

PainWeek®

Muscles' Little Helper: Spasms vs Spasticity

Mark Garofoli, PharmD, MBA, BCGP, CPE

Faculty



- Family of 8 Pharmacists
 - *Wife, In-Laws, & Cousins*
- Family Vineyard in the Marche Region of Italy

Disclosures

- Expert Witness: U.S. Department of Justice, Consumer Protection Branch
- Expert Witness: Cardinal Health

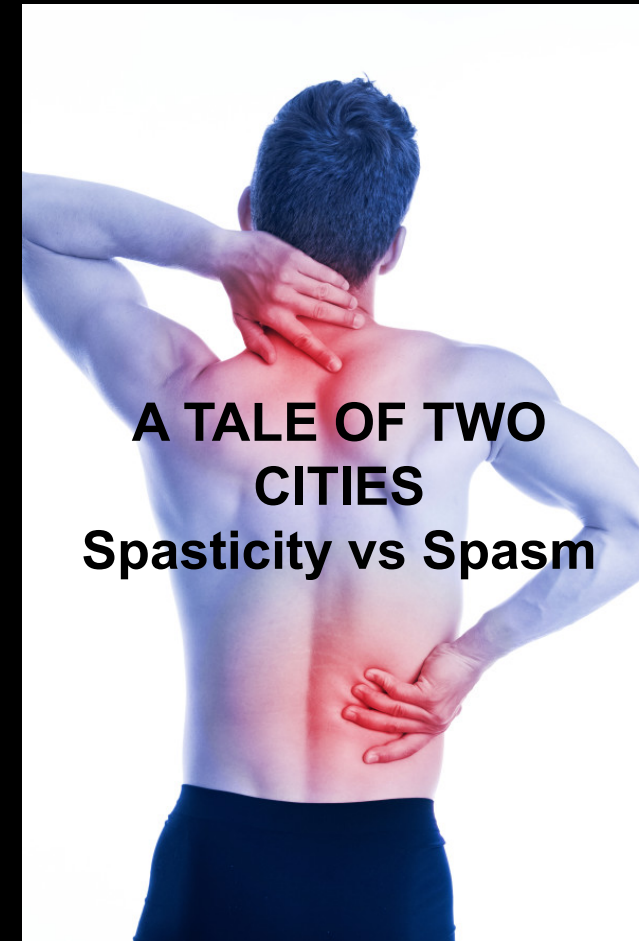
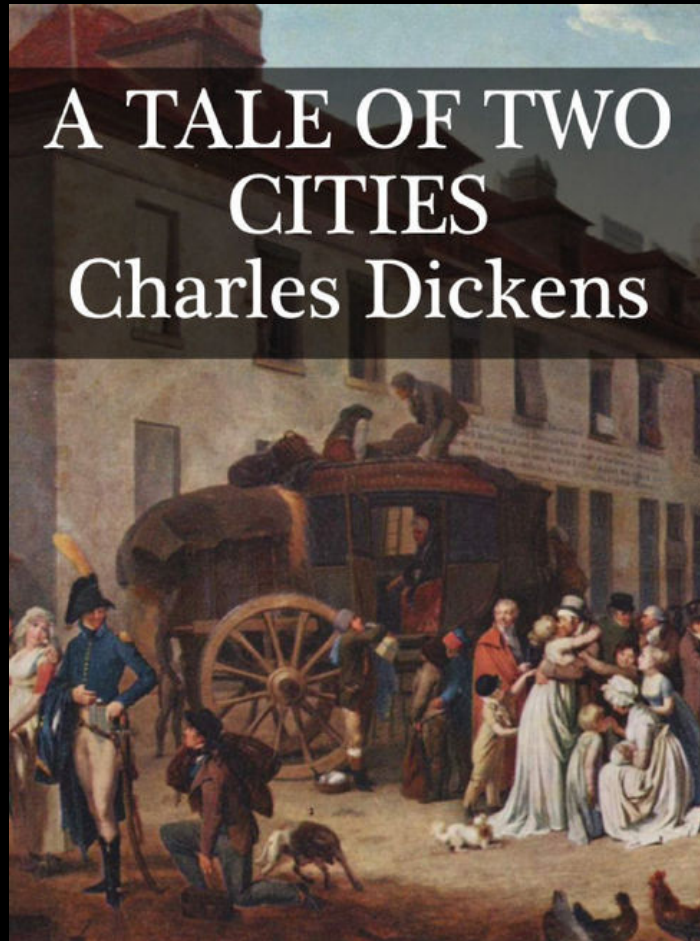
This presentation was not a part of the presenter's official duties at the WVU and does not represent the opinion of WVU

Learning Objectives

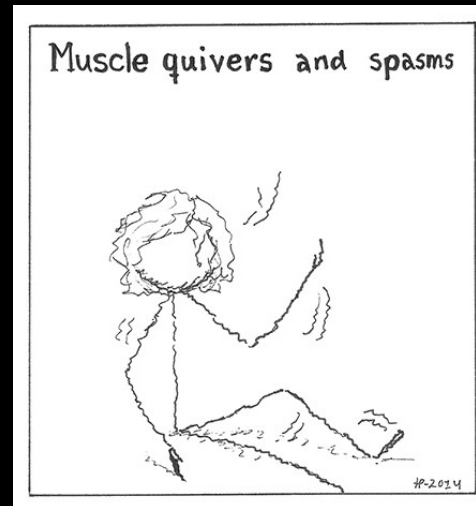
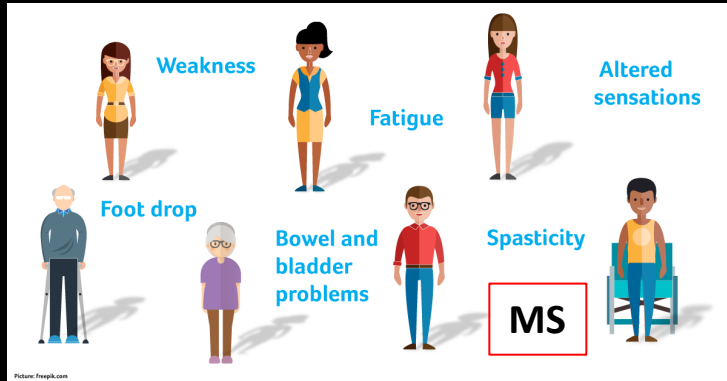
- Distinguish treatments of muscle spasticity versus muscle spasms
- Summarize the unique individual characteristics of “muscle relaxants”
- Recall the appropriate use and dosage of “muscle relaxants”

“Muscle Relaxants”

It was the best of times, it was the worst of times...



Stiffness or Twitching What's the Diff Dx?



Rabies

How it spreads

ANIMAL BITE: The farther away from brain, the longer virus takes to spread

VIRUS: Spreads through central nervous system

Common carriers of rabies

Infected animals: Show no fear for humans; act very agitated

Bat

Fox

Cat

Skunk

Dog: Another common rabies source

Symptoms in humans

- Fever, depression
- Agitation
- Painful spasms followed by excessive saliva
- Death within a week without vaccine

Treatment: Hospitalization, immune globulin injections, anti-rabies vaccine

Foaming at mouth after drinking: Produced by spasms in throat

SOURCE: The World Book Medical Encyclopedia KRT

Stiffness or Twitching

What's the Diff Dx?

	Spasticity	Spasms
Definition	Velocity-dependent muscle tone increase caused by the increased excitability of the muscle stretch reflex	Involuntary muscle contractions
Etiology	Central disorder of upper motor neurons	Peripheral muscle sprain or nerve compression
Symptoms	STIFFNESS	TWITCHING
Causes	MS, cerebral palsy, spinal cord or brain injury, motor neuron disease, or post-stroke syndrome	musculoskeletal, fibromyalgia, herniated disk, mechanical lower back pain, spinal stenosis, sciatica, or myofascial pain
FDA Approved Medications	<ul style="list-style-type: none"> • botulinum toxin • baclofen • dantrolene • diazepam • riluzole • tizanidine 	<ul style="list-style-type: none"> • carisoprodol • chlorzoxazone • cyclobenzaprine • metaxalone • methocarbamol • orphenadrine

Stiffness or Twitching

What's the Diff Dx?

	Spasticity	Rigidity
Description	Velocity-dependent muscle tone increase	Non-velocity-dependent muscle tone increase
Etiology	Central disorder of upper motor neurons	Extrapyramidal lesions (e.g., Parkinson's)
Symptoms	<p>STIFFNESS</p> <ul style="list-style-type: none"> • More resistance in one direction 	<p>STIFFNESS</p> <ul style="list-style-type: none"> • Same resistance in all directions
Causes	MS, cerebral palsy, spinal cord or brain injury, motor neuron disease, or post-stroke syndrome	Parkinson's disease

Modified Ashworth Scale (Muscle Twitching Dx)

- Place the patient in a supine position
- If testing a muscle that primarily flexes a joint, place the joint in a maximally flexed position and move to a position of maximal extension over one second
- If testing a muscle that primarily extends a joint, place the joint in a maximally extended position and move to a position of maximal flexion over one second

Score	
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2	More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3	Considerable increase in muscle tone, passive movement difficult
4	Affected part(s) rigid in flexion or extension

Rigidity vs Spasm Treatments

Rigidity (Spasticity)



SPASMS (Musculoskeletal)



“Muscle Relaxants”

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

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

baclofen

gabapentinoids & benzos

PERIPHERAL ACTING

dantrolene

botulinum toxin

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

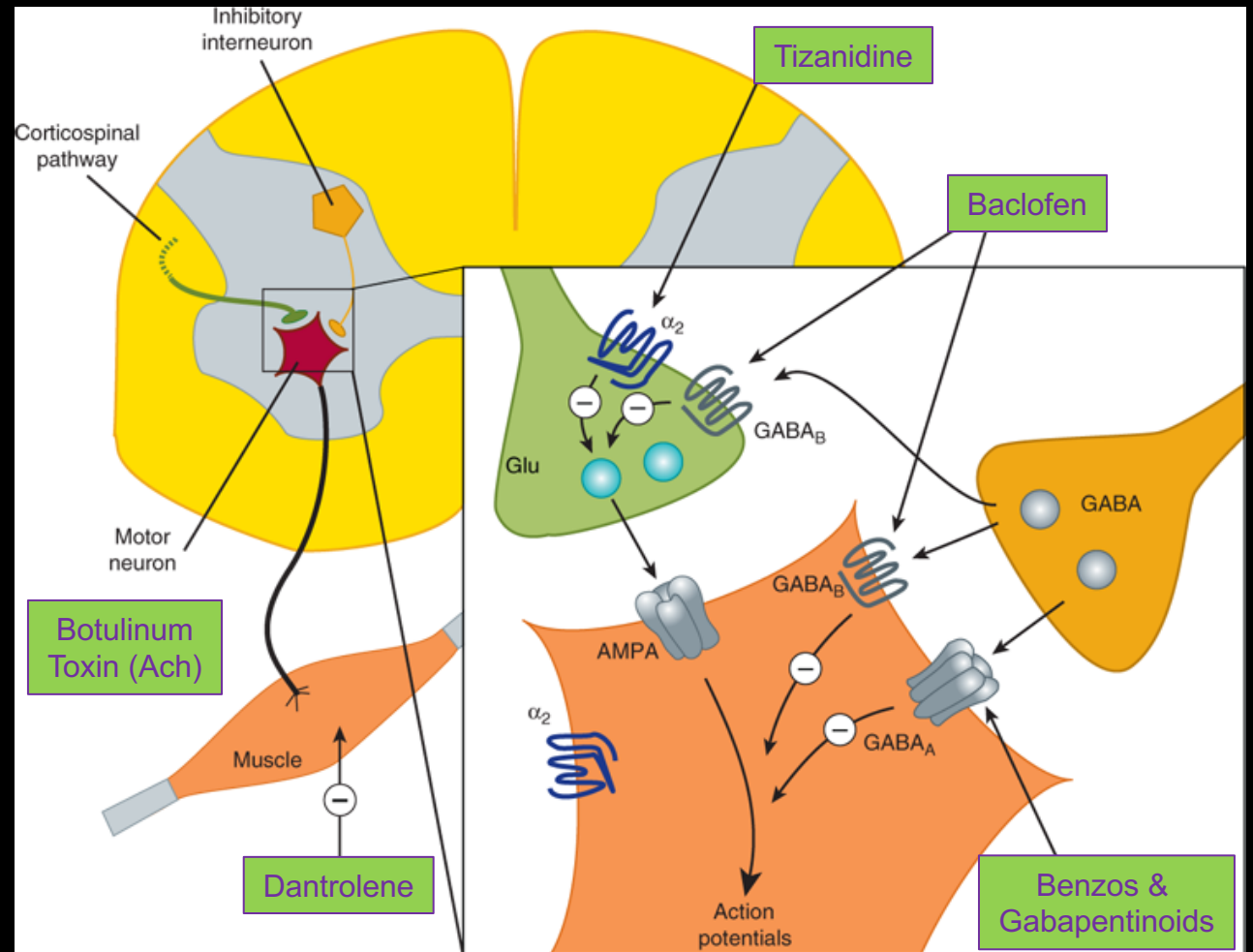
chlorzoxazone

metaxalone

“Muscle Relaxants”

