



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Hospitalization for the Initiation of a Ketogenic Diet

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Intracranial Electroencephalography (IEEG)
 Nutritional Counseling
 Quantitative Electroencephalography (QEEG)
 Vagus Nerve Stimulation
 Video Electroencephalographic (V-EEG) Monitoring

INSTRUCTIONS FOR USE

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Coverage Policy

CIGNA covers inpatient hospitalization for the initiation of a ketogenic diet as medically necessary for ANY of the following:

- management of refractory epilepsy in individuals under age 19 when there is documented failure of, contraindications to, or intolerance of a minimum of three (3) antiepileptic medications
- pyruvate dehydrogenase complex deficiency (PDCD)
- glucose transporter protein deficiency

General Background

The ketogenic diet is a high-fat, low-carbohydrate, low-protein diet that has been used in the treatment of patients with epilepsy that is refractory to conventional medications. The composition of this diet induces ketosis, a physiological state in which fatty acids and ketones are used as the primary source of energy. The exact mechanism by which the diet obtains seizure control is unknown. Dehydration and acidosis, in addition to ketosis, appear to play a role.

Epilepsy is a chronic disorder characterized by recurrent seizures.. Antiepileptic drugs (AEDs) are the first-line treatment for epilepsy. Other treatment options for epilepsy include vagus nerve stimulation and surgical resection. More than half of those with refractory epilepsy are not candidates for resective surgery. In adults,

refractory epilepsy is generally defined as the persistence of seizures despite at least two appropriately prescribed AEDs that have been progressively increased in dosage until toxicity has been experienced. In most children, at least three AEDs should be tried before the child is said to have refractory or intractable epilepsy (Wolf and McGoldrick, 2006; Sheth, et al., 2002).

Certain inborn errors of metabolism, such as the glucose transporter protein deficiency syndrome (Glut1-DS) and pyruvate dehydrogenase complex deficiency (PDCD), have also been treated with the ketogenic diet. Glut1-DS is caused by impaired glucose transport into the brain resulting in an epileptic encephalopathy, developmental delay, and a complex motor disorder. In Glut1-DS, a ketogenic diet provides ketones as an alternative fuel to the brain and effectively controls seizures (Klepper, 2005). PDCD is a rare disorder of carbohydrate metabolism and is characterized by an inability to metabolize pyruvate for energy production within the body. Tissues that require the greatest amounts of oxygen (e.g., brain) are most sensitive to deficiencies in the PDC. While ketogenic diets for the treatment of PDCD have yielded variable success rates, this type of diet along with thiamine, is the primary therapy for infants with this condition (Nordli, et al., 2001).

The ketogenic diet is most commonly initiated during a three- to five-day hospitalization. Inpatient hospitalization has been considered important because of potential complications, such as hypoglycemia or other metabolic problems that may occur during the period of fasting and initial administration of the diet. Fasting begins upon admission along with a modest fluid restriction until urinary ketones reach 3+ to 4+, as measured by urine dipsticks. The diet is then started and gradually increased to a full-calorie, ketogenic diet by the fifth day. The diet ratio, or grams of fat to grams of protein plus carbohydrate, is specifically prescribed for each patient. Most patients remain on the diet for at least two years, during which time AEDs may be reduced or discontinued. Potential side effects of this diet include constipation, growth inhibition, kidney stones and, less commonly, prolonged QT syndrome, cardiomyopathy and bruising. Medical contraindications to the ketogenic diet include metabolic disorders with defects in fat or ketone metabolism; mitochondrial disorders; and liver or renal disease.

The Atkins diet, which is used for weight reduction, has been evaluated as an alternative to ketogenic diet for the treatment of refractory epileptic seizures. The Atkins diet is less restrictive than the traditional ketogenic diet in terms of protein, fluid, and calorie content and also has the ability to induce ketosis (Gaby, 2007). A few small retrospective and prospective uncontrolled studies (n=14–20) have reported that the diet is effective in reducing seizure frequency and is well tolerated with few side effects (Kossoff, et al. 2006; Kang, et al., 2006). However, larger studies with longer-term data are needed to determine the role of the Atkins diet in the treatment of refractory seizures.

Literature Review

In general, inclusion criteria for reported studies of the effects of ketogenic diets have been children with mixed seizure type who failed treatment with 2–3 AEDs (Neal, et al., 2008; Marsh, et al., 2006; Bergqvist, et al., 2005; Than, et al., 2005; Nordli, et al., 2001). The safety and effectiveness of the ketogenic diet has also been assessed in and is supported by a meta-analysis (Henderson et al. (2006) and several systematic reviews (Henderson, et al., 2006; Keene, 2006; Levy and Cooper, 2003; Lefebvre and Aronson, 2000).

Few studies have examined the safety and effectiveness of initiating the ketogenic diet on an outpatient basis. A case series (n=44) by Vaisleib et al. (2004) reported on patients who had outpatient initiation of the ketogenic diet. Outcomes were compared to retrospectively to patients (n=21) who were hospitalized for initiation of the diet. No significant differences were found between the outpatient and inpatient groups regarding seizure control.

There is evidence in the published, peer-reviewed medical to support the safety and effectiveness of the ketogenic diet. However prospective, randomized controlled trials are needed to determine the role of inpatient versus outpatient initiation of the diet.

Professional Societies/Organizations

The National Institute for Clinical Excellence (NICE) clinical guidelines for the management of epilepsy in adults and children state that the ketogenic diet may be considered as an adjunctive treatment in children with drug-resistant epilepsy. However, the diet should not be recommended for adults with epilepsy (NICE, 2004).

Summary

Despite the paucity of randomized controlled trials (RCTs) to support its efficacy, the ketogenic diet is recognized as an effective alternative treatment for children with refractory epilepsy. There is very limited evidence that adult patients with refractory epilepsy may benefit from the ketogenic diet. Additional well-designed studies are needed to further define patient selection criteria and to determine the diet's efficacy in the adult population.

Although data supporting the use of the ketogenic diet for pyruvate dehydrogenase complex deficiency (PDCD) and glucose transporter protein deficiency (Glut1-DS) are based on a very limited number of uncontrolled studies, ketogenic diets have become incorporated into the standard of care for the treatment of both conditions (Weber, et al., 2001; Rowland, 2005).

The ketogenic diet is a restrictive medical regimen that requires nutritional counseling, as well as a highly motivated patient and family, in order to maintain compliance. For optimal administration of the ketogenic diet, an interdisciplinary program is recommended, including a neurologist, dietician, nurse and social worker. This dietary method utilizes readily accessible food items, so the patient/family is usually self-sufficient upon discharge from the hospital setting.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT ^{®*} Codes	Description
	No specific codes

ICD-9-CM Diagnosis Codes	Description
271.8	Other specified disorders of carbohydrate transport and metabolism
271.9	Unspecified disorder of carbohydrate transport and metabolism
345.00 – 345.91	Epilepsy

*Current Procedural Terminology (CPT[®]) ©2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	5/15/2008	0359	Hospitalization for the Initiation of a Ketogenic Diet for Intractable Seizure Disorder
Great-West Healthcare	3/12/2007	95.282.04	Ketogenic Diet, Hospitalization for Initiation of Diet

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