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Coverage Policy Number **IP0409**

Stiripentol

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for **Diacomit®** (stiripentol) capsules and powder for oral suspension.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Stiripentol (Diacomit) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Documented diagnosis of Dravet Syndrome.** Individual meets **ALL** of the following criteria (A, B, and C):
    A. Individual is 6 months of age or older and weighs at least 7 kg
    B. Individual meets **ONE** of the following criteria (i or ii):
        i. Individual is taking concomitant clobazam
        ii. Documentation the individual is unable to take clobazam due to intolerance
    C. The medication is being prescribed by, or in consultation with, a neurologist

2. **Documented diagnosis of one of the following specific conditions when causing treatment-refractory seizures/epilepsy** (such as, Lennox-Gastaut Syndrome; infantile spasms; tuberous sclerosis complex; Sturge-Weber syndrome; Doose syndrome; infection-related or anoxo-ischemic epilepsy syndromes; cortical malformation/dysplasia; epileptic encephalopathies associated with sodium channel mutations; and epilepsy with myoclonic absences). Individual meets **ALL** of the following criteria (A, B, and C):
    A. Individual is 6 months of age or older and weighs at least 7 kg
    B. There is documentation that the individual has had an inadequate response, contraindication, or intolerance to **TWO** other antiepileptic drugs
    C. The medication is being prescribed by, or in consultation with, a neurologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Stiripentol (Diacomit) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response (for example, reduced seizure severity, frequency, and/or duration).

Authorization Duration

Initial approval duration: up to 12 months.

Reauthorization approval duration: up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Diacomit, an antiepileptic drug (AED), is indicated for the treatment of seizures associated with **Dravet syndrome** in patients ≥ 6 months of age and weighing ≥ 7 kg taking clobazam.[1] There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome.

Disease Overview
Dravet syndrome is a rare genetic epileptic encephalopathy (dysfunction of the brain) marked with frequent and/or prolonged seizures.[2,3] 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] Two or more 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, reduction in overall seizure frequency, and minimization of treatment side effects.[4,5]

Clinical Efficacy in Other Refractory Seizures
In one study (n = 212), Diacomit was studied in children with different types of epilepsy syndromes (including Lennox-Gastaut Syndrome [LGS]; infantile spasms; infection□related or anoxo-ischemic epilepsy syndromes; tuberous sclerosis complex; Sturge□Weber syndrome; Doose syndrome; cortical malformation/dysplasia; and epilepsy with myoclonic absences) whose seizures were refractory to more than two AEDs (including vigabatrin).[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 sodium voltage-gated channel alpha subunit 1 (SCN1A) mutations or other sodium channel mutations under compassionate use protocols.[7] A single-blind, exploratory trial evaluated Diacomit in combination with standard treatment in 16 patients with 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. Additionally, a published study of Diacomit added to carbamazepine in childhood partial epilepsy (n = 67) demonstrated seizure response in 32 patients with conditions including herpetic encephalitis, LGS, and tuberous sclerosis complex.[9]

Guidelines/Recommendations

At this time, there are three drugs approved for the treatment of seizures associated with Dravet syndrome: Diacomit, Epidiolex® (cannabidiol oral solution), and Fintepla® (fenfluramine oral solution).[1,10,11] An expert panel considers valproic acid and clobazam to be the first-line treatment for Dravet syndrome.[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. The Dravet Foundation states that Diacomit, Epidiolex, and Fintepla are considered first-line agents for the treatment of Dravet syndrome.[2] If control is still inadequate, other therapies to consider are clonazepam, levetiracetam, and zonisamide.[2,4,5] Sodium channel blockers (e.g., carbamazepine, oxcarbazepine, lamotrigine, and phenytoin) can worsen seizures in Dravet syndrome. Additionally, vigabatrin and tiagabine may increase the frequency of myoclonic seizures and should be avoided.

References

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