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

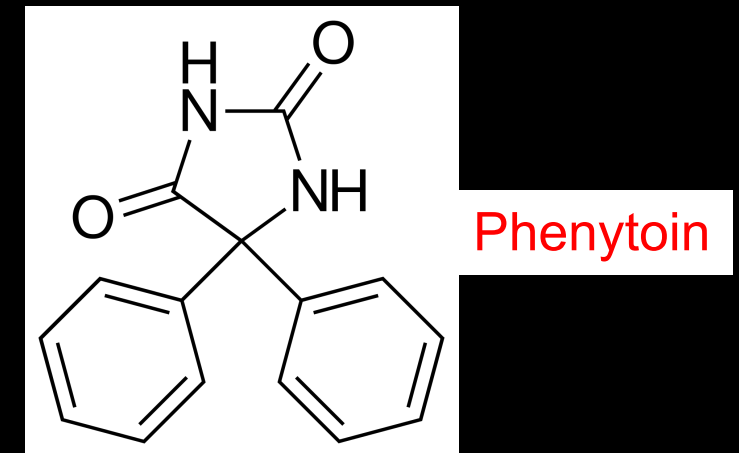
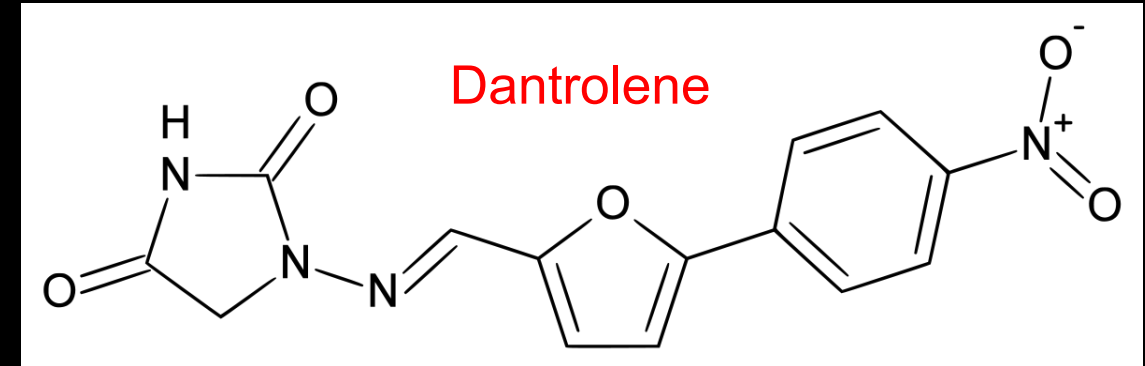
SPASTICITY (Stiffness)
CENTRAL ACTING
tizanidine
baclofen
gabapentinoids & benzos
PERIPHERAL ACTING
dantrolene
botulinum toxin



Source: A.J. Trevor, B.G. Katzung, M. Kruidering-Hall: Katzung & Trevor's Pharmacology: Examination & Board Review, 11th Ed. www.accesspharmacy.com Copyright © McGraw-Hill Education. All rights reserved.

Dantrolene

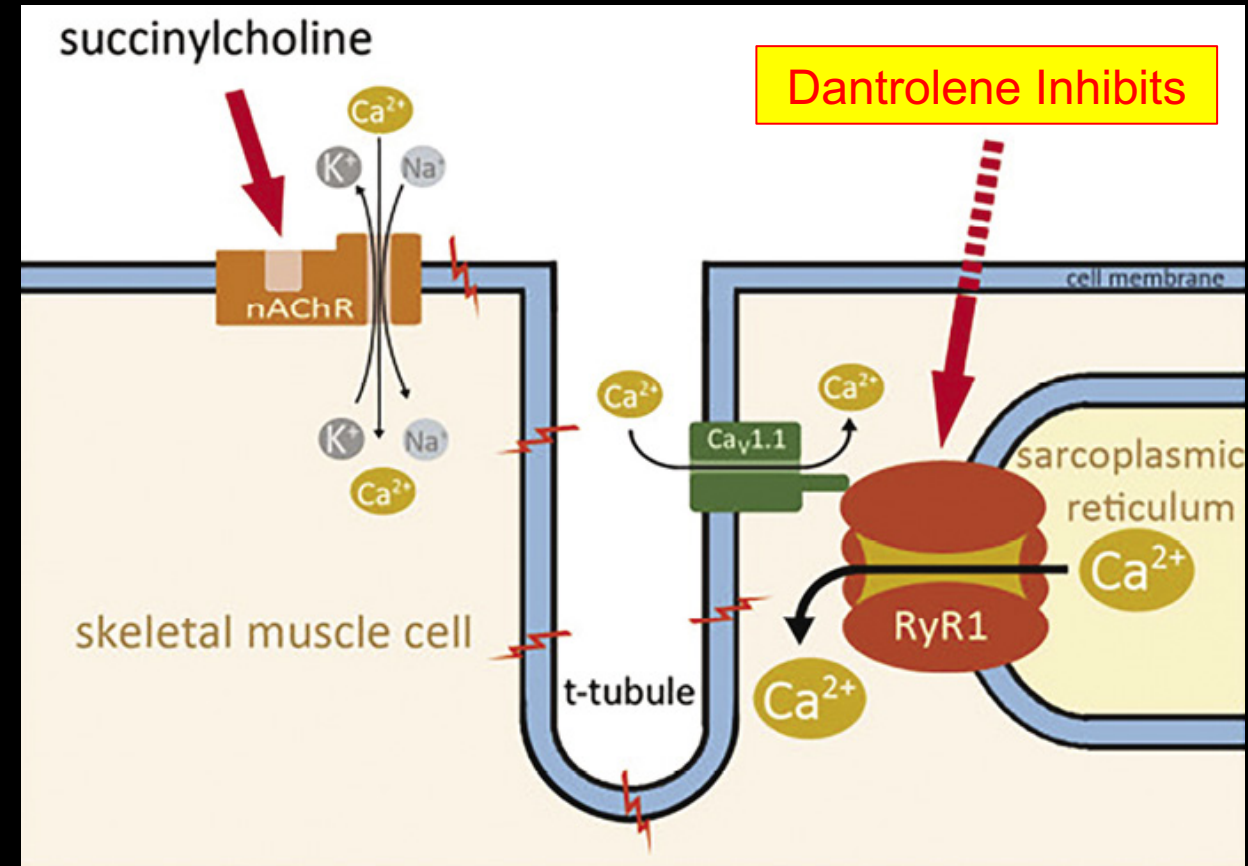
- Hydantoin derivative structurally related to phenytoin
- Uses
 - Upper motor neuron disorders
 - Malignant hyperthermia



Dantrolene

Mechanism of Action

- Blocks ryanodine channel, which inhibits Ca release, thus reducing muscle contraction
 - Counteracts succinylcholine
- Does NOT interfere with Ca entry at the cell surface as with Ca channel blockers



Dantrolene

Side Effects

- Skeletal muscle weakness
- Troubled breathing (dyspnea)
- Troubled swallowing (dysphasia)
- Somnolence
 - Diarrhea (dose dependent)
 - Hepatotoxicity (Black Box Warning)
 - >800 mg/day
 - >3 month utilization

Products

- Dantrium[®] 25mg & 50mg capsules
 - Generic 25mg, 50mg, & 100mg
- Revonto[®] 20mg powder for injection
- Ryanodex[®] 250mg injection powder

Island of Misfit “Muscle Relaxants”

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

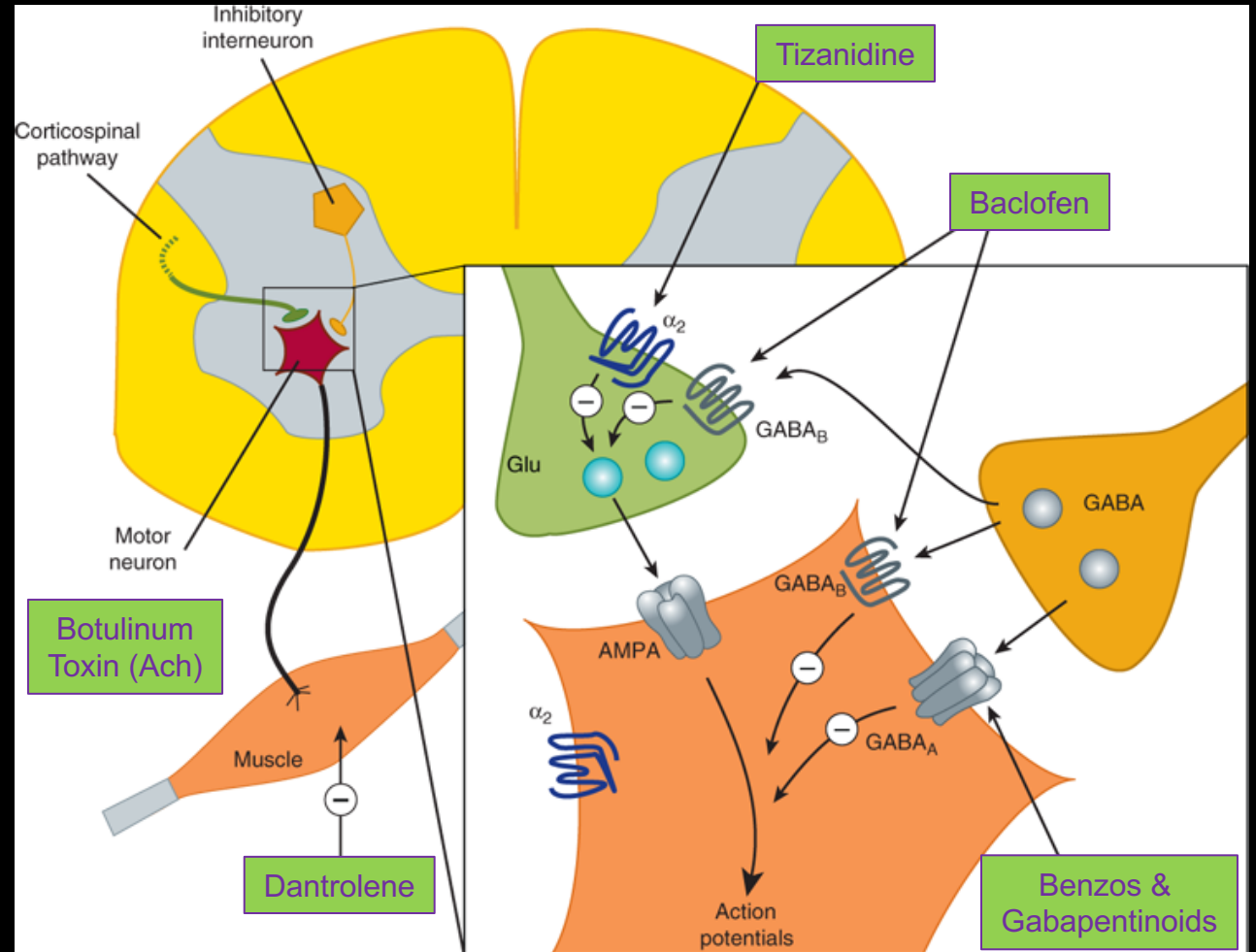
baclofen



“Muscle Relaxants”

