



## Newborn Screening ACT Sheet

# Elevated C5 Acylcarnitine Isovaleric Acidemia (IVA) / 2-Methylbutyrylglycinuria (2MBG)

**Differential Diagnosis:** Isovaleric acidemia (IVA), 2-Methylbutyrylglycinuria (2MBG) (also referred to as short/branched chain acyl-CoA dehydrogenase deficiency or SBCAD deficiency); antibiotic-related (pivalic acid derived) artifact.

**Condition Description:** IVA and 2MBG result from different defects in the metabolism of the branched chain amino acids, leucine (isovaleryl-CoA dehydrogenase in IVA) and isoleucine (short/branched chain acyl-CoA dehydrogenase in 2MBG). In both conditions specific metabolites accumulate and are potentially toxic.

**Conditions associated with this analyte have been identified by the Society of Inherited Metabolic Disorders (SIMD) as critical, and require immediate action.**

### **MEDICAL EMERGENCY - Take the Following IMMEDIATE Actions:**

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Immediate telephone consultation with pediatric metabolic specialist. (See attached list.)
- Evaluate the newborn.
- If infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport IMMEDIATELY to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Initial testing: Plasma acylcarnitine profile, urine organic acids, and urine acylglycine.
- Repeat newborn screen if second screen not yet done.
- Educate family about signs/symptoms and need for urgent treatment of metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Report findings to newborn screening program.

**Diagnostic Evaluation:** Plasma acylcarnitine analysis confirms the increased C5. Urine organic acid analysis will show isovalerylglycine in IVA and 2-methylbutyrylglycine in most cases of 2MBG. Urine acylglycine and acylcarnitine analysis may also be informative.

**Clinical Considerations:** Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a “sweaty feet” odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist. Long-term prognosis of IVA with appropriate therapy is good. The clinical spectrum of 2MBG is variable. To date, most patients identified by newborn screening with 2MBG are of Hmong descent and remain asymptomatic.

#### **Additional Information:**

**American College of Medical Genetics and Genomics (ACMG)**

<https://www.acmg.net/StaticContent/ACT/C5.pdf>

#### **Genetics Home Reference**

<http://ghr.nlm.nih.gov/condition=isovalericacidemia>

#### **STAR G FELSI**

<http://www.newbornscreening.info/Parents/organicaciddisorders/IVA.html>