotype)
  - Change from baseline in the $\log_{10}$-transformed SPD of index lesions
  - Change from baseline in percentage of naïve B cells out of total B cells
- Secondary and exploratory end point assessments
- Safety assessment

Long-Term Safety[1,5]

- A nonrandomized open-label extension (OLE) study to evaluate the long-term safety, tolerability, efficacy, and pharmacokinetics of Joenja in patients with APDS (N=37)
  - Thirty-five patients from Parts 1 and 2
  - Two patients previously treated with an investigational PI3Kδ inhibitor
- Primary outcome measure: long-term safety and tolerability

BID, twice a day; SPD, sum of product diameters.

Select Safety Information

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

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Joenja significantly reduced lymphadenopathy, helping to restore immune balance[1]

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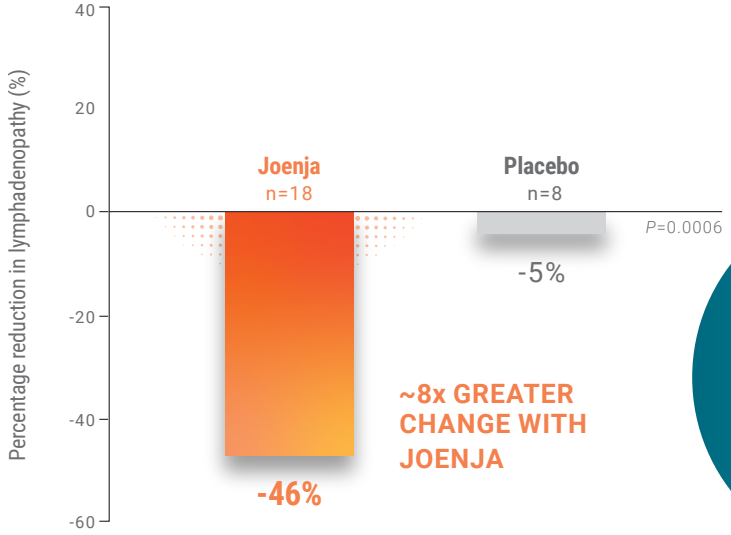
Log_{10}-transformed SPD of index lesions (excluding patients with 0 lesions at baseline) at week 12[1]*

	Joenja (n/N=18/21)†	Placebo (n/N=8/10)†
Baseline mean (SD)	**3.03** (0.42)	**3.05** (0.39)
Change from baseline, LS mean (SE)	**-0.27** (0.04)	**-0.02** (0.05)
Difference vs placebo (95% CI)		**-0.25** (-0.38, -0.12)

P=0.0006

- Improvement in lymphoproliferation as measured by a change from baseline in lymphadenopathy measured by the log_{10}-transformed SPD of index lymph nodes[1,2]

At week 12, patients saw a significant reduction in lymphadenopathy*† with Joenja vs placebo[1,7]



- Reduction computed based on estimates for the adjusted mean changes[7]

46%
REDUCTION WITH JOENJA VS 5% WITH PLACEBO[7]

Note: The LS mean change from baseline, difference in LS mean change from baseline between Joenja and placebo and its *P* value were obtained from an ANCOVA model with treatment, glucocorticoids use and IRT at baseline, and baseline measurement as covariates.[1]
*Change in index lesion size was measured using the log_{10}-transformed SPD of the largest lymph nodes (maximum of 6) identified as per the Cheson criteria on CT/MRI.[1]
†The analysis excluded 2 patients from each treatment group due to protocol deviations and 1 Joenja patient having complete resolution of the index lesion identified at baseline.[1]
ANCOVA, analysis of covariance; CI, confidence interval; CT, computed tomography; IRT, immunoglobulin replacement therapy; LS, least squares; MRI, magnetic resonance imaging; SD, standard deviation; SE, standard error.

