A Progressive, Debilitating, Inherited Metabolic Disease[1-3]

ARGINASE 1 DEFICIENCY

Arginase 1 Deficiency (ARG1-D) is a urea cycle disorder, resulting from mutations in the *ARG1* gene that encodes the arginase-1 enzyme (ARG1).[3]

- In the absence of a functional enzyme, arginine and arginine-related metabolites accumulate and are associated with neuromotor pathology, leading to significant morbidity and early mortality[1,3-6]

Verify high levels of arginine, which cause the manifestations of ARG1-D, with routine testing[2,3]

DIAGNOSING ARG1-D

Key manifestations[3,6-11]

- Progressive spasticity
- Aversion to protein
- Impaired mobility/gait

AND/OR

Medical history[3,6,7,10,12,13]

- Atypical cerebral palsy (CP)
- Idiopathic spasticity
- Hereditary spastic paraplegia (HSP) with unknown etiology
- Episodes of hyperammonemia

Other manifestations may include:

Neurological[3,6-11]

- Seizures
- Speech impairment
- Intellectual disability

Developmental[3,6,7,9,10,14,15]

- Global developmental delay
- Behavioral abnormalities
- Learning disabilities

Functional[3,6-10]

- Lower and upper limb spasticity
- Tiptoe walking
- Growth impairment

ELEVATED LEVELS OF ARGININE ARE THE HALLMARK OF ARG1-D[1,13,16]

Evaluate the results of a plasma amino acid panel for high levels of plasma arginine (>115 µmol/L)[4]

If high levels of plasma arginine are present, confirm with a **genetic test*†**

Newborn screening for ARG1-D is not routinely performed and testing is inconsistent, causing potential delays in diagnosis.[12,17]

Newborn screening for ARG1-D is **NOT** available in the following 13 states[17]:

- Alabama
- Arizona
- Arkansas
- Florida
- Kansas
- Maryland
- Montana
- Nebraska
- South Carolina
- Virginia
- Washington
- West Virginia
- Wisconsin

THINK ARGININE™

Order a NO-CHARGE sponsored plasma amino acid panel and genetic test*† now at ThinkArginine.com

*Due to the genetic heterogeneity of *ARG1* genotypes, not all mutations causing ARG1-D have been identified.
†Please see reverse side for plasma amino acid panel and genetic test eligibility criteria.

For important differential diagnosis information, see reverse side.

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Arginase 1 Deficiency:

EARLY AND ACCURATE DIAGNOSIS IS CRUCIAL[12,18]

Persistently high levels of plasma arginine ultimately distinguish ARG1-D from other neurometabolic and neurologic disorders[3,6,10,12,13,18,19]

	High plasma arginine level	Seizures	Intellectual disability	Spasticity	Progressive spasticity	Hyperammonemia
Arginase 1 Deficiency	✓	✓	✓	✓	✓	✓
Cerebral palsy		✓	✓	✓		
Hereditary spastic paraplegia				✓	✓	
Other UCDs		✓	✓			✓

ARG1-D is a rare genetic metabolic disease that requires a multidisciplinary management plan directed by a metabolic specialist

The Aeglea THINK ARGININE™ Diagnostic Program provides easy access to NO-CHARGE sponsored testing*† and services for ARG1-D

If your patient displays neuromotor manifestations that could be associated with a neurologic condition, our program is designed to help you. Confirm ARG1-D to avoid delays in diagnosis, treatment, and management.

Benefits for you and your patients:

- Plasma amino acid panel: measuring arginine levels, as part of your metabolic screen
- Genetic test: confirming a diagnosis
- Continuum of care solutions
- Disease management resources
- Genetic counseling
- Ongoing patient monitoring services

THINK ARGININE™

DON'T MISS ARG1-D IN YOUR PRACTICE

Diagnose this progressive condition by ordering a NO-CHARGE sponsored plasma amino acid panel* and genetic test† now at ThinkArginine.com

*Plasma amino acid panel: a health care professional (HCP) *is required to confirm* no pathogenic variant by previous genetic testing for HSP.
†Genetic testing: spasticity or global developmental delay and arginine ≥115 µmol/L. HCP is required to provide level of plasma arginine.

References:
1. Diez-Fernandez C et al. *Hum Mutat*. 2018;39:1029-1050. 2. Carvalho DR et al. *Gene*. 2012;509:124-130. 3. Carvalho DR et al. *Pediatr Neurol*. 2012;46:369-374. 4. Lüneburg N et al. *J Nutr*. 2011;141:2186-2190. 5. Batshaw ML et al. *Mol Genet Metab*. 2014;113:127-130. 6. Crombez EA, Cederbaum SD. *Mol Genet Metab*. 2005;84:243-251. 7. Schlune A et al. *Amino Acids*. 2015;479:1751-1762. 8. Cai X et al. *Medicine (Baltimore)*. 2018;97:e9880. 9. Sin YY et al. *J Mol Med (Berl)*. 2015;93:1287-1296. 10. Scaglia F, Lee B. *Am J Med Genet C Semin Med Genet*. 2006;142:113-120. 11. Sun A et al. In: Adam MP et al, eds. *GeneReviews®*. Seattle, WA: University of Washington, Seattle; 2020. https://www.ncbi.nlm.nih.gov/books/NBK1159/. Accessed August 19, 2021. 12. Huemer M et al. *J Inherit Metab Dis*. 2016;39:331-340. 13. Burrage LC et al. *Hum Mol Genet*. 2015;24:6417-6427. 14. Amayreh W et al. *Dev Med Child Neurol*. 2014;56:1021-1024. 15. Bélanger SA et al. *Paediatr Child Health*. 2018;23(6):403-419. 16. Häberle J et al. *Orphanet J Rare Dis*. 2012;7:32. 17. Therrell BL et al. *Mol Genet Metab*. 2017;121:308-313. 18. Edwards RL et al. *J Inherit Metab Dis*. 2009;32:S197-S200. 19. NORD. The Physician's Guide to Urea Cycle Disorders. 2012. http://www.nucdf.org/documents/NORD_Physician_Guide_to_Urea_Cycle_Disorders.pdf. Accessed August 2, 2021.

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