NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pegzilarginase as an add-on treatment for arginase-1 deficiency

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pegzilarginase within its marketing authorisation as an add-on 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 presents in early childhood and symptoms may include developmental delay, stiffness, vomiting and seizures. If untreated, the condition progresses to 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, the sensitivity of newborn screening for ARG1 deficiency is unknown because 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) is a novel, recombinant modified form of the human enzyme arginase 1 that metabolises arginine to ornithine and urea, thereby lowering blood arginine levels. Pegylation improves blood circulation times and cobalt substitution increases the catalytic activity of arginase 1. It is administered as an intravenous infusion or subcutaneous injection.

Pegzilarginase does not currently have a marketing authorisation in the UK for ARG1 deficiency. It has been studied in a clinical trial compared with placebo in children and adults with ARG1 deficiency.

Intervention	Pegzilarginase
Population	People with arginase-1 deficiency
Subgroups	If the evidence allows, the following subgroups will be considered: • age (children and adults)
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 • 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

Questions for consultation

What is the prevalence of arginase-1 deficiency in England?

Is it routine to perform a genetic test in the NHS to confirm diagnosis of arginase-1 deficiency?

Where do you consider pegzilarginase will fit into the existing care pathway for arginase-1 deficiency?

Would pegzilarginase be a candidate for managed access? Would hyperammonemic episodes/crises be considered a key outcome measure?

Do you consider that the use of pegzilarginase 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 pegzilarginase 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. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-tehnology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. National Organization for Rare Disorders (2019) Arginase-1 deficiency. Accessed December 2022.

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 December 2022.