Select Safety Information

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

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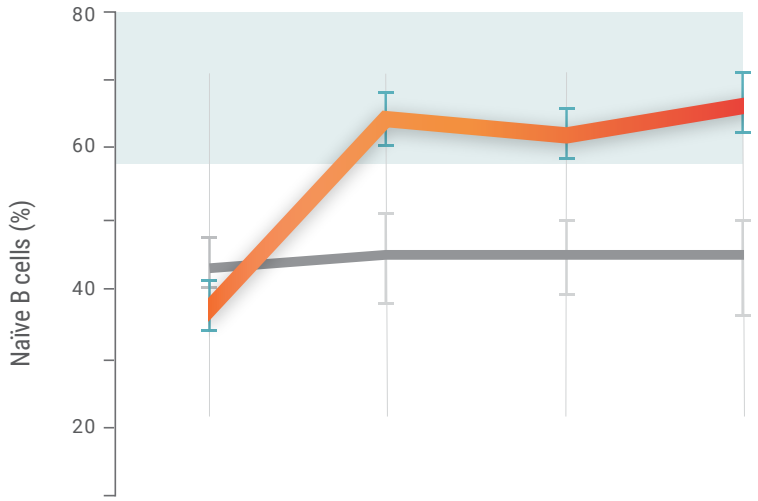
Joenja significantly increased naïve B cells[2]

Significantly improved immunophenotype vs placebo at week 12[1,2]

- In patients with <48% of naïve B cells at baseline,* the adjusted mean difference between Joenja (n=8) and placebo (n=5) in the percentage of naïve B cells out of total B cells was 37.30 (95% CI: 24.06, 50.54), *P*=0.0002†
- The adjusted mean change from baseline (SE) for Joenja was 37.39 (5.34) and 0.09 (6.66) for placebo†

Absolute percentage of naïve B cells over time[2]



		Baseline	Week 4	Week 8	Week 12
Joenja	n	20	19	19	16
Placebo	n	10	9	9	10

MEAN NAÏVE B-CELL LEVELS WITHIN NORMAL RANGE BY WEEK 4 AND MAINTAINED THROUGH WEEK 12 WITH JOENJA

*Cell surface markers used to distinguish naïve B cells on flow cytometry were CD19+, CD27-, and CD10-. Baseline is defined as the arithmetic mean of the baseline and day 1 values when both were available, and if either value was missing, the existing value was used.[1]
†The analysis excluded 2 patients from each treatment group due to protocol deviations, 5 Joenja patients and 3 placebo patients with ≥48% naïve B cells at baseline, 5 Joenja patients with no day 85 measurement, and 1 Joenja patient with no baseline measurement.[1]

Select Safety Information

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended. There is no recommended dosage for patients weighing less than 45 kg.

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Joenja safety results in the randomized, placebo-controlled pivotal study

Adverse reactions reported by ≥2 Joenja-treated patients and more frequently than placebo[1]

	Joenja (n=21) n (%)	Placebo (n=10) n (%)
Headache	**5** (24)	**2** (20)
Sinusitis	**4** (19)	**0**
Dermatitis atopic*	**3** (14)	**0**
Tachycardia†	**2** (10)	**0**
Diarrhea	**2** (10)	**0**
Fatigue	**2** (10)	**1** (10)
Pyrexia	**2** (10)	**0**
Back pain	**2** (10)	**0**
Neck pain	**2** (10)	**0**
Alopecia	**2** (10)	**0**

- No serious drug-related adverse reactions were reported[2]
- No patients withdrew due to an adverse drug reaction[2]
- The most common adverse reactions (>10%) were headache, sinusitis, and dermatitis atopic[1]

*Dermatitis atopic: including dermatitis atopic and eczema.[1]
†Tachycardia: including tachycardia and sinus tachycardia.[1]

Select Safety Information

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

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IN THE OLE STUDY

Additional safety results from an interim analysis

At the data cutoff

- Thirty-seven of 38 patients received Joenja 70 mg orally twice daily for at least 25 weeks; 66% were exposed for 96 weeks or longer[1]
- Median duration of Joenja treatment was approximately 2 years[1]
- Four patients had more than 5 years of Joenja exposure[1]
- In the open-label clinical trial, 5 patients (14%) experienced weight gain[1]

