

Clinical Policy Title:	clobazam
Policy Number:	RxA.429
Drug(s) Applied:	Onfi®, Sympazan®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Clobazam (Onfi®, Sympazan®)	LGS	<p>Patients ≤ 30 kg body weight: initiate at 5 mg PO daily and titrate as tolerated up to 20 mg daily</p> <p>Patients > 30 kg body weight: initiate at 10 mg PO daily and titrate as tolerated up to 40 mg daily</p> <p>A daily dose of Onfi greater than 5 mg should be administered in divided doses twice daily; a 5 mg daily dose can be administered as a single dose.</p>	<p>≤ 30 kg body weight: 20 mg/day</p> <p>> 30 kg body weight: 40 mg/day</p>
	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

Dosage Forms

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

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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 \geq 2 years;
4. Failure of 2 preferred agents for LGS (e.g., clonazepam, valproic acid (divalproex), lamotrigine, topiramate, felbamate), unless all are contraindicated or clinically significant adverse effects are experienced;
5. For Onfi and Sympazan requests, medical justification supports the inability to use generic clobazam tablets and oral suspension (e.g., contraindications to excipients in generic formulations);
6. Dose does not exceed 40 mg per day (2 tablets per day, 16 mL per day, or 2 films per day).

Approval Duration

Commercial: 12 months

Medicaid: 12 months

HIM: 12 months

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 \geq 2 years;
4. Failure of \geq 4 anti-seizure drugs (*see Appendix B*), unless all are contraindicated or clinically significant adverse effects are experienced;
5. For Onfi and Sympazan requests, medical justification supports the inability to use generic clobazam tablets and oral suspension (e.g., contraindications to excipients in generic formulations);
6. Dose does not exceed 40 mg per day (2 tablets per day, 16 mL per day, or 2 films per day).

Approval Duration

Commercial: 12 months

Medicaid: 12 months

HIM: 12 months

C. Dravet Syndrome (off-label) (must meet all):

1. Diagnosis of Dravet syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age \geq 2 years;
4. For Onfi and Sympazan requests, medical justification supports the inability to use generic clobazam tablets and oral suspension (e.g., contraindications to excipients in generic formulations);
5. Dose does not exceed 2 mg/kg per day.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

HIM: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Onfi or Sympazan for Lennox-Gastaut syndrome, intractable/refractory epilepsy, or 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 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

Commercial: 12 months

Medicaid: 12 months

HIM: 12 months

III. Appendices

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®)		
valproic acid (Depakene®)	See full prescribing information	See full prescribing information
AMPA glutamate receptor antagonists		
Fycompa® (perampanel)	See full prescribing information	See full prescribing information
valproic acid (Depakene®)	See full prescribing information	See full prescribing information
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

References

1. Onfi Prescribing Information. Deerfield, IL: Lundbeck; June 2018. Available at: <https://www.onfihcp.com/>. Accessed July 30, 2020.
2. Sympazan Prescribing Information. Warren, NJ: Aquestive Therapeutics; November 2018. Available at:

www.sympazan.com. Accessed July 30, 2020.

3. Hancock EC, Cross JH. Treatment of Lennox-Gastaut syndrome. *Cochrane Database Syst Rev*. 2013 Feb 28;(2).
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. French JA, Kanner AM, Bautista J, et al. Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2004 Apr 27;62(8):1261-73.
6. 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.
7. Gauthier AC, Mattson RH. Clobazam: a safe, efficacious, and newly rediscovered therapeutic for epilepsy. *CNS Neurosci Ther*. 2015 Jul;21(7):543-8.
8. Montenegro MA, Arif H, Nahm EA, et al. Efficacy of clobazam as add-on therapy for refractory epilepsy: experience at a US epilepsy center. *Clin Neuropharmacol*. 2008 Nov- Dec;31(6):333-8.
9. Cross JH, Auvin S, Falip M, et al. Expert Opinion on the Management of Lennox–Gastaut Syndrome: Treatment Algorithms and Practical Considerations. *Frontiers in Neurology*. 2017;8:505.
10. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed July 30, 2020.
11. Wirrell EC, Laux L, Jette N, et al. Optimizing the diagnosis and management of Dravet syndrome: recommendations from a North American consensus panel. *Pediatr Neurol*. 2017; 68: 18-34.
12. Epilepsies: diagnosis and management. National Institute for Health and Care Excellence (NICE) website. <https://www.nice.org.uk/guidance/CG137/chapter/Appendix-E-Pharmacological-treatment>. Updated Feb 2020. Accessed July 30, 2020.
13. Wirrell EC. Treatment of Dravet syndrome. *Can J Neurol Sci*. 2016; 43 Suppl 3: S13-8. doi: 10.1017/cjn.2016.249. <https://www.ncbi.nlm.nih.gov/pubmed/27264138>.

Practice Guideline Update: Efficacy and Tolerability of the New Antiepileptic Drugs II: Treatment-resistant Epilepsy. American Academy of Neurology. Available at: <https://www.aan.com/Guidelines/Home/GetGuidelineContent/922>. Accessed July 30, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed. <ol style="list-style-type: none"> 1. Clinical Policy table updated 2. Initial Therapy and Continued Therapy Approval duration updated from length of benefit to 12 months for commercial and for HIM updated to 12 months for Onfi and Sympazan both 3. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 4. Reference reviewed and updated. 	07/30/2020	09/14/2020