BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 07/31/12**
SECTION: DRUGS	**LAST REVIEW DATE: 07/20/17**
	LAST CRITERIA REVISION DATE: 07/20/17
	ARCHIVE DATE:

ONFI® (clobazam) oral suspension and tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

ONFI® (clobazam) oral suspension and tablet (cont.)

Description:

Onfi (clobazam) is indicated for adjunctive treatment of seizures associated with LGS in individuals 2 years of age or older. The exact mechanism of action for clobazam, a 1,5-benzodiazepine, is not fully understood but is thought to involve potentiation of gamma-aminobutyric acid (GABA) neurotransmission resulting from binding at the benzodiazepine site of the GABA-A receptor. It is listed in Schedule IV of the Controlled Substance Act (CSA).

Lennox–Gastaut Syndrome (LGS), also known as Lennox syndrome, is a severe and difficult-to-treat form of childhood-onset epilepsy that most often appears between the second and sixth year of life. It is characterized by frequent seizures and can include different seizure types, such as, tonic, atonic, atypical absence, and myoclonic seizures. There may be periods of frequent seizures mixed with brief, relatively seizure-free periods. Most children with LGS experience some degree of impaired intellectual functioning or information processing, along with developmental delays, and behavioral disturbances.

Treatment for LGS includes anti-epileptic medications such as clobazam, clonazepam, felbamate, lamotrigine, levetiracetam, rufinamide, topiramate, valproate, or zonisamide. There is usually no single antiepileptic medication that will control seizures. Children who improve initially may later show tolerance to a drug or have uncontrollable seizures.

Definitions:

The Child-Pugh classification system:

	Score: 1 point	**Score: 2 points**	**Score: 3 points**
Serum Albumin (g/dL)	>3.5	3.0 - 3.5	<3.0
Serum Bilirubin (mg/dL)	<2.0	2.0 - 3.0	>3.0
Prothrombin time (seconds)	1 - 4	4 - 6	>6
Ascites	none	moderate	severe
Encephalopathy	none	mild	severe

The three classes and their scores are:
- **Class A** is score 5 – 6: Well compensated
- **Class B** is score 7 – 9: Significant functional compromise
- **Class C** is score >9: Decompensated disease

ONFI® (clobazam) oral suspension and tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Onfi (clobazam) is considered ***medically necessary*** for individuals 2 years of age or older with medical record documentation of **ALL** of the following:

  1. Diagnosis of **EITHER** of the following:
     - Adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS)
     - Non-LGS refractory seizure disorder on multiple anticonvulsants that includes Clonazepam **AND** experienced **ONE** of the following:
       - Uncontrolled seizures while on multiple anticonvulsants and Clonazepam
       - Adverse effect or intolerance to Clonazepam
     - Non-LGS refractory seizure disorder on multiple anticonvulsants experiencing uncontrolled seizure **AND** Clonazepam is contraindicated

  2. Absence of **ALL** of the following contraindications:
     - Hypersensitivity to clobazam or any ingredient in Onfi

  3. Absence of **ALL** of the following exclusions:
     - Woman of child bearing potential who is pregnant or not currently using effective contraception
     - Woman who is breast feeding an infant or child
     - Severe renal impairment (creatinine clearance less than 30 mL/min) or end stage renal disease (ESRD)
     - Severe hepatic impairment (Child-Pugh score greater than 9)

- **Initial approval duration**: 12 months

- **Criteria for continuation of coverage (renewal request):** Onfi (clobazam) is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. The individual has benefited from therapy but remains at high risk

  2. The condition has not progressed or worsened while on therapy

  3. Individual has not developed any contraindications or other exclusions to its continued use

- **Renewal duration**: 12 months

Resources:

Onfi® package insert revised by the manufacturer February 2017 reviewed on 07-11-2017.

Onfi® package insert revised by the manufacturer on December 2014 reviewed on 06-14-2015.

Onfi™ package insert revised by manufacturer on November 2013 reviewed on August 7, 2014.

ONFI® (clobazam) oral suspension and tablet (cont.)

Onfi™ package insert revised by manufacturer on October 2011 (reference ID: 3033069) reviewed on February 21, 2012.

Klonopin® package insert revised by manufacturer on August 2010 (PID2010-04836) reviewed on July 30, 2013.