Most common AEs[5,8]	n
Upper respiratory tract infection	9
Headache	6
Pyrexia	6
Otitis externa	5
Weight increase	5
COVID-19 positive	5
COVID-19 negative	14

Distribution and grades* of AEs

- Thirty-two of 37 patients had ≥1 AE (333 AEs reported)[5]
- 78.4% were grade 1, 48.6% were grade 2, and 27% were grade 3[5]
- No grade 4 AEs were reported[5]
- One patient who had a grade 5 AE with significant baseline comorbidities suffered cardiac arrest resulting in death on day 879; investigator determined that the death was not related to study drug[5]
- No serious AEs were related to Joenja treatment[5]

AEs associated with Joenja

- The AEs reported as related to study drug were weight increase (3 patients), arthralgia (1 patient), hyperglycemia (1 patient), and decreased neutrophil count (1 patient)[5]

* CTCAE were used to determine AE grade. If CTCAE grading did not exist for an AE, the following definitions were used: 1, mild; 2, moderate; 3, severe; 4, life-threatening; 5, death.[8]

AE, adverse event; CTCAE, common terminology criteria for adverse events.

Select Safety Information

The most common adverse reactions (incidence >10%) were headache, sinusitis, atopic dermatitis, and weight gain.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

The open-label extension study is complete

Additional findings in the open-label extension study include[8]:

- Annual infection rates
- Immunoglobulin replacement therapy reductions and discontinuations

Not actual patients

Select Safety Information

Seven (33%) patients receiving JOENJA developed an absolute neutrophil count (ANC) between 500 and 1500 cells/microL. No patients developed an ANC <500 cells/ microL and there were no reports of infection associated with neutropenia.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Take a closer look at 6 patients from the open-label extension trial[9]

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See how Joenja treatment helped them over 6 years[9]

- These patient cases are from a retrospective analysis of 6 patients enrolled in the dose-finding trial and the open-label extension study. These patients were not enrolled in the pivotal efficacy and safety evaluation trial for Joenja. They represent the cohort of patients who have been on Joenja for the longest period of time[9]
- People with APDS suffer from a wide range of symptoms and response to treatment varies[7,10-12]
  - The clinical significance of these patient case observations is not known. Study limitations included variable timing of patient visits and treatment gaps up to roughly 1 year[9]
    - The clinician-reported questionnaire utilized was subject to recall and investigator bias, and the data captured were subjective by nature, which limited generalizability[9]
      - For all patients discussed, names and images were changed to protect their identity
      - Individual results may vary


REGULAR ARTICLE

blood advances

Check for updates

Long-term treatment with selective PI3Kδ inhibitor leniolisib in adults with activated PI3Kδ syndrome

Koneti Rao,[1] Elaine Kulm,[2] Jennifer Grossman,[3] David Buchbinder,[4] Hey Chong,[5] Jason Bradt,[6] Sharon Webster,[1] Anna Šedivá,[7] Dalm,[8] and Gulbu Uzel[1]

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Activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) is an inborn error of immunity that manifests as immune deficiency and dysregulation; symptoms include frequent infections and lymphoproliferation. In our dose-finding and phase 3 placebo-controlled trials, treatment with the selective PI3Kδ inhibitor leniolisib reduced lymphoproliferation and normalized lymphocyte subsets. Here, we present 6 years of follow-up from the 6 adult patients in the original dose-finding trial receiving leniolisib. We used data from the ongoing open-label extension study, which was supplemented at later time points by investigators, including health-related quality of life (HRQoL) assessed through a clinician-reported questionnaire. We observed improvements in HRQoL: 5 of 6 patients experienced an increase in physical capabilities and socialization, and a decrease in prescribed medications. Immune subsets improved in all patients; mean transitional B

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• Patients with APDS receiving leniolisib saw

Blood Advances is a registered trademark of the American Society of Hematology, Inc.

