

# Texas Vendor Drug Program

## Drug Use Criteria: Skeletal Muscle Relaxants

### Publication History

1. Developed October 2008.
2. Revised **July 2022**; June 2020; May 2018; May 2016; September 2014; December 2012; March 2011.

***Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.***

### Prepared by:

- Drug Information Service, UT Health San Antonio.
- The College of Pharmacy, The University of Texas at Austin.



**TEXAS**  
Health and Human  
Services

Medical and  
Social Services

# 1 Dosage

## 1.1 Adults

The skeletal muscle relaxants (SMRs), carisoprodol, chlorzoxazone, cyclobenzaprine, methocarbamol, metaxalone, and orphenadrine, are FDA-approved for short-term use to manage discomfort associated with acute, painful musculoskeletal conditions such as strains, sprains, and other muscle injuries.<sup>1-10</sup> These agents should be used as an adjunct to non-pharmacologic treatments, including rest and physical therapy. **Baclofen is FDA approved to alleviate signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. Baclofen may also be useful in patients with spinal cord injuries and other spinal cord diseases.**<sup>1,2,11-14</sup> **Tizanidine is FDA approved for the management of spasticity, and dantrolene is FDA approved for managing spasticity due to upper motor neuron disorders (e.g., spinal cord injury, cerebral palsy, multiple sclerosis, or stroke).**<sup>1,2,15,16</sup> Maximum recommended dosages for SMRs are summarized in Table 1. Dosages exceeding these recommendations will be reviewed.

**Table 1. Skeletal Muscle Relaxant Maximum Recommended Dosages (Adults):  
Monotherapy<sup>1-16</sup>**

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
baclofen (generic, <b>Lyvispah®</b> , <b>Ozobax®</b> , <b>Fleqsuvy®</b> )	5 mg, 10 mg, 20 mg tablets ( <b>generic</b> ); <b>5 mg, 10 mg, 20 mg oral granules (Lyvispah®)</b> ; <b>5 mg/ 5 mL oral solution (Ozobax®, generic)</b> ; 5 mg/mL oral suspension ( <b>Fleqsuvy®</b> )	spasticity	80 mg/day, in divided doses
carisoprodol (Soma®, generic)	250 mg, 350 mg tablets	muscle spasm	1400 mg/day, in divided doses
chlorzoxazone (generic)	250 mg, 375 mg, 500 mg tablets, 750 mg tablets	muscle spasm	3000 mg/day, in divided doses
chlorzoxazone (Lorzone®)	375 mg, 750 mg tablets	muscle spasm	3000 mg/day, in divided doses
cyclobenzaprine tablet (Fexmid®, generic)	5 mg, 7.5 mg ( <b>Fexmid®</b> ), 10 mg tablets	muscle spasm	30 mg/day, in divided doses
cyclobenzaprine capsule, extended- release (Amrix®, generic)	15 mg, 30 mg capsules	muscle spasm	30 mg/day
dantrolene (Dantrium®, generic)	25 mg, 50 mg, 100 mg capsules	spasticity	400 mg/day, in divided doses
metaxalone (Skelaxin®, generic)	400 mg, 800 mg tablets	muscle spasm	3200 mg/day, in divided doses
methocarbamol (Robaxin®, generic)	500 mg, 750 mg tablets	muscle spasm	8 g/day, in divided doses

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
orphenadrine ER (generic)	100 mg extended-release tablet	muscle spasm	200 mg/day, in divided doses
tizanidine	2 mg, 4 mg tablets (Zanaflex®, generic); 2 mg, 4 mg, 6 mg capsules (Zanaflex®, generic)	spasticity	36 mg/day, in divided doses

**Table 2. Skeletal Muscle Relaxant Maximum Recommended Dosages (Adults):  
Combination Therapy<sup>1,2,17,18</sup>**

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
carisoprodol/ ASA/codeine (generic)	200 mg/ 325 mg/ 16 mg tablets	<b>acute pain associated with musculoskeletal conditions</b>	400 mg/650 mg/32 mg (2 tablets) four times daily
orphenadrine/ ASA/ caffeine (Norgesic Forte®, generic)	25 mg/ 385 mg/ 30 mg, 50 mg/ 770 mg/ 60 mg tablets	Mild to moderate pain of acute musculoskeletal disorders	200 mg/ 3080 mg/ 240 mg daily