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

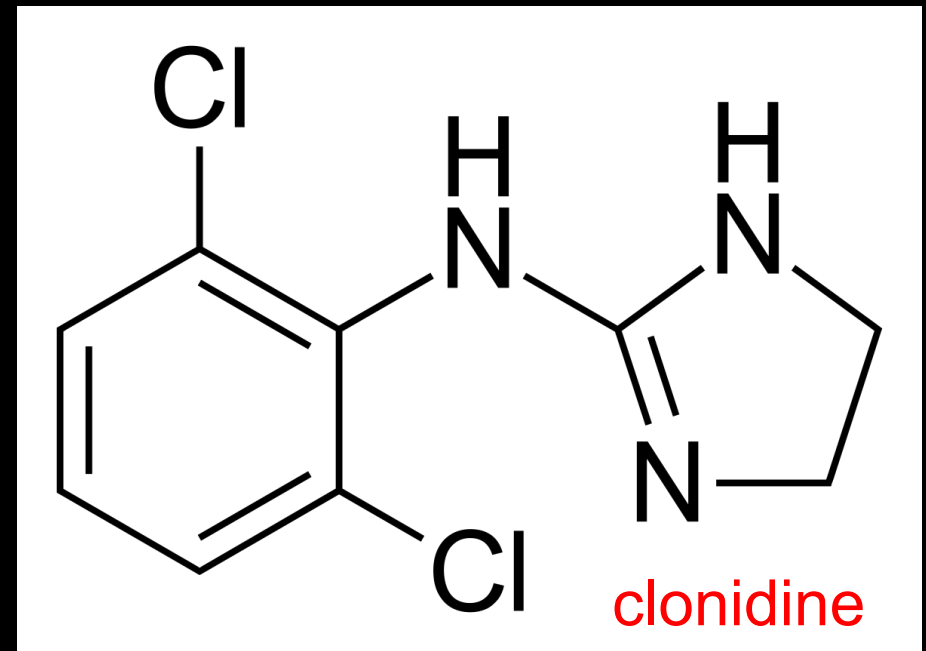
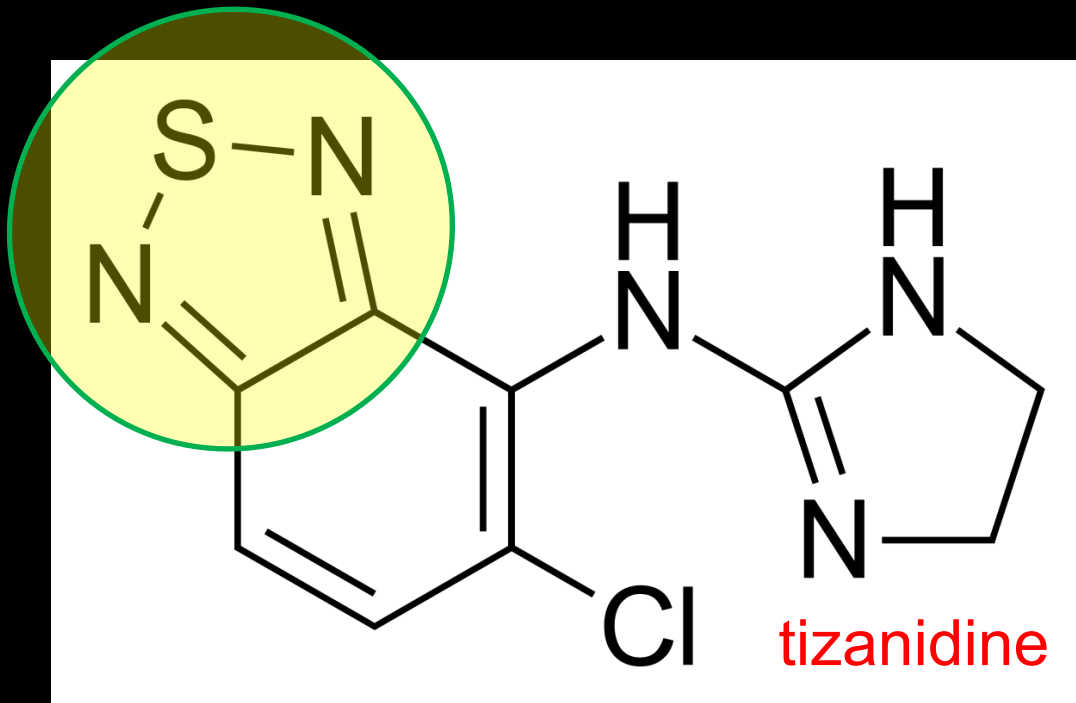
SPASTICITY (Stiffness)
CENTRAL ACTING
tizanidine
baclofen



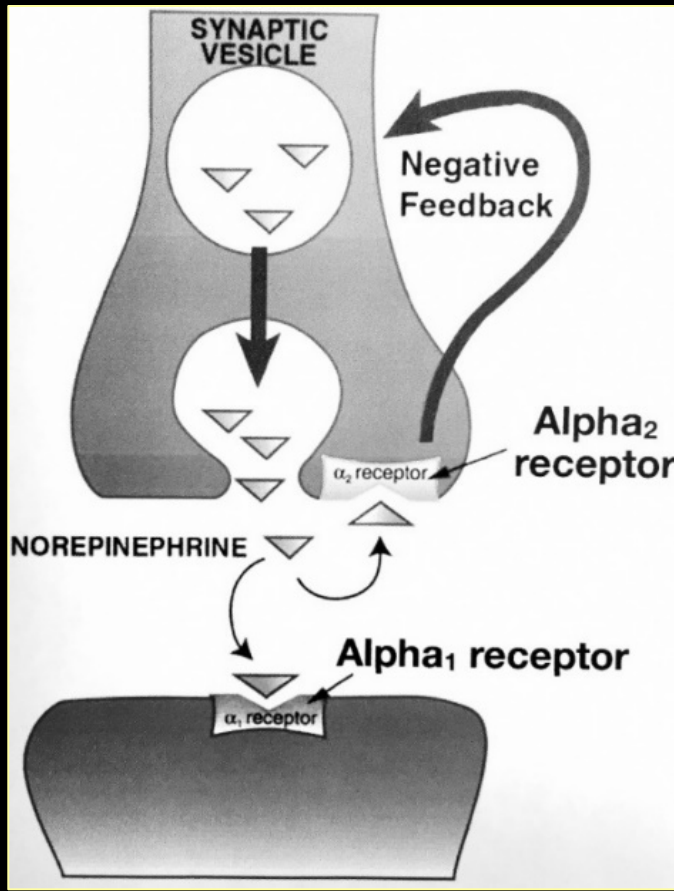
Source: A.J. Trevor, B.G. Katzung, M. Kruidering-Hall: Katzung & Trevor's Pharmacology: Examination & Board Review, 11th Ed. www.accesspharmacy.com Copyright © McGraw-Hill Education. All rights reserved.

Tizanidine

Tizanidine is a structural analog of clonidine



Tizanidine



Mechanism of Action

- Blocks *afferent* sensory spine neuron firing (alpha-2 agonist)
- Central analgesia (dorsal horn receives sensory info from periphery)

Inhibits presynaptic NE release

Vasoconstriction

Tizanidine

Notable Side Effects

- Elevated liver function tests (LFTs)
- Weakness & lack of energy (asthenia)
- Somnolence
 - More sedation than baclofen, so dose HS
- Hypotension

Tizanidine

Interactions

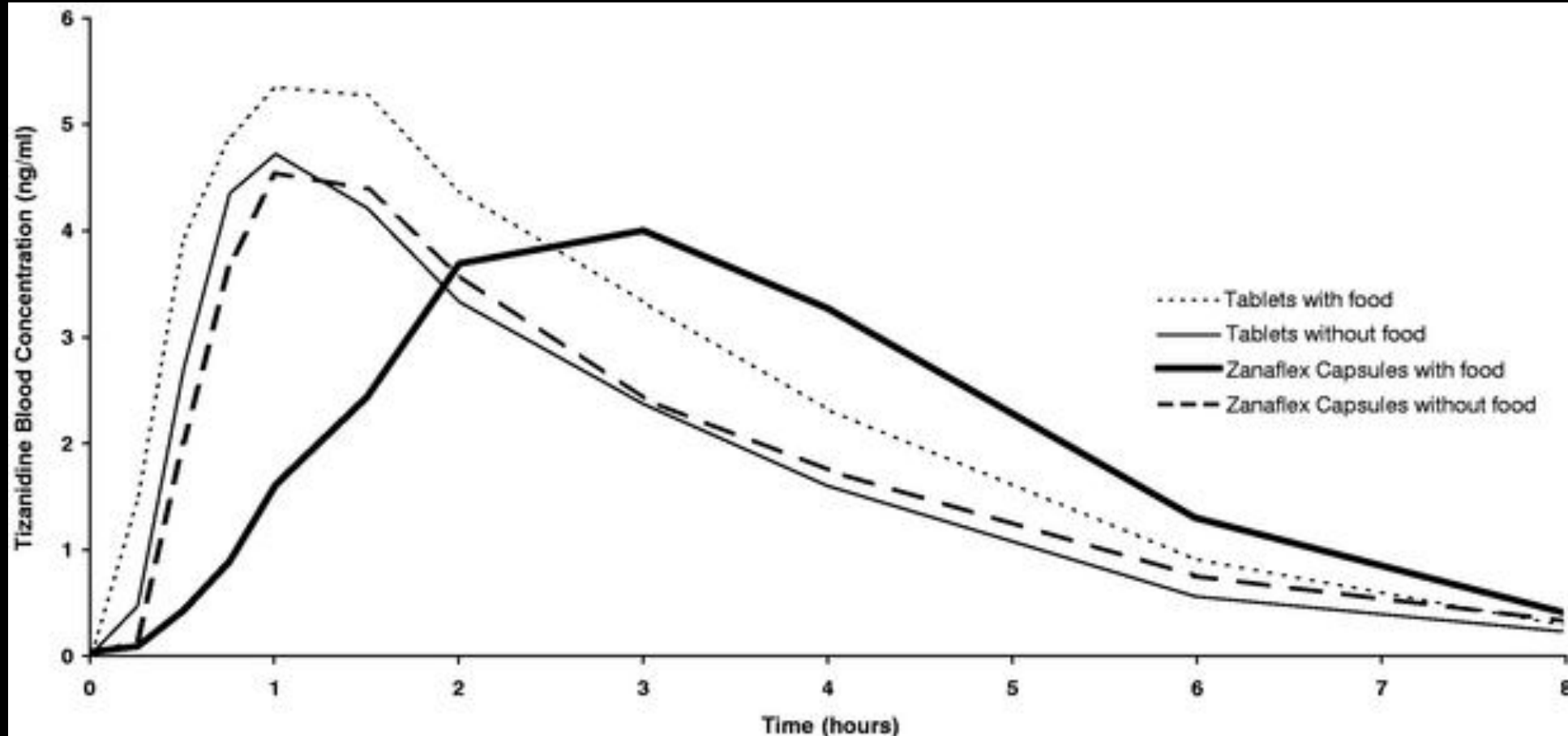
- CYP1A2 inhibitors
 - Major: ciprofloxacin & fluvoxamine
 - Minor: cimetidine, famotidine, verapamil, & ethinyl estradiol
- ACEIs/ARBs → severe hypotension

Clin Pharmacol Ther. 2004 Dec;76(6):598-606.

