Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Diacomit (stiripentol)

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Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for **Diacomit (stiripentol)** when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered

Diacomit (stiripentol) may be considered **medically necessary** when all of the following criteria are met:

FDA-Approved Indications:

1. **Dravet Syndrome.** Approve for 1 year if the patient meets ONE of the following criteria **(A or B)**:
   - A. Initial Therapy: Approve for 1 year if the patient meets the following criteria (**i, ii, and iii)**:
     - i. The patient is ≥ 6 months of age and weighing ≥7 kg; **AND**
     - ii. The patient meets ONE of the following criteria **(a or b)**:
       - a. The patient is taking concomitant clobazam; **OR**
       - b. The patient is unable to take clobazam due to adverse events as determined by the prescribing physician; **AND**
     - iii. Diacomit is prescribed by, or in consultation with, a neurologist; **OR**
   - B. Patient is Currently Receiving Diacomit: Approve for 1 year if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescribing physician.

There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome.[1]

Other Uses with Supportive Evidence:

2. **Treatment-Refractory Seizures/Epilepsy, Including Lennox-Gastaut Syndrome.** Approve for 1 year if the patient meets ONE of the following criteria **(A or B)**:
    A. Initial Therapy: Approve for 1 year if the patient meets the following criteria **(i, ii, and iii)**
        i. The patient is ≥ 2 years of age; **AND**
        ii. The patient has tried at least two other antiepileptic drugs (e.g., valproic acid, lamotrigine, topiramate, clonazepam, Banzel, felbamate, clobazam, Fycompa, Sabril, levetiracetam, zonisamide, others); **AND**
        iii. Diacomit is prescribed by, or in consultation with, a neurologist; **OR**
    B. Patient is Currently Receiving Diacomit: Approve for 1 year if the patient is responding to therapy (e.g., reduced seizure severity, frequency, and/or duration) as determined by the prescribing physician.

In one study (n = 212), Diacomit was studied in children with different types of epilepsy syndromes whose seizures were refractory to more than two AEDs [including Sabril].6 In the 88 patients who completed the 3-month placebo-controlled study, 56.8% of patients with partial epilepsy responded (with 14% becoming seizure free) compared with 41.9% of patients with generalized epilepsy and 38.4% of patients with myoclonic epilepsy. Diacomit has also been administered to patients with epileptic encephalopathies associated with SCN1A mutations or other sodium channel mutations under compassionate use protocalls.7 A single-blind, multicenter, exploratory trial evaluated Diacomit in combination with standard treatment in 16 patients with Lennox-Gastaut syndrome (LGS) and eight patients with symptomatic generalized epilepsy of the Lennox-Gastaut type.8 There were 15 evaluable patients with LGS. The overall results identified some benefit for LGS where 60% of patients were responders (based on 50% responder rate). Diacomit treatment produced a mean 62% seizure reduction and median -80% reduction from baseline.

When Policy Topic is not covered

Diacomit (stiripentol) is considered **not medically necessary** when the above criteria is not met and **investigational** for all other uses.

Considerations

Diacomit (stiripentol) requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, local medical policies of other health plans, Medicare (CMS), local providers.

Description of Procedure or Service

Diacomit, an antiepileptic drug (AED), is indicated for the treatment of seizures associated with Dravet syndrome in patients ≥ 2 years of age taking clobazam. There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome. The mechanism by which Diacomit exerts its anticonvulsant effect is not known. Possible mechanisms of action include direct effects mediated through the gamma-aminobutyric acid (GABA)A receptor and indirect effects involving inhibition of cytochrome P450 (CYP) activity with resulting increase in blood levels of clobazam and its active metabolite.

Disease Overview

Dravet syndrome is a rare genetic epileptic encephalopathy (dysfunction of the brain) marked with frequent and/or prolonged seizures.[2,3] It's been estimated that 1 out of 15,700 infants born in the US are affected with Dravet syndrome. The seizures generally begin in the first year of life in an otherwise healthy infant. Affected individuals can develop many seizure types: myoclonic, tonic-clonic, absence, atypical absence, atonic, focal aware or impaired awareness (previously called partial seizures), and status epilepticus.[3] As the seizures continue, most of the children develop some level of developmental disability and other conditions associated with the syndrome. Two or more antiepileptic drugs (AEDs) are often needed to control the seizures; most of the seizures are refractory to medications. The goals of treatment are cessation of prolonged convulsions, reductions in overall seizure frequency, and minimization of treatment side effects.[4,5] Some patients respond to the ketogenic diet and/or vagus nerve stimulation.

Guidelines/Recommendations

Valproic acid and clobazam are considered to be the first-line treatment for Dravet syndrome.[2,4,5] If seizure control is suboptimal, Diacomit and topiramate are second-line treatment. Ketogenic diet is moderately effective and can also be considered second-line. If control is still inadequate, other therapies to consider are clonazepam, levetiracetam, and zonisamide. Sodium channel blockers (e.g., carbamazepine, oxcarbazepine, lamotrigine, and phenytoin can worsen seizures in Dravet syndrome. Additionally, Sabril® (vigabatrin tablet, oral packet for suspension [generics]) and tiagabine may increase the frequency of myoclonic seizures and should be avoided.

