Clinical Policy Title:	stiripentol
Policy Number:	RxA.104
Drug(s) Applied:	Diacomit®
Original Policy Date:	02/07/2020
Last Review Date:	10/19/2022
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
stiripentol (Diacomit®)	Seizures associated with Dravet syndrome	50 mg/kg/day orally in 2-3 divided doses	3,000 mg/day

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Seizures associated with Dravet Syndrome (must meet all):

1. Diagnosis of seizures associated with Dravet syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 6 months;
4. Member's weight ≥ 7 kg;
5. Will be used as adjunctive therapy (see Appendix B) with at least one other antiepileptic drug;
6. Hematologic testing should be obtained prior to starting treatment to monitor for neutropenia and thrombocytopenia;
7. Dose does not exceed 50 mg/kg (up to a maximum of 3,000 mg) per day.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

II. Continued Therapy Approval

A. Seizures associated with Dravet Syndrome (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance, 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. Hematologic testing conducted every 6 months to monitor for neutropenia and thrombocytopenia;
5. 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
EEG: electroencephalography
MRI: Magnetic resonance imaging
NICE: National Institute for Health and Care Excellence
SMEI: severe myoclonic epilepsy of infancy

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
clobazam (Onfi®, Sympazan®)	Initial: 0.2-0.3 mg/kg/day orally divided twice daily	2 mg/kg/day
valproic acid (Depakote®)	Initial: 10-15 mg/kg/day orally, given in 2-3 equally divided doses	25-60 mg/kg/day
Epidiolex®	Maintenance: 5 mg/kg orally twice daily	20 mg/kg/day
topiramate (Topamax®, Trokendi® XR, Qudexy® XR)	Initial: 0.5-2 mg/kg/day orally	8-12 mg/kg/day
levetiracetam (Spritam®, Keppra®)	Initial: 10-20 mg/kg/day orally, divided in 2-3 doses	60-80 mg/kg/day
Other antiepileptic drugs: clonazepam (Klonopin®), zonisamide (Zonegran®), ethosuximide (Zarontin®), phenobarbital	Varies	Varies

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - 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 c
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.
- Although only recently FDA-approved in August 2018, Diacomit® has been long used in clinical practice in Canada, Japan, and European countries as well as off-label in the United States through a compassionate-use program.

References

1. Diacomit® Prescribing Information. San Mateo, CA, USA: Biocodex; July 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=58304ba8-9779-4658-811e-94ffe08c3f16&type=display. Accessed September 15, 2022.
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. Available at: https://pubmed.ncbi.nlm.nih.gov/28284397/. Accessed September 15, 2022.
3. National Institute for Health and Care Excellence (NICE). Epilepsies: diagnosis and management. Available at: https://www.nice.org.uk/guidance/CG137/chapter/Appendix-EPharmacological-treatment. Accessed September 15, 2022.

4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2022. Available at: http://www.clinicalkey.com. Accessed September 15, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
1. Criteria added to initial and continued therapy: Hematologic testing should be obtained prior to starting treatment and every 6 months to monitor for neutropenia and thrombocytopenia. 2. Updated References	4/30/2020	5/20/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to All lines of business. 2. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance. 3. Therapeutic alternatives were updated: Deleted the discontinued drugs. 4. Appendix B standard verbiage has been changed and updated.	01/14/2021	03/09/2021
Policy was reviewed: 1. Dosing Information, Indication: Updated from Dravet syndrome to Seizures associated with Dravet syndrome. 2. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial Approval Criteria, I.A, I.A.1: Updated indication from Dravet syndrome to Seizures associated with Dravet syndrome. 4. Continued Therapy Approval Criteria, II.A: Updated indication from Dravet syndrome to Seizures associated with Dravet	11/24/2021	1/17/2022

syndrome. 5. Continued Therapy Approval Criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance”…". 6. Appendix A: Updated to include abbreviation SMEI. 7. Appendix B, Epidiolex®: Updated to remove unavailable generic therapeutic alternative cannabidiol. 8. Appendix B, Dosing Regimen, Onfi®, Sympazan®: Updated dosing information from Initial: 0.2-0.3 mg/kg/day PO to Initial: 0.2-0.3 mg/kg/day orally divided twice daily. 9. Statement about drug listing format in Appendix B is rephrased “o "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic o”ly". 10. References were reviewed and updated.		
Policy was reviewed: 1. Background: Updated information regarding age from 2 years of age to 6 months of age. 2. Background: Updated to include new information regarding patient’s weight, "weighing 7 kg or more ". 3. Initial Approval Criteria, I.A.3: Updated age criteria from 2 years of age to 6 months of age. 4. Initial Approval Criteria, I.A.4: Updated to include new weight criteria Member’s weight ≥ 7 kg. 5. Appendix B, Maximum Dose,	9/15/2022	10/19/2022

clobazam (Onfi®, Sympazan®): Updated maximum dose information from 0.5-2 mg/kg/day to 2 mg/kg/day for indication Seizures associated with Dravet syndrome. 6. References were reviewed and updated.		