PRIOR AUTHORIZATION POLICY

POLICY: Antiepileptics – Diacomit Prior Authorization Policy
- Diacomit® (stiripentol capsules and powder for oral suspension – Biocodex)

REVIEW DATE: 02/03/2021

OVERVIEW

Diacomit, an antiepileptic drug (AED), is indicated for the treatment of seizures associated with **Dravet syndrome** in patients ≥ 2 years of age 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, reductions 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 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, 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 are considered 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Diacomit. Because of the specialized skills required for evaluation and diagnosis of patients treated with Diacomit as well as the monitoring required for adverse events and efficacy, initial approval requires Diacomit to be prescribed by, or in consultation with, a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Diacomit is recommended in those who meet the following criteria:

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.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient meets ONE of the following criteria (a or b):
       - **a)** Patient is taking concomitant clobazam; OR
       - **b)** Patient is unable to take clobazam due to adverse events as determined by the prescriber; AND
     - **iii.** The medication 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 prescriber.

Other Uses with Supportive Evidence

2. **Treatment-Refractory Seizures/Epilepsy [specific rare conditions]** (i.e., 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). 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.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient has tried at least two other antiepileptic drugs; AND
       Note: Examples of other antiepileptic drugs include valproic acid, lamotrigine, topiramate, clonazepam, Banzel® (rufinamide tablet, oral suspension), felbamate, clobazam, Fycompa® (perampanel tablet, oral suspension), vigabatrin, levetiracetam, zonisamide, others.
     - **iii.** The medication 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 prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Diacomit is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Diacomit® capsules and oral suspension [prescribing information]. Redwood City, CA: Biocodex; August 2018.
2. Dravet Foundation – Dravet Syndrome. Available at: https://www.dravetfoundation.org/what-is-dravet-syndrome/. Accessed on February 1, 2021.
3. Shafer PO. Epilepsy Foundation – Dravet Syndrome. Updated September 2, 2018. Available at: https://www.epilepsy.com/learn/types-epilepsy-syndromes/dravet-syndrome. Accessed on February 1, 2021.
4. Knupp KG, Wirrell EC. Treatment Strategies for Dravet Syndrome. *CNS Drugs*. 2018;32(4):335-350.
5. Wirrell EC, Laux L, Donner, et al. Optimizing the diagnosis and management of Dravet syndrome: recommendations from a North American Consensus Panel. *Pediatr Neurol*. 2017;68:18-34.
6. Perez J, Chiron C, Musial C, et al. Stiripentol: efficacy and tolerability in children with epilepsy. Epilepsia. 1999;40(11):1618-1626.
7. Perry MS. Expanded access use of stiripentol in Dravet syndrome or sodium channel mutation epileptic encephalopathies. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2021 Feb 1]. Available at: https://www.clinicaltrials.gov/ct2/show/NCT02239276?term=stiripentol&rank=2. NLM Identifier: NCT02239276.
8. Center for Drug Evaluation and Research. Clinical review of Diacomit. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/206709Orig1s000,207223Orig1s000MedR.pdf. Accessed on February 1, 2021.
9. Chiron C, Tonnelier S, Rey E, et al. Stiripentol in childhood partial epilepsy: randomized placebo-controlled trial with enrichment and withdrawal design. *J Child Neurol*. 2006;21(6):496-502.
10. Epidiolex® oral solution [prescribing information]. Carlsbad, CA: Greenwich Biosciences, Inc; October 2020.
11. Fintepla® oral solution [prescribing information]. Emeryville CA: Zogenix Inc; June 2020.