NICE National Institute for Health and Care Excellence

Highly Specialised Technology Evaluation

Leniolisib for untreated activated phosphoinositide 3-kinase delta syndrome in people 12 years and over [ID6130]

Patient Organisation Submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on conditions and their treatment that is not typically available from other sources.

To help you give your views, please use this questionnaire with our guide for patient submissions.

You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type. [Please note that declarations of interests relevant to this topic are compulsory].

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 10 pages.

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About you

1.Your name	Dr Susan Walsh
2. Name of organisation	Immunodeficiency UK
3. Job title or position	CEO
4a. Brief description of the organisation (including who funds it). How many members does it have?	Immunodeficiency UK is a small, registered charity. We support people and families affected by primary and secondary immunodeficiency work through a range of activities including providing a helpline, medically reviewed information, patient events and hardship grants. Our mission is to work with patients, healthcare professionals and other relevant organisations to ensure those affected have the knowledge needed to manage their condition effectively and to ensure their health needs are understood and addressed by those involved in policy and delivery of healthcare. We currently have 1400 members. We are funded through community fundraising, trusts and foundations and pharmaceutical companies. The latter currently include Takeda, CSL Behring, LFB Ltd and Grifols. We have a published policy of how we work with pharmaceutical companies.
4b. Has the organisation received any funding from the company bringing the treatment to NICE for evaluation or any of the comparator treatment companies in the last 12 months? [Relevant companies are listed in the evaluation stakeholder list.]	None in the financial year 2023-2024. Immunodeficiency UK received funding in 2022 (£10,000) from Pharming for the development of five patient stories about the importance of an early diagnosis of PID (a mixture of PID conditions) for Rare Disease Day, addition of information on APDS (developed with our medical panel) and two patient stories about APDS, which are available on our website. This information carries the following statement 'This patient story was developed with the help of funding from Pharming to Immunodeficiency UK in 2022. Pharming had no contact with the author and no editorial control.' Over the last 12 months we have developed two other patient stories about APDS.
4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No. It is our policy not to accept funding from these sources.

5. How did you gather information about the experiences of patients and carers to include in your submission?	Through telephone conversations with affected individuals and their carers, developing patient stories 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. There was a formal survey collaboration agreement between ID UK and NICE. A report of the findings is found in Appendix 1. 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 it is important that their views are taken into consideration.
6. Living with the condition. **Impact on daily life and carers.**	The impact on APDS on daily life is significant. Respondents reported affects on family life (n=8), daily activities (n=7), ability to do hobbies (n=6), ability to socialise (n=5), ability to work (n=4). Of 13 respondents only four reported satisfaction with quality of life. 10 respondents reported an extreme or moderate amount of tiredness associated with having APDS. A major factor was the impact on the ability to attend school/educational activities (n=10), with 12 respondents reported significant days off. The range was several weeks each term, 1-4 years. *Recurrent infections, stunted growth, hearing issues impacting learning in school, ability to do physical sport, coordination issues.' Mum to an affected child.* *'Ear and lymph glands problems. Behind in schoolwork and development both socially and academically'. Mum to an affected child.* Ten respondents reported that APDS **impacted their mental health.** Reasons were burden of care, isolation and loneliness, depression, frustration. A major concern is worry of the risk of infection with 11/13 respondents reporting an extreme amount of concern. The vulnerability to COVID was mentioned specifically. Eleven respondents reported an extreme or moderate extent of worry about future health. *"Makes me feel so down and depressed, isolated". "Anxiety, uncertainty, having a condition no one understands."*

	Pain and discomfort: Only 3 of 12 respondents reported little or no pain associated with having APDS. Four respondents reported extreme/moderate pain (scale 7-10, where 10 is extreme pain). '*Xxxx struggles with discomfort in her ears, stomach and chest. She has had reoccurring lung collapse which would be more on a level of 10 for pain when this occurs.' Mum to an affected child.* *'I'm struggling. I suffer from swollen lymph nodes, lymphoid polyps, enlarged spleen. I'm continuously out of breath'. Patient directly affected by APDS.* *'Tough, exhausting, damaging, poorly, sick, irritable from coughing and all the infections, painful'. Adult patient directly affected by APDS.* Four respondents reported an impact of APDS on **carer's ability to work** with subsequent loss of income. *'I am unable to work due to xxx's condition as she is constantly getting infections and needs iv medication at least 2/3 monthly.' Mum to an affected child.* *'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.'* *"delayed development so not potty trained and can't wash himself".* *"2-3 physio sessions a day, medicine administrations, weekly subq infusions, frequent soiling as on antibiotics regularly".* **On living with APDS**: *'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'* Tough, exhausting, damaging, poorly, sick, irritable from coughing and all the infections, painful.'

