TEXAS Health and Human Services

# Medicaid Drug Use Criteria

## *Skeletal Muscle Relaxants*

- Developed October 2008.
- Revised June 2020; May 2018; May 2016; September 2014; December 2012; March 2011.

Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

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

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# 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. These agents should be used as an adjunct to non-pharmacologic treatments,

including rest and physical therapy. The SMRs, baclofen, dantrolene, and tizanidine are FDA-approved for managing spasticity due to upper motor neuron disorders (e.g., spinal cord injury, cerebral palsy, multiple sclerosis, stroke). 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**

| Treatment Indication | Drug Name | Dosage Form/ Strength | Maximum Recommended Dosage |
|---|---|---|---|
| muscle spasm | carisoprodol (Soma®, generic) | 250 mg, 350 mg tablets | 1400 mg/day, in divided doses |
| muscle spasm | chlorzoxazone (generic) | 250 mg, 375 mg, 500 mg tablets, 750 mg tablets | 3000 mg/day, in divided doses |
| muscle spasm | chlorzoxazone (Lorzone®) | 375 mg, 750 mg tablets | 3000 mg/day, in divided doses |
| muscle spasm | cyclobenzaprine tablet (Fexmid®, generic) | 5 mg, 7.5 mg, 10 mg tablets | 30 mg/day, in divided doses |
| muscle spasm | cyclobenzaprine capsule, extended-release (Amrix®, generic) | 15 mg, 30 mg capsules | 30 mg/day |
| muscle spasm | metaxalone (Skelaxin®, Metaxall®, generic) | 400 mg, 800 mg tablets | 3200 mg/day, in divided doses |
| muscle spasm | methocarbamol (Robaxin®, generic) | 500 mg, 750 mg tablets | 8 g/day, in divided doses |
| muscle spasm | orphenadrine ER (generic) | 100 mg extended-release tablet | 200 mg/day, in divided doses |
| spasticity | baclofen (generic) | 5 mg, 10 mg, 20 mg tablets, 5 mg/mL suspension | 80 mg/day, in divided doses |
| spasticity | dantrolene (Dantrium®, generic) | 25 mg, 50 mg, 100 mg capsules | 400 mg/day, in divided doses |
| spasticity | tizanidine | 2 mg, 4 mg tablets (Zanaflex®, generic); 2 mg, 4 mg, 6 mg capsules (Zanaflex®, generic) | 36 mg/day, in divided doses |

**Table 2. Skeletal Muscle Relaxant Maximum Recommended Dosages (Adults): Combination Therapy**

| Treatment Indication | Drug Name | Dosage Form / Strength | Maximum Recommended Dosage |
|---|---|---|---|
| moderate pain associated with musculoskeletal conditions, muscle spasm | carisoprodol/ ASA/codeine (generic) | 200 mg/ 325 mg/ 16 mg tablets | 400 mg/650 mg/32 mg (2 tablets) four times daily |
| moderate pain associated with musculoskeletal conditions, muscle spasm | carisoprodol/ASA [carisoprodol compound] (generic) | 200 mg/ 325 mg tablets | 400 mg/650 mg (2 tablets) four times daily |
| Mild to moderate pain of acute musculoskeletal disorders | orphenadrine/ ASA/ caffeine (Norgesic Forte®, generic) | 25 mg/ 385 mg/ 30 mg, 50 mg/ 770 mg/ 60 mg tablets | 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.

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.

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.

Administer baclofen cautiously in patients with renal impairment as the drug is primarily renally excreted.

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.

Dosage adjustments for methocarbamol may be necessary for patients with hepatic impairment, as the drug is extensively metabolized in the liver.

Metaxalone is contraindicated for use in patients with significantly impaired renal and/or hepatic function.

Dantrolene should not be prescribed to patients with hepatic disease due to risk of hepatic injury associated with this drug.

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.

## 1.2 Pediatrics

Except for dantrolene, skeletal muscle relaxants are not FDA-approved for use in children. Safety and efficacy of cyclobenzaprine extended-release capsules (Amrix®) have not been evaluated in pediatric patients, including adolescents. 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.

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

| Treatment Indication | Drug Name | Maximum Recommended Dosage |
|---|---|---|
| muscle spasm | carisoprodol | Greater than or equal to 16 years of age: 1400 mg/day, in divided doses |
| muscle spasm | cyclobenzaprine tablets | Greater than or equal to 15 years of age: 30 mg/day, in divided doses |
| muscle spasm | metaxalone | Greater than 12 years of age: 3200 mg/day, in divided doses |
| muscle spasm | methocarbamol | Greater than or equal to 16 years of age: 8 g/day, in divided doses |
| spasticity | baclofen | Greater than or equal to 12 years of age: 80 mg/day, in divided doses |

| Treatment Indication | Drug Name | Maximum Recommended Dosage |
|---|---|---|
| spasticity | dantrolene | Greater than or equal to 5 years of age: 400 mg/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.

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. 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# |
|---|---|---|---|---|
| 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# |
|---|---|---|---|---|
| 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)<br>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)<br>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)<br>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)<br>3-moderate (CP) |
| 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)<br>1-severe (CP) |

| Target Drug | Interacting Drug | Interaction | Recommendation | Clinical Significance Level# |
|---|---|---|---|---|
| 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) |

- #CP = Clinical Pharmacology
- CNS = central nervous system
- MAOIs = monoamine oxidase inhibitors
- SNRIs = serotonin/norepinephrine reuptake inhibitors
- SSRIs = selective serotonin reuptake inhibitors
- TCAs = tricyclic antidepressant

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