

## 351 Inborn Errors of Metabolism

### Kansas Risk Factor Summary

Risk Factor Code	Kansas Risk Factor Title	High Risk	Auto-Assigned	Based on MD Diagnosis	Category and Priority					USDA Revised Date
					PG	BF	PP	I	C	
351	Inborn Errors of Metabolism	X		X	1	1	3	1	3	05/11

### Kansas Risk Factor Definition

Presence of inherited metabolic disorder caused by a defect in the enzymes or their co-factors that metabolize protein, carbohydrate, or fat, diagnosed by a physician as self-reported by caregiver; or as reported or documented by a physician, or someone working under physician's orders. Inborn errors of metabolism (IEM) generally refer to gene mutations or gene deletions that alter metabolism in the body, including but not limited to:

- Amino Acid Disorders - Amino Acid Metabolism Disorders are characterized by the inability to metabolize a certain essential amino acid. The build-up of the amino acid that is not metabolized can be toxic. Treatment of amino acid disorders involves restricting one or more essential amino acids to the minimum required for growth and development and supplying the missing product due to the blocked reaction.
  - [Phenylketonuria \(includes clinically significant hyperphenylalaninemia variants\);](#)
  - [Maple syrup urine disease;](#)
  - [Homocystinuria;](#)
  - [Tyrosinemia;](#)
- Carbohydrate Disorders - This group of disorders includes an enzyme deficiency or its cofactor that affects the catabolism or anabolism of carbohydrate. Carbohydrate disorders are complex and affect neurological, physical, and nutritional status.
  - [Galactosemia](#)
  - [Glycogen storage disease type I](#)
  - [Glycogen storage disease type II](#) (see also [Pompe disease](#))
  - [Glycogen storage disease type III](#)
  - [Glycogen storage disease type IV \(Andersen Disease\)](#)
  - [Glycogen storage disease type V](#)
  - [Glycogen storage disease type VI](#)
  - Hereditary Fructose Intolerance ([Fructose 1-phosphate aldolase deficiency](#), Fructose 1, 6, biphosphatase deficiency, fructose kinase deficiency)
- Fatty Acid Oxidation Disorders - Fatty acid oxidation defects include any enzyme defect in the process of mitochondrial fatty acid oxidation (FAO) system. The biochemical characteristic of all FAO defects is abnormally low ketone production as a result of the increased energy demands. This results in fasting hypoglycemia with severe acidosis secondary to the abnormal accumulation of intermediate metabolites of FAO, which can result in death.
  - [Medium-chain acyl-CoA dehydrogenase deficiency](#)

- [Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency](#)
- [Trifunctional protein deficiency type 1](#) (LCHAD deficiency)
- [Trifunctional protein deficiency type 2](#) (mitochondrial trifunctional protein deficiency)
- [Carnitine uptake defect](#) (primary carnitine deficiency)
- [Very long-chain acyl-CoA dehydrogenase deficiency](#)
- [Organic Acid Metabolism Disorders](#) - Organic Acid Disorders are characterized by the excretion of non-amino organic acids in the urine. Most of the disorders are caused by a deficient enzyme involving the catabolism of specific amino acid(s). As a result, the non-metabolized substance accumulates due to the blockage of the specific metabolic pathway, which is toxic to certain organs and may also cause damage to the brain.
  - [Isovaleric acidemia](#)
  - [3-Methylcrotonyl-CoA carboxylase deficiency](#)
  - [Glutaric acidemia type I](#)
  - [Glutaric acidemia type II](#)
  - [3-hydroxy-3-methylglutaryl-coenzyme A lyase deficiency](#)
  - [Multiple carboxylase deficiency](#) (Biotinidase deficiency, [Holocarboxylase synthetase deficiency](#))
  - [Methylmalonic acidemia](#)
  - [Propionic acidemia](#)
  - [Beta-ketothiolase deficiency](#)
- [Lysosomal Storage Diseases](#) - Lysosomal storage diseases are a group of related conditions characterized by increased storage of undigested large molecules in lysosomes. Lysosomes are cellular organelles responsible for intracellular degradation and recycling of macromolecules. Due to a defect in a specific lysosomal enzyme, the macromolecule that normally would be metabolized is not broken down; instead, it accumulates in the lysosomes. This leads to tissue damage, organ failure and premature death. Common clinical features include bone abnormalities, organomegaly, developmental impairment and central, peripheral nervous system disorders.
  - [Fabry disease](#) ( $\alpha$ -galactosidase A deficiency)
  - [Gauchers disease](#) (glucocerebrosidase deficiency)
  - [Pompe disease](#) (glycogen storage disease Type II, or acid  $\alpha$ -glucosidase deficiency)
- [Mitochondrial Disorders](#) - Mitochondrial Disorders are caused by the dysfunction of the mitochondrial respiratory chain, or electron transport chain (ETC). Mitochondria play an essential role in energy production. The ETC dysfunction increases free radical production, which causes mitochondrial cellular damage, cell death and tissue necrosis and further worsens ETC dysfunction and thus forms a vicious cycle. The disorders can affect almost all organ systems. However, the organs and cells that have the highest energy demand, such as the brain and muscles (skeletal and cardiac) are most affected. The clinical features vary greatly among this group of disorders, but most have multiple organ dysfunctions with severe neuropathy and myopathy.
  - [Leber hereditary optic neuropathy](#)
  - [Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes](#) (MELAS)
  - [Mitochondrial neurogastrointestinal encephalopathy disease](#) (MNGIE)

- [Myoclonic epilepsy with ragged-red fibers \(MERRF\)](#)
- [Neuropathy, ataxia, and retinitis pigmentosa \(NARP\)](#)
- [Pyruvate carboxylase deficiency](#)
- Peroxisomal Disorders - There are two types of peroxisomal disorders: single peroxisomal enzyme deficiencies and peroxisomal biogenesis disorders. These disorders cause severe seizures and psychomotor retardation. Peroxisomes are small organelles found in cytoplasm of all cells. They carry out oxidative reactions which generate hydrogen peroxides. They also contain catalase (peroxidase), which is important in detoxifying ethanol, formic acid and other toxins. Single peroxisomal enzyme deficiencies are diseases with dysfunction of a specific enzyme, such as acyl coenzyme A oxidase deficiency. Peroxisomal biogenesis disorders are caused by multiple peroxisome enzymes such as Zellweger syndrome and neonatal adrenoleukodystrophy.
  - [Zellweger Syndrome Spectrum](#)
  - [Adrenoleukodystrophy \(x-ALD\)](#)
- [Urea Cycle Disorders](#) - Urea Cycle Disorders occur when any defect or total absence of any of the enzymes or the cofactors used in the urea cycle results in the accumulation of ammonia in the blood. The urea cycle converts waste nitrogen into urea and excretes it from the kidneys. Since there are no alternate pathways to clear the ammonia, dysfunction of the urea cycle results in neurologic damages.
  - [Citrullinemia](#)
  - [Argininosuccinic aciduria](#)
  - [Carbamoyl phosphate synthetase I deficiency](#)

#### [USDA Justification](#)

**Note:** USDA Justification is provided because it explains nicely why the risk is important. However, you must use the Kansas risk factor names and definitions which may differ slightly from the USDA document.