Clinical Policy: Clobazam (Onfi, Sympazan)

Reference Number: CP.PMN.54
Effective Date: 11.01.12
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Clobazam (Onfi®, Sympazan®) is a benzodiazepine.

FDA Approved Indication(s)

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

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 Centene Corporation® that Onfi and Sympazan are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Lennox-Gastaut Syndrome (must meet all)**:**

1. Diagnosis of LGS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. Failure of 2 preferred agents for LGS (e.g., clonazepam, valproic acid (divalproex), lamotrigine, topiramate, felbamate), unless clinically significant adverse effects are experienced or all are contraindicated;
5. For Onfi and Sympazan requests, member must use generic clobazam tablets or oral suspension, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Dose does not exceed 40 mg per day (2 tablets per day, 16 mL per day, or 2 films per day).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Intractable/Refractory Epilepsy (off-label) (must meet all)**:**

1. Diagnosis of intractable/refractory epilepsy;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. Failure of ≥ 4 anti-seizure drugs (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;

5. For Onfi and Sympazan requests, member must use generic clobazam tablets or oral suspension, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Dose does not exceed 40 mg per day (2 tablets per day, 16 mL per day, or 2 films per day).

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

C. Dravet Syndrome (off-label) (must meet all)**:**
1. Diagnosis of Dravet syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 2 years;
4. For Onfi and Sympazan requests, member must use generic clobazam tablets or oral suspension, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Dose does not exceed 2 mg/kg per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Onfi or Sympazan for a covered indication 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 one of the following (a or b):
   a. LGS or intractable/refractory epilepsy: 40 mg per day (2 tablets per day, 16 mL per day, or 2 films per day);
   b. Dravet syndrome: 2 mg/kg per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
LGS: Lennox-Gastaut syndrome

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Anticonvulsants-benzodiazepines		
clonazepam (Klonopin®)	See full prescribing information	See full prescribing information
diazepam rectal gel (Diastat®)		
Carbamates		
felbamate (Felbatol®)	See full prescribing information	See full prescribing information
GABA modulators		
vigabatrin (Sabril®)	See full prescribing information	See full prescribing information
tiagabine (Gabitril®)		
Hydantoins		
Peganone® (ethotoin)	See full prescribing information	See full prescribing information
phenytoin (Dilantin®)		
Succinimides		
ethosuximide (Zarontin®)	See full prescribing information	See full prescribing information
Celontin® (methsuximide)		
Valproic acid		
divalproex sodium (Depakote®)	See full prescribing information	See full prescribing information
valproic acid (Depakene®)		
AMPA glutamate receptor antagonists		
Fycompa® (perampanel)	See full prescribing information	See full prescribing information

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Anticonvulsants-miscellaneous		
Briviact® [brivaracetam], carbamazepine [Tegretol®, Tegretol XL®], Aptiom® [eslicarbazepine], Potiga® [ezogabine], gabapentin [Neurontin®], Vimpat® [lacosamide], lamotrigine [Lamictal®], levetiracetam [Keppra®, Spritam®], oxcarbazepine [Oxtellar XR®, Trileptal®], Lyrica® [pregabalin], primidone [Mysoline®], Banzel® [rufinamide], topiramate [Topamax®, Qudexy XR®, Trokendi XR®], zonisamide [Zonegran®])	See full prescribing information	See full prescribing information

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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of hypersensitivity to the drug or its ingredients
- Boxed warning(s): risks from concomitant use with opioids; abuse, misuse, and addiction; dependence and withdrawal reactions

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
LGS	Patients ≤ 30 kg body weight: initiate at 5 mg PO daily and titrate as tolerated up to 20 mg daily Patients > 30 kg body weight: initiate at 10 mg PO daily and titrate as tolerated up to 40 mg daily A daily dose greater than 5 mg should be administered in divided doses twice daily; a 5 mg daily dose can be administered as a single dose.	≤ 30 kg body weight: 20 mg/day > 30 kg body weight: 40 mg/day
Intractable/refractory epilepsy (off-label)	See LGS	See LGS
Dravet syndrome (off-label)	Initial: 0.2-0.3 mg/kg/day PO Maximum: 0.5-2 mg/kg/day PO	See regimen

VI. Product Availability

Drug Name	Availability
Clobazam (Onfi)	Tablet with a functional score: 10 mg, 20 mg Oral suspension: 2.5 mg/mL in 120 mL bottles
Clobazam (Sympazan)	Oral film: 5 mg, 10 mg, 20 mg

VII. References

1. Onfi Prescribing Information. Deerfield, IL: Lundbeck; February 2021. Available at: https://www.onfihcp.com/. Accessed August 20, 2021.
2. Sympazan Prescribing Information. Warren, NJ: Aquestive Therapeutics; March 2021. Available at: www.sympazan.com. Accessed August 20, 2021.
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4. Arzimanoglou A, French J, Blume WT, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Lancet Neurol. 2009 Jan;8(1):82-93.
5. Mills JK, Lewis TG, Mughal K, et al. Retention rate of clobazam, topiramate and lamotrigine in children with intractable epilepsies at 1 year. Seizure. 2011 June;20(5): 402-405.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Lennox-Gastaut: modified requirement related to treatment failure with clonazepam in conjunction with a PDL anticonvulsant to allow trial and failure of any 2 PDL anti-epileptics for Lennox-Gastaut	03.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
since a neurologist is involved in the patient's care; removed requirement that Onfi "must be used as adjunctive therapy with any of the following PDL anticonvulsants: valproic acid (divalproex), lamotrigine, topiramate, or felbamate" since specialist is involved in patient's care and is better able to select appropriate therapy Created criteria for treatment of intractable/refractory epilepsy (off-label) Converted to new template- Removed age restriction per new template update Modified weight-based dose criteria to max dose of drug per new template update Added criteria for continuity of care and documentation of positive response to therapy for re-auth. Updated references		
2Q 2018 annual review: no significant HIM added; added age; added QL of 2 tablets/day, or 16 mL/day to max dose; increased initial approval duration from 6 to 12 months; references reviewed and updated.	12.18.17	05.18
3Q 2018 annual review: LGS-removed duration of trial of formulary alternatives since specialist is involved in care; references reviewed and updated.	05.03.18	08.18
Added criteria for off-label use in Dravet syndrome.	09.20.18	11.18
RT4: added Sympazan to the policy.	06.21.19	
4Q 2019 annual review: added Commercial line of business; added redirection to generic formulations; for HIM approval duration, added reference to non-formulary policy for Sympazan; reference reviewed and updated.	07.25.19	11.19
4Q 2020 annual review: no significant changes; for HIM line of business removed references to non-formulary policy for Sympazan; references reviewed and updated.	08.04.20	11.20
4Q 2021 annual review: no significant changes; revised "Medical justification…for clobazam tablets and oral suspension…" to "Member must use clobazam tablets or oral suspension…"; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.20.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.