Healthcare Improvement Scotland | SMC Advice on new medicines

www.scottishmedicines.org.uk

Patient Group Submission Form

The Scottish Medicines Consortium (SMC) is committed to working in partnership with patient groups to capture patient and carer experiences, and use them to inform decision-making.

Before you make a submission

You are required to complete a patient group partner registration form before you make a submission. The registration form requests general information about your organisation. It only needs to be completed once (and annually updated) and should save you time with any further submissions to SMC. If you have not already completed a registration form, please do this before you make your submission.

You will find it helpful to read our *Guide for Patient Group Partners*, which gives details about the type of information you need to capture in the submission form. **Please read this before you make your submission and use it to help you complete each question.**

You can find the registration form and *Guide for Patient Group Partners* in the Public involvement and Making a submission sections of our website.

Contact us

If you have any more questions after reading the guide, the SMC Public Involvement Team can support you throughout the submission process. You can email us at: his.smcpublicinvolvement@nhs.scot

Please do not hesitate to get in touch, as we are here to help you.

Name of medicine:

Leniolisib (Joenja)

Indication: (what the medicine is used for)

Activated phosphoinositide 3-kinase delta syndrome (APDS)

Submission date:

18th August 2025

Name of organisation making submission:

Immunodeficiency UK

Who is the main contact for submissions to SMC?

Name:	Dr Susan Walsh
Position held in organisation:	CEO
Email address:	susan.walsh@immunodeficiencyuk.org
Phone number:	0800 987 8986
Postal address:	Registered address: Nightingale House, 46-48 East Street, Epsom, Surrey KT17 1HQ.

Summary of key points

Please summarise the key points of your submission which you would like to emphasise to SMC Committee – bullet points may be helpful.

(See P11 of *A Guide for Patient Group Partners*)

- Living with APDS can have a profound negative impact on the physical and mental health, and quality of life of those affected, their carers, and families.
- Health problems that have an extreme impact on quality of life were respiratory infections, chronic cough, autoimmune problems, enlarged lymph nodes, gastrointestinal problems, enlarged spleen, and hearing problems.
- The health of people with APDS deteriorates with age due to the accumulating damage to body organs caused by infections, autoimmunity, and inflammation.
- Current medicines manage the condition but do not address the underlying dysregulation of the immune system that is seen in APDS, which can result in a higher incidence of lymphoma, autoimmunity, and inflammatory problems.
- Leniolisib is the only targeted pathway-specific drug available for patients with APDS that helps address the underlying problems of the dysregulated, overactive immune system seen in APDS.
- Patients and carers reported significant health benefits of taking Leniolisib, including reducing lymph node size, reducing hospital admissions, improved energy levels, and a reduction in antibiotic use. The drug was well tolerated.
- The availability of Leniolisib will lead to a better quality of life for those affected, their carers, and families because it will help reduce their treatment burden.
- By helping to normalise the immune system in people with APDS, the drug will help improve long-term health outcomes, rather than them experiencing a progressive deterioration in health.
- The drug has the potential to decrease the chance of developing lymphoma in people with APDS, giving reassurance and hope for the future.

Please provide details of any individuals who have had a significant role in preparing your submission and who have an interest to declare.

(See P11 of *A Guide for Patient Group Partner*s)

300 words maximum

Dr Susan Walsh (SW), CEO of Immunodeficiency UK, prepared this submission.

SW has not received payments of any kind from the submitting company and is not a shareholder or director of the pharmaceutical company who have developed this medicine.

Please tell us how you gathered information about the experiences of patients and carers to help inform your submission.

(See P11 of *A Guide for Patient Group Partners*)

We gathered information through telephone conversations with affected individuals and their carers, developing patient stories (available on our website) and through a joint survey project with NICE. The survey involved the co-production of survey questions, NICE hosting the survey and ID UK highlighting the survey to people affected by APDS through our e-newsletter, social media and reach out to immunology specialist centres.

The survey attracted 14 responses: four people were directly affected by APDS and ten identified themselves as a carer, a family member or friend of the family. These included parents/family members of affected children under the age of 12 years. APDS is a life-long condition and based on mortality data, children affected by APDS are likely to reach 12 years of age and over so would be offered this treatment. Therefore, their opinion is valid, and their views must be taken into consideration.

1. How does this condition affect the day-to-day lives of people living with it?

(See P11 of *A Guide for Patient Group Partners*)

APDS is a rare immunodeficiency affecting approximately 40 people in the UK. It affects males and females and is an inherited disorder, although cases can occur without a family history. Mutations in the genes that control the production of the enzyme called PI3K delta occur, causing it to be overactive. PI3K delta is important for the normal development and proliferation of B and T-cells. In APDS, the B-cells and T-cells, are abnormal and can't recognise and attack bacteria and viruses to prevent infection (immunodeficiency). Other consequences are due to having an unregulated immune system. There is an increased risk of developing cancer (lymphoma) and having autoimmune and autoinflammatory complications. The current survival rate for people affected by APDS is 68% at age 40.