Safety

The most common AEs in patients treated with Diacomit in the placebo-controlled studies were somnolence (67%), decreased appetite (45%), agitation (27%), ataxia (27%), weight decreased (27%), hypotonia (24%), nausea (15%), tremor (15%), dysarthria (12%), and insomnia (12%). Hematologic testing should be obtained prior to starting treatment with Diacomit and every 6 months. During a clinical trial, a decrease in neutrophil count from normal at baseline to < 1,500 cells/mm3 was observed in 13% of patients treated with Diacomit but not in patients treated with placebo. Also during this clinical trial, a decrease in platelet count from normal at baseline to < 150,000/µL during the trial was observed in 13% of these patients but not in patients on placebo. Also during this clinical trial,

a decrease in platelet count from normal at baseline to < 150,000/µL during the trial was observed in 13% of these patients but not in patients on placebo.

Diacomit powder for suspension contains phenylalanine, a component of aspartame. Each 250 mg packet contains 1.4 mg phenylalanine; each 500 mg packet contains 2.8 mg phenylalanine. Consider the combined daily amount of phenylalanine from all sources, including Diacomit, in patients with phenylketonuria (PKU). Diacomit capsules do not contain phenylalanine.

Warnings and Precautions

- Somnolence: DIACOMIT can cause somnolence. In controlled studies in patients with Dravet syndrome, the incidence of somnolence was 67% in DIACOMIT-treated patients, compared to 23% in patients on placebo. All patients in both groups were on concomitant clobazam, which is also known to cause somnolence. Co-administration of DIACOMIT with clobazam results in increased levels of clobazam and its active metabolite. Other central nervous system CNS depressants, including alcohol, could potentiate the somnolence effect of DIACOMIT.

  Prescribers should monitor patients for somnolence. If somnolence occurs during coadministration with clobazam, consider an initial reduction of clobazam by 25%. If somnolence persists, further clobazam reduction by an additional 25% should be considered, as should adjustment of the dosage of other concomitant anticonvulsant drugs with sedating properties. Prescribers should caution patients against engaging in hazardous activities requiring mental alertness, such as operating dangerous machinery or motor vehicles, until the effect of DIACOMIT on mental alertness is known.

- Decreased Appetite and Decreased Weight: DIACOMIT can cause decreases in appetite and weight. In controlled studies in patients with Dravet syndrome, the incidence of decreased appetite was 46% in DIACOMIT-treated patients, compared to 10% in patients on placebo. The incidence of decreased weight was 27% in DIACOMIT-treated patients, compared to 6% in patients on placebo. Nausea and vomiting also occurred more frequently in DIACOMIT-treated patients. Given the frequency of these adverse reactions, the growth of pediatric patients treated with DIACOMIT should be carefully monitored. In some cases, decreasing the dose of concomitant valproate by 30% per week can reduce the decrease in appetite and weight.
- Neutropenia and Thrombocytopenia: DIACOMIT can cause a significant decline in neutrophil count. In controlled studies in patients with Dravet syndrome, there were 31 patients treated with DIACOMIT who had both a baseline and end-of-study neutrophil count obtained. A decrease in neutrophil count from normal at baseline to less than 1500 cells/mm3 during the trial was observed in 13% of these DIACOMIT treated patients, but not in any placebo-treated patients.

DIACOMIT can cause a significant decline in platelet count. In controlled studies in patients with Dravet syndrome, there were 31 patients treated with DIACOMIT who had both a baseline and end-of-study platelet count. A decrease in platelet count from normal at baseline to less than 150,000/μL during the trial was observed in 13% of these DIACOMIT-treated patients, but not in any placebo-treated patients.

Hematologic testing should be obtained prior to starting treatment with DIACOMIT, and then every 6 months.

- Withdrawal Symptoms: As with most antiepileptic drugs, DIACOMIT should generally be withdrawn gradually to minimize the risk of increased seizure frequency and status epilepticus.

  In situations where rapid withdrawal of DIACOMIT is required (e.g., in the setting of a serious adverse reaction), appropriate monitoring is recommended.

- Risks in Patients with Phenylketonuria: Phenylalanine can be harmful to patients with phenylketonuria (PKU). DIACOMIT Powder for Suspension contains phenylalanine, a component of aspartame. Each 250 mg packet contains 1.40 mg phenylalanine; each 500 mg packet contains 2.80 mg phenylalanine. Before prescribing DIACOMIT Powder for Suspension to a patient with PKU, consider the combined daily amount 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 in patients taking these drugs for any indication. 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.

  Anyone considering prescribing DIACOMIT or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

  Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the

emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Rationale

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Diacomit (stiripentol) while maintaining optimal therapeutic outcomes.

REFERENCES

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Billing Coding/Physician Documentation Information

N/A	Oral; pharmacy benefit

Additional Policy Key Words

N/A

Policy Implementation/Update Information

10/2019	New policy titled Diacomit (stiripentol)

10/2020	Annual review – no changes made
10/2021	Annual review – no changes made
10/2022	Annual review – changed age from ≥2 years or age to ≥6 months of age and weighing ≥7 kg and adding Warnings and Precautions
10/2023	Annual review – no changes made
