For the benefit of patients for whom you prescribe DIACOMIT, we are providing this sample letter of medical necessity, which can be customized by your office and submitted to insurers as part of the prior authorization, medical exception, or pre-determination process. This sample includes general information on Dravet Syndrome and DIACOMIT. You may use this to supplement your patient-specific assessment, clinical judgement and rationale for the medical necessity of DIACOMIT.

The sample letter of medical necessity can be customized by your office and submitted to insurers as part of the prior authorization, medical exception, or pre-determination process.

Please fax this letter to US Bioservices at 833-871-4137 and send a copy to the patient.

If you would like more information on how to utilize this template letter, please contact the Support Center by calling toll-free at 833-248-0467, Monday through Friday, 8 AM to 8 PM ET.

**\*\*\*Remove this section prior to sending this letter\*\*\***



**[Practice Letterhead]**

**[Date]**

**[Name of Medical Director] [Title] [Name of Insurer]
[Address of Insurer]
[City, State, Zip Code]**

**Re: [Patient’s Name]
[Patient ID Number]
[Diagnosis Code(s) and Description(s)]**

I am writing to provide additional information regarding the medical necessity of treating one of your members, **[Patient Name]**, with DIACOMIT® (stiripentol) capsules for oral use or powder for oral suspension. DIACOMIT was approved by the FDA on August 20, 2018 and is indicated for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam.

This letter provides information about my patient’s medical history, an explanation for the use of DIACOMIT, and my rationale for this course of treatment.

**DISEASE OVERVIEW**

Dravet syndrome (DS) is a rare, catastrophic epileptic syndrome currently affecting approximately 2,800 young patients (from 2-18 years old) in the United States (US).1,2 DS is viewed as one of the most medically intractable forms of epilepsy with frequent generalized tonic-clonic seizures, often extending into *status epilepticus*, which results in patient hospitalization. Over the long term, DS patients present with intellectual disability, motor impairment, and care-giver dependence in adulthood.3

DS is associated with a high mortality rate.4,5 Premature mortality effects up to 21% of patients, most frequently between 3 to 7 years of age. Mortality is often from sudden unexcepted death in epilepsy (SUDEP) or from *status epilepticus*.

Additionally, DS is associated with frequent emergency room visits, monthly neurology and pediatric office visits, multiple hospitalizations per year, ongoing drug therapy, diagnostics (including electroencephalography (EEG) and magnetic resonance imaging (MRI)), and eventually institutional care.6

Given the severity of DS, the life-threatening condition of the disease, and its burden both for patients and caregivers, it is of critical importance to manage patients with an optimal therapy as soon as the diagnosis is made. Since DS can be exacerbated by some antiepileptic drugs, early diagnosis and appropriate treatments are important for better prognosis.7

**DIACOMIT CLINICAL STUDIES AND REAL WORLD DATA**

Two phase 3, randomized, double-blind, clinical trials, STICLO-France (N=42) and STICLO-Italy (N=23), evaluated the safety and efficacy of DIACOMIT in DS patients. The pooled findings of the trials were that 70% of patients taking DIACOMIT achieved at least 50% reduction in seizure frequency (the primary endpoint), vs. 5% of the patients on placebo. Of the DIACOMIT patients who achieved the primary endpoint, 36% vs none on placebo were completely free of generalized tonic and tonic-clonic seizures after 8 weeks of treatment.8,9

In these clinical trials, DIACOMIT also reduces the frequency and the duration of seizures and the occurrence of *status epilepticus*.10 Adverse events reported in the clinical trials with an incidence over 10% and at least twice the placebo rate included: nausea (15% vs 3%), weight decreased (27% vs. 6%), decreased appetite (46% vs. 10%), somnolence (67% vs. 23%), and dysarthria (12% vs. 0%).

Additionally, a US study assessing real-world safety and efficacy of DIACOMIT in 82 patients reported that compared to the baseline, most children who received DIACOMIT showed reductions in overall seizure frequency and in frequency of both use of rescue medications and emergency room/hospital visits.11 The long-term safety and efficacy of DIACOMIT in DS is supported by over 25 years of clinical experience, extensive data collection, and analysis.

Cochrane Database Systematic Reviews concluded that DIACOMIT is significantly efficient for reducing seizure frequency and achieving seizure freedom.12 The International League Against Epilepsy and the North American Consensus Panel stated that after first-line treatment with clobazam or valproic acid, DIACOMIT is the second-line therapy in DS guidelines based on strong clinical evidence.13,14

**PATIENT’S DIAGNOSIS AND HISTORY**

The history and course of DS for **[Patient Name]** are as follows:

Diagnosis: **[Insert information regarding the date and method of diagnosis]**

* **[Include bullets of information around patient’s past medical history, such as, types of seizures, how often seizures have occurred, types of medication and reactions.]**

**Clinical course of disease: [Insert patient information regarding disease progression, including past/present comments on working diagnosis prior to DS confirmation, response to any antiepileptic drugs taken (such as, clobazam or valproic acid), occurrence of any type of seizures including myoclonic seizures and later consequences of the disease (such as, ataxia, occurrence of developmental delay, mental retardation, psychiatric and behavior problems, orthopedic and movement issues, and sleep disorders)]**

