Quarterly HOTLINE: Effective January 4, 2019

New Test **3001132** **Capillary Malformation-Arteriovenous Malformation (*EPHB4 and RASA1*) Sequencing, and (*RASA1*) Deletion/Duplication** **CMAVM PAN**

Available Now

Methodology: Polymerase Chain Reaction/Sequencing/Multiplex Ligation-dependent Probe Amplification
Performed: Sun- Sat
Reported: Within 1 month

Specimen Required: Collect: Lavender (EDTA), Pink (K_2EDTA), or Yellow (ACD).
Specimen Preparation: Transport 3 mL whole blood. (Min: 1 mL)
Storage/Transport Temperature: Refrigerated.
Stability (collection to initiation of testing): Ambient: 1 week; Refrigerated: 1 month; Frozen: 6 months

Interpretive Data:

Background Information for Capillary Malformation-Arteriovenous Malformation (*EPHB4* and *RASA1*) Sequencing and (*RASA1*) Deletion/Duplication:
Characteristics: Multifocal, randomly distributed, capillary malformations (CM) of the skin that may be associated with a fast-flow lesion (arteriovenous malformations [AVM] or arteriovenous fistula). Fast-flow lesions in the skin, muscle, bone, or central nervous system can cause life-threatening complications such as bleeding, congestive heart failure, or neurological consequences. Capillary malformation-arteriovenous malformation syndrome type 1 (CM-AVM1) is caused by *RASA1* pathogenic variants; capillary malformation-arteriovenous malformation syndrome type 2 (CM-AVM2) is caused by *EBHB4* pathogenic variants.
Incidence: Estimated at 1 in 20,000 for CM-AVM1 and 1 in 12,000 for CM-AVM2.
Inheritance: Autosomal dominant; approximately one-third of *RASA1* pathogenic variants are de novo.
Penetrance: 90-95 percent.
Cause: Pathogenic *RASA1* and *EPHB4* variants.
Clinical Sensitivity: Not well-established, but at least 65 percent.
Methodology: Bidirectional sequencing of all coding regions and intron-exon boundaries of the *EPHB4 and RASA1* genes; Multiplex Ligation-dependent Probe Amplification (MLPA) to detect large *RASA1* deletions/duplications.
Analytical Specificity and Sensitivity: 99 percent.
Limitations: Diagnostic errors can occur due to rare sequence variations. Regulatory region variants and deep intronic variants will not be detected. Large deletions/duplications will not be detected in *EPHB4*. The breakpoints of large *RASA1* deletions/duplications will not be determined.

See Compliance Statement C: www.aruplab.com/CS

CPT Code(s): 81479

New York DOH approval pending. Call for status update.

HOTLINE NOTE: Refer to the Test Mix Addendum for interface build information.