Minnesota Department of Labor and Industry

STATEMENT OF NEED AND REASONABLENESS

Proposed Amendment to Rules Governing Workers' Compensation Treatment Parameters, Minnesota Rules, Parts 5221.6030 to 5221.6305.

ALTERNATIVE FORMAT

Upon request, this Statement of Need and Reasonableness can be made available in an alternative format, such as large print, Braille, or cassette tape. To make a request, contact Carrie Rohling at the Department of Labor and Industry in any of the following ways: by mail at 443 Lafayette Road North, St. Paul, MN 55155; by phone at 651-284-5006; by FAX at 651-284-5725; or by e-mail at dli.rules@state.mn.us. TTY users may call the Department at 651-297-4198.

STATUTORY AUTHORITY AND INTRODUCTION

Statutory Authority

In 1992 the legislature enacted Minn. Stat. § 176.83, subd. 5, which granted the commissioner of the Department of Labor and Industry the authority to promulgate emergency and permanent rules establishing standards and procedures for treatment of workers' compensation injuries. The current statute provides:[1]

> Subd. 5. **Treatment standards for medical services.** In consultation with the Medical
> Services Review Board or the rehabilitation review panel, the commissioner shall adopt rules establishing standards and procedures for health care provider treatment. The rules shall apply uniformly to all providers including those providing managed care under section 176.1351. The rules shall be used to determine whether a provider of health care services and rehabilitation services, including a provider of medical, chiropractic, podiatric, surgical, hospital, or other services, is performing procedures or providing services at a level or with a frequency that is excessive, unnecessary, or inappropriate under section 176.135, subdivision 1, based upon accepted medical standards for quality health care and accepted rehabilitation standards.
> The rules shall include, but are not limited to, the following:
> (1) criteria for diagnosis and treatment of the most common work-related injuries including, but not limited to, low back injuries and upper extremity repetitive trauma injuries;
> (2) criteria for surgical procedures including, but not limited to, diagnosis, prior conservative treatment, supporting diagnostic imaging and testing, and anticipated outcome criteria;
> (3) criteria for use of appliances, adaptive equipment, and use of health clubs or other exercise facilities;
> (4) criteria for diagnostic imaging procedures;
> (5) criteria for inpatient hospitalization; and

1. The underlined language was added by the legislature in 1995. See, 1995 Minn. Laws, ch. 231, art. 2, sec. 99

> (6) criteria for treatment of chronic pain.
> If it is determined by the payer that the level, frequency or cost of a procedure or service of a provider is excessive, unnecessary, or inappropriate according to the standards established by the rules, the provider shall not be paid for the procedure, service, or cost by an insurer, self-insurer, or group self-insurer, and the provider shall not be reimbursed or attempt to collect reimbursement for the procedure, service, or cost from any other source, including the employee, another insurer, the special compensation fund, or any government program unless the commissioner or compensation judge determines at a hearing or administrative conference that the level, frequency, or cost was not excessive under the rules in which case the insurer, self-insurer, or group self-insurer shall make the payment deemed reasonable. A rehabilitation provider who is determined by the Rehabilitation Review Panel Board, after hearing, to be consistently performing procedures or providing services at an excessive level or cost may be prohibited from receiving any further reimbursement for procedures or services provided under this chapter. A prohibition imposed on a provider under this subdivision may be grounds for revocation or suspension of the provider's license or certificate of registration to provide health care or rehabilitation service in Minnesota by the appropriate licensing or certifying body. The commissioner and Medical Services Review Board shall review excessive, inappropriate, or unnecessary health care provider treatment under section 176.103.

Additional authority for the rules is in Minn. Stat. § 176.103, subd. 2, which provides that the commissioner, in consultation with the Medical Services Review Board (MSRB), "shall adopt rules defining standards of treatment, including inappropriate, unnecessary or excessive treatment and the sanctions to be imposed for inappropriate, unnecessary or excessive treatment.[2] As discussed in the Rule - by - Rule analysis section, the Department has extensively consulted with the MSRB in the development of the proposed rules. The MSRB was established by Minnesota Statutes §176.103 in 1983. The MSRB is composed of two chiropractic representatives, one hospital administrator representative, one registered nurse, one physical therapist, six physicians of different specialties, one employee representative, one employer/insurer representative and one general public representative.[3] Under M.S. §176.103, the MSRB advises the department about workers' compensation medical issues and is a liaison between the department and the medical-provider community.

