Pharmacy Policy Bulletin

Title: Lennox-Gastaut and Dravet Syndrome Agents
Policy #: Rx.01.209

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:
The intent of this policy is to communicate the medical necessity criteria for Epidiolex® (cannabidiol), Diacomit® (stiripentol), Onfi® (clobazam), and Banzel® (rufinamide) as provided under the member's prescription drug benefit.

Description:
Lennox-Gastaut syndrome: A form of severe epilepsy that begins in childhood. It is characterized by multiple types of seizures and intellectual disability. People with Lennox-Gastaut syndrome begin having frequent seizures in early childhood, usually between ages 3 and 5 years.

Dravet syndrome (DS): A severe form of epilepsy which appears during the first year of life characterized by frequent, prolonged seizures often triggered by high body temperature (hyperthermia), developmental delay, speech impairment, loss of full control of bodily movements, low muscle tone, sleep disturbances, and other health problems.

Epidiolex® (cannabidiol (CBD)); the exact mechanism by which CBD produces its anticonvulsant effects is unknown. CBD may exert a cumulative anticonvulsant effect, modulating a number of endogenous systems including, but not limited to, neuronal inhibition (synaptic and extrasynaptic GABA channels), modulation of intracellular calcium (TRPV, VDAC, GPR55), and possible anti-inflammatory effects (adenosine).

Diacomit® (stiripentol); the mechanism of action by which stiripentol exerts its anticonvulsant effect in humans is unknown. Possible mechanisms of action include direct effects mediated through the gamma-aminobutyric acid (GABA)A receptor and indirect effects involving inhibition of cytochrome P450 activity with resulting increase in blood levels of clobazam and its active metabolite.

Onfi® (clobazam); The exact mechanism of action for clobazam, a 1,5-benzodiazepine, is not fully understood but is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABAA receptor.

Banzel® (rufinamide); The precise mechanism(s) by which rufinamide exerts its antiepileptic effect is unknown. The results of in vitro studies suggest that the principal mechanism of action of rufinamide is modulation of the activity of sodium channels and, in particular, prolongation of the inactive state of the channel. Rufinamide (≥ 1 μM) significantly slowed sodium channel recovery from inactivation after a prolonged prepulse in cultured cortical neurons, and limited sustained repetitive firing of sodium-dependent action potentials (EC50 of 3.8 μM).
Epidiolex ® is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.

Diacomit® is indicated for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of Diacomit® as monotherapy in Dravet syndrome.

Onfi® is indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older.

Banzel® indicated for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in pediatric patients 1 year of age and older, and in adults.

**Policy:**

### Initial criteria

Epidiolex ® (cannabidiol) is approved when ALL of the following are met:

A. Member is 2 years of age or older; AND
B. Baseline CBC, serum transaminases and total bilirubin obtained prior to initiating therapy; AND
C. ONE of the following
   1. Diagnosis of Dravet syndrome and inadequate response or inability to tolerate ONE of the following
      1. Clobazam; OR
      2. Valproic acid; OR
      3. Levetiracetam; OR
      4. Topiramate;
   OR
   2. Diagnosis of Lennox-Gastaut syndrome and inadequate response or inability to tolerate ONE of the following
      1. Valproic acid; OR
      2. Lamotrigine; OR
      3. Topiramate; OR
      4. Felbamate; OR
      5. Rufinamide*; OR
      6. Clobazam* AND
D. Documentation of concurrent use with additional anti-epileptic(s); AND
E. Prescribed by a neurologist

Authorization length: 6 months

Continuation criteria: Documentation of reduction in seizure activity or intensity

Authorization length: Indefinite

Diacomit® (Stiripentol) is approved when ALL of the following criteria are met:

A. Diagnosis of seizures associated with Dravet syndrome; AND
B. Member is 2 years of age or older; AND
C. Used in combination with clobazam; AND
D. Prescribed by or in consultation with a neurologist

Clobazam (Onfi®) tablets and oral suspension, clobazam (Sympazan®) is approved when ONE of the following is met:

A. All of the following:
1. Member is 2 years of age and older; and
2. Diagnosis of seizures associated with Lennox-Gastaut syndrome (LGS); and
3. Used as adjunctive therapy; and
4. Prescribed by or in consultation with a neurologist; and
5. One of the following:
   i. Inadequate response or inability to tolerate generic clobazam tablets or oral suspension (applies to brand Onfi® and Sympazan® only); or
   ii. For continuation of prior therapy if the member is established on brand Onfi® or brand Sympazan®

OR

B. All of the following:
1. Diagnosis of seizures associated with Dravet Syndrome (DS); and
2. Used in combination with Diacomit®; and
3. Prescribed by or in consultation with a neurologist; and
4. One of the following:
   i. Inadequate response or inability to tolerate generic clobazam tablets or oral suspension (applies to brand Onfi® and Sympazan® only); or
   ii. For continuation of prior therapy if the member is established on brand Onfi® or brand Sympazan®

Rufinamide (Banzel®) is approved when ONE of the following:

A. All of the following:
1. Diagnosis of seizures associated with Lennox-Gastaut Syndrome (LGS); and
2. Used as adjunctive therapy; and
3. Inadequate response or inability to tolerate ONE of the following generics:
   i. Valproic acid; or
   ii. Lamotrigine; or
   iii. Topiramate; or
   iv. Felbamate; or
   v. Clobazam*; and
4. Prescribed by or in consultation with neurologist

OR

B. For continuation of prior therapy if the member is established on Rufinamide (Banzel®)

*Please note: prior authorization required

**Black Box Warning as shown in the drug Prescribing Information:**

Onfi® (clobazam): Concomitant use of benzodiazepines, including Onfi®, and opioids may result in profound sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of benzodiazepines and opioids for use in patients for whom alternative treatment options are inadequate. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. If a decision is made to prescribe Onfi® concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. Advise both patients and caregivers about the risks of respiratory depression and sedation when Onfi® is used with opioids.

**Guidelines:**

Refer to the specific manufacturer’s prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company’s products when the medical necessity criteria listed
in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**


**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidiolex®</td>
<td>Cannabidiol</td>
</tr>
<tr>
<td>Diacomit®</td>
<td>Stripentol</td>
</tr>
<tr>
<td>Onfi®</td>
<td>Clobazam</td>
</tr>
<tr>
<td>Banzel®</td>
<td>Rufinamide</td>
</tr>
</tbody>
</table>

**Cross References:**

Off-Label Use Rx.01.33

Applicable Age Edits Rx.01.2

**Policy Version Number:** 4.00

**P&T Approval Date:** April 23, 2020

**Policy Effective Date:** July 01, 2020

**Next Required Review Date:** October 10, 2020
The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.