Ciprofloxacin greatly increases concentrations and hypotensive effect of tizanidine by inhibiting its cytochrome P450 1A2-mediated presystemic metabolism.

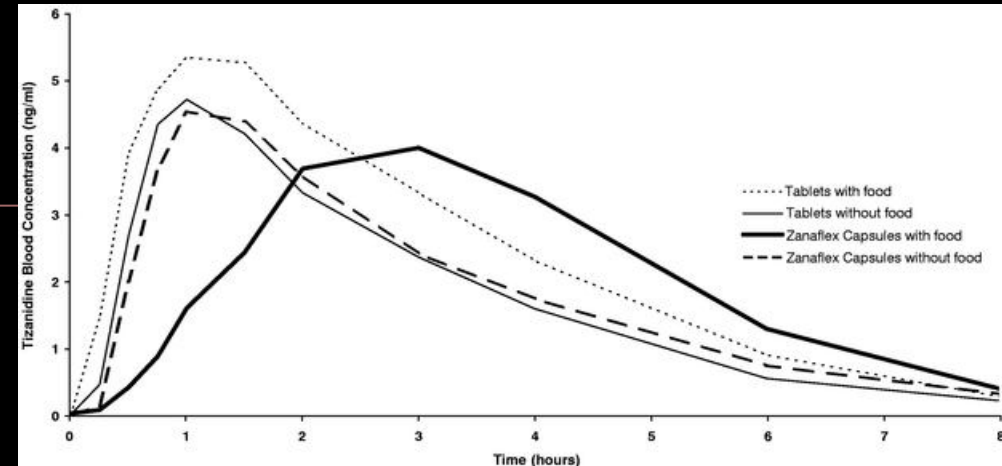
Granfors MT¹, Backman JT, Neuvonen M, Neuvonen PJ.

Tizanidine



Tizanidine

- Capsules & tablets without food bioequivalent
- Capsule (+) food compared to capsule (-) food < concentration & longer absorption
- Tablet (+) food compared to tablet (-) food & capsule (+/-) food > concentration & quicker absorption
- Tablet (-) food compared to capsule (+) food > concentration & quicker absorption



Tizanidine

Products


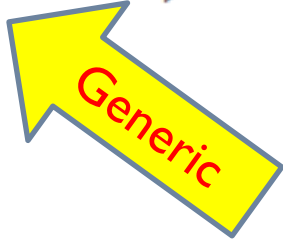
- Zanaflex[®] 2mg, 4mg, 6mg Capsules (generic available)
- Zanaflex[®] 2mg & 4mg Tablets (generic available)

United States Court of Appeals, Second Circuit.

**APOTEX INC., et al., Plaintiffs–Appellants, v. ACORDA THERAPEUTICS, INC.,
Defendant–Appellee.**

Docket No. 14–4353–cv.

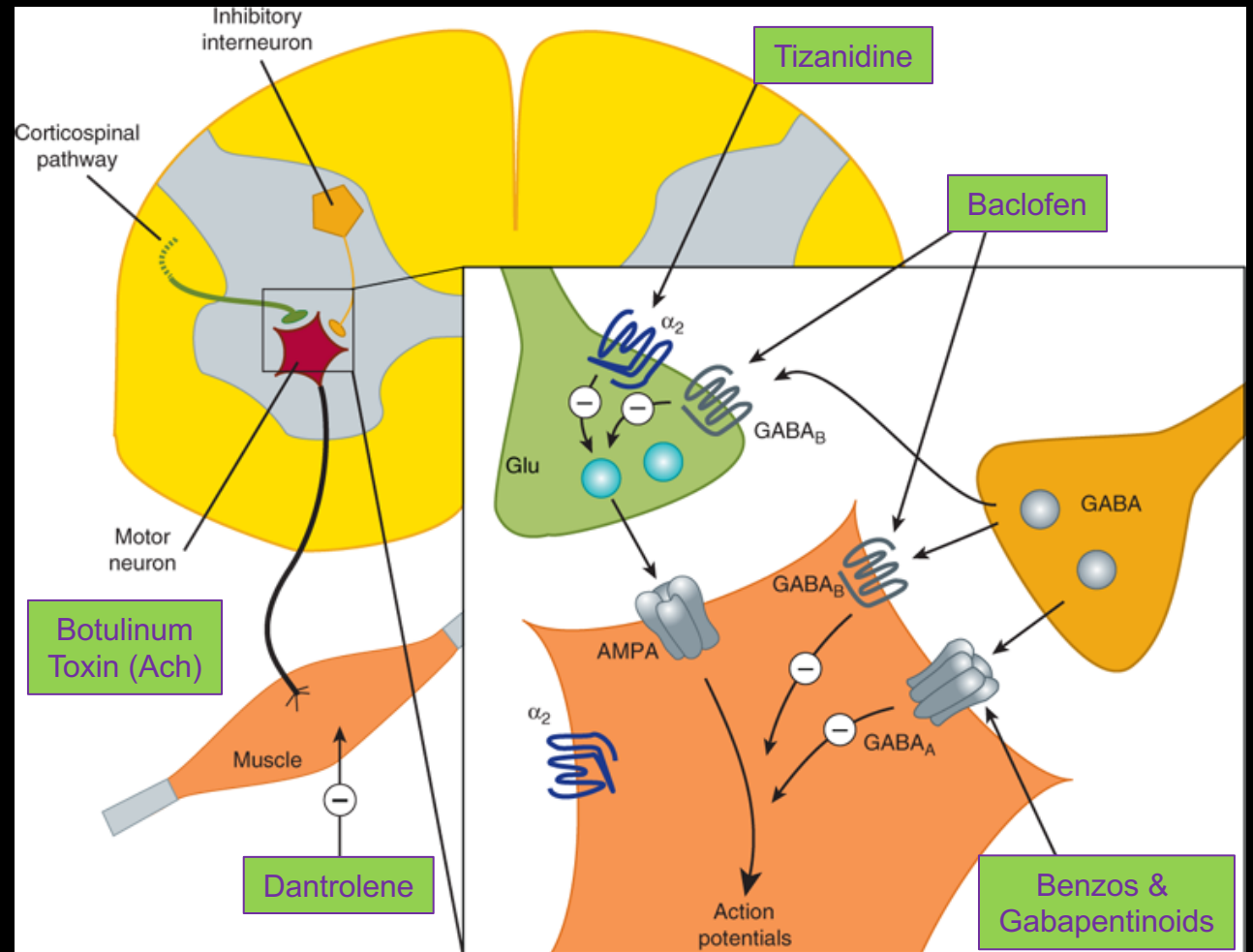
Decided: May 16, 2016



“Muscle Relaxants”

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

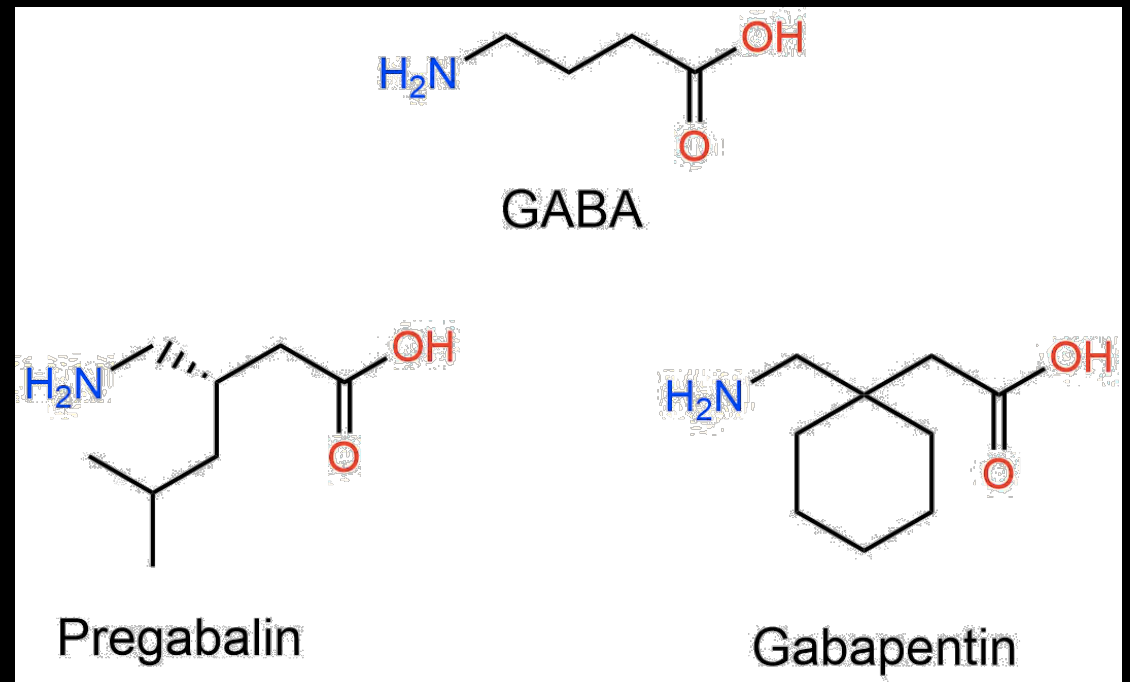
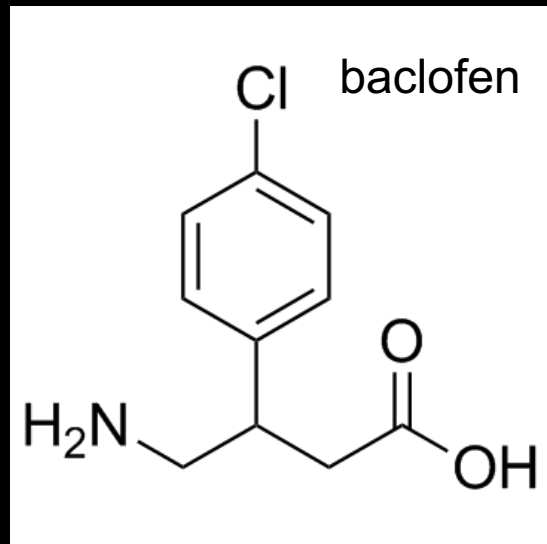
SPASTICITY (Stiffness)
CENTRAL ACTING
tizanidine
baclofen



