NICE National Institute for Health and Care Excellence

Highly Specialised Technologies (HST) criteria checklist

Maralixibat for treating cholestatic disease in Alagille Syndrome [ID3941]

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. For more information, please see section 7 of NICE health technology evaluation topic selection: the manual

Key – Please use the colour key to advise if the technology meets the criteria

Met	There is clear and strong evidence that the criterion is met.
Unclear	There is some evidence, or the evidence available is unclear that the criterion is met.
Not met	There is no evidence or limited evidence that the criterion is met.

Expected MA wording: Treatment of cholestatic disease in patients with Alagille Syndrome aged 1 year and older

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	Incidence at birth (birth prevalence) is estimated between 1 in 30,000 and 1 in 70,000 live births[2,3,4]. Estimates prevalence vary between 1 in 30,000 and 1 in 100,000[1]. This leads to a prevalence of 565 to 1,885 in England (using 2020 mid-year England population estimate, 56,550,000)[5].	Unclear

Number	Criterion	Description of how the technology meets the criteria	Does the technology meet the criteria?
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	There were 610,505 live births in England in 2019[6], so the incidence equates to between 9 and 20 (610,505/30,000 or 610,505/70,000) live births each year in England. Estimates of prevalence vary between 1 in 30,000 and 1 in 100,0001, leading to a prevalence of 565 to 1885 in England. The company estimated a prevalence of 190-440 under 18 in England. Clinicians at the scoping workshop indicated that all patients over and under 18 with cholestasis would be eligible for treatment and that treatment is expected to be lifelong. The incidence and prevalence may be underestimated because Alagille syndrome may be undiagnosed or misdiagnosed due to the varying clinical presentation[7]. Experts at the workshop estimated that the incidence and prevalence could be around 10% higher. Based on 2019 Hospital Episode Statistics (HES) data and NIHR 2021 report, costing comments (Feb 2021) estimated that about 70 people with cholestatic liver disease have Alagille syndrome. However, the HES recording was based on Q44.7 of ICD-10 code which includes but is not specific to Alagille syndrome, and HES data only recorded patients presenting to the NHS with finished consultant episodes.	Not met
3.	The very rare condition significantly shortens life or severely impairs its quality	Likely met for all patients that would receive treatment, although the clinical presentation of Alagille syndrome is very variable. People who are diagnosed in infancy are often diagnosed because of liver disease causing symptoms from the first few months of life. Liver disease in Alagille syndrome, if present, may range in severity from jaundice or mild cholestasis to severe, progressive liver disease that can potentially result in liver failure.[7]	Met

Number	Criterion	Description of how the technology meets the criteria	Does the technology meet the criteria?
		At the scoping workshop, clinical and patient experts explained that the pruritus associated with cholestasis in Alagille syndrome severely impairs the quality of life, impacting on all aspects of the child's life, including sleep, appetite, education, relationships, and ability to take part in everyday activities. This has an impact on the caregivers and the wider family. The disease can stabilise and symptoms may improve, but almost 60% of patients will have a liver transplant before 18 years of age[11] Currently there is no way to predict whether liver symptoms in infancy will resolve or progress[9].	
4.	There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.	Current treatment for Alagille Syndrome focuses on alleviating symptoms. Treatments to reduce itching may include ursodeoxycholic acid, cholestyramine, rifampicin, naltrexone, ondansetron, SSRIs and antihistamines such as chlorphenamine[10]. Nutritional supplements and high-calorie diets are important for many people with Alagille Syndrome, because of the difficulties cholestasis causes with absorbing fats and nutrients[9]. If Alagille Syndrome does not respond to drug and dietary therapies, a partial biliary diversion may be carried out[7] although this is rare in the UK. At the scoping workshop, clinical experts explained that liver transplant is the only treatment for the underlying liver failure. Almost 60% of patients will have a liver transplant before 18 years of age[11].	Met

References

1 Diaz-Frias J, Kondamudi NP. Alagille Syndrome. [Updated 2021 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK507827.

2 Leonard, L.D. *et al.* (2014) 'Clinical utility gene card for: Alagille Syndrome (ALGS)', *European Journal of Human Genetics*, 22(3).

3 Kamath, B. *et al.* (2003) 'Consequences of JAG1 mutations', *Journal of Medical Genetics*, 40(12), pp. 891–895. doi:10.1136/jmg.40.12.891.

4 MedLine Genetics (2021) *Alagille syndrome: MedlinePlus Genetics*. Available at: https://medlineplus.gov/genetics/condition/alagille-syndrome (Accessed December 2021)

5 Office for National Statistics (2021) Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland. Available at https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland Accessed December 2021.

6 Office for National Statistics (2020) Births in England and Wales: summary tables. Available at https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/datasets/birthsummarytables. Accessed September 2021.

7 National Organization for Rare Disorders. Alagille Syndrome. Available at https://rarediseases.org/rare-diseases/alagille-syndrome/. Accessed September 2021.

8 Orphanet. Alagille Syndrome. Available at https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=52. Accessed September 2021.

9 Genetic and Rare Diseases Information Center. Alagille Syndrome. Available at https://rarediseases.info.nih.gov/diseases/804/alagille-syndrome. Accessed September 2021.

10 Children's Liver Disease Foundation. Alagille Syndrome. Available at https://childliverdisease.org/liver-information/childhood-liver-conditions/alagille-syndrome/ Accessed September 2021.

11 Vandriel, S, Liting, L et al. (2020). Clinical Features and Natural History of 1154 Alagille Syndrome Patients: Results from the International Multicenter GALA Study Group.