*ASA- aspirin*

### 1.1.1 Dosing in Renal and Hepatic Disease

Carisoprodol dosing adjustments should be considered for patients with severe hepatic insufficiency, as carisoprodol is extensively metabolized by the liver. Carisoprodol is also renally eliminated and should be dosed cautiously in patients with severe renal impairment.<sup>1-3</sup>

Chlorzoxazone should be administered cautiously, if at all, in patients with a history of hepatic disease as hepatotoxicity has been reported with chlorzoxazone use. Chlorzoxazone should not be prescribed to patients with active hepatic disease, including hepatitis.<sup>1,2,4</sup>

Cyclobenzaprine is extensively metabolized by liver and is not recommended for use in patients with moderate to severe hepatic impairment. Cyclobenzaprine dosage adjustments are necessary in patients with mild hepatic impairment.<sup>1,2,5-7</sup>

Administer baclofen cautiously in patients with renal impairment as the drug is primarily renally excreted.<sup>1,2,11</sup>

Orphenadrine should be administered cautiously to patients with renal and hepatic disease, as the drug is extensively metabolized in the liver, with metabolites and unchanged drug eliminated by the kidneys.<sup>1,2,10</sup>

Dosage adjustments for methocarbamol may be necessary for patients with hepatic impairment, as the drug is extensively metabolized in the liver.<sup>1,2,9</sup>

Metaxalone is contraindicated for use in patients with significantly impaired renal and/or hepatic function.<sup>1,2,8</sup>

Dantrolene should not be prescribed to patients with hepatic disease due to risk of hepatic injury associated with this drug.<sup>1,2,16</sup>

Tizanidine is extensively metabolized by the liver and eliminated by the kidneys; therefore, tizanidine should be prescribed cautiously to patients with hepatic and renal impairment.<sup>1,2,15</sup>

## 1.2 Pediatrics

With the exception of dantrolene, skeletal muscle relaxants are not FDA-approved for use in children.<sup>1,2,16</sup> Safety and efficacy of cyclobenzaprine extended-release capsules (Amrix®) have not been evaluated in pediatric patients, including adolescents.<sup>1,2,7</sup> Select skeletal muscle relaxants are FDA-approved for use in adolescents. Recommended pediatric dosages and age limitations for skeletal muscle relaxants are summarized in Table 2.

Although not FDA-approved, baclofen has been used for spasticity in pediatric patients 2 to 7 years of age in doses up to 40 mg/day and in children 8 to 11 years of age in maximum doses of 60 mg/day.<sup>1</sup>

### **Table 3. Maximum Recommended Dosages for Skeletal Muscle Relaxants (Pediatric Patients)**

Drug Name	Treatment Indication	Maximum Recommended Dosage
baclofen	spasticity	$\geq 12$ years of age: 80 mg/day, in divided doses
dantrolene	spasticity	$\geq 5$ years of age: 400 mg/day, in divided doses
carisoprodol	muscle spasm	$\geq 16$ years of age: 1400 mg/day, in divided doses
cyclobenzaprine tablets	muscle spasm	$\geq 15$ years of age: 30 mg/day, in divided doses
metaxalone	muscle spasm	$>12$ years of age: 3200 mg/day, in divided doses
methocarbamol	muscle spasm	$\geq 16$ years of age: 8 g/day, in divided doses

## 2 Duration of Therapy

For muscle spasm, centrally acting skeletal muscle relaxants have been evaluated for short-term use in managing acute pain associated with musculoskeletal conditions. Therefore, with the exception of carisoprodol and cyclobenzaprine, patient profiles documenting prolonged skeletal muscle relaxant use for greater than three months will be reviewed.

Cyclobenzaprine therapy for muscle spasm should not last longer than three weeks as efficacy beyond this time period has not been demonstrated.<sup>1,2,5-7</sup>

Limited information exists regarding carisoprodol therapy duration for muscle spasm. As carisoprodol has been evaluated only for use in the treatment of acute painful musculoskeletal conditions, patient profiles documenting prolonged carisoprodol or carisoprodol combination therapy use (greater than 21 days) will be reviewed. Cases of psychological dependence have been reported following carisoprodol administration.<sup>19,20</sup> Therefore, carisoprodol should be administered cautiously, if at all, to patients with a history of drug or alcohol abuse and/or dependence.