Source: A.J. Trevor, B.G. Katzung, M. Kruidering-Hall: Katzung & Trevor's Pharmacology: Examination & Board Review, 11th Ed.
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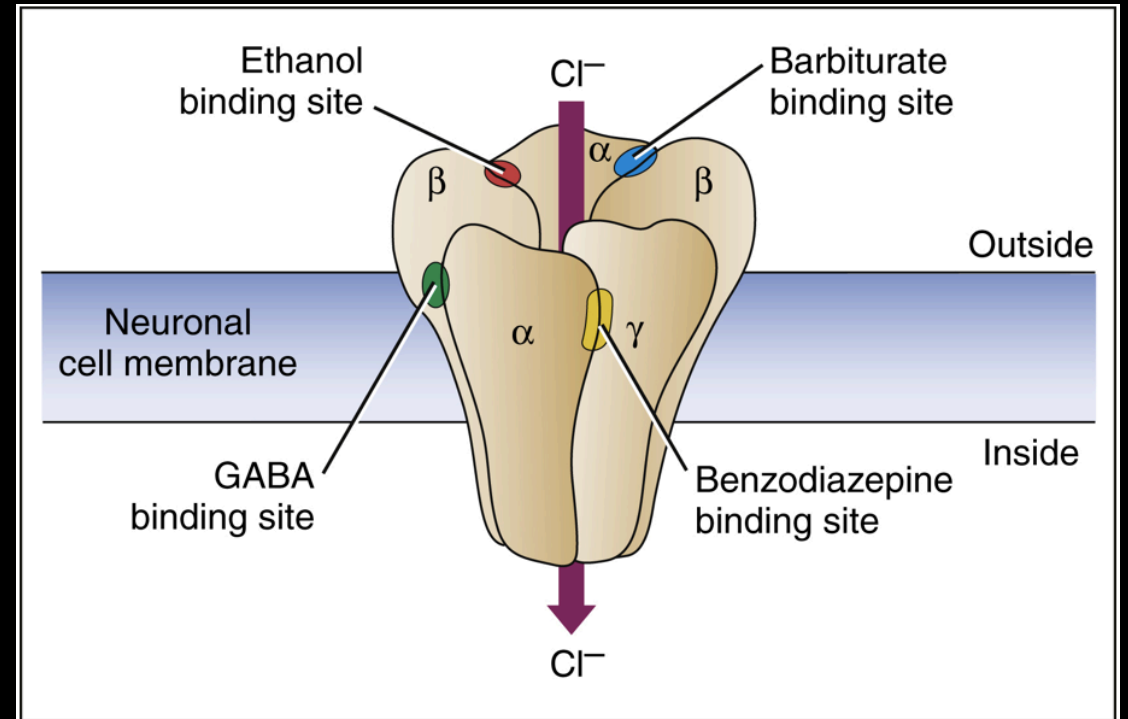
Baclofen

- Structural analog gamma-amino-butyric acid (GABA)
- Originally designed to treat epilepsy
- Being studied for alcohol-use disorder



Baclofen

- Mechanism of Action
 - Activates GABA chloride channel
 - Blocks central afferent sensory neurons



Baclofen

- Notable side effects
- Decreased muscle tone (hypotonia)
 - More so than tizanidine
- Drowsiness
- Abrupt discontinuation → withdrawal (benzo-Like)
 - Seizures, tachycardia, hyperthermia, anxiety, hallucinations, etc.

Products

- Baclofen 10mg & 20mg (Generic ONLY)
- Lioresal[®] & Gablofen[®] Solutions for Injection

Island of Misfit “Muscle Relaxants”

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

baclofen



Carisoprodol

C-IV

- 2007: European Medicines Agency recommends suspension of marketing
- 2012: US/DEA reclassified as a controlled substance
 - Only “relaxant” controlled substance
- 2012: European Medicines Agency withdrew from market
- 2013: Canada & Indonesia withdrew from market



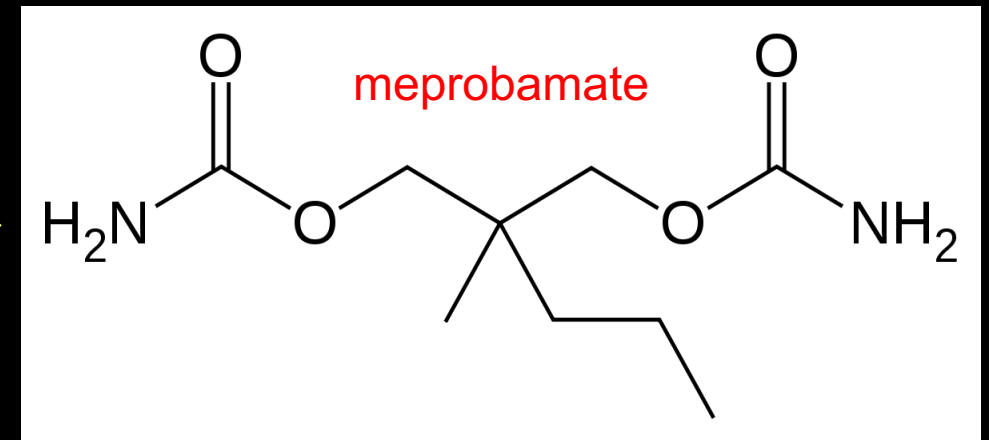
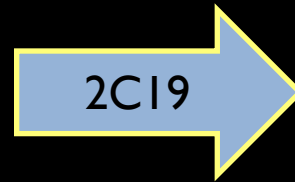
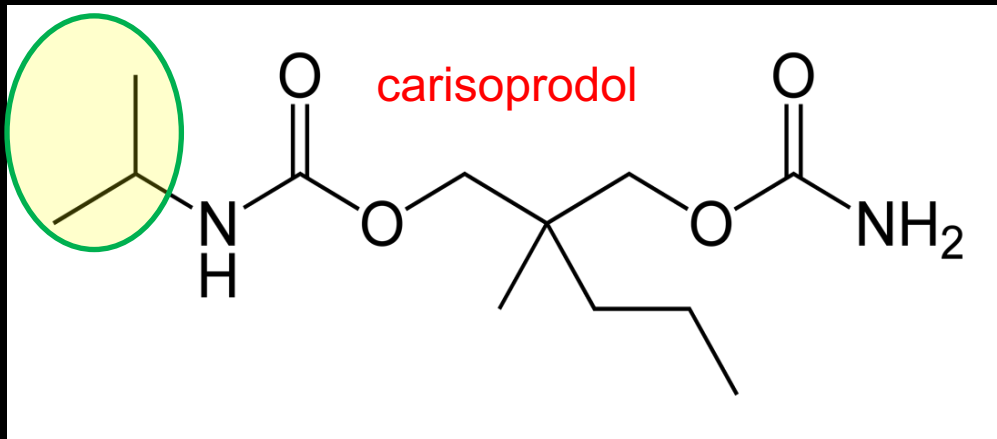
Carisoprodol

C-IV

■ Metabolism

–CYP-2C19 metabolizes carisoprodol to meprobamate (barbiturate)

- Meprobamate was 1st blockbuster psychotropic medication



Carisoprodol

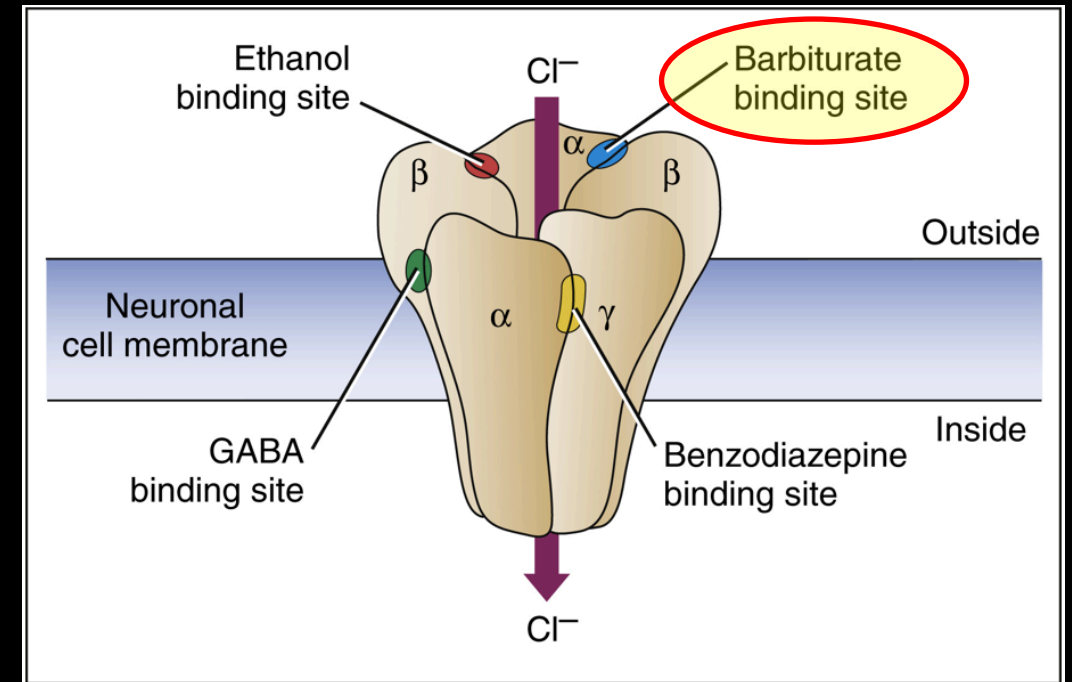
C-IV

Mechanism of Action

- GABA-related (barbiturate)

Products

- Soma[®] 250mg & 350mg Tablets (generic available)
- Carisoprodol 200mg & Aspirin 325mg (generic only)
- Carisoprodol 200mg, Aspirin 325mg, & Codeine 16mg (generic only)



“Muscle Relaxants”

