Clinical Policy: Stiripentol (Diacomit)

Reference Number: CP.PMN.184
Effective Date: 09.25.18
Last Review Date: 11.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Stiripentol (Diacomit®) is an anticonvulsant.

FDA Approved Indication(s)

Diacomit is indicated for the treatment of seizures associated with Dravet syndrome in patients taking clobazam who are 6 months of age and older and weighing 7 kg or more. There are no clinical data to support the use of Diacomit as monotherapy in Dravet syndrome.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Diacomit is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Dravet Syndrome (must meet all)**:**

1. Diagnosis of Dravet syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 6 months;
4. Member weighs ≥ 7 kg;
5. Will be used as adjunctive therapy (*see Appendix B*) with at least one other antiepileptic drug;
6. Failure of ≥ 3 month trial of Epidiolex® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 50 mg/kg (up to a maximum of 3,000 mg) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Dravet Syndrome (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Diacomit for Dravet syndrome and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Diacomit will continue to be used as adjunctive therapy (*see Appendix B*) with at least one other antiepileptic drug;
4. If request is for a dose increase, new dose does not exceed 50 mg/kg (up to a maximum of 3,000 mg) per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
EEG: electroencephalography
MRI: magnetic resonance imaging
NICE: National Institute for Health and Care Excellence

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
clobazam (Onfi®, Sympazan®)	Initial: 0.2-0.3 mg/kg/day PO*	0.5-2 mg/kg/day
valproic acid (Depakene®, Depakote®, Stavzor®)	Initial: 10-15 mg/kg/day PO, given in 2-3 equally divided doses*	25-60 mg/kg/day
topiramate (Topamax®, Trokendi® XR, Qudexy® XR)	Initial: 0.5-2 mg/kg/day PO*	8-12 mg/kg/day
levetiracetam (Spritam®, Keppra®)	Initial: 10-20 mg/kg/day PO, divided in 2-3 doses*	60-80 mg/kg/day
Other antiepileptic drugs: clonazepam (Klonopin®), zonisamide (Zonegran®), ethosuximide (Zarontin®), phenobarbital	PO; off-label dosing information not available	Off-label dosing information not available
Epidiolex® (cannabidiol)	Initial: 2.5 mg/kg PO BID Maintenance: 5 mg/kg PO BID	20 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Dravet syndrome, also known as severe myoclonic epilepsy of infancy (SMEI), is a severe form of epilepsy with an incidence of 1 in 15,700 to 1 in 40,900. Diagnosis is largely based on clinical presentation as magnetic resonance imaging (MRI) is usually normal and electroencephalography (EEG) findings are nonspecific.

- Complete seizure control is typically not achievable, so the primary goal of therapy is to reduce seizure frequency. The following therapies are recommended for the management of Dravet syndrome by the United Kingdom National Institute for Health and Care Excellence (NICE; April 2018) and a North American Consensus Panel (January 2017):

	NICE	North American Consensus Panel
1st line	Valproic acid or topiramate	Valproic acid or clobazam *If first choice is not effective, then add the other*
2nd line	Addition of clobazam or Diacomit	Addition of Diacomit or topiramate
3rd line	Refer to tertiary specialist	Addition of clonazepam, levetiracetam, zonisamide, ethosuximide, or phenobarbital

- Diacomit increases plasma concentrations of clobazam through inhibition of CYP3A4 and 2C19.
- FDA-approved in August 2018, Diacomit had long prior been used in clinical practice in Canada, Japan, and European countries as well as off-label in the United States through a compassionate-use program.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Dravet syndrome	Age ≥ 6 months and weighing 7 kg to < 10 kg: 25 mg/kg twice daily Age ≥ 1 year and weighing ≥ 10 kg: 25 mg/kg twice daily or 16.67 mg/kg three times daily	50 mg/kg/day (not to exceed 3,000 mg/day)

VI. Product Availability

- Capsules: 250 mg, 500 mg
- Powder for oral suspension: 250 mg, 500 mg

VII. References

1. Diacomit Prescribing Information. Beauvais, France: Biocodex; July 2022. Available at: www.diacomit.com/downloads/pdf/DIACOMIT_US_PI.pdf. Accessed July 5, 2023.
2. Wirrell EC, Laux L, Jette N, et al. Optimizing the diagnosis and management of Dravet syndrome: recommendations from a North American consensus panel. Pediatr Neurol. 2017; 68:18-34.
3. National Institute for Health and Care Excellence (NICE). Epilepsies: diagnosis and management. Available at: https://www.nice.org.uk/guidance/CG137/chapter/Appendix-E-Pharmacological-treatment. Accessed August 1, 2019.
4. Wirrell EC, Hood V, Knupp KG et al. International consensus on diagnosis and management of Dravet syndrome. Epilepsia. 2022;63:1761-77. DOI: 10.1111/epi.17274.
5. Strzelczyk A, Schubert-Bast S. A practical guide to the treatment of Dravet syndrome with anti-seizure medication. CN Drugs. 2022;36:217–237. https://doi.org/10.1007/s40263-022-00898-1.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2019 annual review: added requirement that Diacomit continue to be used as adjunctive therapy for reauthorization; references reviewed and updated.	08.01.19	11.19
Added HIM line of business per SDC and prior clinical guidance.	10.07.19	
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.04.20	11.20
Per November SDC and prior clinical guidance, added redirect to Epidiolex	11.16.20	
4Q 2021 annual review: no significant changes; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.22.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
4Q 2022 annual review: no significant changes; RT4: updated the policy to reflect the new indication expansion to patients ≥ 6 months of age and weighing ≥ 7 kg; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.25.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	08.16.23	11.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.