	"Tiredness and chest infections are a major concern as well as the mental anxiety the condition causes." **Symptoms which were reported as having an extreme impact** were bronchiectasis, respiratory infections, chronic cough, infections, autoimmunity problems, enlarged lymph nodes, gastrointestinal problems, enlarged spleen and hearing problems. **Impact of disease burden on patients and the NHS.** 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 (Table 3; Appendix 1).

Current treatment of the condition in the NHS

7. What do patients or carers think of current treatments and care available on the NHS?	A wide range of treatments are used in APDS. This was reflected in the survey data (table 2, Appendix 1). The burden of treatment is high but was variable within the respondents (Appendix 1), reflecting the differences in how having the condition APDS can impact on patients. Three respondents were taking 5 treatments, one patient had four treatments, one had 3 treatments, four had 2 treatments and five had 1 treatment (immunoglobulin only). All survey respondents reported they or the patient were currently on medication: 12 were on immunoglobulin therapy, 9 prophylactic antibodies, 5 prophylactic anti-virals, 6 immunosuppressants and 3 were taking Sirolimus. Respondents reported symptoms that are not addressed by current treatments (Page 13, Appendix 1).

8. Is there an unmet need for patients with this condition?	APDS is an ultra-rare disease with no approved therapies and is considered by the clinical community as a serious life-threatening condition. It is our understanding that there are 41 people in the UK with APDS. There is an unmet need for treating the consequences of having a dysregulated immune system which Leniolisib can address. Leniolisib is a targeted therapy and represents a 'first of its kind' treatment to address the fundamental cause of immune dysfunction in people with APDS by acting specifically on the overactive PI3K delta kinase. The drug Leniolisib can help address autoimmunity and malignancy (lymphoma) which occur in APDS. Current therapeutic options such as antibiotics, immunoglobulin therapy only manage the symptoms of this immunodeficiency and help with infections. Having access to Leniolisib could result in reduced hospital admissions, lower use of antibiotics, and health improvements may translate into ability to have a full education and working life and improved quality of life. All (5 of 5) survey responses thought that everyone should have access to Leniolisib and all (8 of 8) survey respondents would recommend Leniolisib to other patients.

Advantages of the technology

9. What do patients or carers think are the advantages of the technology?	Six of 14 respondents had been treated with Leniolisib (one, only for one month), with one respondent saying they were unsure if they taking this medication. 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 hospitial additions'. Mum to an affected child.* '*Reduced coughing, reduced the amount of need of antibiotics.' Person directly affected who is taking Lenio.* *'Reduced lymph nodes. More appetite and energy.' Person directly affected by APDS.* *'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) and who is on Leniolisib.* HSCT is the only curative option for APDS. Leniolisib could act as a bridging treatment to HSCT by stabilising the immune system and preventing organ damage that can decrease the chances of a successful outcome (see section 12).

Disadvantages of the technology

10. What do patients or carers think are the disadvantages of the technology?	Three of six survey respondents who were taking Leniolisib reported drawbacks. This included the possible side effects listed (N=1), having mouth and tongue ulcers for the first time (N=1), and Leniolisib not tackling the infection damage that was caused before starting the Leniosilib (N=1), highlighting the need for improved diagnosis (the majority of respondents reported a time to diagnosis of greater than three years).

Patient population

11. Are there any groups of patients who might benefit more or less from the technology than others? If so, please describe them and explain why.	The survey results (Appendix 1) indicate that the effects of having APDS can vary between individuals. This is not a surprise as clinicians tell us that some patients are more severely affected than others. It is widely known that the same genetic abnormality can cause different effects in different people. This variability may arise from complicated interactions between genes, and other factors related to the patient and his or her environment. The fact that gene defects can have such variable effects has been known for many years. This variation of severity between individuals is also reflected in the survey findings on treatments taken to manage symptoms and outpatient and in hospital stays. Clinicians would be able to select the patients who would benefit most and develop guidelines for the treatment of APDS to ensure all those affected get the best standard of care.

Equality

12. Are there any potential equality issues that should be taken into account when considering this condition and the technology?	There are no specific ethnic groups that are affected by APDS however people with an ethnic background may find it difficult to find a suitably matched unrelated donor for HSCT. 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 have HSCT 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.

Other issues

13. Are there any other issues that you would like the committee to consider?	Leniosilib could be a bridging treatment to the potential of a cure by HSCT by normalising the immune system in APDS.

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Key messages

14. In up to 5 bullet points, please summarise the key messages of your submission.	• Living with APDS can have a profound impact on physical, mental health, daily and family life and quality of life of those affected, their carers,and families. • Patients and carers reported significant health benefits of taking Leniolisib including reducing lymph nodes, reducing hospital admission, improved energy levels and reduction in antibiotic use. • Leniolisib may reduce inequality by improving health of people who are unable to benefit from HSCT because of the lack of tissue-matched stem cell donors. • There is overwhelming patient support for the availability of Leniolisib for the treatment of APDS.

Thank you for your time.

Please log in to your NICE Docs account to upload your completed submission.

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