Fazio C, Manfredi M, Piccinelli A: Treatment of epileptic seizure with Clonazepam: A reappraisal. Arch Neuol 1975 May; 32(5):304-307. [Abstract only]

Browne TR: Clonazepam: A review of a new anticonvulsant drug. Arch Neurol 1976 May; 33(5):326-332. [Abstract only]

Pinder RM, Brogden RN, Speight TM, Avery GS: Clonazepam: A review of its pharmacologic properties and therapeutic efficacy in epilepsy. Drugs 1976 Nov; 12(5):321-361. [Abstract only]

Nanda RN, Johnson, RH, Keoh HL, et al: Treatment of epilepsy with Clonazepam and its effect on other anticonvulsants. J Neurol Neurosurg Psychiatry 1977 June; 40(6):538-543. [Abstract only]

Mireles R, Leppik IE: Valproate and Clonazepam comedication in patients with intractable epilepsy. Epilepsia 1985 Mar-Apr; 26(2):122-126. [Abstract only]

Farrell K: Benzodiazepines in the treatment of children with epilepsy. Epilepsia 1986; 27 (Suppl 1):S45-S52. [Abstract only]

Robertson MM: Current status of the 1,4- and 1,5-benzodiazepines in the treatment of epilepsy: The place of Clobazam. Epilepsia 1986; 27 (Suppl 1):S27-S41. [Abstract only]

Henriksen O: An overview of benzodiazepines in seizure management. Epilepsia 1998; 39 (Suppl 1):S2-S6.

Tassinari CA, Michelucci R, Riguzzi P, et al: The use of Diazepam and Clonazepam in epilepsy. Epilepsia 1998; 39 (Suppl 1):S7-S14.

Riss J, Cloyd J, Gates J, Collins S: Benzodiazepines in epilepsy: Pharmacology and pharmacokinetics. Acta Neurol Scand 2008; 118:69-86.

van Rijckevorsel K: Treatment of Lennox-Gastaut syndrome: Overview and recent findings. Neuorpsych Disease Treatment 2008; 4(6):1001-1019.

Machado VH, Palmini A, Bastos FA, Rotert R: Long-term control of epileptic drop attacks with combination of Valproate, Lamotrigine, and a Benzodiazepine: A “proof of concept,” open label study. Epilepsia 2011; 52(7):1303-1310.

Montenegro MA, Arif H, Naham EA, et al: Efficacy of Clobazam as add-on therapy for refractory epilepsy: Experience at a US epilepsy center. Clin Neuropharmacol 2008; 31(6):333-338.

Montenegro MA, Noronha AL, Mory SB, et al: Efficacy of Clobazam as add-on therapy in patients with refractory epilepsy. Epilepsia 2001; 42(4):539-542.

ONFI® (clobazam) oral suspension and tablet (cont.)

Buchanan N: Clobazam in the treatment of epilepsy: Prospective follow-up to 8 years. J Royal Soc Med 1993 July; 86: 378-380.

Schmidt D, Rohde M, Wolf P, Roeder-Wanner U: Clobazam for refractory focal epilepsy: A controlled trial. Arch Neurol 1986 Aug; 43:824-826.

Allen JW, Oxley J, Robertson MM, et al: Clobazam as adjunctive treatment in refractory epilepsy. Br Med J 1983 April; 286:1246-1247.

Refer to package insert for complete dosing information.

Indication	Recommended Dose
A benzodiazepine indicated for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older. Safety and effectiveness in patients <2 years of age have not been established.	ONFI should be administered in divided doses twice daily (the 5 mg dose can be administered as a single daily dose). Patients should be dosed according to body weight. Within each body weight group, dosing should be individualized based on clinical efficacy and tolerability. Each dose in Table 1 has been shown to be effective, although effectiveness increases with increasing dose. Dose escalation should not proceed more rapidly than weekly, because serum concentrations of clobazam and its active metabolite require 5 and 9 days, respectively, to reach steady-state. ONFI tablets can be administered whole, or crushed and mixed in applesauce and can be taken without regard to timing of meals Table 1: Recommended Total Daily Dosing by weight group ≤ 30 kg body weight / > 30 kg body weight Starting dose: 5 mg / 10 mg Starting Day 7: 10 mg / 20 mg Starting day 14: 20 mg / 40 mg As with all antiepileptic drugs and benzodiazepines, ONFI should be withdrawn gradually, abrupt discontinuation should be avoided. Taper by decreasing the total daily dose by 5-10 mg/day on a weekly basis until discontinued

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.