Relax, All Antispasmodics Are the Same…Right?

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Disclosure

- None

Learning Objectives

- Describe the pharmacokinetic profile of each class of anti-spasmodic medication
- Discuss pearls for selection and dosing of anti-spasmodic medications
- Choose an appropriate anti-spasmodic based on patient specific information

PAINWEEK

Pathophysiology

- Spasticity
  - Upper motor neuron syndrome
- Spasm
  - Peripheral musculoskeletal conditions

PAINWEEK

Medications

- Antispastic agents
  - Baclofen
  - Tizanidine
  - Dantrolene
- Antispasmodic
  - Baclofen
  - Clyclobenzaprine
  - Methocarbamol
  - Carisoprodol
  - Orphenidrine
  - Tizanidine
  - Metaxalone

PAINWEEK

Common Uses

- Low back pain
- Neck pain
- Fibromyalgia
- Tension headaches
- Myofascial pain syndrome

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What Does the Literature Say?

- Better than placebo, but NOT better than NSAIDs alone
- Cyclobenzaprine is better than placebo, but inferior to antidepressants
- No difference between metaxalone and placebo
- Some evidence that supports carisoprodol, cyclobenzaprine, orphenadrine and tizanidine for low back pain

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Cyclobenzaprine

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Clinical Information

MOA	Acts at brain stem w/in CNS, decreases tonic somatic motor activity influencing both alpha and gamma motor neurons
Similar Structure	Amitriptyline
Dosing	5-10mg TID
Preparations	5mg and 10mg tablets
Onset	< 1 hour
Brought to Market	1977

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Clinical Pearls

- Caution in hepatic impairment
- Potential for serotonin syndrome
- Contraindications:
  - Heart block
  - Cardiac conduction issues
- Use past 2-3 weeks lacks efficacy

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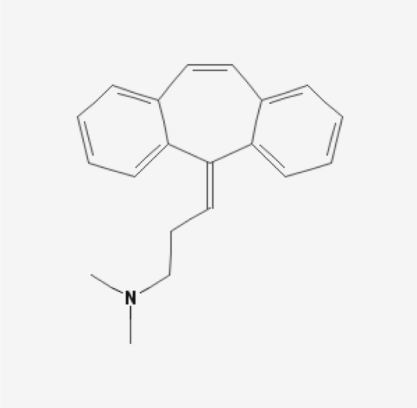
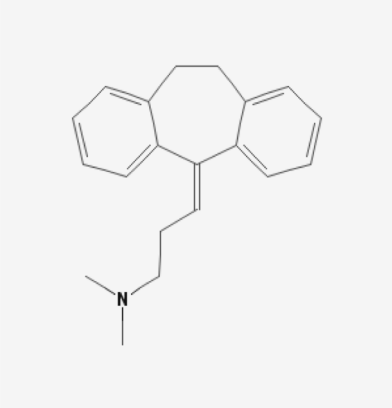
Pop Quiz





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Methocarbamol

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Clinical information

MOA	General CNS depression
Similar Structure	Derivative of guaifenesin
Dosing	1.5g PO four times daily for 2-3 days, then decrease to TDD of 4-4.5g 1g IM/IV Q8H, max of 3g/day
Preparations	500mg and 750mg tablets 100mg/mL injection
Onset	30 minutes
Brought to Market	1960s

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Clinical Pearls

- Caution in patients with a seizure disorder
- Contraindications:
  - Injectable formulation in renal impairment
- Less drowsiness than other agents

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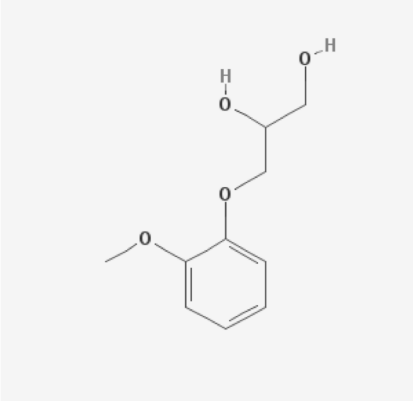
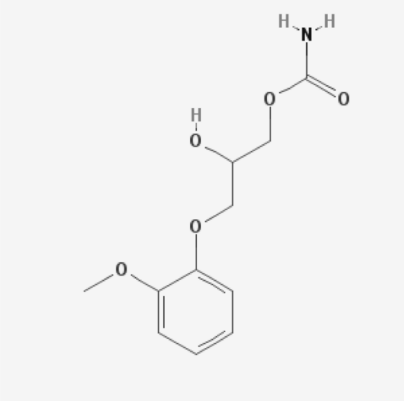
Pop Quiz





