BlueCross BlueShield Arizona

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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE:**	**5/16/2019**
SECTION: DRUGS	**LAST REVIEW DATE:**	**5/19/2022**
	LAST CRITERIA REVISION DATE:	**5/20/2021**
	ARCHIVE DATE:	

DIACOMIT® (stiripentol)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Diacomit (stiripentol) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
  2. Individual is 2 years of age or older
  3. A confirmed diagnosis of seizures associated with Dravet syndrome (DS) in a patient taking clobazam and having at least four generalized clonic or tonic-clonic seizure per month
  4. Documented failure, contraindication per FDA label, intolerance to valproate as first-line therapy and clobazam as first-line add-on therapy
  5. Will not be used as monotherapy, if approved, it will be added to treatment with clobazam
  6. Individual does not have moderate or severe renal impairment
  7. Individual does not have moderate or severe hepatic impairment

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Diacomit (stiripentol) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Neurologist
  2. Individual's condition responded while on therapy
     a. Response is defined as **ALL** of the following:
        i. No evidence of disease progression
        ii. Experienced at least a 50% decrease in frequency (per 30 days) of generalized clonic or tonic-clonic seizures compared to baseline
  3. Individual has been adherent with the medication
  4. Individual has not developed any significant adverse drug effects that may exclude continued use
     a. Significant adverse effect such as:
        i. Emergence or worsening of depression, suicidal thoughts, behavior, or thoughts of self-harm and/or any unusual changes in mood or behavior
        ii. Phenylketonuria from use of powder for suspension formulation
        iii. Neutropenia
        iv. Thrombocytopenia

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5. Will not be used as monotherapy, treatment includes clobazam
6. Individual does not have moderate or severe renal impairment
7. Individual does not have moderate or severe hepatic impairment
8. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Diacomit (stiripentol) is indicated for the treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of Diacomit (stiripentol) as monotherapy in DS. The mechanism by which Diacomit (stiripentol) exerts its anticonvulsant effect in humans is unknown. Possible mechanisms of action include direct effects mediated through the gamma-aminobutyric acid (GABA) receptor and indirect effects involving inhibition of cytochrome P450 activity with resulting increase in blood levels of clobazam and its active metabolite.

The package label states the effectiveness of Diacomit (stiripentol) in the treatment of DS was established in two multicenter placebo-controlled double-blinded studies in DS patients. Lack of control was defined as individual having at least four generalized clonic or tonic-clonic seizure per month. In both studies, patients were required to be **3 years of age** to less than 18 years of age who were inadequately controlled on clobazam **and** valproate. Diacomit (stiripentol) was added to their treatment with clobazam **and** valproate. The effectiveness of Diacomit (stiripentol) for treatment of DS in patients 2 years of age to less than 3 years of age was **extrapolated** from the demonstration of effectiveness in patients 3 years of age to less than 18 years of age.

DS, previously known as severe myoclonic epilepsy of infancy, is a rare early-onset epileptic encephalopathy characterized by refractory epilepsy and neurodevelopmental problems beginning in infancy. Patients present in the first year of life with a prolonged, often febrile, clonic seizure in the setting of normal cognitive and motor development prior to seizure onset. In most, febrile and afebrile seizures, including episodes of status epilepticus, recur repeatedly in the weeks to months after the initial event, and psychomotor impairment begins thereafter. Myoclonus, both epileptic and non-epileptic, occurs frequently. The majority of older children and young adults with DS have motor system dysfunction, gait and postural abnormalities, and cognitive and behavioral impairment.

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DS seizures tend to be refractory to most anti-seizure drugs, and some patients derive benefit from a ketogenic diet and vagus nerve stimulation. The most commonly used anti-seizure drugs include valproate, clobazam, topiramate, levetiracetam, stiripentol, and cannabidiol. Most patients require two or more agents to achieve reasonable seizure control.

Valproate is considered a first-line agent for DS with clobazam added as a second agent if valproate does not control seizures despite adequate valproate dosing and serum levels. Topiramate is a broad spectrum antiseizure agent that is also used as added on therapy. Stiripentol is also considered as add-on therapy. Clonazepam, levetiracetam, zonisamide, ethosuximide, and vegal nerve stimulation are considered third-line treatments for DS. Cannabidiol (or CBD) is also approved for treatment for DS.

Resources:

Diacomit (stiripentol) product information, revised by Biocodex, Inc. 05-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 07, 2022.

Andrade DM, Nascimento FA. Dravet syndrome: Genetics, clinical features, and diagnosis. In: UpToDate, Nordil DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated April 12, 2022. Accessed May 07, 2022.

Andrade DM, Nascimento FA. Dravet syndrome: Management and prognosis. In: UpToDate, Nordil DR, Dashe JF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated November 15, 2021. Accessed May 07, 2022.