NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of leniolisib within its marketing authorisation for untreated activated phosphoinositide 3-kinase delta syndrome in people 12 years and over.

Background

Activated phosphoinositide 3-kinase delta syndrome (APDS) is an inherited disorder where people are unable to fight infections because their immune system does not work properly. It is caused by defects in the genes that control the production of a protein called phosphoinositide 3-kinase delta. The defects make phosphoinositide 3-kinase delta overactive, interfering with the normal development of B and T cells and their ability to fight infections.[1] The main symptoms usually occur in the first two years of life and include ear, sinus and respiratory tract infections; herpes; gastrointestinal symptoms; chronic cough; enlarged tonsils, lymph nodes or spleen; autoimmune and autoinflammatory disorders; low number of blood cells; lymphoma; and failure to grow and develop normally.[1,2]

The prevalence of APDS is estimated to be approximately 0.01 in 10,000 people in the European population.[3]

There are currently no licensed targeted treatments for APDS. Standard management of people with ADPS depends on their individual symptoms. Infections are treated with antibiotics and antivirals. Immunoglobin replacement therapy can be used for people with poor antibody production. Haematopoietic stem cell transplantation can be used as a curative option for some people with severe APDS or who have developed a lymphoma. Steroids, sirolimus or rituximab can be used to modify the response of the immunity system for people with autoimmunity such as people with low numbers of blood cells, kidney disease, arthritis, or inflammation of the colon.[1]

The technology

Leniolisib (brand name unknown, Pharming Group) does not currently have a marketing authorisation in the UK for ADPS. It has been studied in a phase II/III clinical trial of people with APDS genetic PI3K delta mutation.

Intervention(s)	Leniolisib
Population(s)	People with activated phosphoinositide 3-kinase delta syndrome 12 years and older.
Comparators	• Established clinical management without leniolisib.
Outcomes	The outcome measures to be considered include: • Percentage of naïve B cells • Reduction in lymph node size • Reduction in spleen volume • Fatigue • Mortality • Disease severity • Adverse and serious effects of treatment • Health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. • Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	None.
Related National Policy	NHS England, 2013/2014. NHS Standard Contract For Specialised Immunology (all ages), Section B Part 1 - Service Specifications. B09/S/a

	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Are any of the following treatments used to treat APDS in the NHS as standard practice?

- Haematopoietic stem cell transplantation
- Immunoglobulin Replacement Therapy (IRT)
- Steroids
- Mammalian target of rapamycin (mTOR) inhibitors
- Rituximab
- Antimicrobials

How many people have APDS in England, and how many would be offered leniolisib?

Are the genetic tests to establish the correct diagnosis of APDS a standard practice in the NHS?

Where do you consider leniolisib will fit into the existing care pathway for APDS?

Are the outcomes listed appropriate? Are there any other outcomes that should be

included in the scope?

Is there any data/evidence available on how long people live with APDS/the impact of APDS on quality of life?

Are there any subgroups of people in whom leniolisib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Do you consider that the use of leniolisib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which leniolisib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

References

1.International Patient Organisation for Primary Immunodeficiencies (IPOPI). APDS- Activated PI3K Delta Syndrome. Accessed September 2022.

2. Immune Deficiency Foundation. Learn about APDS. Accessed September 2022.

3. European Medicines Agency. EU/3/20/2339: Orphan designation for the treatment of activated phosphoinositide 3-kinase delta syndrome. Accessed September 2022.