"Spasticity vs Spasms" An Island of Misfit Medications

Faculty
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Assistant Professor, West Virginia University School of Pharmacy

In professional practice, numerous medications are disguised as “muscle relaxants”, however just how many actually are true relaxants of peripheral muscle? In this discussion on the overall classes of “muscle relaxants”, we will endeavor to evaluate these medications based on respective mechanisms of action and truly decipher just what actual type of medications the stereotypical “muscle relaxants” actually are. We will also aim to improve patient care by providing a strategic thought process into the appropriate selection of these medications for use in patients with muscle spasticity and/or muscle spasms. At the conclusion of our discussion, we will be able to declare that “the gig is up!” and reveal the true identity of these so-called “muscle relaxants”!

Learning Objectives

**Pharmacist**
1. Distinguish between “muscle relaxant” treatments for muscle spasticity versus those for muscle spasms.
2. Recognize the unique characteristics of the stereotypical class of “muscle relaxants” in order to improve patient care.
3. Recall the appropriate use and dosage of the stereotypical class of “muscle relaxants” in order to improve patient care.

**Pharmacy Technician**
1. Recognize the difference between treating muscle spasticity versus treating muscle spasms.
2. Recall the unique characteristics of the stereotypical class of muscle relaxants.
3. Recall the appropriate use and dosage of the stereotypical class of muscle relaxants.

**Nurse**
1. Distinguish between “muscle relaxant” treatments for muscle spasticity versus those for muscle spasms.
2. Recognize the unique characteristics of the stereotypical class of “muscle relaxants” in order to improve patient care.
3. Recall the appropriate use and dosage of the stereotypical class of “muscle relaxants” in order to improve patient care.
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Target Audience
Pharmacists, Pharmacy Technicians, Nurses

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0798-0000-19-007-L01-T
Nurse
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Pharmacist Learning Objectives

• Distinguish between “muscle relaxant” treatments for muscle spasticity versus those for muscle spasms.

• Recognize the unique characteristics of the stereotypical class of “muscle relaxants” in order to improve patient care.

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Pharmacy Technician Learning Objectives

• Recognize the difference between treating muscle spasticity versus treating muscle spasms.

• Recall the unique characteristics of the stereotypical class of muscle relaxants.

• Recall the appropriate use and dosage of the stereotypical class of muscle relaxants.
“Muscle Relaxants”
“It was the best of times, it was the worst of times…”

A TALE OF TWO CITIES

Charles Dickens

“Muscle Relaxants”
“It was the best of times, it was the worst of times…”

A Tale of Two Cities: Spasticity versus Spasm

"Spasticity vs Spasms" An Island of Misfit Medications
Stiffness or Twitching Differential Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Spasticity</th>
<th>Spasms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Velocity-dependent increase in muscle tone caused by the increased excitability of the muscle stretch reflex</td>
<td>Involuntary muscle contractions</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
<td>Central disorder of upper motor neurons</td>
<td>Peripheral muscle sprain or nerve compression</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td><strong>STIFFNESS</strong></td>
<td><strong>TWITCHING</strong></td>
</tr>
<tr>
<td><strong>Causes</strong></td>
<td>MS, Cerebral Palsy, Spinal Cord or Brain Injury, Motor Neuron Disease, or Post-Stroke Syndrome</td>
<td>Musculoskeletal, Fibromyalgia, Herniated Disk, Mechanical Lower Back Pain, Spinal Stenosis, Sciatica, or Myofascial Pain</td>
</tr>
</tbody>
</table>
| **FDA Approved Medications** | • botulinum toxin  
• baclofen  
• dantrolene  
• diazepam  
• riluzole  
• tizanidine | • carisoprodol  
• chlorzoxazone  
• cyclobenzaprine  
• metaxalone  
• methocarbamol  
• orphenadrine |


"Spasticity vs Spasms" An Island of Misfit Medications
Pain Management Treatments