APDS has a significant burden on quality of life. It is challenging living with frequent infections and managing treatments. People directly affected by APDS may also be caring for affected children. There is a need to attend multiple appointments, often with different medical specialities and there is an associated financial impact of taking time off work and the cost of travel to the hospital. Those affected can require hospitalisation, and some people interviewed report spending months in hospital.

From our survey APDS symptoms that were reported as having a moderate or extreme impact on the lives of those affected by APDS were infections (74% of respondents), autoimmunity (66%), enlarged lymph nodes (54%), enlarged spleen (33%), lymphoma (18%), gastrointestinal problems (69%), hearing problems due to infections (66%).

Ten of 14 (71%) respondents reported that APDS impacted their mental health. Reasons were the burden of care, isolation and loneliness, and depression. 84% of respondents reported an extreme amount of concern. The vulnerability to COVID was mentioned specifically. 71% of respondents reported an extreme or moderate extent of worry about future health.
Pain and discomfort: Only 3 of 12 (25%) respondents reported little or no pain associated with having APDS. Four respondents reported extreme/moderate pain (scale 7-10, where 10 is extreme pain).

Impact of disease burden on patients and the NHS. The average number of outpatient visits over the last twelve months was 24.6 visits (n=13; range 2-200 visits). Average number of days in hospital over the last twelve months was 17.6 days (n=13; range 0 -80 days). These results highlight the impact on individuals and families in spent of time spent managing the condition and disruption to their lives through time spent in hospital.

'I'm struggling. I suffer from swollen lymph nodes, lymphoid polyps, enlarged spleen. I'm continuously out of breath'. Directly affected adult patient.

'Tough, exhausting, damaging, poorly, sick, irritable from coughing and all the infections, painful'. Directly affected adult patient.

'On my worse days I am in pain from weak joints, or headaches from sinus flare-ups, chest always hurts with coughing so hard. 'Directly affected adult patient.

'I'm terrified to go out'. 'Directly affected adult patient.

'Not easy, always on the edge, always following to the dot the doctors /CNS instructions/ admissions a lot in hospital and missing out on his childhood/not being able to do a lot due to extreme precautions of the condition/not being able to see a lot of the family, etc' Mum to an affected child.

2. How well do medicines which are currently available in NHSScotland help patients manage this condition? (See P12 of *A Guide for Patient Group Partners*)

500 words maximum

Agreed pathways of care are not available in the UK and there are no international guidelines for the management of APDS. The burden of treatment for those affected is high.

Medications are needed to prevent infections. These include taking prophylactic antibiotics (daily tablets), antivirals (daily tablets), and/or immunoglobulin therapy. Immunoglobulin (IG) therapy replenishes the immune system of people affected by APDS with antibodies to combat infections. IG therapy requires regular infusions (weekly or monthly) either by intravenous (mainly by hospital visits) or subcutaneous infusions (people are trained to self-administer at home). The side effects of taking antibiotics, including their impact on the gut microbiome and the development of antimicrobial resistance, are well-documented. Despite these medications and lifestyle changes to reduce the chances of infection, breakthrough infections may occur, resulting in hospital admissions. Furthermore, these treatments do not prevent the development of autoimmunity and lymphoproliferation.

Other medications manage other health complications of APDS by acting on the immune system to reduce the inflammation and autoimmune complications. These medicines suppress how the immune system works, so they may themselves result in people being more prone to infection. These medicines include steroids (daily tablets), which can cause stomach problems, fluid retention, and weight gain.

The medicine called Sirolimus (daily/tablets) is also used. The side effects include fever, nausea, stomach pains, fungal infections, diarrhoea, and headaches. A more serious complication can be infection of the brain.

Rituximab can be used to treat lymphoma. It is given by IV infusion in a hospital. It takes a couple of hours and needs two doses, with about two weeks between the doses.

Chemotherapy may also be used to treat cancer caused by APDS. The side effects of chemotherapy are well-documented and can include toxicity to unaffected tissues.

Have you been able to consult with patients who have used this medicine?

(See P12 of *A Guide for Patient Group Partners*)

Yes ☐X No ☐

3. Would this medicine be expected to improve the patient's quality of life and experience of care, and if so, how?

(See P12 of *A Guide for Patient Group Partners*)

500 words maximum

Leniolisib would improve and treat symptoms and disease complications and prevent its progression. It is a targeted treatment that corrects the overactive PI3K delta enzyme to help the immune system work in a more normal way. The treatment has fewer reported side effects than other medicines that are used to manage APDS. It is likely to reduce infection through improvements in how the immune system works and by improving or preventing autoimmune and autoinflammatory complications.

