# ONFI® (clobazam)Ⓒ Dosing Guide

## Two Formulations Available

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

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.

Onfi®
(clobazam)Ⓒ
10 mg, 20 mg Tablets
2.5 mg/mL Oral Suspension

**Please see Important Safety Information, including Boxed Warning for risks from concomitant use with opioids, on pages 6 and 7. For more information, please see the full Prescribing Information, Medication Guide, and Instructions for Use; or go to ONFI.com.**

# ONFI® (clobazam)℞ Oral Suspension Provides Dosing in a Liquid Formulation

**Oral Suspension Formulation: 2.5 mg/mL[1]**


Berry flavor

Store at room temperature

Available in a 120 mL glass bottle

Can be taken with or without food

- Shake well before each use

**Oral Suspension:** Recommended Total Daily Dosing by Weight Group[1]

| | ≤30 kg Body Weight | >30 kg Body Weight |
|---|---|---|
| Starting Dose | 5 mg (2 mL) | 10 mg (4 mL) |
| Starting Day 7 | 10 mg (4 mL) | 20 mg (8 mL) |
| Starting Day 14 | 20 mg (8 mL) | 40 mg (16 mL) |

The total daily dose should be divided and given twice daily.
A 5 mg (2 mL) daily dose can be given once daily.

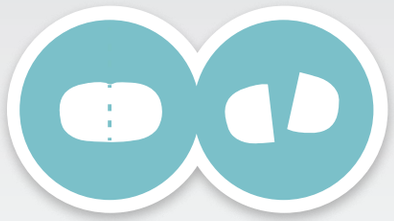
- Do not proceed with dose escalation more rapidly than weekly[1]
- Titration schedule and final dose should be based on response to therapy and tolerability[1]
- The relative bioavailability between ONFI tablets and oral suspension is approximately 100%
- Advise patients to use within 90 days of first opening bottle
- Store and dispense in the original bottle in an upright position
- Instruct patients to read the "Instructions for Use" carefully

ONFI oral suspension contains potential carbohydrates in the form of sucralose, propylene glycol, and maltitol. The potential carbohydrate content is 0.19 g/mL.[2]



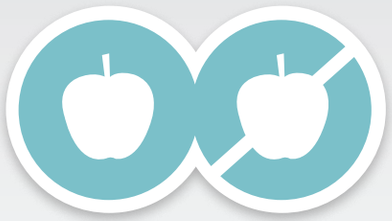
# ONFI Scored Tablets Can Be Broken in Half or Administered Whole

**Scored Tablets: 10 mg and 20 mg**



Apply pressure on the score to split tablet


Available in 10 mg and 20 mg scored tablets (not actual size)



Can be taken with or without food

- Can be administered whole, halved along the score, or crushed and mixed with applesauce

**Scored Tablets:** Recommended Total Daily Dosing by Weight Group[1]

| | ≤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 |

The total daily dose should be divided and given twice daily.
A 5 mg daily dose can be given once daily.

- As with all antiepileptic drugs (AEDs) and benzodiazepines, withdraw ONFI gradually. Taper by decreasing the total daily dose by 5 - 10 mg/day on a weekly basis until discontinued[1]
- ONFI causes somnolence and sedation. In clinical trials, somnolence or sedation was reported at all effective doses and was dose-related. In general, somnolence and sedation begin within the first month of treatment and may diminish with continued treatment. Monitor patients for somnolence and sedation, particularly with concomitant use of other CNS depressants[1]

**Please see Indication and Important Safety Information, including Boxed Warning for risks from concomitant use with opioids, on pages 6 and 7.**

# Additional Dosing Recommendations

**Recommended Dosing in Specific Populations[1]**

| **Specific Populations** Dose Escalation Should Proceed Slowly | **Starting Dose** | **Titration Based on Weight** | **Starting Day 21** |
|---|---|---|---|
| - Geriatric<br>- Known CYP2C19 poor metabolizers<br>- Mild to moderate hepatic impairment | 5 mg/day | One-half of the recommended total daily dose | Maximum dosage of 20 or 40 mg/day* |

*If necessary and based on clinical response, an additional titration to the maximum dose may be started on day 21.

- No dose adjustment is required for patients with mild and moderate renal impairment
- No definitive data available in patients with severe hepatic impairment, severe renal impairment, or end-stage renal disease

## Combining ONFI® (clobazam)℠ With Other AEDs[1]

The effects of concomitant AEDs were evaluated using data from clinical trials.

- CYP3A4 inducers (phenobarbital, phenytoin, and carbamazepine)
- CYP2C19 inducers (valproic acid, phenobarbital, phenytoin, and carbamazepine)
- CYP2C19 inhibitors (felbamate and oxcarbazepine)

Results of population pharmacokinetic analysis show that these concomitant AEDs did not significantly alter the pharmacokinetics of clobazam or N-desmethylclobazam at steady state.

