BlueCross BlueShield of Alabama

Name of Policy:
Nutritional Supplements for Phenylketonuria (PKU)

Policy #: 029
Category: Supplies

Latest Review Date: July 2014
Policy Grade: D

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Classic phenylketonuria (PKU) is a rare metabolic disorder that usually results from a deficiency of a liver enzyme known as phenylalanine hydroxylase (PAH). This enzyme deficiency leads to elevated levels of the amino acid phenylalanine (Phe) in the blood and other tissues. Mental retardation, microcephaly, delayed speech, seizures, eczema, behavior abnormalities and other symptoms characterize the untreated state. Approximately 1 of every 15,000 infants in the United States is born with PKU.

The current treatment for this disorder involves strict metabolic control using a low-Phe diet that includes specialized medical foods. Metabolic control of PKU can be difficult to achieve, and poor control can result in significant decline of mental and behavioral performance. Women with PKU must also maintain strict metabolic control before and during pregnancy to prevent fetal damage.

Implementing a Phe-restricted diet early in life can significantly reduce mental deficiencies associated with PKU. Metabolic control via medical nutrition therapy involves the use of medical foods including medical protein sources and modified low-protein products in addition to the provision of required amounts of Phe through small amounts of natural protein. The response is monitored throughout periodic measurement of blood Phe levels in conjunction with analysis of nutritional intake and review of nutritional status. Most experts advocate lifelong dietary treatment for metabolic control of blood Phe levels. Data suggest that elevated Phe levels in adolescents and adults adversely affect cognitive function and case reports have documented deterioration of adult patients with PKU after diet discontinuation.[1]

Policy:

Nutritional supplements for phenylketonuria (PKU) (ICD-9 code 270.1), (ICD-10 code E70.0) meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage throughout the lifespan of the patient.

These medical food nutrients are not prescription drugs; they are, however, not products that one can walk into a drug store and purchase off the shelf. They must be special ordered through a pharmacy or pharmaceutical organization.

The available medical foods include:

- ~~Lofenalac~~ (No longer available through manufacturer)
- Phenyl Free 1
- Phenyl Free 2
- Phenyl Free 2 HP
- Milupa PKU-1
- Milupa PKU-2
- Milupa PKU-3
- Crystalline amino acid mix plus Protein Free Diet Powder (MJ80056)
- Periflex
- X Phe Analog

- X Phe Maxamaid
- X Phe Maxamum
- Phenex-1
- Phenex-2
- Phlexy-10
- Phenylade Blend, PheBLOC tablets
- Lophlex
- Phlexy-Vits
- Add-Ins
- Phenyl Ade
- PKU Gel
- PKU Express
- PKU Cooler
- Camino Pro

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Hyperphenylalaninemia results from impaired metabolism of Phe caused by deficient activity of the enzyme PAH. People with PKU have a complete absence or profound deficiency of enzyme activity, typically show very high elevation of blood Phe (>20 mg/dL), and accumulate phenylketones. A partial deficiency of PAH results in non-PKU hyperphenylalaninemia and a lower degree of blood Phe elevation without phenylketone accumulation. Both forms of hyperphenylalaninemia, which account for the vast majority of cases, are autosomal recessive disorders caused by mutations in the *PAH* gene.

Since the early 1960s, newborns in the United States have been screened for PKU through the collection of neonatal blood samples on special paper cards within the first days of life. Blood samples are evaluated for the presence of abnormally elevated Phe levels, and infants found to have high levels of Phe are referred for diagnostic evaluation and comprehensive treatment and care.

Implementing a Phe-restricted diet early in life can significantly reduce mental deficiencies associated with PKU.[1]

Pharmacological interventions have been investigated to assess the impact they have on brain levels of phenylalanine (Phe) in adults with PICU.[2] Dietary supplementation with large neutral

amino acids seems to lower the brain Phe in adults with PKU. [2] In addition, these amino acids assist with the protein requirements needed for adolescents and adults. [3]

Key Words:

Inborn errors of metabolism, PKU, nutritional supplements, medical food, medical nutrients

Approved by Governing Bodies:

Not applicable

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: No special consideration
Pre-certification/Pre-determination requirements: Not applicable

Coding:

HCPCS code: **S9435** Medical foods for inborn errors of metabolism

Effective for dates of service on or after April 1, 2009:

S9433 Medical food nutritionally complete, administered orally, providing 100% of nutritional intake

References:

1. Bodamer OA. Overview of Phenylketonuria. www.uptodate.com/contents/overview-or-phenylketonuria?view=print.
2. Comparative Effectiveness of Treatment for Phenylketonuria. Research Protocol, February 8, 2011: www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/.
3. Howell R.R., et al. National institutes of health consensus development conference statement: Phenylketonuria: screening and management. Pediatrics, October 2001; 108: 4.
4. Moats RA, Moseley KD, Koch R, and Nelson M, Jr. Brain phenylalanine concentrations in phenylketonuria: Research and treatment of adults. Pediatrics, December 2003; 112(6 Pt 2): 1575-9.
5. Rohr JF, Munier AW and Levy HL. Acceptability of a new modular protein substitute for the dietary treatment of phenylketonuria. Journal of Inherited Metabolic Disease, November 2001; 24(6): 623-30.
6. Schindeler S, Ghosh-Jerath S,Thompson S, et al. The effects of large neutral amino acid supplements in PKU: an MRS and neuropsychological study. Mol Genet Metab May 2007; 91(1): 48-54.

Policy History:

Medical Policy Group, December 2000
Medical Policy Group, August 2001
Benefit and Policy Committee, October 2001
Medical Policy Administration Committee, November 2001
Medical Policy Group, March 2003
Medical Policy Administration Committee, March 2003
Medical Policy Group, January 2004
Medical Policy Administration Committee, January 2005
Medical Policy Group, July 2006 **(1)**
Medical Policy Group, January 2008 **(1)**
Medical Policy Group, July 2009 **(1)**
Medical Policy Group, June 2012 **(2)**: 2012 Update to Policy; update available medical foods list; Key Points and References
Medical Policy Administration Committee, July 2012
Available for comment July 9 through August 24, 2012
Medical Policy Group, July 2014 **(5):** Under Policy Statement added ICD-10 code and removed a medical food that is no longer being manufactured. Policy statement is unchanged; literature review completed and references updated through July 1, 2014.