Six of 14 survey respondents had been treated with Leniolisib (one, only for one month).

Five survey respondents reported benefits:

- Reduction in use of antibiotics (n=2)
- Bringing bloods (blood counts) up (n=1)
- Increasing energy and appetite (n=1)
- Reducing hospital admissions (n=1)
- Reducing lymph nodes (n=1).
- Reduced coughing (n=1).

'xxx had been on antibiotics for 5 years with several hospital additions where so as starting treatment to date of 8 months xxx has only had 3 antibiotics and no hospital additions'. Mum to an affected child.

'*Reduced coughing, reduced the amount of need of antibiotics.' Person directly affected who is taking Leniolisib.*

'Reduced lymph nodes. More appetite and energy.' Person directly affected who is taking Leniolisib..

'100% would recommend the medication. As a parent you want what is best for your children, just having the chance to try a medication for a condition of this nature gives us just that little bit of hope that she will one day be healthier then what she is today and for that reason I would always recommend it.' Mum to an affected child (<12 years old) on Leniolisib.

4. What kind of impact would treating a patient with this medicine have on the patient's family or carers? (See P13 of *A Guide for Patient Group Partners*)

Treatment with leniolisib would improve quality of life by potentially decreasing the number of medications people take. People would have to attend fewer hospital appointments with potentially less time spent in hospital. It would help alleviate the stress and anxiety caused by living with APDS and allow people to live a more normal life. It would give relief to know that this therapy has the potential to alleviate autoimmune, inflammatory health problems and lymphoma development. These impacts would lead to less stress and anxiety within the family and for carers.

'Unable to work and socialise. Tired and lack of sleep. Difficult to maintain routine'.

'*Significantly, my mother had to give up work, family holidays had to be cancelled, hobbies for my siblings had to be cancelled, time my parents spent with my siblings was compromised as they were always with me.'*

5. Are there any disadvantages of the new medicine compared to current standard treatments? (See P13 of *A Guide for Patient Group Partners*)

500 words maximum

Overall, this treatment was reported as being well-tolerated. The medication is given daily as a tablet.

Three of the six survey respondents who were taking Leniolisib, reported side effects. This included headache (n=1), fatigue and diarrhoea (n=1), having mouth and tongue ulcers (n=1).

Another survey comment mentioned Leniolisib not tackling the tissue damage caused by infections before starting the Leniolisib. This highlights the need for improved diagnosis (most respondents reported a time to diagnosis of greater than three years).

6. Are there any potential equality issues that should be taken into account when considering this condition and medicine? (See P13 of *A Guide for Patient Group Partners*)

There will be people living in areas in Scotland not served by a specialist immunology service or there may be areas where referral to specialist services occurs less frequently due to staff shortages.

The Scottish Paediatric and Adult Infection and Immunology Network (SPAIIN), Annual Report 2023 / 24, highlighted that adult immunology services face a national staffing shortage, and concluded in its Risks and Issues closing statement:

'The adult immunology services face difficult challenges due to depleted staffing levels. There have been continued vacancies in NHS GGC, Grampian, and Tayside, meaning currently only two adult immunologists are covering all of Scotland. By July 2025 there will be only one trained Immunologist (in Edinburgh) covering the needs of a population of 5.6 million people.'

There are no known ethnic groups specifically affected by APDS, however, people with an ethnic background may find it difficult to find a suitably matched unrelated donor for a bone marrow transplant (BMT), a procedure which offers a potential cure for APDS. Information from the charity DKMS, who, with the help of other partners, help recruit stem cell donors, states that *'Patients from black, Asian or other minority backgrounds have a 20% chance of finding the best possible blood stem cell match from an unrelated donor, compared to 69% for northern European backgrounds.'* The availability of Leniolisib for those patients who are unable to find a donor for a BMT will help tackle this inequality.

'*XXX is unable to have a bone marrow transplant due to her ethnicity. I feel like if this medication was used for patients in the uk who are unable to get a transplant they would have more of a chance of living a more fulfilled quality of life.' Mum to a child affected by APDS.*

7. Is there any additional information you think may be useful for the SMC committee to consider? (Optional)

500 words maximum

Leniolisib could serve as a bridging treatment to the potential of a cure for APDS by a BMT by helping normalise the immune system, before a transplant. This could improve the success rates of this potential cure for APDS.

The use of Leniolisib may reduce the need for antibiotics and immunoglobulin replacement therapy.

8. Do you consent for a summary of your submission to be included in the Detailed Advice Document for this medicine?

Yes ☒ X No ☐

Thank you for completing this form.

The Public Involvement Team is available to advise you on how to complete this form to ensure the patient and carer experience is fully captured, to help inform the SMC decision making process.
If you have any questions about completing this form, please email it to:
his.smcpublicinvolvement@nhs.scot