NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

Remit/evaluation objective

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

Background

Activated phosphoinositide 3-kinase delta syndrome (APDS) is a rare 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] Living with APDS can negatively affect the quality of life due to frequent infections, hospitalisations, and fatigue.

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 immune 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 (Joenja, Pharming) 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 12 years and over.

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: • Infections • Lung function • Fatigue • Mortality • Disease severity • Immunophenotype measures (lymphocyte counts, immunoglobulin levels, cytokine and chemokine levels) • Immune system function (lymph node size, spleen and liver volume size, use of immunoglobulin replacement therapy) • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
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)

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.