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Meet a 24-year-old male with APDS

whose progress was followed in the Joenja open-label extension study for 6 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

No longer struggling with school attendance, this patient has graduated from high school and an online university

He has a full-time job, can walk and drive without difficulty, and manages his own medical care

Select Safety Information

Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

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Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• Experienced fatigue from IRT infusions, anxiety, and difficulty coping with treatment burden • Hospitalized yearly for infections • Frequently prescribed antibiotics	• Stopped IRT infusions and fatigue got better • No hospitalizations • He had 7 infections, none of which returned • Only doctor he visits regularly is his immunologist
Clinical manifestations	• Low blood platelet counts • Damaged lung airways • Gastrointestinal issues and migraines	• Blood platelet count increased • Damaged lung airways did not get worse

Additional information[9]

Over the course of the trial, he received 14 prescription medicines, receiving 2 at year 6.

He experienced some side effects within the first 2 years of treatment that were mild and cleared up, including:

- Gastroparesis (slowed stomach emptying)
- Hypertriglyceridemia (too much fat in the blood)

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Meet a 27-year-old male with APDS

whose progress was followed in the Joenja open-label extension study for 6 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

No longer struggling with shortness of breath, this patient can go on extended walks and his outlook on life has improved noticeably

His family members saw differences in his physical capacities and noted that he has become more social

Select Safety Information

JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• Recurrent infections which occasionally required hospitalization • Infectious pneumonia • Discontinued IRT	• **No hospitalizations** • **Infectious pneumonia improved within a year, but infiltrates (substances that stay in the lungs, such as blood) were present**
Clinical manifestations	• Low body weight for his age • Low red and white blood cell counts • Damaged lung airways (due to infectious pneumonia)	• **Gained weight** • **Red blood cell count improved within 6 weeks of starting the extension trial** • **White blood cell counts improved through year 6** • **Damaged lung airways did not worsen and stabilized at year 6**

Additional information[9]

Although 5 medications were prescribed during the 6-year period, only 3 medications were taken regularly and he was down to 2 medications by year 6.

He experienced some side effects, including:

- Lyme disease in the first year, which was mild and cleared up
- Low white blood cell counts, which occurred shortly after the open-label extension trial started and resolved around year 2

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Meet a 31-year-old female with APDS

whose progress was followed in the Joenja open-label extension study for 6 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

After being homeschooled due to illness, she is continuing her education and now has a full-time job

Now with more energy, she takes aerobics classes and walks. She's traveled overseas to visit friends and manages her own medical care

Select Safety Information

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• Frequent nose and lower respiratory infections • Diagnosed with stage IV diffuse large B-cell lymphoma at 19 years old, and had a full remission before starting Joenja* * No known recurrence of lymphoma during the study period.	• She had 2 infections during the first 2 years of treatment
Clinical manifestations	• Low blood platelet counts • Low white blood cell counts	• Improved blood platelet counts • White blood cell counts were within normal limits by year 2 and remained normal

Additional information[9]

She has received 8 prescription medicines, receiving 3 at year 6, and visits her local doctor regularly.

She experienced some side effects, including:

- Hay fever, dental cavities, low white blood cell counts, and elevated liver enzymes
- These side effects were mild and cleared up

She also experienced some side effects that were more serious, but cleared up:

- Alanine aminotransferase (increase in liver enzymes)
- Reactive arthritis (which happened in year 4)

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Meet a 39-year-old male with APDS

whose progress was followed in the Joenja open-label extension study for 6 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

No longer affected by fatigue, he is able to participate in activities with his children

Within 2 months of starting treatment, he returned to work and socializes with colleagues after work

