



Medical Coverage Policy

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Hospitalization for the Initiation of a Ketogenic Diet

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Related Coverage Resources

[Vagus Nerve Stimulation \(VNS\)](#)

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The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses the ketogenic diet for the treatment of intractable (e.g., medically refractory, drug-resistant) epilepsy and select inborn errors of metabolism.

Coverage Policy

Inpatient hospitalization for the initiation of a ketogenic diet is considered medically necessary for ANY of the following:

- management of intractable (e.g., medically refractory, drug-resistant) epilepsy in individuals under age 19 when there is documented failure of, contraindications to, or intolerance of antiepileptic medication (i.e., polytherapy)
- pyruvate dehydrogenase complex deficiency (PDCD)
- glucose transporter protein deficiency

General Background

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. Patients with epilepsy whose seizures do not respond to antiseizure drug therapy are considered to have drug-resistant epilepsy (DRE). Drug resistant epilepsy is also referred to as intractable, medically refractory, or pharmacoresistant epilepsy. Patients with DRE are those who have failed at least two fair trials of appropriate medications. (Mikati and Tchapyjnikov, 2020; Sirven, 2020; Wolf and McGoldrick, 2006; Sheth, et al., 2002).

The ketogenic diet is a high-fat, low-carbohydrate, low-protein diet that has been used in the treatment of patients with epilepsy that does not successfully respond to antiseizure drug therapy. 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.

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 (Kossoff, 2021; Klepper, et al., 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 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.

The Atkins diet, which is used for weight reduction, has been evaluated as an alternative to ketogenic diet for the treatment of intractable 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 (Kang, et al., 2007; Kossoff, et al. 2006). Sharma et al. (2013) conducted a randomized controlled trial of 102 children aged 2–14 years who had daily seizures with appropriate use of at least three anticonvulsant drugs were randomized to receive either the modified Atkins diet (n=50) or no dietary intervention (n=52) for a period of three months. The percentage of children with > 90% seizure reduction, and > 50% seizure reduction 52% and 11.5% respectively, was significantly higher in the diet group (p<0.001). Constipation experienced by those on the diet was the most common adverse event. Although study results suggest a modified Atkins diet may be effective in reducing seizures in the pediatric population, larger studies with longer-term data are needed to determine the role of this diet in the treatment of drug intractable 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. These studies demonstrating the safety and effectiveness of the ketogenic diet have included randomized controlled trials (RCTs) and case series with patient populations ranging from 48–557 (Lambrechts, et al., 2017; Suo, et al., 2013; Caraballo, et al., 2011; 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 diet have also been assessed in and is supported by a meta-analysis Henderson et al. (2006) and several systematic reviews (Martin-McGill, et al., 2018; Levy, et al., 2012; Henderson, et al., 2006; Keene, 2006; Levy and Cooper, 2003; Lefevre and Aronson, 2000).

A Hayes Directory Report reviewed the available evidence (n=17 prospective studies) on the ketogenic diet for refractory seizures. Studies were found to be consistent and demonstrated a reduction in seizure frequency significantly for 33%–90% of primarily pediatric patients. Less evidence was found to support the efficacy of ketogenic diets in adult patients. Complications of the diet included gastrointestinal symptoms, acidosis, and nutritional deficiency in pediatric patients, menstrual irregularities in women, and impaired concentration in adult patients. It was summarized that the ketogenic diet is an effective therapy for patients with seizure disorders who do not respond adequately to AEDs or who have unacceptable side effects from AED treatment (Hayes, 2011; updated 2015).

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. The paucity of evidence investigating the efficacy of ketogenic diet in adult patients with intractable epilepsy is not sufficient to draw conclusions (Hayes, 2019). Despite the lack of robust evidence, hospitalization for the initiation of the diet is the standard of care due to potential complications associated with fasting and dehydration in the pediatric 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, the ketogenic diet has been incorporated into the standard of care for the treatment of both conditions (Klepper, et al., 2005; Weber, et al., 2001).

Professional Societies/Organizations

There is no current statement on the use of a ketogenic diet for seizure disorders from the American Academy of Neurology (AAN) or The Child Neurology Society (CNS).

Use Outside of the US

The National Institute for Clinical Excellence (NICE) clinical guideline for the management of epilepsy in adults and children stated that the ketogenic diet has long been used in the treatment of intractable epilepsy in children, although the exact mechanism of action is unclear. NICE recommends that children and young people with whose seizures have not responded to the appropriate AEDs be referred to a specialist for consideration of the use of a ketogenic diet (NICE, 2012; updated 2020).

According to the 2018 updated consensus recommendations on the ketogenic diet for children from the International Ketogenic Diet Study Group, the diet should be strongly considered in a child who has failed two to three anticonvulsant drugs and for several epilepsy syndromes. The ketogenic diet is considered the treatment of choice for two distinct disorders of brain metabolism, GLUT-1 deficiency syndrome and PDHD. It is recommended that before starting ketogenic diet therapy, that inborn errors of metabolism be considered and ruled out if there is a clinical suspicion for these disorders. The guidelines also stated that the initiation of ketogenic diets should be flexible, with fasting and inpatient initiation optional and regular follow-up with labs and side effect monitoring at each visit (Kossoff, et al., 2018).

Medicare Coverage Determinations

	Contractor	Policy Name/Number	Revision Effective Date
NCD		No National Coverage Determination found	
LCD		No Local Coverage Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
	No specific codes

*Current Procedural Terminology (CPT®) ©2020 American Medical Association: Chicago, IL.

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