January 23, 2021

Department of Medical Genetics
737 Broadway North, Route 1220
Fargo, ND 58122
701.234.2362
701.234.2995 (fax)

Dear North Dakota Senate Human Services Committee Members,

I'm writing in support of SB 2224, for coverage of metabolic supplements which are medically necessary for standard treatment for individuals with inborn errors of metabolism. For many years, North Dakota newborns with phenylalanine hydroxylase deficiency (also known as phenylketonuria or PKU) have received phenylalanine-free metabolic formula through the North Dakota state formula program, which has prevented devastating neurological disease among these individuals. With growth and diversification of our state's population, improvements and additions to our state newborn screening panel, and advancements in the field of clinical biochemical genetics, there are now North Dakota newborns being diagnosed with a wide variety of other treatable inborn errors of metabolism. These babies deserve equitable access to metabolic formulas and supplements which might be life-saving and/or may provide protection against neurological disease, vision loss, hearing loss, and other medical complications. Below are some examples of metabolic supplements which are medically necessary and standard in the treatment of individuals with inborn errors of metabolism.

Hydroxycobalamin, when administered intramuscularly, dramatically improves metabolic function in individuals with vitamin B12-responsive forms of methylmalonic acidemia, as well as individuals with homocystinuria. I am aware of at least two North Dakota children who require hydroxycobalamin injections, one for treatment of Cobalamin A complementation type methylmalonic acidemia, and the other for treatment of combined methylmalonic acidemia and homocystinuria due to defects in adenosylcobalamin and methylcobalamin synthesis. These disorders, when untreated, may result in metabolic encephalopathy, stroke, seizures, vision, loss, renal disease, and even death.

Biotin, given orally, is the sole treatment required to prevent medical complications of biotinidase deficiency. If untreated, individuals with biotinidase deficiency may develop intellectual disability, seizures, vision loss, hearing loss, hair loss, and skin disease. Several North Dakota newborns have been diagnosed with biotinidase deficiency and are being successfully treated with biotin. Families are typically paying out of pocket for this medically necessary treatment with biotin.

Thiamine, given orally, is used for treatment of individuals with thiamine-responsive maple syrup urine disease (MSUD). Among such individuals, thiamine increases the activity of branched-chain alpha-keto acid dehydrogenase. This prevents accumulation of leucine and associated metabolic encephalopathy, seizures, coma, and even death. There are at least two North Dakota residents with MSUD.

Riboflavin, given orally, is used for treatment of individuals with multiple acyl-CoA dehydrogenase deficiency (MADD) and multiple different mitochondrial diseases. Riboflavin may boost activity of flavoenzymes which are deficient in such disorders. Treatment with riboflavin may therefore prevent complications such as metabolic acidosis, skeletal myopathy, cardiomyopathy, neuropathy, seizures, coma, and even death. Patients with MADD and mitochondrial diseases often pay out of pocket for riboflavin and other components of their "mitochondrial cocktails", which are essential for preventing metabolic crises and progression of their disease.

Thank you, in advance, for consideration of the medical needs of North Dakotans with inborn errors of metabolism, in particular those diagnosed via the North Dakota state newborn screening program.

Sincerely,

Kari Casas, MD
Clinical Associate Professor, Department of Pediatrics, UND School of Medicine & Health Sciences
Medical Genetics and Metabolism, Sanford Broadway Clinic