Select Safety Information

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

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Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• Recurrent respiratory tract infections • Continually taking antibiotics • Malignancy of the lymph nodes at age 20, with a full remission before starting Joenja	• Discontinued IRT at year 4 after 2 years of dose adjustments. After stopping IRT, he had 4 mild infections and the frequency and severity of infections declined • Periodic infections through year 4 • 2 confirmed cases of COVID-19, 1 in year 5 (with mild inflammation of nasal passages) and 1 in year 6 • He visits immunology-pulmonology clinic yearly, and remains under the care of his otolaryngologist. He sees them less frequently
Clinical manifestations	• Low blood platelet counts	• Low blood platelet counts resolved around the end of year 1

Additional information[9]

He received 14 prescription medications over 6 years. He received 2 at year 6 and no longer needed preventative antibiotics.

He experienced some side effects that were mild and cleared up, including hearing loss, nosebleeds, diarrhea, headache, inflammation at his bone-anchored hearing aid, jaw pain, sore throat, tickling cough, painful wrist, reflux esophagitis, and Fuchs heterochromic iridocyclitis (swelling and inflammation of the middle layer of the eye).

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Joenja® leniolisib

Meet a 23-year-old female with APDS

whose progress was followed in the Joenja open-label extension study for 5 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

She graduated from college and started working full-time as a schoolteacher

With her anxiety better controlled, she became more assertive, remained active, and expanded her circle of friends. She discontinued her anxiety medication and regularly visits her therapist

Select Safety Information

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended. There is no recommended dosage for patients weighing less than 45 kg.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja leniolisib

Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• Frequent throat and nose infections that required consistent antibiotics • Recurrent Epstein-Barr virus infections	• 12 infections occurred that were managed efficiently • Highest Epstein-Barr virus levels were clinically significant, but no infection was observed • Contracted COVID-19 but had mild symptoms (cough and runny nose) that resolved • She visits her immunologist and pulmonologist less frequently
Clinical manifestations	• Low white blood cell counts	• Low white blood cell counts resolved around the end of year 1

Additional information[9]

She received 17 prescription medications, receiving 7 at year 6, with pulmonary medications prescribed as needed.

She experienced some side effects that were mild and cleared up, including rash, sunburn, hair loss, oral ulcer, seborrheic dermatitis (dandruff, scaly patches, and/or inflamed skin), and temporomandibular joint pain (pain and discomfort in the jaw joint).

Weight gain and myalgia (muscle aches and pain) were unresolved side effects.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Meet a 32-year-old male with APDS

whose progress was followed in the Joenja open-label extension study for 6 years[9]

- In clinical studies, patients taking Joenja saw a reduction in lymph node size and an improvement in naive B-cell counts[1,2]
- Joenja has not been proven to impact quality of life

At the most recent check-in

He works a full-time, labor-intensive job. As symptoms improved, he experienced positive changes in his mood

He did not report any changes in shortness of breath, but he has airway damage from lymphoma chemotherapy in 2011

Select Safety Information

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Before and after starting Joenja treatment[9]

	Before study enrollment	Since starting Joenja treatment
Infections and treatment burden	• IRT • Repeated airway infections • Prophylactic antibiotics • Diagnosed with Hodgkin lymphoma at 11 years old and had a full remission before starting Joenja	• IRT dose was reduced • Frequency and severity of infections reduced with 8 relapses of respiratory infections • Prophylactic antibiotics stopped • Acute infections cleared more quickly • He is only monitored by his pneumologist and visits have decreased
Clinical manifestations	• Low white blood cell counts • Bronchiectasis • Rash, joint stiffness, and swelling • Gastrointestinal issues • Shortness of breath	• Low white blood cell counts resolved by year 2 • Bronchiectasis remained stable out to year 6 • Rash and joint pain resolved • Gastrointestinal conditions improved

Additional information[9]

He received 22 prescription medications, receiving 7 at year 6, 3 of which were deemed crucial.

He experienced some side effects that were mild and cleared up, including pruritus (itching), sore throat, seborrheic dermatitis (dandruff, scaly patches, and/or inflamed skin), diarrhea, productive cough (produces mucus), and anxiety.

