

New Drug Overview

Tonmya (cyclobenzaprine)

PDL Category: Muscle Relaxants

Introduction

Disease Background:

- Fibromyalgia, described as extensive musculoskeletal pain, is a chronic, non-inflammatory pain condition known to inhibit daily activities of living. In addition, it is associated with fatigue, sleep difficulties, and nonspecific symptoms such as depressed mood or cognitive dysfunction (*Clauw et al 2025, Goldenberg and Kaplan 2025*).
 - This condition is more common in women than men, frequently having onset of symptoms between 20 to 55 years of age. Nevertheless, fibromyalgia may occur in children (*Clauw et al 2025*).
 - The estimated prevalence is between 1% to 8% in adults and between 1% to 6% in children.
 - An associated increased risk includes family history of fibromyalgia.
- While extensive, generalized pain is the main characteristic of fibromyalgia, other symptoms may include issues with sleep (reported in >90% of patients), depression and anxiety, fatigue (reported in close to 70% of patients), difficulty in concentrating, stiffness of muscles, and sensitivities such as to cold, intolerance to odors, or photophobia (*Clauw et al 2025*).
- The goal for managing fibromyalgia includes improving overall quality of life through pain reduction, improvement in sleep, and improvement of physical and mental health (*Clauw et al 2025*).
 - Nonpharmacologic and pharmacologic treatment should be utilized in a multidisciplinary method, individualizing treatment per patient symptoms, comorbidities, and preferences.
 - Note that in managing chronic pain, a reduction of 30-50% is thought to be significant.
 - There are several agents FDA-approved to treat fibromyalgia, including pregabalin, milnacipran, and duloxetine; however, other drugs are utilized for fibromyalgia but use is considered off-label.
- Tonmya (cyclobenzaprine) was FDA approved in 2025.

Pharmacology/Usage

- Tonmya (cyclobenzaprine) is a sublingual (SL) tablet and contains D&C Yellow No. 10 as well as mannitol. The mechanism of action for its approved indication is not known. In in vitro pharmacology studies, cyclobenzaprine demonstrated functional antagonism of 5HT_{2A}, α₁-adrenergic, H₁-histaminergic, and M₁-muscarinic acetylcholine receptors. In addition, pharmacological studies in animals demonstrated a similarity between the effects of cyclobenzaprine and the structurally related tricyclic antidepressants (TCAs), including reserpine antagonism, norepinephrine potentiation, potent peripheral and central anticholinergic effects, and sedation.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Tonmya (cyclobenzaprine)
• For treatment of fibromyalgia in adults.	✓

(Prescribing information: Tonmya 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Tonmya (cyclo- benzaprine)	Sublingual (SL) tablets	Oral	Once daily at bedtime. -There is dosage titration with the target dose to be started on day 15 and thereafter with a maximum recommended dosage of 5.6mg daily.	<ul style="list-style-type: none"> • Administer after brushing teeth and finishing other oral care. • Avoid eating or drinking for ≥ 15 minutes after the SL tablet(s) has/have completely dissolved and preferably avoid any hot, cold, or acidic beverages until the morning. • Avoid talking for at least 5 minutes after administration. • If a dose is missed, take the dose the next evening. Do not take a missed dose during the day. • Pregnancy testing is recommended in females of reproductive potential prior to starting Tonmya treatment. • The recommended dosage and the maximum recommended dosage in geriatric patients is 2.8mg SL once daily at bedtime. • The recommended dosage and the maximum recommended dosage in patients with mild hepatic impairment is 2.8mg SL once daily at

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				bedtime. Tonmya is not recommended in patients with moderate or severe hepatic impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Tonmya was assessed in three randomized, two-arm, parallel-group, double-blind, placebo-controlled multicenter trials (TRIAL 1, TRIAL 2, and TRIAL 3) that enrolled patients (N=1,474) aged 18 to 65 years who met the 2016 American College of Rheumatology (ACR) criteria for diagnosis of fibromyalgia (including generalized pain, defined as pain in at least 4 of 5 regions; symptoms that had been present at a similar level for at least 3 months; and widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 , OR WPI between 4 to 6 and SSS score ≥ 9).
 - In the trials, 95% were female, 86% were White, the mean age of included patients was 49 years (range 18 to 65) and the mean duration of fibromyalgia was 9 years (range 0 to 49 years).
 - Patients were randomized to receive SL treatment of either Tonmya or placebo through week 14.
- The primary endpoint in all three trials was the change from baseline to week 14 in the weekly average of daily 24-hour recall pain intensity scores.
 - As measured by the 11-point (0-10) numeric rating scale (NRS), the minimum mean baseline pain score required for enrollment was 4. Within each trial, at baseline, the Tonmya and placebo groups had similar mean weekly averages of daily diary pain scores.
 - In Trials 1 and 3, Tonmya demonstrated a statistically significant reduction in pain intensity scores as compared to placebo.
 - In Trial 2, there was no statistically significant treatment group difference (Tonmya minus placebo). Results of this trial may not have been generalizable due to the presence of factors outside the conduct of the study.
 - The least squares (LS) mean change from baseline in the weekly average of daily 24-hour recall pain intensity scores at week 14 in adult patients with fibromyalgia for the Tonmya and placebo groups in Trial 1 and Trial 3 are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