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

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

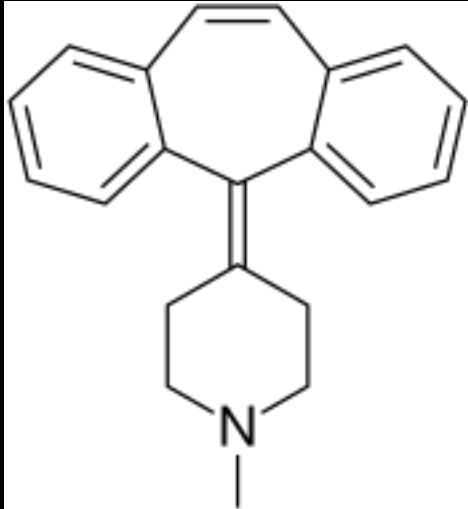
chlorzoxazone

metaxalone

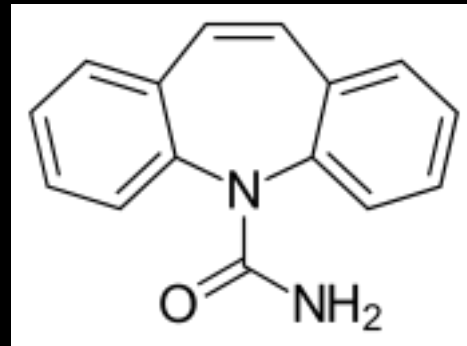


Tricyclic Medications

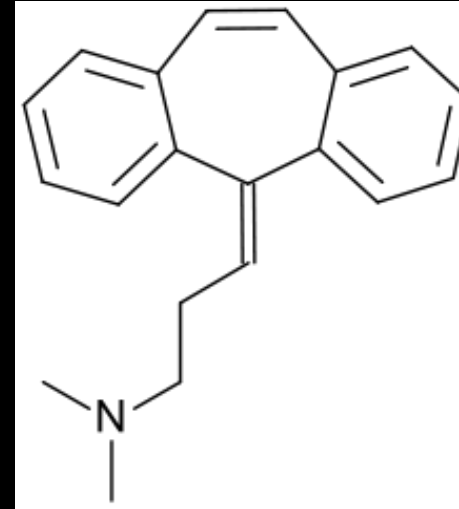
cyproheptadine



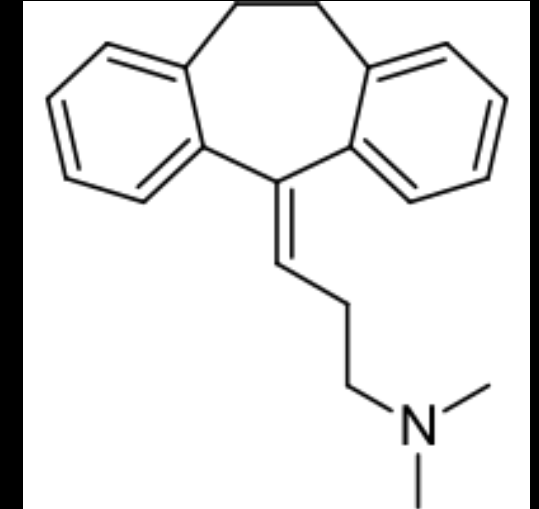
carbamazepine



cyclobenzaprine



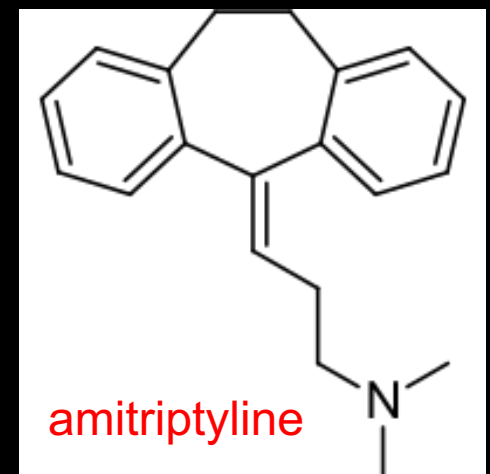
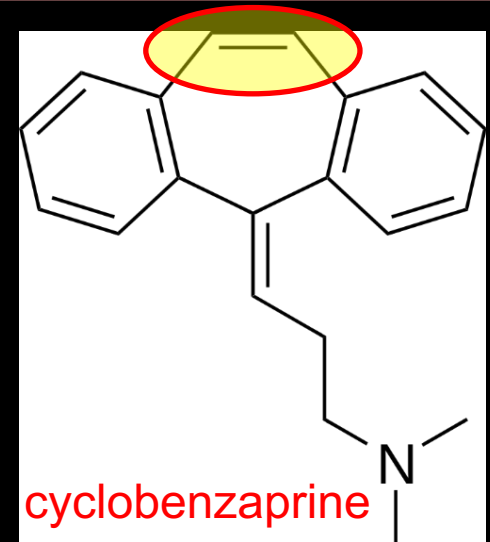
amitriptyline



➤ Urine drug screening false positives???

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



Cyclobenzaprine

Notable Side Effects

- Remote cases of serotonin syndrome with other serotonergic agents

Metabolism

- CYP3A4, CYP1A2, & very little CYP2D6






Products

- ER: Amrix[®] 15mg & 30mg (generic available)
- IR: Flexeril[®] 5mg & 10mg (generic available)
- IR: Fexmid[®] 7.5mg (generic available)

MNEMONIC MONDAY

SEROTONIN SYNDROME

"SHIVERS" ❄️❄️❄️❄️

S	HIVERING 
H	YPERREFLEXIA + MYOCLONUS
I	NCREASED TEMPERATURE (> 41 C) 
V	ITAL SIGNS INSTABILITY - HR ↑ - RR ↑ - BP ↓ 
E	NCEPHALOPATHY (ALTERED LOC)
R	ESTLESNESS 
S	WEATING 

MIRIAMSRXNOTES.COM

“Muscle Relaxants”

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

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

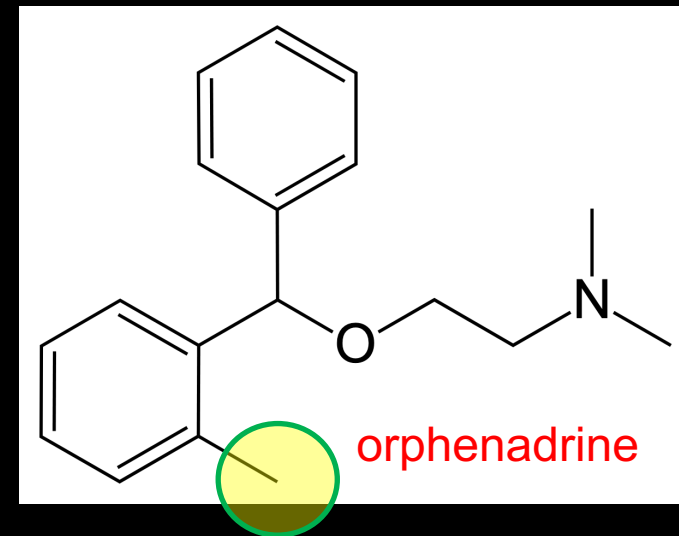
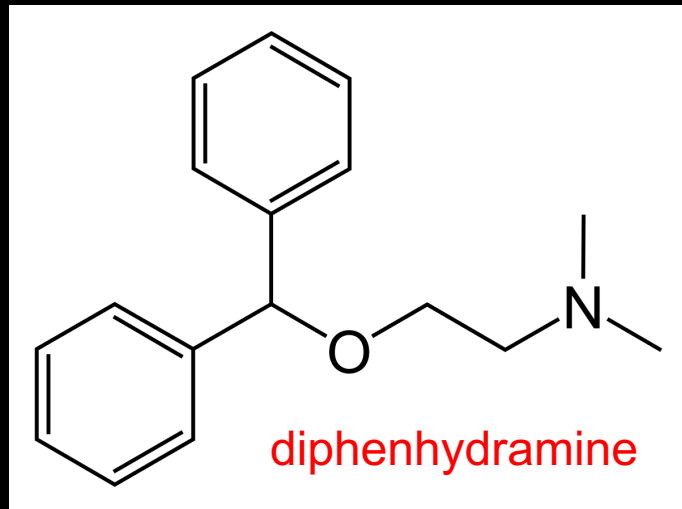
chlorzoxazone

metaxalone



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



Orphenadrine

Mechanisms of Action

- H1 receptor antagonist (stronger than diphenhydramine)
- Anticholinergic (muscarinic receptor antagonist)
- NMDA antagonist
- NE reuptake inhibitor

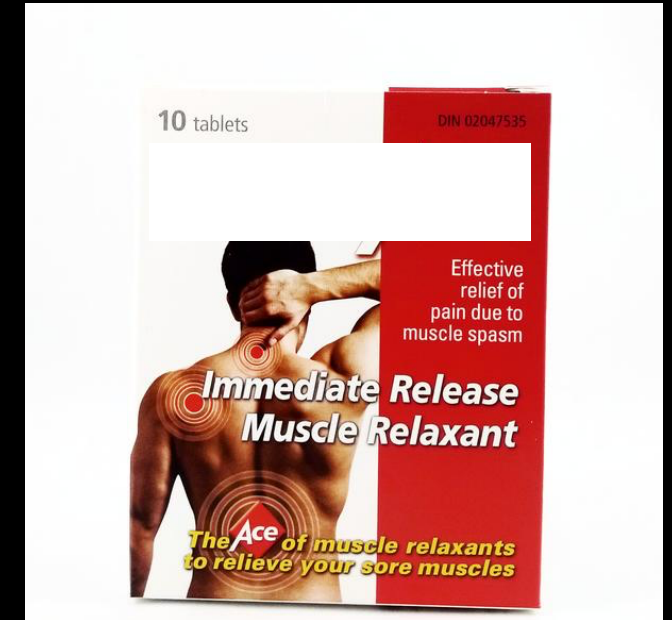
Notable Side Effects

- Antihistamine sedation effect
- Anticholinergic effects (e.g., “drying”)
- Aplastic anemia (rare)

Orphenadrine

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

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methocarbamol

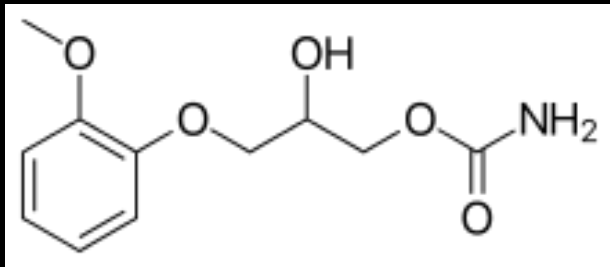
chlorzoxazone

metaxalone

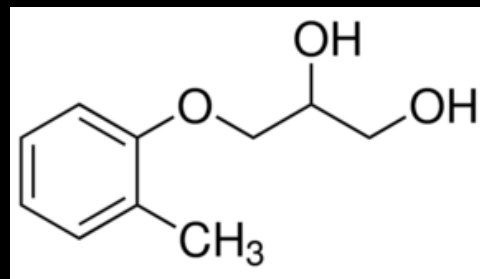


Methocarbamol

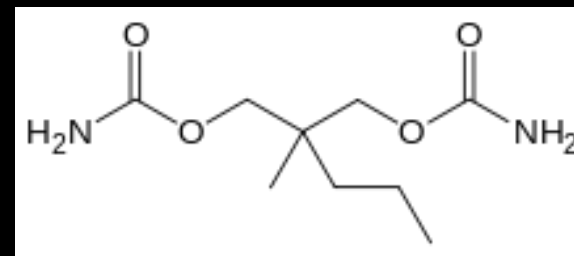
- Structural analog of mephenesin
 - NTI: respiratory depression
 - Antidote for strychnine poisoning
 - 1950s: utilized to develop meprobamate (barbiturate)
- Carbamate derivative of guaifenesin



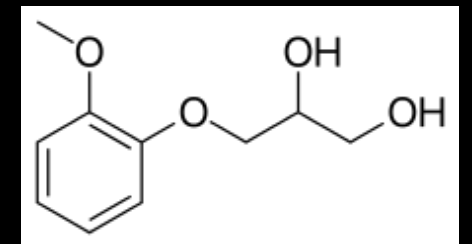
methocarbamol



mephenesin



meprobamate



guaifenesin

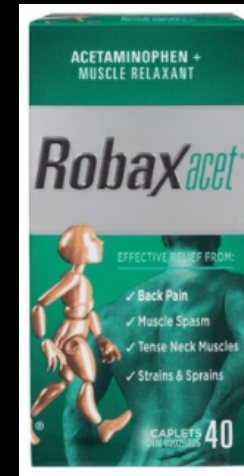
Methocarbamol

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

- No CYP Interactions
- Does not produce guaifenesin as a metabolite (carbamate bond not hydrolyzed)

Notable Side Effect

- **Brown/black/green urine**










Urine Color



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

AM I HYDRATED? Urine Color Chart		
1		If your urine matches these colors, you are drinking enough fluids
2		Drink more water to get the ideal color in Shade 1 and 2.
3		Dehydrated
4		You may suffer from cramps and heat-related problems
5		Health risk! Drink more water.
6		Health risk! Drink more water.
7		Health risk! Drink more water.
8		Health risk! Drink more water.

Urine Color

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

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

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

metaxalone



Chlorzoxazone

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

Mechanism of Action

- Unknown (GABA? 5HT? MAOI?)

