Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

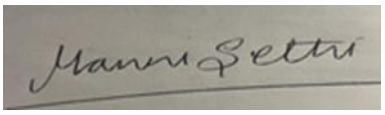
Plan: AmeriHealth Caritas Pennsylvania Community HealthChoices & Keystone First Community HealthChoices	Submission Date: 5/1/2025
Policy Number: CCP.1222	Effective Date: 7/1/2016 Revision Date: 4/2025
Policy Name: Ketone monitor for ketogenic diet in epilepsy	

Type of Submission:

☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☒ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	Signature of Authorized Individual: 

Keystone First
Community HealthChoices

Ketone monitor for ketogenic diet in epilepsy

Clinical Policy ID: CCP.1222

Recent review date: 4/2025

Next review date: 8/2026

Policy contains: Ketone monitoring device; ketogenic diet in epilepsy.

Keystone First Community HealthChoices has developed clinical policies to assist with making coverage determinations. Keystone First Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First Community HealthChoices, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First Community HealthChoices will update its clinical policies as necessary. Keystone First Community HealthChoices' clinical policies are not guarantees of payment.

Coverage policy

Ketone monitoring devices for members with epilepsy prescribed ketogenic diets are investigational/not clinically proven, and therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Urine test kits to test for ketones in members on the ketogenic diet for epilepsy.

Background

An estimated 3.4 million have active epilepsy, including 470,000 children (Centers for Disease Control and Prevention, 2020). In two-thirds of people with epilepsy, anti-seizure medications are effective at lessening or eliminating seizures. Surgery may be an option for focal seizures. Vagus nerve stimulation and ketogenic diets are options when medications are ineffective and surgery is not possible (Centers for Disease Control and Prevention, 2022).

The ketogenic diet is a special high-fat, low-carbohydrate diet developed in the 1920s to control epileptic seizures. While the underlying mechanism of action is not completely understood, the higher levels of ketones formed when the body uses fat for its primary energy source often lead to improved seizure control. The diet fell out of favor with the development of the seizure controlling medications. However, approximately 35% have medically intractable epilepsy, and there has been a resurgence of interest in the ketogenic diet as an effective treatment option (D'Andrea Meira, 2019).

The traditional ketogenic diet is administered under medical supervision. It entails an initial fasting and dehydration period, during which patients receive no food, and fluid intake is limited until ketones are present in the urine. Thereafter, a diet high in fat and low in carbohydrates and protein is introduced. Hospitalization may be necessary during an initial starvation period to induce marked ketosis and weight loss. The length of hospital stay depends on the proposed initial starvation period and generally should not exceed three days. More recently, low glycemic index treatment designed to simplify the implementation of the ketogenic diet, the modified Atkins diet, and the medium chain triglyceride diet have been introduced to improve adherence (D'Andrea Meira, 2019; Rezaei, 2018).

Strict compliance with this unpalatable dietary regimen is essential, along with careful monitoring of patient-reported seizure activity, growth (in children), health, and adverse effects. Ketone monitoring of serum or urine levels may be performed to assess ketosis and serve as a strategy to improve long-term dietary adherence. Urine testing, the most commonly-used technique, measures acetoacetate levels, while blood testing measures beta-hydroxybutyrate. Newer breath tests measure acetone (Keyto, 2020). In children with epilepsy on a ketone diet, monitoring is performed by physicians every one to three months, including growth (Kossoff, 2017).

There are several ketone monitoring devices on the market for patient use, which are mainly used for managing diabetes. Some examples are:

- FreeStyle® Optium Neo, which has a choice of tools designed to help people who use insulin.
- Precision Xtra® system and Precision Xtra blood ketone test strips.
- Ketonix® breath ketone monitor, which is a reusable breath ketone analyzer that measures the level of breath ketones. Measurements indicate the acetone in a user's breath, which is produced from the breakdown of acetoacetate in the person's blood.
- Nova Max® Plus glucose and ketone monitoring system.
- Walgreens TRUEresult® system.