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Carisoprodol

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Clinical information

MOA	Unclear, but likely due to CNS depression, active metabolite has anxiolytic and sedative effects
Similar Structure	Meprobamate
Dosing	250-350mg TID and at bedtime for max of 2-3 weeks
Preparations	350mg tablet
Onset	30 minutes with a peak response after 4 hours
Brought to Market	1959

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Clinical Pearls

- Caution in patients with hx of drug abuse due to possibility of dependence
- Taper slowly after prolonged use

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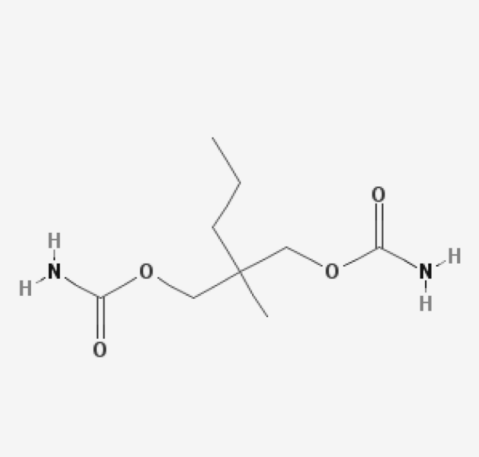

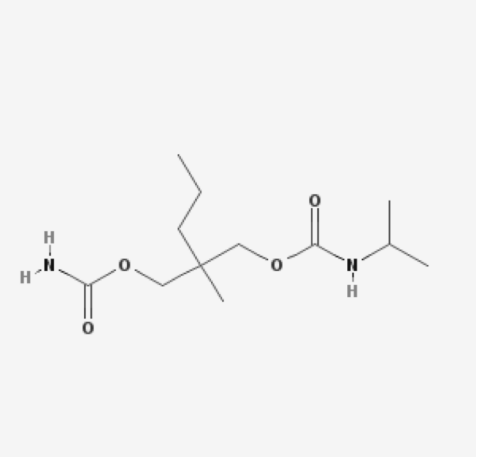

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Orphenadrine

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Clinical information

MOA	Not defined, potentially due to analgesic and euphoric effects. Indirect skeletal muscle relaxant through central anticholinergic effects
Similar Structure	Diphenhydramine
Dosing	IM/IV: 60mg Q12H
Preparations	30mg/mL injection
Onset	1 hour
Brought to Market	1940s

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Clinical Pearls

- Caution in patients with tachycardia or arrhythmias
- Contraindicated in myasthenia gravis and glaucoma
- Potential to be very sedating

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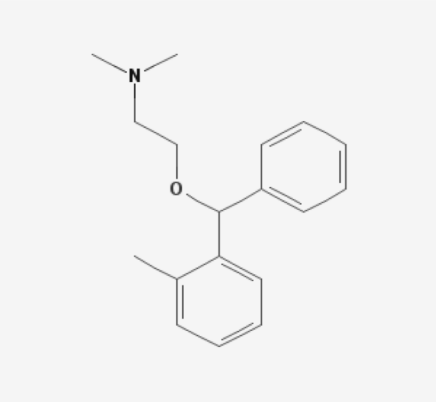

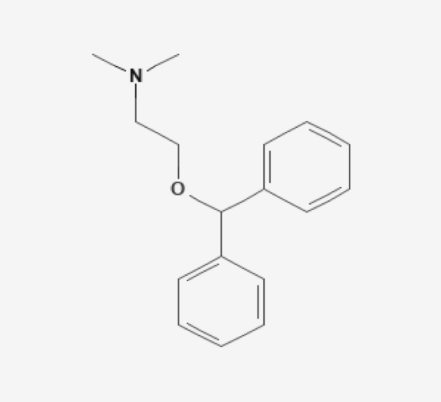

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Baclofen

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Clinical information

MOA	Acts on spinal end of upper motor neurons to cause muscle relaxation, general CNS depressant
Similar Structure	Derivative of the GABA neurotransmitter
Dosing	5mg TID, max of 80mg/day
Preparations	5mg, 10mg tablets Injectable
Onset	3-4 days
Brought to Market	1992

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Clinical Pearls

- Black Box Warning: Avoid abrupt discontinuation, use a slow taper
- Dose reduction required in CrCl < 80mL/min
- Potential to cause acute urinary retention
- Caution in patients with GI disorders