<table>
<thead>
<tr>
<th>Pain Management Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Pharmacological</td>
</tr>
<tr>
<td>Active (Exercise, Yoga, etc.) &amp; Passive (e.g. Massage, Acupuncture, etc.)</td>
</tr>
<tr>
<td>Non-Opioid</td>
</tr>
<tr>
<td>Acetaminophen, NSAIDs, OTC/Supplements, etc.</td>
</tr>
<tr>
<td>Opioids</td>
</tr>
<tr>
<td>Phenanthrenes (morphine, hydrocodone, oxycodone, etc.) &amp; others</td>
</tr>
<tr>
<td>Adjuvants</td>
</tr>
<tr>
<td>Antidepressants, Alpha-2 Agonists, &quot;Muscle Relaxants&quot;, Benzodiazepines, Gabapentinoids, Anti-Epileptic Drugs, Antiarrhythmics, &amp; NMDA Antagonists</td>
</tr>
<tr>
<td>Interventional</td>
</tr>
<tr>
<td>Injections, Nerve Blocks, Spinal Cord Stimulation, Pumps, etc.</td>
</tr>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>Various Procedures (e.g. Knee Replacement, etc.)</td>
</tr>
</tbody>
</table>

Adjuvant Therapies

<table>
<thead>
<tr>
<th>Adjuvant Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
</tr>
<tr>
<td>TCAs, SNRIs, bupropion, &amp; mirtazapine</td>
</tr>
<tr>
<td>Alpha-2 Agonists</td>
</tr>
<tr>
<td>Clonidine</td>
</tr>
<tr>
<td>&quot;Muscle Relaxants&quot; &amp; Benzodiazepines</td>
</tr>
<tr>
<td>Spasticity &amp; Spasm medications</td>
</tr>
<tr>
<td>Gabapentinoids</td>
</tr>
<tr>
<td>Alprazolam, lorazepam, diazepam, etc.</td>
</tr>
<tr>
<td>Gabapentin, pregabalin, baclofen, etc.</td>
</tr>
<tr>
<td>Anti-Epileptic Drugs</td>
</tr>
<tr>
<td>1st &amp; 2nd Generation AEDs</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
</tr>
<tr>
<td>mexiletene &amp; flecainide</td>
</tr>
<tr>
<td>NMDA Antagonists</td>
</tr>
<tr>
<td>methadone, dextromethorphan, ketamine, &amp; amantadine</td>
</tr>
</tbody>
</table>
Musculoskeletal Disorders (Spasms)
- carisoprodol (Soma®)
- cyclobenzaprine (Flexeril®)
- orphenadrine (Norflex®)
- methocarbamol (Robaxin®)
- chlorzoxazone (Parafon Forte DSC®, Lorzone®, Relax-DS®)
- metaxalone (Skelaxin®)

Muscle Relaxants
Not recommended for chronic pain, except for acute flare-ups

Spasticity (Stiffness)
Central Acting
- tizanidine (Zanaflex®)
- baclofen (Lioresal®)
- Gabapentinoids & Benzos

Peripheral Acting
- dantrolene (Dantrium®)
- Botulinum Toxin

Spasticity vs Spasms: An Island of Misfit Medications
Dantrolene

- Hydantoin derivative structurally related to phenytoin
- Used for Upper motor neuron disorders & Malignant hyperthermia

**Mechanism of Action**
- Blocks ryanodine channel, which inhibits Ca$^{2+}$ release, thus reducing muscle contraction
- Does NOT interfere with Ca$^{2+}$ entry at the cell surface as with Ca$^{2+}$ Channel Blockers

**Side Effects**
- Skeletal muscle weakness
- Troubled breathing (Dyspnea)
- Troubled swallowing (Dysphasia)
- Somnolence
  - Dose-dependent diarrhea
  - Black Box warning of hepatotoxicity
    - Associated with high doses (>800 mg/day) & long-term use (>3 months)

**Products**
- Dantrium® 25mg & 50mg Capsules
  - Generic available as 25mg, 50mg, & 100mg
- Revonto® 20mg Powder for Injection
- Ryanodex® 250mg Powder for Injection
Island of Misfit “Muscle Relaxants”

Tizanidine

- Structural Analog of clonidine
- Blocks Afferent sensory spine neuron firing (Alpha-2 Agonist)
- Central Analgesia (Dorsal Horn receives sensory info from periphery)

Inhibits presynaptic NE release

Vasoconstriction

Rudolph the Red-Nosed Reindeer (TV special); NBC & General Electric, 1964.