**Previous treatments: [Insert information on patient’s current therapy and previous treatments to help manage DS (diet modification, discontinuation of specific antiepileptic drugs), therapy (eg, occupational/physical therapy) received for developmental delays or mental retardation, medications and/or therapy for psychiatric and behavior problems, medications or treatments for orthopedic and movement disorders, and medications or treatments for sleep disorders (eg, surgery, CPAP)]**

Despite the use of treatments and therapies to treat the symptoms of DS described in this letter, my patient continues to experience severe seizures not controlled by the current treatments **[he/she/they]** is given, and quality of life is significantly affected by DS. The daily effects of DS my patient experiences include **[long-lasting seizures, developmental delays, mental retardation, psychiatric and behavior problems, orthopedic and movement issues, and sleep disorders]**. It is my opinion that DIACOMIT is appropriate for my patient and may lead to a reduction in a host of seizures and improving my patient’s life. If the patient does not have DIACOMIT, they are likely to experience more of the following services:15

* **[list other possible services such as emergency room visits, hospitalizations, or tests (EEGs or MRIs, etc.)]**

Given the results of the DIACOMIT clinical trials demonstrating significant reduction in seizure frequency and duration, as well as the real-world safety and efficacy information, it is my professional medical opinion that **[Patient Name]** should receive DIACOMIT in order to improve seizure control.

I trust that this information is helpful to you in understanding why I have prescribed treatment with DIACOMIT. If you require any additional information, please do not hesitate to contact me at **[(XXX) XXX-XXXX].**

Sincerely,
**[Physician’s name and title]**

Enclosures: **[Please list and include any additional clinic notes, prescribing Information, FDA approval letter, other supportive medical literature]**

**REFERENCES**

1. Villas N, et al. *Epilepsy Behav*. 2017;74:81-86.
2. Wu YW, et al. *Pediatrics*. 2015 Nov;136(5):e1310-1315.
3. Dravet C. *Epilepsia*. 2011;52(Suppl 2):3-9.
4. Shmuely S, et al. *Epilepsy Behav*. 2016;64(Pt A):69-74.
5. Cooper MS, et al. *Epilepsy Res*. 2016;128:43-47.
6. Whittington MD, et al. *Epilepsy Behav*. 2018;80:109-113.
7. Knupp KG, et al. *CNS Drugs*. 2018;32(4):335-350.
8. Chiron C, et al. *Lancet*. 2000;356:1638-1642.
9. Chiron C. *Neurotherapeutics.* 2007;4:123-125.
10. Thanh TN, et al. *Archives de Pediatrie*. 2002;9 :1120-1127.
11. Wirrell EC, et al. *Epilepsia*. 2013;54(9):1595-1605.
12. Brigo F, et al. *Cochrane Database Syst Rev*. 2017;5:CD010483. 13. Brigo F, et al. *Expert Opin Emerg Drugs.* 2018;23(4):261-269. 14. Wilmshurst JM, et al. *Epilepsia*. 2015;56(8):1185-1197.
15. Wirrell EC, et al. *Pediatr Neurol*. 2017;68:18-34.

**INDICATION**

DIACOMIT (stiripentol) capsules for oral use or powder for oral suspension are indicated for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of DIACOMIT as monotherapy in Dravet syndrome.

**IMPORTANT SAFETY INFORMATION CONTRAINDICATIONS**

No contraindications are listed.

**WARNINGS & PRECAUTIONS**

**Somnolence**

DIACOMIT can cause somnolence. Monitor patients for somnolence, particularly when DIACOMIT is used concomitantly with other CNS depressants or clobazam, which is also known to cause somnolence.

**Decreased Appetite and Decreased Weight**

DIACOMIT can cause decreases in appetite and weight. The growth and weight of pediatric patients treated with DIACOMIT should be carefully monitored.

**Neutropenia and Thrombocytopenia**

DIACOMIT can cause significant declines in neutrophil and platelet counts. Hematologic testing should be obtained prior to starting treatment with DIACOMIT and then every 6 months.

**Withdrawal Symptoms**

As with most antiepileptic drugs (AEDs), DIACOMIT should be gradually withdrawn to minimize the risk of increased seizure frequency and status epilepticus.

**Risks in Patients with Phenylketonuria (PKU)**

DIACOMIT powder for suspension contains phenylalanine, which can be harmful to patients with PKU. Before prescribing DIACOMIT powder for suspension to a patient with PKU, consider the total daily intake of phenylalanine from all sources, including DIACOMIT powder for suspension. DIACOMIT capsules do not contain phenylalanine.

**Suicidal Behavior and Ideation**

AEDs, including DIACOMIT, increase the risk of suicidal thoughts or behavior. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

**ADVERSE REACTIONS**

The most common adverse reactions that occurred in at least 10% of DIACOMIT-treated patients and more frequently than on placebo were somnolence, decreased appetite, agitation, ataxia, decreased weight, hypotonia, nausea, tremor, dysarthria, and insomnia.

**PREGNANCY**

There are no adequate data on the developmental risks associated with the use of DIACOMIT in pregnant women. Based on animal data, DIACOMIT may cause fetal harm.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to AEDs, such as DIACOMIT, during pregnancy. Physicians are advised to recommend that pregnant patients taking DIACOMIT enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry (information at http://www.aedpregnancyregistry.org). This can be done by calling the toll-free number 1-888-233-2334, and must be done by patients themselves or their caregiver.

To report suspected adverse reactions, contact BIOCODEX at 1-866-330-3050 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.