Visit/Statistics	Placebo		Tonmya	
	Value	Change from baseline	Value	Change from baseline
Trial 1 Baseline				
N	255		248	
Mean	6.0		6.1	
(Minimum, Maximum)	(4, 9)		(4, 9)	
Week 14				

	Placebo		Tonmya	
Visit/Statistics	Value	Change from baseline	Value	Change from baseline
Least Squares (LS) mean	4.6	-1.5	4.2	-1.9
95% confidence interval (CI)	(4.3, 4.8)	(-1.7, -1.3)	(3.9, 4.4)	(-2.1, -1.7)
Difference in LS mean				
Difference in LS mean			-0.4	
95% CI for difference in LS mean			(-0.7, -0.1)	
p-value for difference			0.010	
Trial 3 Baseline				
N	225		231	
Mean	5.9		5.9	
(Minimum, Maximum)	(4, 9)		(4, 9)	
Week 14				
LS mean	4.7	-1.2	4.1	-1.8
95% CI	(4.5, 5.0)	(-1.4, -0.9)	(3.8, 4.3)	(-2.0, -1.6)
Difference in LS mean				
Difference in LS mean			-0.7	
95% CI for difference in LS mean			(-1.0, -0.3)	
p-value for difference			<0.001	

- In Trial 1 and Trial 3, the percentage of Tonmya-treated patients who achieved at least a 30% improvement from baseline in their weekly average of daily 24-hour recall pain intensity score at week 14 was 47% and 46%, respectively.

Clinical guidelines

- **European League Against Rheumatism (EULAR) revised recommendations for the management of fibromyalgia** (Macfarlane et al 2017).

- The authors note that fibromyalgia management should be guided by improvement of health-related quality of life balancing benefit and risk of treatment that may need a multidisciplinary method using both pharmacological and non-pharmacological treatment.
 - Initially, non-pharmacologic therapies should be utilized to manage this condition.
 - Recommended non-pharmacologic therapies include:
 - Aerobic and strengthening exercise.
 - Cognitive behavioral therapies.
 - Multicomponent therapies.
 - Defined physical therapies.
 - Meditative movement therapies as well as mindfulness-based stress reduction.
 - Pharmacological treatment can be considered for patients with severe pain (duloxetine, pregabalin, tramadol) or sleep disturbance (amitriptyline, cyclobenzaprine, pregabalin).
 - Recommended pharmacologic therapies include:
 - Amitriptyline (low dose).
 - Duloxetine or milnacipran.
 - Tramadol.
 - Pregabalin.
 - Cyclobenzaprine.

Safety summary

• Contraindications:

- Hypersensitivity to cyclobenzaprine or any inactive ingredient of the product.
- Concomitant use of monoamine oxidase (MAO) inhibitors or within 14 days after discontinuation of a MAO inhibitor.
- During the acute recovery phase of myocardial infarction, and in patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure.
- Hyperthyroidism.

• Box Warning: None.

• Warnings and precautions:

- Based on data from animal reproduction studies, Tonmya may cause an increased risk of neural tube defects when administered to a pregnant female two weeks prior to conception and during the first trimester of pregnancy. Advise females of reproductive potential of the potential risk to the fetus and avoid use of Tonmya two weeks prior to conception and through the first trimester of pregnancy.
 - Perform a pregnancy test prior to initiation of treatment.
 - Advise females of reproductive potential to use effective contraception during treatment and for two weeks after the final dose.
- The development of a potentially life-threatening serotonin syndrome has been reported with cyclobenzaprine when used in combination with other drugs, such as selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), TCAs, tramadol, bupropion, meperidine, verapamil, or MAO inhibitors. Tonmya is contraindicated with MAO inhibitor use.
 - Treatment with Tonmya and any concomitant serotonergic agents should be discontinued immediately if serotonin syndrome symptoms occur and supportive symptomatic treatment should be started. If concomitant treatment with Tonmya and other serotonergic drugs is clinically warranted, careful observation is advised, especially during treatment initiation or dosage increases.