**Please see Indication and Important Safety Information, including Boxed Warning for risks from concomitant use with opioids, on pages 6 and 7.**

# Special Considerations

## Opioids[1]

- Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death
- When benzodiazepines and opioids are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists
- Limit dosage and duration of concomitant use of benzodiazepines and opioids, and follow patients closely for respiratory depression and sedation

## CNS Depressants and Alcohol[1]

- Concomitant use with other CNS depressants may increase the risk of sedation and somnolence
- Alcohol, as a CNS depressant, will interact with ONFI in a similar way and also increases the maximum plasma exposure of clobazam by approximately 50%

## Effect of ONFI on Other Drugs[1]

- ONFI is a weak CYP3A4 inducer. As some hormonal contraceptives are metabolized by CYP3A4, their effectiveness may be diminished when given with ONFI. Additional non-hormonal forms of contraception are recommended when using ONFI
- ONFI is a CYP2D6 inhibitor. Dose adjustment of drugs metabolized by CYP2D6 may be necessary

## Effect of Other Drugs on ONFI[1]

- Dosage adjustment of ONFI may be necessary when coadministered with strong CYP2C19 inhibitors (eg, fluconazole, fluvoxamine, ticlopidine) or moderate CYP2C19 inhibitors (eg, omeprazole) due to increased risk of dose-related adverse events

## Pregnancy and Nursing[1]

- Based on animal data, ONFI may cause fetal harm and should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus
- ONFI is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from ONFI, discontinue nursing or discontinue the drug

## Indications and Usage

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

## Important Safety Information

**WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS**
***See full Prescribing Information for complete boxed warning.***

**Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.**

- **Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

**Contraindication: Hypersensitivity**
ONFI is contraindicated in patients with a history of hypersensitivity to the drug or its ingredients. Hypersensitivity reactions have included serious dermatological reactions.

**Risks from Concomitant Use with Opioids (see Boxed Warning)**
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. Advise both patients and caregivers about the risks of respiratory depression and sedation when ONFI is used with opioids.

**Potentiation of Sedation from Concomitant Use with Central Nervous System (CNS) Depressants**
ONFI has a CNS depressant effect. Caution patients or their caregivers against simultaneous use with other CNS depressant drugs or alcohol and that the effects of other CNS depressant drugs or alcohol may be potentiated.

**Somnolence or Sedation**
ONFI causes somnolence and sedation. In clinical trials, somnolence or sedation was reported at all effective doses and was dose-related. In general, somnolence and sedation begin within the first month of treatment and may diminish with continued treatment. Monitor patients for somnolence and sedation, particularly with concomitant use of other CNS depressants. Caution patients against engaging in hazardous activities that require mental alertness, such as operating dangerous machinery or motor vehicles, until the effect of ONFI is known.

**Withdrawal Symptoms**
As with all antiepileptic drugs (AEDs), withdraw ONFI gradually to minimize the risk of precipitating seizures, seizure exacerbation, or status epilepticus. Withdrawal symptoms occurred following abrupt discontinuation of ONFI; the risk of withdrawal symptoms is greater with higher doses.

**Serious Dermatological Reactions**
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. Discontinue ONFI at the first sign of rash, unless the rash is clearly not drug-related.

**Physical and Psychological Dependence**
Carefully monitor patients with a history of substance abuse when receiving ONFI or other psychotropic agents because of the predisposition of such patients to habituation and dependence. In clinical trials, cases of dependency were reported following abrupt discontinuation of ONFI. The risk of dependence increases with increasing dose and duration of treatment.

**Suicidal Behavior and Ideation**
AEDs, including ONFI, increase the risk of suicidal thoughts or behavior in patients. Inform patients, their caregivers, and families of the risk and advise them to monitor and report any emergence or worsening of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts of self-harm. If these symptoms occur, consider whether it may be related to the AED or illness, because epilepsy itself can increase these risks.

**Pregnancy, Registry and Nursing Mothers**

- Based on animal data, ONFI may cause fetal harm and should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.
  - Encourage patients to call the toll-free number 1-888-233-2334 to enroll in the Pregnancy Registry or visit http://www.aedpregnancyregistry.org/.
- ONFI is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from ONFI, discontinue nursing or discontinue the drug.

**Adverse Reactions**
The most commonly observed adverse reactions reported in an LGS randomized, double-blind, placebo-controlled, parallel group clinical trial of patients who received clobazam as adjunctive therapy (≥10% in any treatment group and at least 5% greater than placebo, respectively) were somnolence or sedation (32% vs. 15%), somnolence (25% vs. 12%), pyrexia (17% vs. 3%), lethargy (15% vs. 5%), aggression (14% vs. 5%), drooling (14% vs. 3%), irritability (11% vs. 5%), ataxia (10% vs. 3%), and constipation (10% vs. 0%).

**Please see the full Prescribing Information, including Boxed Warning for risks from concomitant use with opioids; Medication Guide; and Instructions for Use; or go to ONFI.com for more information.**

**References:**
**1.** ONFI [package insert]. Deerfield, IL: Lundbeck. **2.** Data on file. Lundbeck, Deerfield, IL.

Contact your account manager or visit **ONFIhcp.com** to learn more.

Lundbeck Your Partner in Epilepsy™



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2.5 mg/mL Oral Suspension

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