Clinical Policy: Stiripentol (Diacomit)
Reference Number: ERX.NPA.100
Effective Date: 09.25.18
Last Review Date: 11.18

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 2 years of age and older taking clobazam.

Limitation(s) of use: 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 Envolve Pharmacy Solutions™ 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 ≥ 2 years;
      4. Will be used as adjunctive therapy (see Appendix B) with at least one other antiepileptic drug;
      5. Dose does not exceed 50 mg/kg (up to a maximum of 3,000 mg) per day.
   Approval duration: Length of Benefit

   B. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. Dravet Syndrome (must meet all):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. 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: Length of Benefit

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
      Approval duration: Duration of request or 12 months (whichever is less); or
      2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).
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 policy – ERX.PA.01 or
evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
- FDA: Food and Drug Administration
- NICE: National Institute for Health and Care Excellence
- EEG: electroencephalography
- MRI: magnetic resonance imaging

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 and may require prior authorization.

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

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):

<table>
<thead>
<tr>
<th>NICE</th>
<th>North American Consensus Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st line</td>
<td>Valproic acid or topiramate</td>
</tr>
<tr>
<td></td>
<td>Valproic acid or clobazam</td>
</tr>
<tr>
<td></td>
<td>If first choice is not effective, add the other</td>
</tr>
<tr>
<td>2nd line</td>
<td>Addition of clobazam or Diacomit</td>
</tr>
<tr>
<td></td>
<td>Addition of Diacomit or topiramate</td>
</tr>
<tr>
<td>3rd line</td>
<td>Refer to tertiary specialist</td>
</tr>
<tr>
<td></td>
<td>Addition of clonazepam, levetiracetem,</td>
</tr>
<tr>
<td></td>
<td>zonisamide, ethosuximide, or phenobarbital</td>
</tr>
</tbody>
</table>

- 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.
V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dravet syndrome</td>
<td>50 mg/kg/day PO in 2-3 divided doses</td>
<td>3,000 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability
- Capsules: 250 mg, 500 mg
- Powder for oral suspension: 250 mg, 500 mg

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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