Clinical Pharmacology Online Database. 2018.
https://www.sciencedirect.com/science/clonidine tizanidine
## Tizanidine

### Notable Side Effects
- Hypotension
- Weakness & Lack of Energy (Asthenia)
  - More sedation than baclofen, so dose at bedtime
- Elevated Liver Function Tests (LFTs)

### Products
- Zanaflex® 2mg, 4mg, 6mg Capsules (generic available)
  - Capsule w/ Food < Concentration & Absorption
- Zanaflex® 2mg & 4mg Tablets (generic available)
  - Tablet w/ Food > Concentration & Absorption

### Interactions
- **CYP1A2 Inhibitors**
  - Major: ciprofloxacin & fluvoxamine
  - Minor: cimetidine, famotidine, verapamil, & ethinyl estradiol
- **ACEIs/ARBs** $\rightarrow$ severe hypotension
Baclofen

• Structural Analog of Gama-Amino-Butyric Acid (GABA)
• Originally designed to treat epilepsy
• Being studied for alcohol-use disorder

Mechanism of Action
• Activates GABA chloride channel
• Blocks Central Afferent sensory neurons

Notable Side Effects
• Decreased muscle tone (Hypotonia)
  ➢ More so than tizanidine
• Drowsiness
  ➢ Abrupt discontinuation → Withdrawal (Benzo-Like)
    ▪ Seizures, tachycardia, hyperthermia, anxiety, hallucination, etc.

Products
• Baclofen 10mg & 20mg (Generic ONLY)
• Lioresal® Solution for Injection

https://basicmedicalkey.com/sedative-hypnotic-and-anxiolytic-drugs-2/
“Muscle Relaxants”
Not recommended for chronic pain, except for acute flare-ups

<table>
<thead>
<tr>
<th>Spasticity (Stiffness)</th>
<th>Musculoskeletal Disorders (Spasms)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Acting</strong></td>
<td>carisoprodol (Soma®)</td>
</tr>
<tr>
<td>tizanidine (Zanaflex®)</td>
<td>cyclobenzaprine (Flexeril®)</td>
</tr>
<tr>
<td>baclofen (Lioresal®)</td>
<td>orphenadrine (Norflex®)</td>
</tr>
<tr>
<td>Gabapentinoids &amp; Benzos</td>
<td>methocarbamol (Robaxin®)</td>
</tr>
<tr>
<td><strong>Peripheral Acting</strong></td>
<td>chlorzoxazone (Parafon Forte DSC®, Lorzone®, Relax-DS®)</td>
</tr>
<tr>
<td>dantrolene (Dantrium®)</td>
<td>metaxalone (Skelaxin®)</td>
</tr>
<tr>
<td>Botulinum Toxin</td>
<td></td>
</tr>
</tbody>
</table>

**Spasticity vs Spasms**: An Island of Misfit Medications

**Muscle Relaxants**

- Not recommended for chronic pain, except for acute flare-ups.
- US/DEA reclassified as a controlled substance.
- European Medicines Agency withdrew from market.

**Carisoprodol**

- 2012
  - US/DEA reclassified as a controlled substance
  - Only “relaxant” controlled substance
  - European Medicines Agency withdrew from market
- 2013
  - Canada & Indonesia withdrew from market

**Mechanism of Action**

- GABA-related

**References**

- Clinical Pharmacology Online Database. 2018.

**European Medicines Agency**

Press release: European Medicines Agency recommends suspension of marketing authorisations for carisoprodol-containing medicinal products.
Carisoprodol

Metabolism
• CYP-2C19 metabolizes carisoprodol to meprobamate (barbiturate, Miltown®)

Products
• Soma® 250mg & 350mg Tablets (generic available)
• Carisoprodol 200mg & Aspirin 325mg (only generic is available)
• Carisoprodol 200mg, Aspirin 325mg, & Codeine 16mg (only generic is available)

https://basicmedicalkey.com/sedative-hypnotic-and-anxiolytic-drugs-2/
Clinical Pharmacology Online Database. 2018.