Metabolism

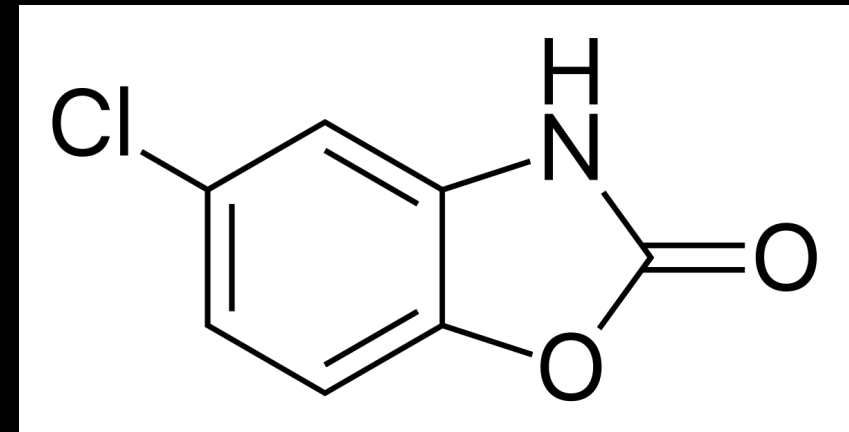
- Hepatic glucuronidation (no CYP interactions)

Notable Side Effects

- Rare cases of idiosyncratic hepatocellular toxicity
 - Monitor LFTs
- **Orange/red/purple** urine

Products

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



“Muscle Relaxants”

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

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

metaxalone



Metaxalone

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

Mechanism of Action

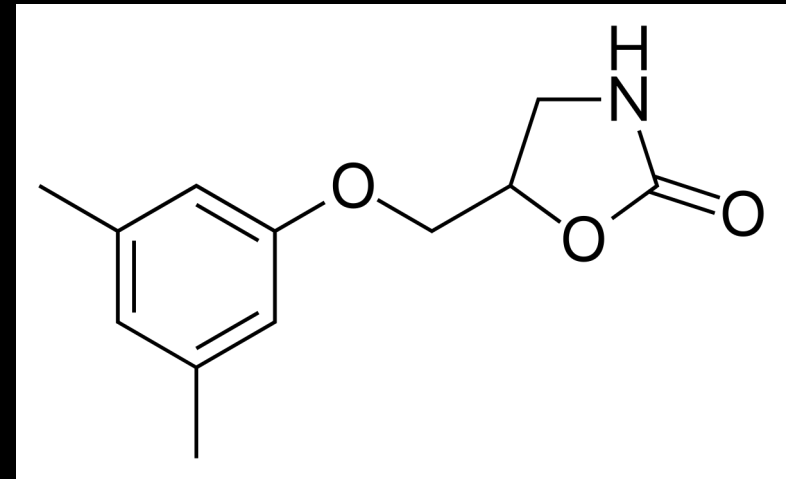
- Unknown (GABA? 5HT? MAOI?)

Kinetics/Metabolism

- High Fat meals > bioavailability & AUC
- Females have an increased $t_{1/2}$ & bioavailability
- CYP1A2, CYP2D6, CYP2E1, & CYP3A4 substrate

Products

- Metaxall[®] & Skelaxin[®] 800mg (generic available)
- Metaxalone 400mg (generic only)



*Watch for confusion with *metolazone* (diuretic)

Island of Misfit “Muscle Relaxants”

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

baclofen



“Muscle Relaxants”

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

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

baclofen

gabapentinoids & benzos

PERIPHERAL ACTING

dantrolene

botulinum toxin

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

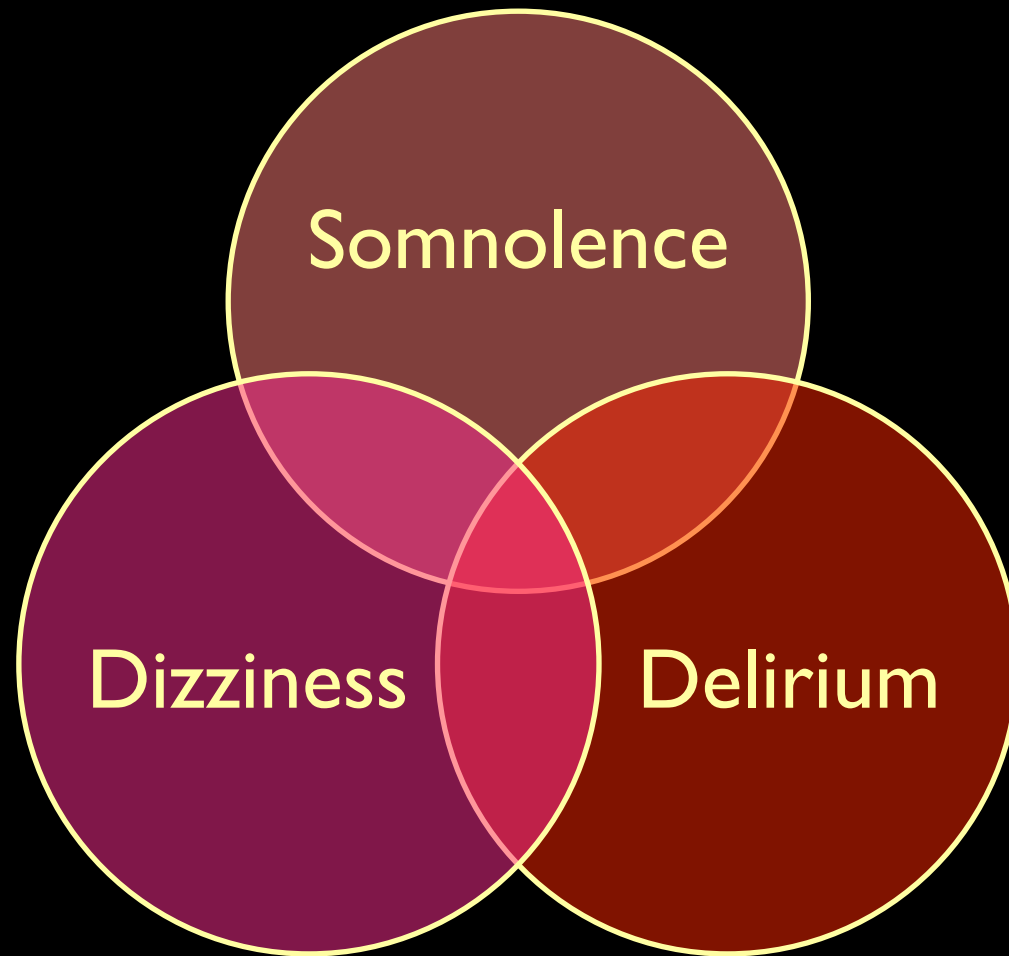
orphenadrine

methocarbamol

chlorzoxazone

metaxalone

Opioids, Benzos, “Relaxants,” & Hypnotics Overlapping Sedative Side Effects...



Opioid-Sedative Interactions

“Name Game”

Drug-Drug Interaction	Proposed Name
Opioid + Benzodiazepine Sedative	“Bozo”
Opioid + “Muscle Relaxant” Sedative	“Relaxoid”
Opioid + Sedative Hypnotic	“Hypoid”
Opioid + One Other Sedative	“Deadly Duo”
Opioid + Two Other Sedatives	“Unholy Trinity”
Opioid + Three Other Sedatives	“Quattro Killer”
Benzodiazepine & Sedative Hypnotic	“Hypzo”
Benzodiazepine & “Muscle Relaxant” Sedative	“Relaxzo”

A Wine Bottle Opener in Every Bag...



oxycodone, alprazolam, carisoprodol, and zolpidem



Flogging a Dead Horse... ???

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

Definitions

Severity:	 Contraindicated	 Major	 Moderate	 Minor	 Unknown
Documentation:	Excellent	Good	Fair	Unknown	

Drug-Drug Interactions (6)

Drugs:	Severity:	Documentation:	Summary:
ALPRAZOLAM -- CARISOPRODOL	 Major	Fair	Concurrent use of BENZODIAZEPINES and CENTRALLY ACTING MUSCLE RELAXANTS may result in additive respiratory depression.
ALPRAZOLAM -- OXYCODONE	 Major	Fair	Concurrent use of OXYCODONE and CNS DEPRESSANTS may result in increased risk of respiratory and CNS depression.
ALPRAZOLAM -- ZOLPIDEM TARTRATE	 Major	Fair	Concurrent use of ZOLPIDEM and SEDATIVES OR HYPNOTICS may result in an increase in CNS depressant effects.
CARISOPRODOL -- OXYCODONE	 Major	Fair	Concurrent use of OXYCODONE and ANTICHOLINERGIC CNS DEPRESSANTS may result in increased risk of paralytic ileus and increased risk of respiratory and CNS depression.
CARISOPRODOL -- ZOLPIDEM TARTRATE	 Major	Fair	Concurrent use of ZOLPIDEM and SEDATIVES OR HYPNOTICS may result in an increase in CNS depressant effects.
OXYCODONE -- ZOLPIDEM TARTRATE	 Major	Fair	Concurrent use of OXYCODONE and CNS DEPRESSANTS may result in increased risk of respiratory and CNS depression.

Medication Database Interaction Screenings

Lexicomp®

Oxycodone, alprazolam, carisoprodol, and zolpidem

A = No known interaction

B = No action needed

C = Monitor therapy

D = Consider therapy modification

X = Avoid combination

View interaction detail by clicking on link.

Drugs in this analysis: ALPRAZolam; Carisoprodol; OxyCODONE; Zolpidem

Drug-Drug Interactions

- D** ALPRAZolam (CNS Depressants) – OxyCODONE
- D** ALPRAZolam (CNS Depressants) – Zolpidem *Depends on Brand Name*
- D** Carisoprodol (CNS Depressants) – OxyCODONE
- D** Carisoprodol (CNS Depressants) – Zolpidem *Depends on Brand Name*
- D** OxyCODONE – Zolpidem (CNS Depressants)
- D** OxyCODONE (CNS Depressants) – Zolpidem *Depends on Brand Name*
- C** ALPRAZolam (CNS Depressants) – Carisoprodol (CNS Depressants)

> Level 1 (Severe) ⓘ (no results)

▼ Level 2 (Major) ⓘ (2 results)

Drug to Drug Interactions

Oxycodone and Skeletal Muscle Relaxants

Oxycodone may cause additive sedative, CNS, and/or respiratory-depressant effects with Skeletal Muscle Relaxants

Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone or oxycodone; naloxone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of oxycodone at one-third to one-half the usual dosage and titrate to clinical response; reduced initial doses of oxycodone; naltrexone, aspirin, ASA; oxycodone, and ibuprofen; oxycodone are also recommended. If a decision is made to start treatment with acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Oxycodone and Alprazolam

Oxycodone may cause additive sedative, CNS, and/or respiratory-depressant effects with Alprazolam

Concomitant use of opiate agonists with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with benzodiazepines to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone is initiated in a patient taking a benzodiazepine, reduce dosages and titrate to clinical response. For acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours, and for other oxycodone products, use an initial dose of oxycodone at one-third to one-half the usual dosage. If a benzodiazepine is prescribed for an indication other than epilepsy in a patient taking an opiate agonist, use a lower initial dose of the benzodiazepine and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Medication Database Interaction Screenings

Clinical Pharmacology[®]

Oxycodone, alprazolam, carisoprodol, and zolpidem

Level 3 (Moderate) ⓘ

(4 results)

Drug to Drug Interactions

Skeletal Muscle Relaxants and Benzodiazepines

Skeletal Muscle Relaxants may result in additive sedative, CNS, and/or respiratory-depressant effects with Benzodiazepines

Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

Zolpidem Tartrate and Carisoprodol

Zolpidem Tartrate may cause additive sedative, CNS, and/or respiratory-depressant effects with Carisoprodol

Carisoprodol can cause additive CNS depression if used concomitantly with other CNS depressants.

Zolpidem Tartrate and Benzodiazepines

Zolpidem Tartrate may cause additive sedative, CNS, and/or respiratory-depressant effects with Benzodiazepines

Concomitant administration of benzodiazepines with zolpidem can potentiate the CNS effects (e.g., increased sedation or respiratory depression) of either agent. If used together, a reduction in the dose of one or both drugs may be needed. For Intermezzo brand of sublingual zolpidem tablets, reduce the dose to 1.75 mg/night. Concurrent use of zolpidem with other sedative-hypnotics, including other zolpidem products, at bedtime or the middle of the night is not recommended. In addition, sleep-related behaviors, such as sleep-driving, are more likely to occur during concurrent use of zolpidem and other CNS depressants than with zolpidem alone.

Zolpidem Tartrate and Oxycodone

Zolpidem Tartrate may cause additive sedative, CNS, and/or respiratory-depressant effects with Oxycodone

Concomitant use of oxycodone with zolpidem may lead to additive respiratory and/or CNS depression. Hypotension, profound sedation, coma, respiratory depression, or death may occur. In addition, sleep-related behaviors, such as sleep-driving, are more likely to occur during concurrent use of zolpidem and other CNS depressants than with zolpidem alone. Prior to concurrent use, assess the level of tolerance to CNS depression that has developed, the duration of use, and the patient's overall response to treatment. Consider the patient's use of alcohol or illicit drugs. If zolpidem is used concurrently with oxycodone, a reduced dosage of oxycodone and/or zolpidem is recommended; use an initial dose of oxycodone at 1/3 to 1/2 the usual dosage. For Intermezzo brand of sublingual zolpidem tablets, reduce the dose to 1.75 mg/night. Monitor for sedation and respiratory depression.

