NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pegzilarginase for treating arginase-1 deficiency

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of pegzilarginase within its marketing authorisation as a treatment for arginase-1 deficiency.

Background

Arginase-1 deficiency (ARG1-D) is a urea cycle disorder in which the body is unable to process arginine, an amino acid used to build protein. It is a metabolic condition caused by mutations in the ARG1 gene, inherited from both parents. A lack of the enzyme arginase in the liver and red blood cells leads to excess nitrogen stored in the form of ammonia (hyperammonaemia) in the blood and arginine (hyperarginemia) in the blood and cerebrospinal fluid.[1]

ARG1 deficiency is a severe condition, presenting in early childhood and symptoms include developmental delay, stiffness, vomiting and seizures. Disease progression is characterised by severe spasticity, inability to walk, complete loss of bowel and bladder control and severe intellectual disability.[1]

It is estimated that ARG1 deficiency occurs in about 1 in 300,000 to 1,000,000 births.[1] However, newborn screening for ARG1 deficiency is not routinely screened for at birth and arginine levels may be within the normal range in the first days of life.[2] It is estimated that the UK population prevalence of ARG1 deficiency is 0.58 cases per million.[3]

Treatment is focused on lowering arginine levels and preventing the build-up of ammonia in the blood. Management includes frequent blood tests to check arginine levels, restricting dietary protein and using oral nitrogen-scavenging medicines such as sodium benzoate and/or sodium phenylbutyrate/phenylacetate for chronic or recurrent hyperammonaemia. Amino acid formulas, multivitamins and calcium supplements may be used.[1,4]

The technology

Pegzilarginase (Loargys, Immedica Pharma) has a marketing authorisation in the UK for ARG1 deficiency, also known as hyperargininemia, in adults, adolescents and children aged 2 years and older.

Intervention	Pegzilarginase
Population	People with arginase-1 deficiency aged 2 years and older

Comparators	Established clinical management without pegzilarginase (including dietary protein restrictions, essential amino acid supplementation and/or the use of ammonia scavengers)
Outcomes	The outcome measures to be considered include: • plasma arginine concentration • level of ornithine and guanidino compounds • mobility • adaptive behaviour • neurocognitive function • adverse 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	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 62. Department of Health (2016) NHS outcomes framework 2016 to 2017: Domains 1–5. NHS England (2013) NHS standard contract for metabolic disorders (adults) E06/s/a. NHS England (2013) NHS standard contract for metabolic disorders (laboratory services) E06/s/c

References

1. National Organization for Rare Disorders (2023) Arginase-1 deficiency. Accessed January 2024.

2. Häberle J, Burlina A, Chakrapani A, et al. (2019) Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. Journal of inherited metabolic disease. 42(6):1192-230.

3. Catsburg C, Anderson S, Upadhyaya N, et al. (2022) Arginase 1 deficiency: using genetic databases as a tool to establish global prevalence. Orphanet J Rare Dis. 2022 Mar 2;17(1):94.

4. Genetic and Rare Diseases Information Center (2021) Arginase deficiency. Accessed January 2024.