FDA Grants Accelerated Approval to Pegzilarginase for Arginase 1 Deficiency

Key Takeaways

- FDA accelerated approval covers hyperargininemia in ARG1-D for adults and children 2 years and older, as adjunct to dietary protein restriction, with ongoing approval contingent on confirmatory postmarketing outcomes.
- PEACE randomly assigned patients 2:1 to weekly pegzilarginase vs placebo plus standard management, demonstrating marked plasma arginine reductions at 24 weeks and normalization in 90.5% of treated patients.
- Mobility measures improved with pegzilarginase, including Gross Motor Function Measure and 2-Minute Walk Test, with benefits maintained through an additional 24 weeks of treatment exposure.
- ARG1-D is an ultrarare urea cycle disorder with neuroprogressive morbidity driven by arginine/toxic metabolite accumulation; pegzilarginase directly addresses the enzyme deficit beyond symptomatic and dietary strategies.

FDA clears pegzilarginase-nbln enzyme therapy for ARG1-D, cutting toxic arginine and boosting mobility.

The FDA has granted accelerated approval of pegzilarginase-nbln (Loargys; Immedica Pharma), an arginine-specific enzyme therapy for the treatment of hyperreninemia in adult and pediatric patients 2 years and older with arginase 1 deficiency (ARG1-D). The drug is indicated to be used alongside dietary protein restriction.[1]

“Today’s FDA accelerated approval of [pegzilarginase] is an important milestone for Immedica and for patients and families affected by ARG1-D in the US,” Anders Edvell, CEO of Immedica, said in a news release. “This outcome is the result of collaborative efforts across the entire ARG1-D community, including patients, advocacy groups, researchers, and clinicians. We are proud to be able to deliver a treatment option for patients and families who have long awaited progress.”[1]

Clinical Trial Supporting Pegzilarginase Accelerated Approval

The approval is primarily supported by data from the multicenter, randomized, double-blind, placebo-controlled phase 3 PEACE trial (NCT03921541), which demonstrated significant reductions in plasma arginine levels.[1,2]

In the study, patients with ARG1-D were randomly assigned 2:1 to receive once-weekly pegzilarginase or placebo in addition to individualized standard disease management. At 24 weeks, pegzilarginase produced a significant reduction in plasma arginine levels compared with placebo, lowering geometric mean levels from 354.0 to 86.4 μmol/L and normalizing plasma arginine in 90.5% of treated patients, whereas no normalization was observed in the placebo group.[3]

Treatment with pegzilarginase was also associated with clinically meaningful improvements in functional mobility, as assessed by the Gross Motor Function Measure and the 2-Minute Walk Test, with benefits sustained through an additional 24 weeks of exposure. The therapy was generally well tolerated, with adverse events mostly mild to moderate in severity and transient.[3]

Understanding ARG1-D and the Role of Pegzilarginase

ARG1-D is an ultrarare, inherited metabolic disorder characterized by the accumulation of plasma arginine and toxic metabolites due to a defect in arginine metabolism. Patients are typically diagnosed in late infancy or early childhood and may experience spasticity, seizures, developmental delay, intellectual disability, and early mortality. Although ARG1-D is a subtype of urea cycle disorders, hyperammonemia is generally less severe than in other forms.[1]

ARG1-D affects an estimated 250 individuals in the US, and the current standard of care focuses on symptom management and includes dietary protein restriction, arginine-free amino acid supplementation, and the use of nitrogen scavenging agents when needed.[1]

Pegzilarginase is a novel recombinant human arginase-1 enzyme that rapidly and sustainably lowers plasma arginine and its toxic metabolites, making it the first therapy proven to reduce plasma arginine levels. It is approved under the FDA's accelerated approval pathway for the treatment of hyperargininemia in adults and children 2 years and older with ARG1-D, in conjunction with dietary protein restriction, with continued approval contingent on confirmation of clinical benefit in a postmarketing trial.[1]

Pegzilarginase is now marked as the first and only treatment that directly targets persistently elevated plasma arginine, the primary driver of ARG1-D.[1]

"Until now, the care of patients with ARG1-D has been limited to symptomatic management and strict dietary control. The accelerated approval of [pegzilarginase] offers a fundamentally new approach that addresses the enzyme deficiency itself. Since persistently elevated arginine and its metabolites have been reported to be the proximal or direct driver of disease progression, this is a major advancement in metabolic medicine." Stephen Cederbaum, MD, professor emeritus of human genetics at UCLA, said in the news release.[1]

REFERENCES

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