- Cyclobenzaprine is structurally related to TCAs. TCAs have been reported to produce arrhythmias, sinus tachycardia, prolongation of the conduction time leading to myocardial infarction and stroke.
 - Caution should be used when TCAs are given to patients with a history of seizure disorder, because TCAs may lower the seizure threshold. Patients with a history of seizures should be monitored during TCA use to identify recurrence of seizures or increase in frequency of seizures.
 - Because of its atropine-like action, Tonmya should be used with caution in patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and in patients taking anticholinergic drugs.
 - Tonmya monotherapy may cause CNS depression and concomitant use of Tonmya with alcohol, barbiturates, or other CNS depressants may increase the risk of CNS depression.
 - Symptoms of CNS depression include somnolence. Advise patients not to operate a motor vehicle or dangerous machinery until they are reasonably certain that Tonmya therapy will not adversely affect their ability to engage in such activities.
 - Oral mucosal adverse reactions, including sensory changes, discomfort, pain, irritation, inflammation, and lesions, occurred more frequently in patients treated with Tonmya compared to placebo (43% vs 8%). Reactions generally occurred within minutes of administration and most resolved within 60 minutes.
 - Advise patients to moisten the mouth with sips of water before administration of Tonmya to reduce the risk of oral sensory changes (hypoesthesia). Advise patients to report severe oral mucosal adverse reactions to their healthcare provider. Consider discontinuation of Tonmya if severe reactions occur.
- **Common adverse drug reactions:** Listed % incidence for adverse drug reactions= reported % incidence for drug (Tonmya) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
 - The most frequently reported adverse events included oral hypoesthesia (22.3%), oral discomfort (8.3%), abnormal product taste (8.3%), somnolence (4%), oral paresthesia (5.6%), oral pain (4%), fatigue (2%), dry mouth (1%), and aphthous ulcer (1.5%).
 - **Drug interactions:**
 - Based on its structural similarity to TCAs, concomitant use of Tonmya with:
 - MAO inhibitors may be life-threatening.
 - Alcohol, barbiturates, and other CNS depressants may increase the risk of adverse reactions associated with these drugs.
 - Tramadol may increase the seizure risk.
 - Guanethidine or other similar acting drugs may block the antihypertensive action of these drugs.
 - Post marketing cases of serotonin syndrome have been reported with the concomitant use of oral cyclobenzaprine and other drugs, such as SSRIs, SNRIs, TCAs, tramadol, bupropion, meperidine, verapamil, or MAO inhibitors.
 - The concomitant use of Tonmya with MAO inhibitors is contraindicated. If serotonin syndrome symptoms occur with the use of other serotonergic drugs, immediately discontinue Tonmya.
 - If concomitant treatment with Tonmya and other serotonergic drugs (besides MAO inhibitors) is clinically warranted, careful observation is advised, especially during dosage increases.
 - **Special populations:**
 - There is no pregnancy category for this medication; however, the risk summary indicates based on animal data, Tonmya may cause fetal harm when given to a pregnant woman. Advise pregnant women about the potential risk to the fetus with maternal exposure to Tonmya and to avoid use of Tonmya two weeks prior to conception and through the first trimester of pregnancy. (Refer to additional information in the warnings and precautions section).

- The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Fibromyalgia, described as extensive musculoskeletal pain, is a chronic, non-inflammatory pain condition known to inhibit daily activities of living. In addition, it is associated with fatigue, sleep difficulties, and nonspecific symptoms such as depressed mood or cognitive dysfunction (*Clauw et al 2025, Goldenberg and Kaplan 2025*).
- Tonmya is a cyclobenzaprine sublingual tablet indicated for the treatment of fibromyalgia in adults.
- Tonmya is contraindicated with concomitant use of MAO inhibitors or within 14 days after discontinuation of a MAO inhibitor. Tonmya is also contraindicated during the acute recovery phase of myocardial infarction, and in patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure. Hyperthyroidism is a contraindication as well.
- Tonmya should be used with caution in patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and in patients taking anticholinergic agents.
- The efficacy of Tonmya was assessed in three randomized, two-arm, parallel-group, double-blind, placebo-controlled multicenter trials that included patients who met the 2016 ACR criteria for fibromyalgia diagnosis.
 - The primary efficacy endpoint in all three trials was the change from baseline to week 14 in the weekly average of daily 24-hour recall pain intensity scores.
 - Results suggested that in Trials 1 and 3, Tonmya demonstrated a statistically significant reduction in pain intensity scores as compared with placebo. However, in Trial 2, there was no statistically significant treatment group difference. Results of this trial may not have been generalizable due to the presence of factors outside the conduct of the study.
- Guidelines do include cyclobenzaprine as a recommended treatment option for fibromyalgia. Tonmya provides patients another dosage formulation of cyclobenzaprine.
- There is no evidence to suggest that Tonmya is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Tonmya remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.
- **PDL Placement:**
 - Preferred
 - Non-Preferred

References

- Clauw DJ, McLean RM, Boackle SA, et al. Fibromyalgia. Dynamed Website. Updated November 13, 2025. Accessed February 9, 2026. <https://www.dynamed.com>.
- Goldenberg DL, Kaplan M. Fibromyalgia: Clinical manifestations and diagnosis in adults. UpToDate Website. Updated August 14, 2025. Accessed February 9, 2026. <https://www.uptodate.com>.
- Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017; 76: 318-328.
- Tonmya. Package insert. Tonix Medicines, Inc; September 2025.

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