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Tizanidine

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Clinical information

MOA	Alpha-2 adrenergic agonist
Similar Structure	Clonidine
Dosing	2mg TID, can titrate up to a max of 36mg/day
Preparations	2mg, 4mg tablets
Onset	1-2 hours
Brought to Market	1996

PAINWEEK

Clinical Pearls

- Reduce dose in CrCl < 25mL/min
- Dose reduce in hepatic impairment
- Contraindications:
  - Use with ciprofloxacin or fluvoxamine
- Can cause hypotension
- Taper recommended

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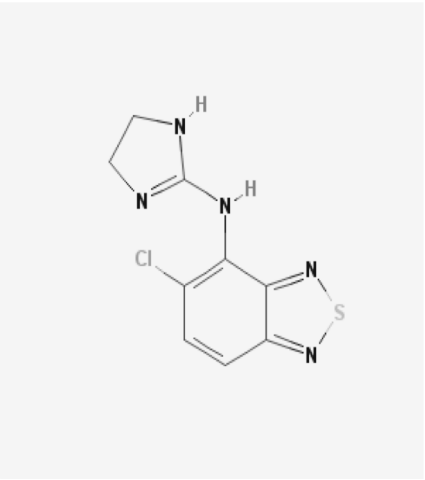

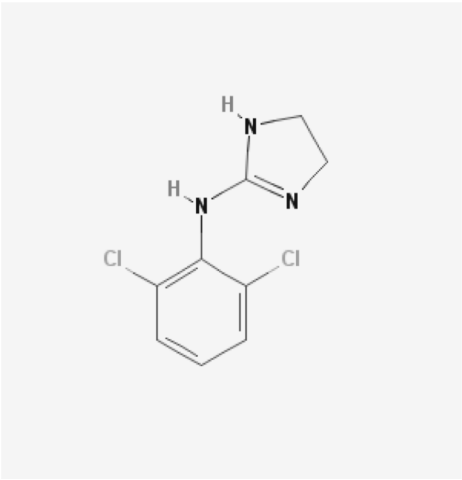

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Metaxolone

PainWeek

Clinical information

MOA	Precise mechanism has not been established; clinical effect may be associated with general depression of the nervous system; no direct effect on the contractile mechanism of striated muscle, the nerve fiber or the motor end plate
Similar Structure	N/A
Dosing	800mg 3-4 times daily
Preparations	400mg, 800mg tablets
Onset	~3 hours
Brought to Market	1962

PainWeek

Clinical Pearls

- Increased bioavailability and half-life in female patients
- No dose adjustments needed
- Serum concentrations may be increased when taken with food

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Benzodiazepines

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Clinical information

MOA	Act at GABA synapse, leading to increased affinity of receptors to GABA and skeletal muscle relaxation. (GABA is major inhibitory neurotransmitter)
Similar Structure	N/A
Dosing	Medication dependent
Preparations	Medication dependent
Onset	Medication dependent

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Clinical Pearls

- Taper recommended with chronic use
- Half-life
  - Clonazepam>diazepam>lorazepam>alprazolam
- Sedating

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Clinical Comparison

Medication	Onset (hours)	Half-life	Active metabolite?	Equivalent Dose	Comments
Alprazolam	1-2	12-15	Yes	1mg	
Clonazepam	1-4	10-46	Yes	0.5mg	Avoid in hepatic impairment
Diazepam	0.25-2.5	>100	Yes	10mg	Avoid in hepatic impairment
Lorazepam	2	10-20	No	2mg	Preferred agent in hepatic and renal failure

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Case 1

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JP is a 44 year old female that was in a recent automobile accident. Works full time and does not want to take medications that cause her to be too sedated, but us also unable to sleep at night.

CC: “Every time I stand up I am in so much pain, feels like my back is tightening up whenever I try to move”
PMH: Old herniated disks at L4/L5 and L5/S1
NKDA

Current medication list:
Gabapentin 600mg at bedtime
Montelukast 10mg at bedtime
Melatonin 2.5mg at bedtime

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Case 2

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MN is an 80 year old male

CC: “My whole body hurts, my legs feel tight”

PMH: Epilepsy, afib, stroke 5 years ago, fibromyalgia

NKDA

Current medication list:

Lisinopril 10mg daily

Metoprolol tartrate 12.5mg BID

Acetaminophen 500mg Q4H prn pain

Pregabalin 75mg BID

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