Carisoprodol
• Structural Analog of amitriptyline
• Synthesized in 1961
• FDA approved in 1977 for ACUTE muscle spasms

Package Insert
• Should be used only for short periods (2-3 weeks)
• Adequate evidence of effectiveness for more prolonged use is NOT available

Cyclobenzaprine

• Structural Analog of amitriptyline
• Synthesized in 1961
• FDA approved in 1977 for ACUTE muscle spasms

Package Insert
• Should be used only for short periods (2-3 weeks)
• Adequate evidence of effectiveness for more prolonged use is NOT available

https://basicmedicalkey.com/sedative-hypnotic-and-anxiolytic-drugs-2/
Clinical Pharmacology Online Database. 2018.
Cyclobenzaprine

Notable Side Effects
- Remote cases of Serotonin Syndrome with other serotonergic agents

Metabolism
- CYP3A4, CYP1A2, and to a lesser extent CYP2D6

Products
- ER: Amrix® 15mg & 30mg (Brand only as of 2017)
- IR: Flexeril® 5mg & 10mg (generic available)
- IR: Fexmid® 7.5mg (generic available)

Urine Drug Screenings
TCA False Positives

cyproheptadine  carbamazepine  cyclobenzaprine  amitriptyline

https://www.dallastox.com/demystifying-urine-drug-testing.html
Orphenadrine

- Structural (methylated) Analog of diphenhydramine
- In 1947, Parke-Davis® led the development of orphenadrine
  - Prior to amantadine (~1960s), anticholinergics were main Parkinson's agents

Mechanisms of Action
- H1 receptor antagonist (stronger than diphenhydramine)
- Anticholinergic (Muscarinic Receptor Antagonist)
- NMDA Antagonist
- NE Reuptake Inhibitor

Notable Side Effects
- Antihistamine Sedation Effect
- Anticholinergic Effects (e.g. “Drying”)
- Aplastic anemia (Rare)

Products (all generic only)
- Orphenadrine 25mg/Aspirin 385mg/Caffeine 30mg IR Tablets
- Orphenadrine 50mg/Aspirin 770mg/Caffeine 60mg IR Tablets
- Orphenadrine ER 100mg Tablets
- Solutions for Injection

Canada → OTC
Methocarbamol

- Structural analog of mephenesin
  - Very Narrow Therapeutic Index involving Respiratory Depression at clinical doses
  - Antidote for Strychnine poisoning
  - Used to develop meprobamate (Miltown®) in the 1950’s as a barbiturate
    - 1st Blockbuster Psychotropic Medication
- Carbamate derivative of guaifenesin (Mucinex®, etc.)

![Structural diagram of methocarbamol, mephenesin, meprobamate, and guaifenesin]

Methocarbamol

Products
- Robaxin® 500mg & 750mg (generic available)
- Robaxin® Solution for Injection
  - Methocarbamol 400mg & Aspiring 325mg Tablets (OFF MARKET)

Canada → OTC
- Robaxin (methocarbamol)
- Robax Platinum (+IBU)
- Robaxacet (+APAP)
- Robaxisal (+ASA)
Methocarbamol

Metabolism
• Does not produce guaifenesin as a metabolite (carbamate bond not hydrolyzed)
• Phase I hydroxylation and O-demethylation, followed by Phase II conjugation

Notable Side Effect
➢ Brown/Black/Green Urine

“\textit{I could go on and on about this. And I will. Get comfortable.}”
Urine Color

• The yellow coloration of urine results from urobilin that is produced as a product of bilirubin degradation