Findings

The National Institute for Health and Clinical Excellence recommended a ketogenic diet under the guidance of a tertiary epilepsy specialist for certain childhood-onset epilepsy syndromes and for drug-resistant epilepsy if other treatment options have been unsuccessful or are not appropriate for adults and children. The recommendation was based on expert consensus acknowledging the benefits for small numbers of people with drug-resistant epilepsy and also the need for more research on the effectiveness and long-term tolerability of ketogenic diets. Therefore, routine use is not recommended. Ketone monitoring was not mentioned (National Institute for Health and Care Excellence, 2022).

A practice paper of the Academy of Nutrition and Dietetics on ketogenic diets for epilepsy included an overview of various diets, a brief literature review on efficacy, guidelines for implementation and coordination of care, and the role of registered dietitian nutritionists. Ketone monitoring is not addressed (Roehl, 2017).

Another guideline from the Dietary Management of Inherited Metabolic Diseases advised laboratory and urine checks at baseline to ensure no pre-existing contraindications or deficiencies, but did not elaborate on the type of testing or frequency of monitoring (van der Louw, 2016).

The Italian League against Epilepsy Dietary Therapy Study Group (De Giorgis, 2023) guideline emphasizes ketone monitoring as essential for successful ketogenic dietary therapy in epilepsy. Regular blood β-hydroxybutyrate measurement (target: 2-5 mmol/L) provides objective verification of therapeutic ketosis, enabling timely dietary adjustments and establishing individual therapeutic thresholds. Blood testing is recommended over urine testing due to superior accuracy and correlation with seizure outcomes. Monitoring should intensify during diet initiation, illness, or medication changes, with home-based protocols empowering

patients while reducing healthcare visits. When properly monitored, ketogenic dietary therapy achieves significant seizure reduction (>50%) in 35-56% of drug-resistant epilepsy patients, with specific conditions like glucose transporter type 1 deficiency potentially requiring higher ketone targets for optimal management (De Giorgis, 2023).

Multiple systematic reviews and meta-analyses described in this policy support the ketogenic diet as an effective treatment for medically refractory epilepsy in adults and children. When tolerated, the ketogenic diet is effective in reducing seizure activity in the short term (≤ three years). Its long-term health implications are not well established. Diet intolerance and lack of efficacy were the main reasons for discontinuing the diet. Most adverse effects were mild and treatable, and serious adverse effects were rare. Since a ketogenic diet is not used as a first-line treatment, its true efficacy may be underestimated, and comparison to other diets require further study.

However, the role of ketone monitoring in epilepsy has received little examination. Ketone monitoring may be used to assess ketosis and monitor compliance with a dietary regimen. Studies comparing patient outcomes with and without ketone monitoring or determining a correlation between ketone level and seizure reduction, the optimal monitoring device for ketosis, or optimal timing are needed.

A Cochrane review of seven randomized controlled trials of 427 children and adolescents found relatively similar results between persons with epilepsy on ketonic diets and modified Atkins diets, but cautioned that more research is necessary to confirm these findings (Martin, 2016). Another Cochrane review of people with epilepsy and intellectual disabilities treated by means other than pharmacology found only one study of poor quality (Jackson, 2015).

Another Cochrane review of 11 studies (n = 778) found evidence supporting use of ketogenic diet, but most studies were small. Moreover, no mention was made of measurement of ketone levels through urine and blood – only reduction in seizures and adverse events (Martin-McGill, 2018). An update by the same team (13 studies, n = 932) found evidence suggesting effective use of the ketogenic diet in treatment-refractory epilepsy in children, but found uncertain results among adults (Martin-McGill, 2020).

A meta-analysis of 70 studies of children and adolescents with epilepsy comparing classical ketogenic diet and modified Atkins diet revealed a non-significant trend toward a higher efficacy within the Atkins group at month-3 and month-6 ($P > .05$). Response rates were insignificantly higher for the ketogenic group, the proportion achieving ≥ 50% seizure reduction at months 1, 3, 6, 12, and 24 were 62%, 60%, 52%, 42%, and 46%; for the Atkins group, reduction rates at 1, 3, 6, and 12 months were 55%, 47%, 42%, and 29% (Rezaei, 2017).

