NICE National Institute for Health and Care Excellence

# Highly Specialised Technologies (HST) criteria checklist

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

**Introduction:** The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable.

**Key – does the technology meet the criteria? Please use the colour key to advise if the technology meets the criteria**

| | |
|---|---|
| Met | There is clear and strong evidence that this criterion is met |
| Not met | There is no evidence or limited evidence that the criterion is met. |

**MA wording:** [redacted]

| Number | Criterion | Description of how the technology meets the criteria | Does the technology meet the criteria? |
|---|---|---|---|
| 1. | The condition is very rare defined by 1:50,000 in England | • The EMA has given this indication an orphan designation, estimating the prevalence across Europe to be 0.01 per 10,000 people (or 0.05 per 50,000).<br>• TSOP noted ADPS has been considered a primary immunodeficiency. Clinical manifestations of PID vary widely but APDS shows similarities to other PIDs which are much more prevalent than APDS. Primary immunodeficiencies are rare diseases, with a reported prevalence of between 1 in 16 000 and 1 in 50 000. | Met |

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| | | TSOP considered the comments from stakeholders about this being a more severe PID, and should be considered one of the combined immunodeficiencies. It was highlighted that genetic testing is standard practice in the UK, and that a specific PID diagnosis must be established, this means that APDS is a distinct and well-defined condition. | |
| 2. | Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications | • When applying the incidence rate above to the total England population (all ages) of 56 million, this would mean 56 people could be eligible to receive leniolisib. This figure is likely to be lower because only people aged 12 and over would be eligible.<br>• Since its first description in 2013, over 200 patients have been reported worldwide.<br>• The company estimated that there would be no more than 60 people with APDS in England who would be offered leniolisib.<br><br>The TSOP panel concluded that this criterion was met but noted potential for misdiagnosis and that prevalence could be likely underestimated. | Met |
| 3. | The very rare condition significantly shortens life or severely impairs its quality | • APDS is a rare, heterogeneous, progressive disease that can lead to end-organ damage and early mortality. Not everyone with APDS is affected to the same extent; living with APDS varies on an individual level.<br>• Most people manifest within 2 years of life but the median age at APDS diagnosis is around 16 years.<br>• The main symptoms include repeated bacterial and viral respiratory tract infections; gastrointestinal disease; chronic cough; enlarged tonsils, lymph nodes or spleen; autoimmune and autoinflammatory | **Met** |

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| | | disorders; low number of blood cells; lymphoma; and failure to grow and develop normally.<br>• Living with APDS can be a significant burden, and negatively affect the quality of life due to frequent infections, hospitalisations, and fatigue.<br>• Children with diseases that affect their immune systems are also less able to cope with social situations, may miss significant amounts of schooling, and are more likely to suffer from anxiety and depression.<br><br>The TSOP panel considered that is reasonable to conclude that APDS reduces the quality and length of life. There is uncertainty about the extent that this would apply for all people with ADPS because of the heterogeneity of this condition and the paucity of available evidence. The panel considered comment from stakeholders that there is a high incidence of lymphomas and lung disease. Cumulative risk of lymphoma and mortality is very high - estimated to be 78% at the age of 40 years. Although there is some heterogeneity with the condition, the TSOP panel agreed that quality of life is severely impacted for the majority of people. This criterion is met. | |
| 4. | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | • There are no licensed or NICE-approved treatment options available for APDS.<br>• The heterogeneous nature of APDS, many people require multiple lines of treatment to control their symptoms. These people may experience multiple treatment failures.<br>People receive non-specific immunosuppressive and symptomatic treatments. Clinical experts at the scoping workshop explained that the treatment people receive depends on their presentation at diagnosis and there are several treatments available. The most common treatment option includes antibiotics for repeated infections. | **Met** |

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|---|---|---|---|
| | | However, some people may require immunoglobulin replacement therapy if they have poor antibody formation and the availability of a treatment like leniolisib might reduce the need for costly immunoglobulin replacement therapy. Drugs such as sirolimus and rituximab are used for people with autoimmune diseases. People with severe APDS and lymphoma receive hematopoietic stem cell transplants (HSCT) and is potentially curative. However, HSCT is mainly reserved for children because risks with HSCT increase with age.<br><br>The TSOP panel acknowledged that:<br><br>• There are no licenced or NICE-approved treatment options available for APDS. People rely on treatments based on presentation and there are unmet needs for people with APDS.<br><br>• Leniolisib is likely reduce lymph node size and increase the percentage of naïve B cells in people with APDS (met co-primary endpoints)<br><br>• The clinical profile of people with APDS varies in a spectrum from mildest forms to severe life-threatening, treatment options may also vary from simple observations to HSCT.<br><br>The panel acknowledged that there are no satisfactory treatment options. TSOP agreed that this criterion was sufficiently met. | |