• Normal urine color: light yellow to golden

<table>
<thead>
<tr>
<th>Urine Color</th>
<th>Medications</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orange</td>
<td>Isoniazid, Phenazopyridine, Warfarin, &amp; Sulfasalazine</td>
<td>Consumption of Carrots</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor for sparse blood in urine (Hematuria)</td>
</tr>
<tr>
<td>Red</td>
<td>Warfarin, Rifampin, Phenazopyridine, Senna, &amp; Ibuprofen</td>
<td>Consumption of Red Beets, Rhubarb, or Carrots</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor for sparse blood in urine (Hematuria)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Myoglobinuria from rhabdomyolysis</td>
</tr>
<tr>
<td>Brown</td>
<td>Metronidazole, Nitrofurantoin, &amp; Acetaminophen</td>
<td>Myoglobinuria from rhabdomyolysis (&quot;Hand Drumming&quot;)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute Renal/Hepatic Disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metastatic melanoma (Rare Reports)</td>
</tr>
<tr>
<td>Black</td>
<td>Methocarbamol</td>
<td>Phenol or Copper Poisoning</td>
</tr>
<tr>
<td></td>
<td>Methyldopa/C-dopa, Senna, &amp; Sorbitol</td>
<td>Consumption of Iodine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metastatic melanoma (Rare Reports)</td>
</tr>
<tr>
<td>Purple</td>
<td>Medications causing Blue (Added to medications causing Red)</td>
<td>Gram-Negative bacteria</td>
</tr>
<tr>
<td>Blue</td>
<td>Methocarbamol</td>
<td>Methylene Blue</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline, Cimetidine, Indomethacin, Zaleplone, &amp; Metoclopramide</td>
<td>Consumption of Asparagus or Black licorice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UTI with Pseudomonas</td>
</tr>
<tr>
<td>Green</td>
<td>Methocarbamol</td>
<td>Calcium or Phosphate Crystals</td>
</tr>
<tr>
<td></td>
<td>Medications causing Blue (Added to yellow urine)</td>
<td>Infection</td>
</tr>
<tr>
<td>White</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
**Chlorzoxazone**

**FDA approved in 1958**
- Adjunct for relief of discomfort associated with acute musculoskeletal conditions

**Kinetics/Metabolism**
- Hepatic glucuronidation into an inactive metabolite that is excreted in the urine
  
  *(Orange/Red/Purple)*

**Products**
- Parafon Forte DSC® & Relax-DS® 500mg (generic available)
- Lorzone® 375mg & 750mg (Brand Only)

**Notable Drug Interactions**
- Diclofenac, acetaminophen, tramadol, & famotidine

**Notable Side Effects**
- Rare cases of idiosyncratic hepatocellular toxicity (Monitor LFTs)
  
  ➢ *Orange/Red/Purple Urine*
Metaxalone

FDA approved in 1962
• Adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute painful musculoskeletal conditions

Kinetics/Metabolism
• High Fat meals > bioavailability & AUC
• CYP1A2, CYP2D6, CYP2E1, & CYP3A4

Products
• Skelaxin® 800mg (generic available)
• Metaxalone 400mg (generic only)

*Watch for confusion with metolazine (diuretic)

"Muscle Relaxant" Products Available

<table>
<thead>
<tr>
<th>Product</th>
<th>Strengths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methocarbamol tablet</td>
<td>500mg, 750mg</td>
</tr>
<tr>
<td>Robaxin® tablet</td>
<td>500mg, 750mg</td>
</tr>
<tr>
<td>Carisoprodol tablet</td>
<td>250mg, 350mg</td>
</tr>
<tr>
<td>Soma® Tablet</td>
<td>250mg, 350mg</td>
</tr>
<tr>
<td>Cyclobenzaprine tablet</td>
<td>5mg, 7.5mg, 10mg</td>
</tr>
<tr>
<td>Flexeril® tablet</td>
<td>5mg, 7.5mg, 10mg</td>
</tr>
<tr>
<td>Amrix® ER Capsule</td>
<td>15mg, 30mg</td>
</tr>
<tr>
<td>Orphenadrine ER tablet</td>
<td>100mg</td>
</tr>
<tr>
<td>Metaxalone tablet</td>
<td>400mg, 800mg</td>
</tr>
<tr>
<td>Metaxall®</td>
<td>800mg</td>
</tr>
<tr>
<td>Skelaxin®</td>
<td>800mg</td>
</tr>
<tr>
<td>Baclofen tablet</td>
<td>10mg, 20mg</td>
</tr>
<tr>
<td>Chlorzoxazone tablet</td>
<td>500mg</td>
</tr>
<tr>
<td>Lorzone® tablet</td>
<td>375mg, 750mg</td>
</tr>
<tr>
<td>Relax-DS®</td>
<td>500mg</td>
</tr>
<tr>
<td>Tizanidine capsule</td>
<td>2mg, 4mg, 6mg</td>
</tr>
<tr>
<td>Zanaflex® capsule</td>
<td>2mg, 4mg, 6mg</td>
</tr>
<tr>
<td>Tizanidine tablet</td>
<td>2mg, 4mg</td>
</tr>
<tr>
<td>Zanaflex® tablet</td>
<td>2mg, 4mg</td>
</tr>
<tr>
<td>Dantrium® capsule</td>
<td>25mg, 50mg, 100mg</td>
</tr>
<tr>
<td>Dantrolene capsule</td>
<td>25mg, 50mg, 100mg</td>
</tr>
</tbody>
</table>
“Muscle Relaxants”
Not recommended for chronic pain, except for acute flare-ups