He experienced some unresolved side effects, including COVID-19–associated mild dyspnea (shortness of breath), hepatopathy (abnormal liver), and hypercholesterolemia. The latter 2 side effects improved.

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APDS Assist—opening doors to help your patients with APDS move forward

APDS Assist provides comprehensive support for you and your patients every step of the way

APDS Care Coordinators

Here to help you navigate coverage, access, and other support options when you prescribe Joenja

ACEs*

Provide one-on-one support and educational resources for you and your patients

APDS Assist Specialty Pharmacists

Available to answer questions you and your patients may have about their Joenja medication

Ways APDS Assist can help your patients with APDS

Our commitment is to **get your patients started on Joenja as quickly as possible** while we work with your office to provide insurance support.

ACEs can help your patients connect with local and nationwide support groups and educational resources along their Joenja journey.

Access to Joenja is our priority. **Depending on the patient's insurance and other eligibility criteria, an APDS Care Coordinator can help identify support resources as needed.**

*Please note that ACEs do not offer medical or treatment advice or replace discussions with a physician.

Learn more about how APDS Assist can support your patients

ACE, APDS Clinical Educator.

Please see Important Safety Information on page 23. Before prescribing JOENJA, please read the full Prescribing Information.

Joenja® leniolisib

Indications and Usage

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

Important Safety Information

Verify pregnancy status in females of reproductive potential prior to initiating treatment with JOENJA.

JOENJA may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus and to use highly effective methods of contraception during treatment with JOENJA and for 1 week after the last dose. Additionally, advise women not to breastfeed during treatment with JOENJA and for 1 week after the last dose.

Live, attenuated vaccinations may be less effective if administered during JOENJA treatment.

JOENJA may cause hypersensitivity reaction(s), including anaphylaxis. Advise patients to discontinue JOENJA and to seek immediate medical attention if they develop any signs and symptoms of serious allergic reactions.

Use of JOENJA in patients with moderate to severe hepatic impairment is not recommended. There is no recommended dosage for patients weighing less than 45 kg.

Avoid co-administration of JOENJA with other medications known to be strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, or BCRP, OATP1B1, and OATP1B3 substrates.

The most common adverse reactions (incidence >10%) were headache, sinusitis, atopic dermatitis, and weight gain.

Seven (33%) patients receiving JOENJA developed an absolute neutrophil count (ANC) between 500 and 1500 cells/microL. No patients developed an ANC <500 cells/ microL and there were no reports of infection associated with neutropenia.

Before prescribing JOENJA, please read the full Prescribing Information.

References: 1. Joenja (leniolisib). Prescribing information. Pharming Healthcare, Inc; 2025. **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. doi:10.1182/blood.2022018546 **3.** Pharming Group. Pharming announces US FDA approval of Joenja® (leniolisib) as the first and only treatment indicated for APDS. Press release. March 24, 2023. Accessed January 9, 2026. https:// www.pharming.com/news/pharming-announces-us-fda-approval-joenja-leniolisib-first-and-only-treatment-indicated-apds **4.** Rao VK, Webster S, Šedivá A, et al. A randomized, placebo-controlled phase 3 trial of the PI3Kδ inhibitor leniolisib for activated PI3Kδ syndrome [supplementary appendix]. *Blood*. 2023;141(9):971-983. doi:10.1182/blood.2022018546 **5.** Rao VK, Kulm E, Šedivá A, et al. Interim analysis: open-label extension study of leniolisib for patients with APDS. *J Allergy Clin Immunol*. 2024;153(1):265-274.e9. doi:10.1016/j.jaci.2023.09.032 **6.** Rao VK, Webster S, Dalm VASH, et al. Effective "activated PI3Kδ syndrome"–targeted therapy with the PI3Kδ inhibitor leniolisib. *Blood*. 2017;130(21):2307-2316. doi:10.1182/blood-2017-08-801191 **7.** Data on file. Pharming Healthcare, Inc. **8.** Rao VK. Interim analysis of safety and hematological parameters of an ongoing long-term open-label extension study of investigational PI3Kδ inhibitor leniolisib for patients with activated PI3K delta syndrome (APDS). Deck presented at: The 64th American Society of Hematology (ASH) Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA. **9.** Rao VK, Kulm E, Grossman J, et al. Long-term treatment with selective PI3Kδ inhibitor leniolisib in adults with activated PI3Kδ syndrome. *Blood Adv*. 2024;8(12):3092-3108. doi:10.1182/bloodadvances.2023011000 **10.** Jamee M, Moniri S, Zaki-Dizaji M, et al. Clinical, immunological, and genetic features in patients with activated PI3Kδ syndrome (APDS): a systematic review. *Clin Rev Allergy Immunol*. 2020;59(3):323-333. doi:10.1007/s12016-019-08738-9 **11.** Deau M-C, Heurtier L, Frange P, et al. A human immunodeficiency caused by mutations in the PIK3R1 gene. *J Clin Invest*. 2014;124(9):3923-3928. **12.** Lucas CL, Chandra A, Nejentsev S, Condliffe AM, Okkenhaug K. PI3Kδ and primary immunodeficiencies. *Nat Rev Immunol*. 2016;16(11):702-714. doi:10.1038/nri.2016.93

