Banzel® (rufinamide) and Onfi® (clobazam)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Onfi® (clobazam) and Banzel® (rufinamide) policy is to ensure appropriate selection of patients for Onfi or Banzel use based on product labeling and/or clinical guidelines and/or clinical studies. The U.S. Food and Drug Administration (FDA) has approved both Banzel and Onfi for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS). Banzel, a triazole derivative that modulates the activity of sodium channels and subsequently prolongs the inactive state of the channel, is indicated for use in patients 1 year of age and older. It is contraindicated in patients with Familial Short QT Syndrome. Onfi, a benzodiazepine, is indicated for use in patients 2 years of age and older.

POLICY

I. Banzel may be considered medically necessary for the initial treatment of Lennox-Gastaut Syndrome when all of the following criteria are met:
   • Diagnosis of Lennox-Gastaut Syndrome
   • At least one year of age
   • Patient is taking another antiepileptic drug (AED) for the treatment of Lennox-Gastaut Syndrome
   • The patient does not have Familial Short QT Syndrome

   Approval will be for 36 months.

II. Onfi may be considered medically necessary for the initial treatment of Lennox-Gastaut when all of the following criteria are met:
   • Diagnosis of Lennox-Gastaut Syndrome
   • At least 2 years of age
   • Patient is taking another antiepileptic drug (AED) for the treatment of Lennox-Gastaut Syndrome

   Approval will be for 36 months.

III. Banzel and Onfi are considered not medically necessary for patients who do not meet the criteria set forth above.
Quantity limits apply:

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Generic Name</th>
<th>Strength</th>
<th>Drug Form</th>
<th>Quantity Limit</th>
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<tbody>
<tr>
<td>Banzel</td>
<td>rufinamide</td>
<td>200 mg, 400 mg</td>
<td>tablet</td>
<td>240 tablets/30 days</td>
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<tr>
<td></td>
<td></td>
<td>40 mg/mL</td>
<td>suspension</td>
<td>2400 mL/30 days</td>
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<tr>
<td>Onfi</td>
<td>clobazam</td>
<td>10 mg</td>
<td>tablet</td>
<td>120 tablets/30 days</td>
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<td>60 tablets/30 days</td>
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<td></td>
<td></td>
<td>2.5mg/mL</td>
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</table>

CLINICAL RATIONALE

Lennox-Gastaut syndrome (LGS) is a rare and debilitating form of childhood-onset epilepsy characterized by frequent seizures and multiple seizure types. Most children with LGS experience some degree of impaired intellectual functioning or information processing, along with developmental delays and behavioral disturbances. LGS seizures are often treatment-resistant, with many patients receiving multiple antiepileptic drugs (AEDs).

**Efficacy**

**Banzel**

The efficacy of Banzel was established in a single, randomized, double-blind, placebo-controlled trial. This 12 week study included 138 patients between 4 and 30 years of age with a diagnosis of inadequately controlled seizures associated with LGS who were being treated with 1 to 3 concomitant stable dose AEDs. After completing a 4 week baseline phase on stable AED therapy, patients were randomized to receive either Banzel (target dose of 45mg/kg/day, maximum of 3200mg/day) or placebo as add-on therapy to their current AED regimen.

Banzel adjunctive therapy was significantly better than placebo in reducing both total seizure frequency per 28 days and tonic-atonic seizure frequency per 28 days. Banzel add-on therapy was also associated with a significantly greater improvement in seizure severity as compared to placebo.

On February 12, 2015, Banzel was approved to be used in pediatric patients ages 1 year and older for the treatment of seizures associated with Lennox-Gastaut Syndrome based on a single multi-center, open label, active-controlled randomized pharmacokinetic bridging study. The pharmacokinetic profile of Banzel is not significantly affected by age either as a continuous covariate (one to 35 years) or as a categorical covariate (age categories: 1 to less than 4 years and 4 years of age and older), after body weight is taken into consideration.

**Onfi**

The efficacy of Onfi as adjunctive therapy for drop seizures associated with LGS was evaluated in two randomized, double-blind controlled studies and one open-label extension (OLE) study. Both randomized, double-blind studies were multicenter trials with similar patient populations in regards to disease characteristics and concomitant antiepileptic drug AED use. In these trials, patients were stratified by weight and then randomly assigned to one of 4 treatment arms: placebo, low-dosage Onfi (target dose of 0.25mg/kg/day, maximum dose of 10mg/day), medium-dosage Onfi (target dose of 0.50mg/kg/day, maximum dose of 20mg/day) or high-dosage Onfi (target dose of 1 mg/kg/day, maximum dose of 40mg/day).

Onfi significantly reduced weekly drop seizure rates in both studies, with the observed benefit of Onfi becoming greater as the dose was increased ($p < 0.0001$).
Safety

Banzel
In all patients treated with Banzel in double-blind, adjunctive therapy studies, the most frequently observed adverse reactions (≥10% and greater than placebo) were headache, dizziness, somnolence, fatigue, vomiting and nausea. The adverse events most frequently responsible for study withdrawal were convulsions, nausea, vomiting, fatigue, headache, dizziness, ataxia and rash.

QT interval shortening has been demonstrated with Banzel use. Although the degree of QT interval shortening is without any known clinical risk, due to their increased risk of sudden death and ventricular arrhythmias, patients with Familial Short QT Syndrome should not take Banzel.

Onfi
The most frequent side-effects of Onfi are drowsiness, sedation and hangover effects; these central nervous system (CNS) depressive effects have occurred in up to 50% of patients treated with Onfi. Other common adverse effects associated with Onfi use include pyrexia, salivary hypersecretion, constipation, aggression, hypomania and mania. The adverse events most frequently responsible for treatment discontinuation were lethargy, somnolence, ataxia, aggression, fatigue and insomnia.

Serious skin reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported with Onfi in both children and adults during the post-marketing period. Patients should be closely monitored for signs or symptoms of SJS/TEN, especially during the first 8 weeks of treatment initiation or when re-introducing therapy. Onfi should be discontinued at the first sign of rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered.

Onfi has been classified as a Schedule IV controlled substance. As such, patients with a history of substance abuse should be monitored closely for signs and symptoms of habituation and dependence during Onfi therapy.

PROCEDURES AND BILLING CODES
To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.
• Code(s), if applicable.

REFERENCES
POLICY HISTORY

Policy #: 05.01.55
Policy Creation: February 2012
Reviewed: July 2017
Revised: May 2016
Current Effective Date: June 11, 2016