**LETTER OF MEDICAL NECESSITY: GLUT1**

**Date:**

**Patient:**

**D.O.B:**

**Policy Number:**

Attention Case Manager:

This letter of medical necessity is regarding the nutrition management of **[PATIENT NAME]**. This patientis a **[AGE] [GENDER]** with a diagnosis **Glucose Transporter Type 1 Deficiency Syndrome (GLUT1) (ICD 10: G93.4)**. GLUT1 is classified as an inborn error of metabolism, a genetic disorder, causing a neurologic disorder with multiple phenotypes. Currently there is not a test to identify it through newborn screening. Low CSF glucose (less than 40 mg/dl) with a low CSF lactate, identified with a lumbar puncture, are diagnostic for the disorder. GLUT1 is an autosomal dominant disorder and can further be confirmed through SLC2A1 gene sequencing.

In GLUT1, the protein that transports glucose across the blood brain barrier is deficient, causing decreased glucose concentration in the central nervous system. The most common symptom, though not present in all cases, is seizures beginning within the first few months of life. Additional symptoms can include movement disorders, developmental delays, with varying degrees of cognitive impairment including speech and language abnormalities. GLUT1 does not respond to traditional epilepsy treatments but has been successfully treated with the ketogenic diet, often resulting in marked clinical improvement of motor and seizure symptoms.

The Ketogenic diet is a high fat, adequate protein, low carbohydrate treatment individually calculated and prescribed to produce ketone bodies which is an alternative fuel source for the glucose-starved brain in the presence GLUT1 deficiency. The efficacy of the ketogenic diet for the management of GLUT1 deficiency is well documented (see clinical references in Appendix A).

Ketogenic therapy severely restricts the intake of dairy products, fruit, vegetables, cereals and grains. As such, the potential for nutrient deficiency is a significant risk. KetoVie 3:1 is a nutritionally complete medical food specifically designed to provide the necessary nutrients to support ketogenic diet therapy in a liquid form for individuals over one year of age. Nutrient deficiencies such as carnitine, selenium, calcium, vitamin D and protein, are common with ketogenic therapies. In order to help prevent these deficiencies, KetoVie 3:1 provides 34 mg carnitine, 16 mcg selenium, 313 mg calcium, 6.3 mcg vitamin D and 7 g protein per 250 mL serving, with a 3:1 (fat to net carbohydrate and protein) ketogenic ratio. KetoVie 3:1 additionally contains medium chain triglycerides (MCTs) which aid in reaching the desired level of ketosis for maximum benefit. KetoVie 3:1 can be offered orally to support optimal levels of ketosis or as a sole source tube feeding.

The term medical food/formula, is defined in section 5(b) of the Orphan Drug Act {21 U.S.C. 360ee (b) (3)}: a “food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”

In order to meet **[PATIENT NAME]** nutritional needs, he/she will require **[# OF CALORIES**] calories per day from KetoVie 3:1 medical food (see monthly volume prescription chart below for corresponding amount of product). KetoVie 3:1 is only available by prescription through a pharmacy, durable medical equipment (DME) company or directly from the manufacturer Ajinomoto Cambrooke, Inc.

Because ketogenic treatment comprises the primary treatment for individuals suffering from GLUT1 deficiency, we are requesting KetoVie 3:1 prescribed for **[PATIENT NAME]** be covered under your policies like other inborn errors of metabolism. If the brain can be protected with a ketogenic formula, more invasive and costly treatments may be avoided, and additional medications may be reduced or even discontinued.

We appreciate your attention to this request for **[PATIENT NAME]** medical food/formula, **KetoVie 3:1**, to be covered by his/her current medical insurance. Please do not hesitate to contact us if you have any questions.

Sincerely,

**[Physician name, M.D. other credentials, contact info, clinic name]**

**[Dietitian name, RD, LDN other credentials Center/Hospital/Institution/Practice]**

Cc: **[Parents’ names] and Medical Records**

Attachments: Prescription, Medical Records, Growth Records (if indicated), and Clinical References for GLUT1 and the Ketogenic Diet

**Monthly Volume Prescription:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Calories per day** | **Calories per month** | **Tetras of KetoVie 3:1 per month** | **Cases per month** |
| 263 or less | 7,890 | 30 | 1 |
| 264 - 526 | 15,780 | 60 | 2 |
| 527 – 789 | 23,670 | 90 | 3 |
| 790 – 1,052 | 31,560 | 120 | 4 |
| 1,053 – 1,315 | 39,450 | 150 | 5 |

**Appendix A: References**

1. Kass, H.R., Parrish Winesett, S., Bessone, S.K., Turner, Z., & Kossoff E.H. (2016). Use of dietary therapies amongst patients with GLUT1 deficiency syndrome. Seizure, 35:83-87.
2. Alter, A.S., Engelstad, K., Hinton, V.J., Montes, J., Pearson, T.S., Akman, C.I., De Vivo, D.C. (2015). Long-term clinical course of Glut1 deficiency syndrome. J Child Neurol. 30(2):160-9.
3. Gumus, H., Bayram, A.K., Kardas, F. Canpolat, M., Cağlayan, A.O., Kumandas, S., et al. (2015). The effects of ketogenic diet on seizures, cognitive functions, and other neurological disorder in classical phenotype of glucose transporter 1 deficiency syndrome. Neuropediatrics 46(5):313-20.
4. Wang D, Pascual JM, De Vivo D. Glucose Transporter Type 1 Deficiency Syndrome. 2002 Jul 30 [Updated 2015 Jan 22]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017.
5. De Vivo, D. (2014). Glucose transporter Type 1 Deficiency Syndrome. National Organization for Rare Disorders. Retrieved 5/3/2017 from https://rarediseases.org/rare-diseases/glucose-transporter-type-1-deficiency-syndrome/.
6. De Giorgis, V., & Veggiotti, P., (2013). GLUT1 deficiency syndrome 2013: current state of the art. Seizure. 22(10):803-11.
7. Harris, M.L., Patel, H., & Garg, B.P., (2008). Intractable seizures, developmental delay, and the ketogenic diet. Semin Pediatr Neurol. 15(4):209-11.
8. Klepper, J., & Leiendecker, B. (2007). GLUT1 deficiency syndrome-2007 update. Dev. Med. Child Neurol. 49: 707-716.
9. Klepper, J., Scheffer, H., Leiendecker, B., Gertsen, E., Binder, S., Leferink, M., et al. (2005). Seizure control and acceptance of the ketogenic diet in GLUT1 deficiency syndrome: a 2- to 5-year follow-up of 15 children enrolled prospectively. Neuropediatrics 36: 302-308.
10. Klepper, J., Leiendecker, B., Bredahl, R., Athanassopoulos, S., Heinen, F., Gertsen, E., (2002). Introduction of a ketogenic diet in young infants. J. Inherit. Metab. Dis. 25: 449-460.
11. De Vivo, D. C., Trifiletti, R. R., Jacobson, R. I., Ronen, G. M., Behmand, R. A., Harik, S. I. (1991). Defective glucose transport across the blood-brain barrier as a cause of persistent hypoglycorrhachia, seizures, and developmental delay. New Eng. J. Med. 325: 703-709.