At a Glance
Homocystinuria (HCU)

Background[1]

Deficient enzyme: Cystathionine Beta-Synthase (CBS)

Cofactor: Pyridoxine (Vitamin B_6)

Toxic Metabolite: Homocysteine

Restricted Amino Acid: Methionine

Clinical presentation, in untreated patients: Ectopic lentis, skeletal abnormalities, intellectual disabilities seizures, thromboembolic disease

***Goal Treatment Range**: Plasma Total Homocysteine (tHcy):

Keep the tHcy concentration as close to normal as possible:

<50 µmol/L for pyridoxine-responsive patients

<100 µmol/L for pyridoxine-unresponsive patients

Plasma Methionine: <1000 µmol/L

Plasma Cystine: normal range

Nutrient Needs by Age[2†]

Age	Methionine mg/kg	Cystine mg/d	Intact Protein	Total Protein	Energy DRI/EER
0-6 mo	15-60	85-150	60-100% DRI based on plasma tHCY and methionine	100-140% DRI or 120-140% DRI for those on medical food	80-120% based on growth trend
6-12 mo	12-43	85-150			
1-4 yr	9-28	60-100			
4-7 yr	7-22	50-80			
7-11 years	7-22	30-50			

†For ages >11 years, see book chapter noted in reference

Simplified Diet

1. At 4-6 months of age, when solid food is introduced, consider implementing a simplified diet
2. Reduce Met allowance (from whole protein source) by 30% (40% in those with more restrictive Met allowances).
3. Allow unmeasured intake of "uncounted foods." These are fruits, vegetables, foods with <20 mg Met/100g

Starting a HCU Diet
(in individuals with CBS deficiency who are non-responsive to vitamin B_6 therapy)

1. Determine goals for Methionine (mg), Cystine (mg), Intact Protein (g), Total Protein (g), Energy (kcal)
   -use 20 mg Met = 1 g protein to calculate mg of methionine from grams of protein
2. Calculate amount of whole protein source (breast milk, infant formula, food) needed to meet Meth goal.
3. Calculate amount of medical food needed in addition to the whole protein source to meet total protein goal.
4. Calculate energy intake from whole protein and medical food sources to ensure total calorie needs are met.

Homocystinuria (HCU)

Medical Food Therapy

	Abbott abbottnutrition.com	Cambrooke Cambrooke.com	Mead Johnson Hcp.meadjohnson.com	Nutricia NutriciaMetabolics.com	Vitaflo www.vitafloUSA.com
Infant (0-1 yr)	Hominex®-1		HCY 1	HCU Anamix® Early Years	
Toddler & Young Children	Hominex-1 Hominex-2	Homactin™AA Plus Powder 15	HCY 1 HCY 2	HCU Anamix Early Years HCU Anamix Next	HCU express™ plus 15 HCU express plus 20 HCU cooler® 15
Older Children & Adults	Hominex-2	Homactin AA Plus Powder 15	HCY 2	HCU Anamix Next HCU Maxamum® HCU Lophlex® LQ	HCU express plus 15 HCU express plus 20 HCU cooler 15

Nutritional Supplementation[1,2]

(dose may vary based on blood laboratory results)

Vitamin B_6 (used as sole therapy in individuals who are pyridoxine responsive)
- -recommended starting dose to assess responsiveness: 100 mg/d
- -maintain unrestricted diet and correct folate and vitamin B_{12} deficiencies prior to assessing response

Correct folate deficiencies (5-10 mg/d folate or 1-5 mg/d folinic acid)
Correct vitamin B_{12} deficiency (dose varies)

Medical Therapy

Cystadane® (betaine anhydrous) www.recordati.com
Betaine anhydrous- www.etonpharma.com
Recommended starting dose[1]:
- Children- 50 mg/kg twice daily
- Adults- 3 g twice daily

Laboratory Monitoring[1]

Total Homocysteine[a]	B_{12}[b]	Zinc, Ferritin, Copper, Selenium[b]
Plasma Methionine[a]	Folate[b]	Essential Fatty Acids[b]
Plasma Amino Acids[b]	Albumin[b]	25-OH Vitamin D[b]

[a] Weekly in infancy, weekly to monthly thereafter
[b] At least annually; if deficiency identified, provide supplementation and repeat in 3-6 months

References

1. Morris et al. Guidelines for the diagnosis and management of cystathionine beta-synthase deficiency. J Inherit Metab Dis 2017, 40: 49-74
2. Roberts, AM. Nutrition Management of Homocystinuria and Cobalamin Disorders. In LE Bernstein, F Rohr, S van Calcar (Eds.) *Nutrition Management of Inherited Metabolic Diseases* (2nd Edition). Springer: 2021