There is no basis for limiting therapy duration for skeletal muscle relaxants prescribed for spasticity (e.g., baclofen, dantrolene, tizanidine) as spasticity due to upper motor neuron disorders (e.g., spinal cord injury, cerebral palsy, multiple sclerosis, stroke) is a chronic disorder.

### 3 Duplicative Therapy

Concurrent administration of two or more skeletal muscle relaxants is not justified as additional therapeutic benefit is not realized and patients may be subjected to enhanced pharmacologic and/or adverse effects. Adjunctive prescriptions for two or more skeletal muscle relaxants will be reviewed.

### 4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically significant for skeletal muscle relaxants are summarized in Table 3. Only those drug-drug interactions identified as major severity or those considered life-threatening which have not been classified will be reviewed.

**Table 4. Skeletal Muscle Relaxant Drug-Drug Interactions**

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>#</sup>
cyclobenzaprine	MAOIs	combined administration may increase risk of hypertensive crises, convulsions, and death; mechanism not determined but may be due to additive norepinephrine effects or serotonin syndrome	combined use contraindicated; do not use cyclobenzaprine within 14 days of MAOI discontinuation	contraindicated (DrugReax) 1-severe (CP)
cyclobenzaprine, tizanidine	QT interval-prolonging medications	Cyclobenzaprine is structurally related to TCAs, which have been associated with QT interval prolongation; combined administration may increase risk of QT interval prolongation; tizanidine also associated with QT interval prolongation in post marketing reports	administer combination cautiously and monitor for QT interval prolongation	contraindicated (DrugReax) 1-severe (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>#</sup>
cyclobenzaprine	SSRIs/SNRIs	combined administration may increase risk of serotonin syndrome (e.g., tremor, fever, agitation, seizures, coma) due to additive serotonergic effects	administer drug combination cautiously; monitor closely for signs/symptoms of serotonin syndrome	major (DrugReax) 2-major (CP)
cyclobenzaprine	tramadol	combined administration may increase seizure risk as cyclobenzaprine is structurally related to TCAs and TCAs may decrease seizure threshold; combined use may also increase risk of serotonin syndrome	avoid combination, if possible, especially in patients predisposed to seizures; if combination necessary, monitor closely for seizure activity and serotonin syndrome sign/symptoms	major (DrugReax) 3-moderate (CP)
orphenadrine	phenothiazines	combined administration may result in decreased phenothiazine serum levels/decreased phenothiazine effectiveness due to orphenadrine anticholinergic effects, which delay phenothiazine gastric emptying and absorption; combined therapy may also produce additive anticholinergic effects	avoid combination, if possible; if combined therapy necessary, adjust phenothiazine doses to effect	moderate (DrugReax) 3-moderate (CP)
skeletal muscle relaxants	CNS depressants	increased risk of additive CNS depressant effects (e.g., sedation, respiratory depression)	administer combined therapy cautiously; adjust doses as necessary	major (DrugReax) 3-moderate (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>#</sup>
tizanidine	potent CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine)	tizanidine is primarily metabolized by CYP1A2; adjunctive administration may result in increased tizanidine levels/enhanced pharmacologic/adverse effects (e.g., hypotension, excessive sedation) due to substantial CYP1A2	combined use contraindicated	contraindicated (DrugReax) 1-severe (CP)
tizanidine	other CYP1A2 inhibitors (e.g., acyclovir, verapamil)	tizanidine primarily metabolized by CYP1A2; adjunctive administration may result in increased tizanidine levels and enhanced pharmacologic/adverse effects (e.g., hypotension, excessive sedation) due to substantial CYP1A2 inhibition	avoid combination, if possible; if adjunctive therapy necessary, administer cautiously and observe for increased adverse effects	major (DrugReax) 2-major (CP)

<sup>#</sup>CP = Clinical Pharmacology

CNS = central nervous system; MAOIs = monoamine oxidase inhibitors; SNRIs =

serotonin/norepinephrine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressant

## 5 References

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