A systematic review of 45 studies, including seven randomized controlled trials, analyzed rates of adverse effects of the ketogenic diet in children with epilepsy. The most common events included gastrointestinal disturbances (40.6%), hyperlipidemia (12.8%), hyperuricemia (4.4%), lethargy (4.1%), infectious diseases (3.8%) and hypoproteinemia (3.8%). Severe adverse effects, such as respiratory failure and pancreatitis, occurred in under 0.5% of cases. Nearly half of the patients discontinued the diet, primarily because of lack of efficacy, not adverse events (Cai, 2017).

A systematic review of 13 studies (n = 341) assessed treatment of infantile spasms with ketogenic diets. A median of 64.7% of patients experienced a spasm reduction > 50% short term, and 9.54% long term. Spasms of unknown etiology had a better chance of achieving freedom from seizures (risk ratio 1.72) (Prezioso, 2018).

Two recent articles arrived at conflicting determinations about ketogenic diets and epilepsy. A systematic literature review found little support for using the diet in patients with refractory status epilepticus (Willems, 2020), while a systematic review of 24 articles concluded various forms of ketogenic diets seem tolerable and effective; in each of the 21 articles addressing epilepsy reported seizure reduction after treatment compared to baseline (Christensen, 2021).

A systematic review/meta-analysis of 18 studies of ketogenic diets in epileptic children showed similar efficacy (seizure remission) at three and six months after treatment started, indicating that three-month results are good predictors for longer periods (Liu, 2019).

A systematic review of 18 articles of families of an epileptic child on the ketogenic diet found the dominant quality of life-related psychological factor was the need for counseling for parents and clear expectations on expected outcomes. Non-adherence and dropout rates were high, and the reasons and timing were not well documented (Poelzer, 2018).

A meta-analysis of 16 studies (n = 338) of adults with drug-resistant epilepsy revealed an efficacy rate of seizure freedom to be 13%; seizure reduction of 50% or more to be 53%; and seizure reduction of 50% or more in adults with intractable epilepsy to be 27%. Adverse reactions were mild, but more common than low glycemic index diet and low-dose fish oil diet (Liu, 2018).

A systematic review/meta-analysis of 33 (n = 534) of infants on the ketogenic diet showed 59% and 33%, respectively, achieved at least half and total seizure reduction. Retention was 84% at three months and 27% at 24 months (Lyons, 2020).

In 2023, we updated the references, including a 2022 National Institute for Health and Clinical Excellence guideline on the diagnosis and management of epilepsy. We identified no newly published, relevant literature to add to the policy. No policy changes are warranted.

In 2024, we identified no newly published, relevant literature to add to the policy. No policy changes are warranted.

In 2025, we added a new guideline Italian League against Epilepsy Dietary Therapy Study Group (2023). We also found several studies that suggested potential clinical utility for ketone monitoring in ketogenic dietary therapies for epilepsy management. A systematic review of 22 studies (n = 703) found that better dietary adherence, as measured by urinary or blood ketone levels, was associated with improved seizure control, although adherence declined from 79.7% at six months to 37.7% at 36 months (Lopes, 2024). An umbrella review covering 5,779 participants reported that the traditional ketogenic diet achieved ≥50% seizure reduction in 60.6% of patients at three months versus 47.7% with modified diets, with both rates decreasing by 12 months (Chen, 2023). In pediatric epilepsy, another review (n = 460) noted that gastrointestinal adverse effects in 45–48% of cases contributed to non-adherence in 30–50% of patients, while formula-based approaches with ketone monitoring reached adherence rates of 81–100% (Faheem, 2024). Additionally, a review of randomized controlled trials (n = 994) suggested that objective ketone monitoring may optimize treatment in medication-resistant cases (Parveen, 2024). Despite these promising findings, methodological limitations across studies warrant cautious interpretation and further cost-effectiveness analyses before revising clinical policies.

References

On March 16, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “ketogenic diet” and “ketone monitoring.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

2/2016: initial review date and clinical policy effective date: 7/2016

2/2017: Policy references updated.

2/2018: Policy references updated.

2/2019: Policy references updated. Policy number changed to CCP.1222.

2/2020:Policy references updated. .

4/2021: Policy references updated.

4/2022: Policy references updated.

4/2023: Policy references updated.

4/2024: Policy references updated.

4/2025: Policy references updated.