



**Indian Health Service
National Pharmacy and Therapeutics Committee
Skeletal Muscle Relaxants
NPTC Formulary Brief
May 2014**



Background:

In May 2014, the IHS National Pharmacy and Therapeutics Committee (NPTC) evaluated current guidelines and recommendations for the use of skeletal muscle relaxants (SMRs). Evaluation criteria included published evidence on the pharmacology, pharmacodynamics, pharmacokinetics, safety, efficacy, utilization and procurement data of the SMRs: baclofen, carisoprodol, cyclobenzaprine, methocarbamol and tizanidine. Carisoprodol is the only federally controlled substance in this class due to its wide potential for abuse.⁵ SMRs are a heterogeneous group of centrally acting medications used to treat spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions.³ SMRs work directly on the contractile mechanism of the skeletal musculature or through transmission in spinal cord motor reflex pathways.³ They act to produce decreased muscle tone and involuntary movement with minimal loss of voluntary motor function and/or consciousness.³

Discussion:

The guideline from the American Pain Society and the American College of Physicians for acute low back pain recommends first-line treatments of acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs).⁸ The guideline recommended to reserve SMRs as an alternative treatment. According to the Clinical Guideline from Chou et al (2007), Medications for Acute and Chronic Low Back Pain (1292 abstracts), the most common medications prescribed are: NSAIDs, SMRs and opioid analgesics. There is good evidence for the short-term effectiveness of SMRs for acute (<4 weeks duration) low back pain. Evidence is insufficient to identify one medication as being overall advantageous due to the complex trade-offs between benefits and harm.² SMRs alone had a total of 36 trials reviewed (all 2 weeks or less in duration) for spasticity and musculoskeletal conditions and one high quality Cochrane review for acute low back pain.² In these reviews, tizanidine was shown to be efficacious for low back pain, but has increased adverse events (ADE's).² Evidence from the Cochrane review identified tizanidine plus APAP or NSAID is consistently better than APAP/NSAIDs alone for short-term pain relief.² Practitioners should consider risk factors for complications, concomitant medication use, baseline severity of pain, duration of low back pain symptoms and cost before adding SMRs to first line pain therapy.² Tizanidine and baclofen are indicated for the treatment of muscle spasticity and carisoprodol, cyclobenzaprine and methocarbamol are indicated for the treatment of musculoskeletal disorders.

A Cochrane Review evaluating muscle relaxants for non-specific low back pain analyzed 30 trials (23 high quality) and indicated strong evidence that any of the SMR's are more effective than placebo alone and are similar in performance, yet adverse events are more prevalent and require caution with use.⁹ Also, further trials are needed to compare SMRs to other analgesics and NSAIDs.⁹ Three high-quality trials (560 patients) showed that tizanidine plus analgesics were more effective in providing pain relief and decreasing muscle spasm than analgesics alone.^{6,8,9} Several reviews consistently confirm that SMRs are associated with increased adverse drug events (ADE), even with short-term use.^{6,8,9} The most common ADEs are dizziness and drowsiness.⁶ However, data is low-quality and limited in quantity.⁶

Comparative Efficacy and Safety of SMRs for Spasticity and Musculoskeletal Conditions: A Systematic Review published in the Journal of Pain and Symptom Management Review was comprised of 101 randomized trials and 98 reports including: systematic reviews, meta-analyses, head-to head trials, and placebo-controlled trials.³ Comparative efficacy of SMRs utilized for spasticity showed no pattern to suggest one SMR was better than others, but a possible increased efficacy of tizanidine.³ Efficacy for musculoskeletal conditions showed that cyclobenzaprine was associated with better 'global improvement' scores.³ Comparative safety of SMRs utilized for spasticity showed increased adverse events, no associated deaths, and abuse was not evaluated.³

Tizanidine showed an asymptomatic increase in LFTs.³ Data for musculoskeletal conditions showed cyclobenzaprine caused more somnolence vs methocarbamol.³ Overall results showed tizanidine was effective for both spasticity and musculoskeletal conditions.³ Spasticity (primarily in multiple sclerosis) showed baclofen and tizanidine had similar effectiveness and rates of ADEs vs. placebo.³ Cyclobenzaprine, carisoprodol and tizanidine are effective vs. placebo.³ Safety and efficacy for many SMRs was not determined with this data.³

See and Ginzburg (2008) recommendations for low back and neck pain include short-term relief with the moderately effective carisoprodol, cyclobenzaprine, or tizanidine.⁸ Cyclobenzaprine is the most heavily studied SMR with consistently proven effectiveness.^{3,8} Cyclobenzaprine with naproxen showed greater decrease of spasm and tenderness.⁸ The authors concluded, SMRs place in therapy is debatable as they are not considered first-line therapy, but rather adjunctive short-term therapy for musculoskeletal conditions or acute low back pain.⁸ Evidence does not clearly support any one SMR medication. Specific selection should be based on side-effect profile, patient preference, abuse potential, drug interaction potential, and any other special characteristics of the SMR.⁸ Effectiveness data is limited and toxicity data is strong. Cyclobenzaprine was useful for low back pain or fibromyalgia.⁸ Methocarbamol was found useful if the sedation from cyclobenzaprine or tizanidine was unwanted.⁸ Carisoprodol is metabolized into meprobamate and should be used as a last-line because of its abuse potential.^{5,8} Standardized high-quality evidence and current primary literature for this class of medications is limited.

Findings:

A wide variety of pain conditions, both acute and chronic, may be accompanied by painful muscle spasm. SMRs can be useful in treating this aspect of the patient's symptoms, but their action may be more the result of sedation rather than muscle relaxation. These medications may also cause CNS depression and should be used cautiously when combined with other CNS depressant medications. SMRs are primarily used as adjunctive medication for pain relief due to spasticity or musculoskeletal conditions. There is some clinical merit for utilizing SMRs based on appropriate patient-specific conditions. Based on the information presented, the committee made no changes to the IHS National Core Formulary (NCF) and did not add a SMR to the NCF. However, these agents may be appropriate for inclusion on local formularies to meet the needs of the patient population. Carisoprodol should be avoided due to its abuse potential. The NPTC will continue to monitor SMR medications for future consideration.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

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