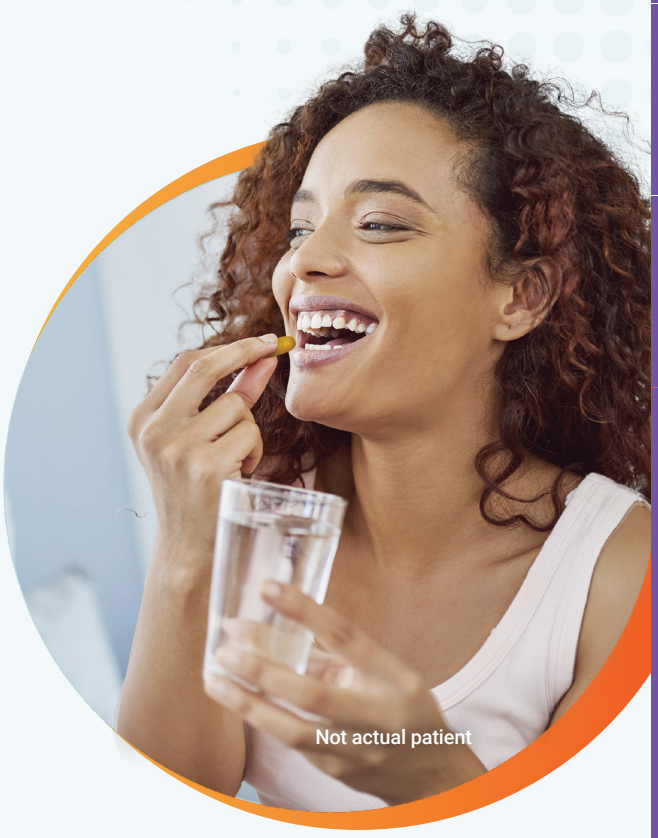
Joenja offers convenient, twice-daily oral dosing[1]

Joenja is taken every 12 hours and can be taken anywhere, with or without food

Recommended administration of Joenja

- 70 mg orally
- Twice daily, ~12 hours apart
- In adult and pediatric patients ≥12 years of age and weighing ≥45 kg*

Advise patients that if a dose is missed by more than 6 hours, they should wait and take the next dose at the usual time.



Adherence counseling may be beneficial for patients who remain on treatment

*There is no recommended dosage for patients 12 years of age and older who weigh less than 45 kg.

Select Safety Information

The most common adverse reactions (incidence >10%) were headache, sinusitis, atopic dermatitis, and weight gain.

Please see Important Safety Information on page 23.
Before prescribing JOENJA, please read the full Prescribing Information.

Pharming®

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Joenja® leniolisib