BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

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

DIACOMIT® (stiripentol) oral capsule & oral powder for suspension

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 seizures 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 valproate and having at least four generalized clonic or tonic-clonic seizure per month
  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - Complete blood count with differential
  5. Will not be used as monotherapy
  6. Will not be used in individuals with moderate or severe renal impairment
  7. Will not be used in individuals with 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 seizures or is in consultation with a Neurologist
  2. Individual's condition responded while on therapy
     - Response is defined as **ALL** of the following:
       - No evidence of disease progression
       - 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 level 4 adverse drug effects that may exclude continued use
     - Significant adverse effect such as:
       - Emergence or worsening of depression, suicidal thoughts, behavior, or thoughts of self-harm and/or any unusual changes in mood or behavior
       - Phenylketonuria from use of powder for suspension formulation
       - Neutropenia
       - Thrombocytopenia

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5. Will not be used as monotherapy
6. Will not be used in individuals with moderate or severe renal impairment
7. Will not be used in individuals with moderate or severe hepatic impairment
8. There are no significant interacting drugs

Renewal duration: 12 months

- Diacomit (stiripentol) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing or frequency outside the FDA-approved dosing and frequency

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 clobazan **and** valproate. Diacomit (stiripentol) was added to their treatment with clobazan **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

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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.

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, stirpentol, 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 accessed 05-10-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=58304ba8-9779-4658-811e-94ffe08c3f16

UpToDate: Dravet syndrome: Genetics, clinical features, and diagnosis. Current through Oct 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/dravet-syndrome-genetics-clinical-features-and-diagnosis?search=Lennox-Gastaut%20syndrome&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

UpToDate: Dravet syndrome: Management and prognosis. Current through Oct 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/dravet-syndrome-management-and-prognosis?search=Lennox-Gastaut%20syndrome&source=search_result&selectedTitle=10~150&usage_type=default&display_rank=10

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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Office notes, labs, and medical testing relevant to the request that show medical justification are required.