At a Glance
Methylmalonic/Propionic Acidemia

Deficient enzyme: MMA-methylmalonyl-CoA mutase (mut^0 or mut^-)
PROP- propionyl-CoA carboxylase

Cofactor: MMA- Adenosylcobalamin (Vitamin B_{12})
PROP- Biotin

Toxic Metabolite: MMA- Methylmalonic Acid
PROP- Propionic Acid

Restricted Amino Acids: Valine, Isoleucine, Methionine, Threonine

Clinical presentation in untreated patients: acute: poor feeding, vomiting, lethargy, tachypnea, acidosis, respiratory distress, coma; longer-term: neurologic complications, optic atrophy, renal dysfunction (MMA), cardiomyopathy (PROP)

***Goal Treatment Range**: Plasma amino acids- maintain within normal range

Nutrient Needs by Age*

Age	Intact Protein g/kg/d	Total Protein g/kg/d	Energy kcal/kg/d
0-3 mo	0.9 – 1.5	1.5 – 1.8	72 - 109
3-6 mo	0.9 – 1.5	1.5 – 1.8	72 - 109
7-12 mo	0.7 – 1.2	1.2 – 1.4	64 - 97
1-3 yrs	0.6 – 1.05	1.05 – 1.3	66 - 99
4-8 yrs	0.6 – 0.95	0.95 – 1.1	56 - 88
9-13 yrs	0.6-0.95	0.95-1.1	39-65
14-18 yrs	0.5-0.85	0.85-1.0	30-53
19->70 yrs	0.5-0.8	0.8-1.0	Varies

*Adapted from SERN/GMDI PROP Nutrition Management Guidelines; https://southeastgenetics.org/ngp/guidelines.php
** See SERN/GMDI PKU Management Guidelines for recommended nutrient needs during pregnancy and lactation

Starting a Diet

1. Determine goals for Intact Protein (g), Total Protein (g), Energy (kcal).
2. Calculate amount of intact protein source (breast milk, infant formula, age-appropriate formula, food) needed to meet intact protein (g) goal.
3. Calculate amount of medical food required to provide remaining protein to meet total protein goal.
4. Calculate energy intake from intact protein and medical food sources to ensure total calorie needs are met.

Methylmalonic/Propionic Acidemia

	Abbott abbottnutrition.com	Mead Johnson hcp.meadjohnson.com	Nutricia nutriciametabolics.com	Vitaflo vitafloUSA.com
Infant (0-1 yr)	Propimex®-1	OA 1	MMA/PA Anamix® Early Years	
Toddler & Young Children	Propimex-1 Propimex-2	OA 1 OA 2	MMA/PA Anamix Early Years MMA/PA Anamix Next	MMA/PA express®15 MMA/PA cooler®15
Older Children & Adults	Propimex-2	OA 2	MMA/PA Anamix Next MMA/PA Maxamum®	MMA/PA express 15 MMA/PA cooler 15

Nutrition Supplementation (doses may vary)

*L-Carnitine: 100-300 mg/kg/d; divided 2-4 doses per day; goal to maintain plasma free carnitine in normal range

*MMA- Hydroxycobalamin: 1.0-2.0 mg intramuscular hydroxycobalamin daily to weekly for those who are vitamin B_{12} responsive (these patients may need little to no dietary restriction)

To determine responsiveness: 1.0 mg (IM or IV) hydroxycobalamin x 5 days; reduction in MMA levels of $\geq$50% indicates responsiveness

**PROP- Biotin: 5-40 mg/d during initial diagnostic work-up; once PROP confirmed, can be discontinued

*Sowa, M. Nutritional Management of Propionic and Methylmalonic Acidemia. In LE Bernstein, F Rohr, S van Calcar (Eds.) Nutritional Management of Inherited Metabolic Diseases (2nd Edition). Springer: 2021

**Jurecki E et al. Nutrition management guideline for propionic acidemia: An evidence- and consensus-based approach. Mol Genet Metab. 2019;126(4):341-54

Medical Therapy

Carbaglu (carglumic acid) (www.recordati.com)

Carglumic acid (generic) (www.etonpharma.com)

Dose for acute hyperammonemia (pediatric and adults) 150 mg/kg patients ≤ 15 kg; 3.3 gm/m^2 patients > 15 kg

Laboratory Monitoring*

Plasma Amino Acids[1]
Serum Methylmalonic Acid[1]
Carnitine (Free and Acyl)[1]
Ketones[5]

CBC, Albumin[2]
Prealbumin[2]
Propionic Acid[3]
Cystatin C[6]

Urine organic acids[3]
25-OH Vitamin D[4]
Folate, ferritin, B_{12}, B_6, zinc, selenium
Complete Metabolic Panel (CMP)[4]

[1] Monthly to every 3 months in infancy; at every clinic visit or every 6 months to annually thereafter
[2] Every 6 to 12 months in infancy; annually thereafter, except prealbumin every 6 to 12 months up until age 18
[3] Baseline then every 6 months in infancy; annually as indicated thereafter
[4] Annually or as indicated
[5] Daily to establish baseline, then weekly or more frequent if clinically unstable in infancy; monthly or daily when clinically unstable thereafter
[6] Every 6 months to monthly as indicated**

*SERN/GMDI PROP Nutrition Management Guidelines; https://southeastgenetics.org/ngp/guidelines.php
**Forny, P et al. Guidelines for the diagnosis and management of methylmalonic acidaemia and propionic acidaemia: First revision. J Inherit Metab Dis. 2021;44(3):566-92