**Musculoskeletal Disorders** (Spasms)
carisoprodol (Soma®)
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methocarbamol (Robaxin®)
chlorzoxazone (Parafon Forte DSC®, Lorzone®, Relax-DS®)
metaxalone (Skelaxin®)

**Spasticity** (Stiffness)
Central Acting
tizanidine (Zanaflex®)
baclofen (Lioresal®)
Gabapentinoids & Benzos

Peripheral Acting
dantrolene (Dantrium®)
Botulinum Toxin

“And, they said that no one would notice if I peed in the pool.”
Opioids, Benzos, “Relaxants”, & Hypnotics
Overlapping Sedative Side Effects...

Drug-Sedative Interactions
“Name Game”

<table>
<thead>
<tr>
<th>Drug-Drug Interaction</th>
<th>Proposed Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid + Benzodiazepine Sedative</td>
<td>“Bozo”</td>
</tr>
<tr>
<td>Opioid + &quot;Muscle Relaxant&quot; Sedative</td>
<td>“Relaxoid”</td>
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<tr>
<td>Opioid + Sedative Hypnotic</td>
<td>“Hypoid”</td>
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<tr>
<td>Opioid + One Other Sedative</td>
<td>“Deadly Duo”</td>
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<tr>
<td>Opioid + Two Other Sedatives</td>
<td>“Unholy Trinity”</td>
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<td>Opioid + Three Other Sedatives</td>
<td>“Quattro Killer”</td>
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<tr>
<td>Benzodiazepine &amp; Sedative Hypnotic</td>
<td>“Hypzo”</td>
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<tr>
<td>Benzodiazepine &amp; &quot;Muscle Relaxant&quot; Sedative</td>
<td>“Relaxzo”</td>
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oxycodone, alprazolam, carisoprodol, and zolpidem

Medication Database Sedative Drug-Drug Interaction Reports
- Micromedex®
- Lexicomp®
- Clinical Pharmacology®
- Facts & Comparisons®

oxycodone, alprazolam, carisoprodol, and zolpidem
Medication Database Interaction Screenings

**Micromedex®**

Oxycodone, alprazolam, carisoprodol, and zolpidem

<table>
<thead>
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<th>Definitions</th>
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<tr>
<td>Severity:</td>
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<td>Occasional</td>
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<td>Moderate</td>
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<td>Minor</td>
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<tr>
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<td>Documentation:</td>
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<td>Excellent</td>
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<td>Good</td>
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<tr>
<td>Fair</td>
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### Drug-Drug Interactions (6)

