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.

[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 long-lasting seizures, often generalized with *status epilepticus*, which result in patient hospitalization. Over the long term, DS patients present with intellectual disability, motor impairment, and dependence in adulthood.[3]

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

Additionally, DS is associated with high direct and indirect costs for the healthcare system and caregiver, including 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 administer 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]

TREATMENT DESCRIPTION AND RATIONALE

Two phase 3, randomized, double-blind, clinical trials, STICLO-France (N=42) and STICLO-Italy (N=23), evaluated the efficacy of DIACOMIT in DS patients. The overall findings of the trials were that 70% of patients achieved at least 50% reduction in seizure frequency with DIACOMIT, of whom 36% vs none on placebo were completely free of generalized tonic and tonic-clonic seizures after 8 weeks of treatment.[8,9] The small numbers of patients in each trial reflect the striking efficacy of DIACOMIT, since these small numbers were enough to demonstrate the very significant superiority of DIACOMIT over the current therapies.

It has also been shown that DIACOMIT reduces the frequency and the duration of seizures and the occurrence of *status epilepticus.*[10] Additionally, a US study assessing real-world safety and efficacy of DIACOMIT in 82 patients reported that compared to baseline, most children who received stiripentol 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]**

- Clinical observations of generalized tonic or tonic-clonic seizures during the first year of life
- Occurrence of myoclonic seizures and ataxia
- Poor response to antiepileptic drugs (clobazam and/or valproic acid)[3]

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

Previous treatments: [Insert information on 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]** 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 **[his/her]** DIACOMIT, the patient is likely to experience more of the following services[15]:

- Emergency room visits
- Hospitalizations
- EEGs and MRIs

DIACOMIT is an FDA-approved orphan product for DS. DIACOMIT comes in capsules and fruit-flavored powder packets so caregivers have options for giving it to their child. DIACOMIT offers clinically meaningful reduction in seizure frequency and duration and finally fills an unmet need in this rare and dramatic disease.

Given the applicability of DIACOMIT clinical trials to this patient and the improvement of seizure frequency and duration, 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], MD

Enclosures: **[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.