Medication Database Interaction Screenings




Clinical Pharmacology[®]

Oxycodone, alprazolam, carisoprodol, and zolpidem

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

 [ALPRAZolam Oral \(Alprazolam\) - Carisoprodol Oral \(Carisoprodol\) - OxyCODONE HCl Oral \(Narcotic Analgesics\)](#)

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.

Flogging a Dead Horse... ???

oxycodone, alprazolam, carisoprodol, and zolpidem

Medication Database Sedative Drug-Drug Interaction Reports

- Micromedex[®]: major
- Lexicomp[®]: consider therapy modification
- Clinical pharmacology[®]: moderate/major
- Facts & comparisons[®]: potentially severe or life-threatening



Pharmacies miss half of dangerous drug combinations

By SAM ROE, RAY LONG and KARISA KING
CHICAGO TRIBUNE | DEC 15, 2016 AT 8:44 AM

The Tribune reporter walked into an Evanston CVS pharmacy carrying two prescriptions: one for a common antibiotic, the other for a popular anti-cholesterol drug.

Taken alone, these two drugs, clarithromycin and simvastatin, are relatively safe. But taken together they can cause a severe breakdown in muscle tissue and lead to kidney failure and death.

Clarithromycin (3A4 Inhibitor) & Simvastatin (3A4 Substrate)

“Muscle Relaxants”

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

SPASTICITY (Stiffness)

CENTRAL ACTING

tizanidine

baclofen

gabapentinoids & benzos

PERIPHERAL ACTING

dantrolene

botulinum toxin

SPASMS (Musculoskeletal)

carisoprodol

cyclobenzaprine

orphenadrine

methocarbamol

chlorzoxazone

metaxalone

www.addictionsurvivors.org

11-20-2008, 12:22 AM #1

sunflower1776
Member
Posts: 250


Skelaxin--abuse potential?

I am wondering if anyone has experience with skelaxin-a muscle relaxer. I was just prescribed them yesterday for an ear problem that the MD thinks is being caused by TMJ- I started a medrol-dose pack and was given the skelaxin to take 3x/day to help relax my jaw. I've been really tense the last few weeks because I've had some pretty bad urges to use again. I didn't take any of them yesterday, but I am taking one tonight. The part of my pill use was the high that I got-the energy. I don't like feeling tired, so I'll be okay if that's all they'll do. If there is any potential for an energetic high if I take too many, could someone please let me know so that I can get them out of the house. I appreciate any responses!

Quote

11-20-2008, 09:05 PM #2

deanna
Senior Member
Posts: 3,083



Hi sunflower. I have TMJ and arthritis in my jaw from a car accident 10 years ago.that is how my pill addiction started in the first place. My dentist would give me pills whenever I asked for them. Anyways, I wear a "night guard" when I sleep.Its like a plastic mouthguard (you probably know what Im talking about).Do you have one? That really helps keep your jaw in place so you dont grind your teeth or clench them like most TMJ sufferers do. Maybe that will help and you dont need the muscle relaxers. I dont know anything about Skelaxin, but IMO I wouldnt take any pill anymore, its brings back bad habits. I know I dint answer the exact question you asked but maybe my idea could help. Good luck!!! Deanna

Spasticity vs Spasms

Choose Wisely
My Friend



Poll Question #1

Ms. Faye Kinet presents this morning to your clinic with a chief complaint of extreme lower back pain and muscle spasming. After a physical exam, you conclude that she does in fact have muscle spasming. Which of the following “muscle relaxants,” if any, would be most appropriate for her treatment?

- a) Baclofen 10mg TID x 3 days
- b) Cyclobenzaprine 10mg TID x 1 month
- c) Methocarbamol 1,500mg QID x 3 days
- d) Tizanidine 2mg TID x 1 month

Poll Question #1 (ANSWER)

Ms. Faye Kinet presents this morning to your clinic with a chief complaint of extreme lower back pain and muscle spasming. After a physical exam, you conclude that she does in fact have muscle spasming. Which of the following “muscle relaxants”, if any, would be most appropriate for her treatment?

- a) Baclofen 10mg TID x 3 days
- b) Cyclobenzaprine 10mg TID x 1 month
- c) **METHOCARBAMOL 1,500MG QID X 3 DAYS [CORRECT ANSWER]**
- d) Tizanidine 2mg TID x 1 month

Poll Question #2

Thomas Payne, a 30yo male pharmacist, presents this morning to an urgent care clinic with a chief complaint of extreme lower back pain and stiffness. Mr. Payne states that he hurt his back at work while moving a case of soda yesterday morning. He notified management and proceeded to work an entire 14 hour shift. Which of the following “muscle relaxants,” if any, would be most appropriate for his treatment?

- a) baclofen
- b) carisoprodol
- c) cyclobenzaprine
- d) methocarbamol



Poll Question #2 (ANSWER)

Thomas Payne, a 30yo Male Pharmacist, presents this morning to an urgent care clinic with a chief complaint of extreme lower back pain and stiffness. Mr. Payne states that he hurt his back at work while moving a case of soda yesterday morning. He notified management and proceeded to work an entire 14 hour shift. Which of the following “muscle relaxants,” if any, would be most appropriate for his treatment?

- a) **BACLOFEN [CORRECT ANSWER]**
- b) carisoprodol
- c) cyclobenzaprine
- d) methocarbamol



Audience Question #3

Thomas Payne was prescribed methocarbamol for his lower back issues. As a pharmacist himself, he knew that his urine may be which of the following colors after ingesting the methocarbamol medication?

- a) Black
- b) White
- c) Yellow
- d) Clear



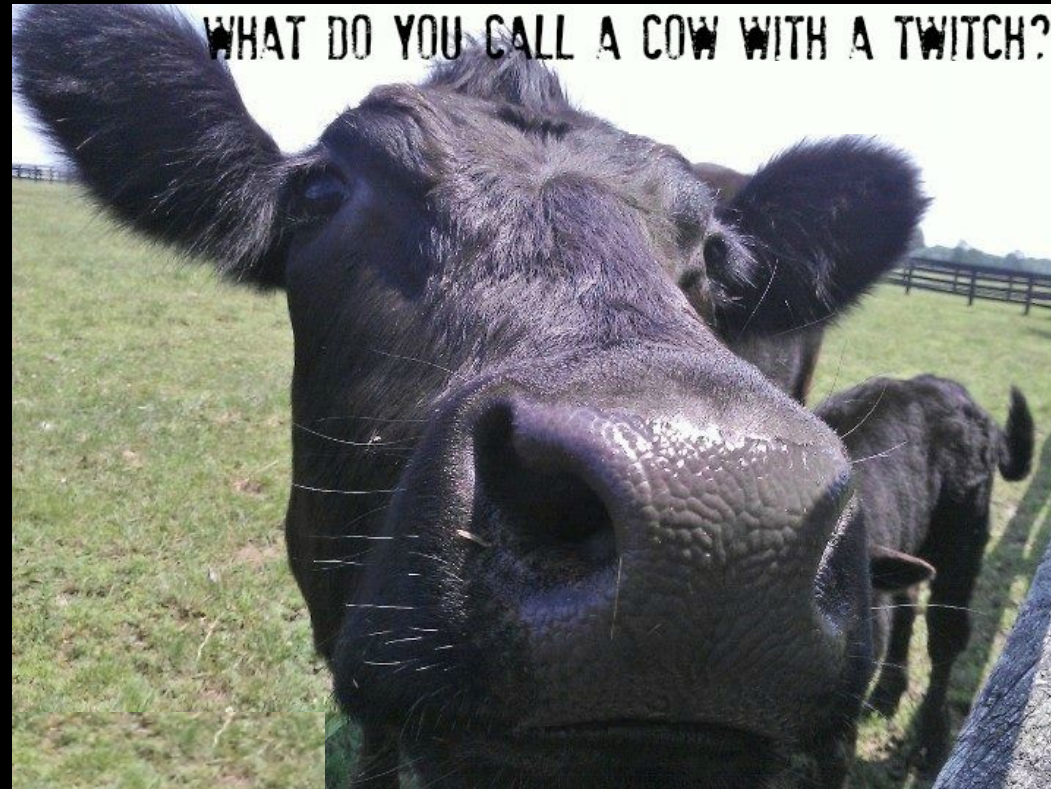
Audience Question #3 (ANSWER)

Thomas Payne was prescribed methocarbamol for his lower back issues. As a pharmacist himself, he knew that his urine may be which of the following colors after ingesting the methocarbamol medication?

- a) **BLACK [CORRECT ANSWER]**
- b) White
- c) Yellow
- d) Clear

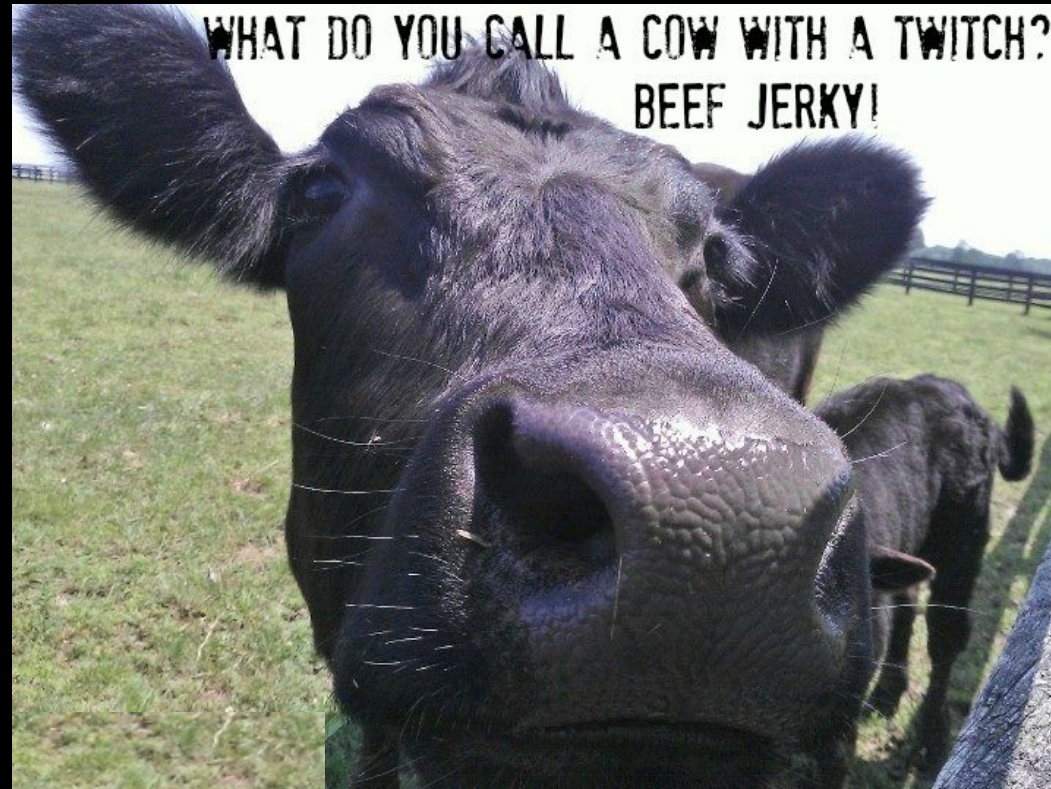


Questions & Discussion



Mark Garofoli, PharmD, MBA, BCGP, CPE
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