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<th>Drugs:</th>
<th>Severity:</th>
<th>Documentation:</th>
<th>Summary:</th>
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<tr>
<td>ALPRAZOLAM - CARISOPRODOL</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of ALPRAZOLAM and CARISOPRODOL may result in increased risk of respiratory depression.</td>
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<tr>
<td>ALPRAZOLAM - OXYCODONE</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of ALPRAZOLAM and OXYCODONE may result in increased risk of respiratory depression and CNS depression.</td>
</tr>
<tr>
<td>ALPRAZOLAM - ZOLPIDEM TARTRATE</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of ALPRAZOLAM and ZOLPIDEM TARTRATE may result in increased risk of respiratory depression and CNS depression.</td>
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<tr>
<td>CARISOPRODOL - OXYCODONE</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of CARISOPRODOL and OXYCODONE may result in increased risk of respiratory depression and CNS depression.</td>
</tr>
<tr>
<td>CARISOPRODOL - ZOLPIDEM TARTRATE</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of CARISOPRODOL and ZOLPIDEM TARTRATE may result in increased risk of respiratory depression and CNS depression.</td>
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<tr>
<td>OXYCODONE - ZOLPIDEM TARTRATE</td>
<td>S Major</td>
<td>Fair</td>
<td>Consumer use of OXYCODONE and ZOLPIDEM TARTRATE may result in increased risk of respiratory depression and CNS depression.</td>
</tr>
</tbody>
</table>

**Lexicomp®**

Oxycodone, alprazolam, carisoprodol, and zolpidem

- **A** = No known interaction
- **B** = Monitor therapy
- **C** = Consider therapy modification
- **E** = Avoid combination

View interaction detail by clicking on link.

Drugs in this analysis: ALPRAZOLAM, Carisoprodol, OXYCODONE, Zolpidem

### Drug-Drug Interactions

- **A** ALPRAZOLAM (CNS Depressants) – OXYCODONE
- **B** ALPRAZOLAM (CNS Depressants) – Zolpidem Depends on Brand Name
- **C** Carisoprodol (CNS Depressants) – OXYCODONE
- **D** Carisoprodol (CNS Depressants) – Zolpidem Depends on Brand Name
- **E** OXYCODONE – Zolpidem (CNS Depressants)
- **F** OXYCODONE (CNS Depressants) – Zolpidem Depends on Brand Name
- **G** ALPRAZOLAM (CNS Depressants) – Carisoprodol (CNS Depressants)
Oxycodone, alprazolam, carisoprodol, and zolpidem

Medication Database
Interaction Screenings

Clinical Pharmacology®

Oxycodone, alprazolam, carisoprodol, and zolpidem

"Spasticity vs Spasms" An Island of Misfit Medications
Medication Database Interaction Screenings
Facts & Comparisons®

Oxycodone, alprazolam, carisoprodol, and zolpidem

Potentially severe or life-threatening reaction/interaction
Reaction/interaction may cause deterioration in the patient’s clinical status
Reaction/interaction may cause minor effects

Drug-Drug Interactions

A strong association exists between illicit drug use and the combination of carisoprodol, alprazolam, and a narcotic analgesic. Clinicians should be vigilant for legitimacy of therapeutic use when presented with prescriptions or prescription requests for this combination of agents. Institutional guidelines for the handling of drug seeking behavior should be followed.

Pharmacies miss half of dangerous drug combinations

“Muscle Relaxants”
Not recommended for chronic pain, except for acute flare-ups

**Musculoskeletal Disorders** (Spasms)
- carisoprodol (Soma®)
- cyclobenzaprine (Flexeril®)
- orphenadrine (Norflex®)
- methocarbamol (Robaxin®)
- chlorzoxazone (Parafon Forte DSC®, Lorzone®, Relax-DS®)
- metaxalone (Skelaxin®)

**Spasticity** (Stiffness)

**Central Acting**
- tizanidine (Zanaflex®)
- baclofen (Lioresal®)
- Gabapentinoids & Benzos
  - **Peripheral Acting**
    - dantrolene (Dantrium®)
- Botulinum Toxin

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www.addictionsurvivors.org

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“Spasticity vs Spasms” An Island of Misfit Medications
“Muscle Relaxants” and Chocolate???

“All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy.”

~Paracelsus

https://www.forbes.com/sites/rosspomeroy/2013/10/31/1900-the-number-of-chocolates-that-will-kill-a-child/#4ec344346d3f

10yo ➔ ~1,900 mini milk bars
16yo ➔ ~800 mini dark bars

Spasticity vs Spasms
Treatment

CHOOSE WISELY

MY FRIEND

CHOOSE WISELY, MY FRIEND