Finally, other subdivisions in Minn. Stat. § 176.83 also provide authority. Subdivision 4 of that section authorizes the commissioner to adopt "rules establishing standards and procedures for determining whether or not charges for health services and rehabilitation services under this chapter are excessive." And Minn. Stat. § 176.83, subd. 3 authorizes "rules establishing standards for reviewing and evaluating the clinical consequences of services provided . . . to an employee by health care providers . . . "

Therefore, the Department has the necessary statutory authority to adopt the proposed

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2. The rules governing the sanctioning process are in part 5221.8900.
3. A list of current MSRB members is at http://www.dli.mn.gov/msrb.asp. The membership of the MSRB was amended effective May 13, 2009 by changing a person representing "hospital administrators" to a person representing "hospitals" and by changing a person representing the "general public" with an "occupational therapist." See, 2009 Minnesota Laws, Chapter 75 at:https://www.revisor.leg.state.mn.us/laws/?view=session&year=2009&type=0

amendments to the treatment parameter rules. [4]

Jacka v. Coca-Cola

The Department adopted permanent treatment parameter rules effective on January 4, 1995. In Jacka v. Coca-Cola Bottling Co., 580 N.W.2d 27 (Minn., 1998), the Minnesota Supreme Court upheld the permanent treatment parameter rules. The Court found that the permanent treatment parameter rules did not exceed the Department's rulemaking authority and did not violate the due process clause of the United States and Minnesota constitutions, because: the rules did not place absolute limits on the duration of treatment; the rule allowing departures (Minn. R. 5221.6050, subp. 8) did not state that it provides the exclusive means of departing from the rules; and because the legislature clarified "how the rules should interact with the compensation judge's role" in the 1995 amendments. The court stated"

> In summary, we hold that the permanent treatment parameter rules adopted by D.O.L.I. are flexible and yielding and, therefore, ensure that reasonably priced, appropriate medical care will not be denied simply because of a time-line or rigid categories. At the same time, the rules are substantial enough to establish standards and procedures based on good medical practice that can be used to regulate provider abuses and reduce litigation over compensable treatment. We recognize, as the broader medical community has done, that rules establishing standards and procedures for managed care do not have to be at odds with the purpose of restoring the employee to good health. We conclude that these rules have struck the right balance between flexibility and substance and should have the respect, force and effect accorded other properly promulgated administrative rules."[5]

Format of the rules

The treatment parameter rules are intended to be used as strategies for managing patient care in workers' compensation according to accepted medical standards for quality health care. They reflect general strategies applicable to all patients as well as specific strategies for patients with certain conditions or circumstances. The parameters are meant to assist health care providers in decision making and to improve the quality of health care while at the same time making it more efficient and cost-effective. They are meant to optimize outcomes for injured workers while reasonably containing costs for employers and insurers. As discussed in more detail in the 1994 Statement of Need and Reasonableness for the permanent treatment parameter rules, the rules are organized to accomplish this as follows: [6]

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4. All sources of statutory authority were adopted and effective prior to January 1, 1996, and so Minnesota Statutes, section 14.125 does not apply. See Minnesota Laws 1995, chapter 233, article 2, section 58. Moreover, these are amendments to existing treatment parameter rules and so Minnesota Statutes, section 14.125, does not apply.

5. Jacka v. Coca-Cola Bottling Co., 580 N.W.2d 27, 36. The court also stated that "in recognition of the fact that the treatment parameters cannot anticipate every exceptional circumstance, we acknowledge that a compensation judge may depart from the rules in those rare cases in which departure is necessary to obtain proper treatment." Id.at 35-36

6. The 1994 Statement of Need and Reasonableness is available from the Department contact person Carrie Rohling by phone at 651-284-5006 or by e-mail at carrie.rohling@state.mn.us

- Part 5221.6030 incorporates by reference the ICD-9 diagnostic coding manual referred to throughout the treatment parameters.[7]

- Part 5221.6040 provides definition of terms used throughout the parameters. A definition of "medical contraindication" is added in subpart 8a.

- Part 5221.6050 provides general treatment parameters. This part identifies standards that apply to treatment of any work-related condition. Treatment must be adequately documented, evaluated for effectiveness and medical necessity, and provided in the least intensive setting with a goal of self-management of the condition. The rules require communication between primary providers and referrals for consultations, and require that a new provider consider prior care in determining an appropriate treatment plan. Excessive treatment is defined in relation to the parameters. Subpart 8 identifies the circumstances under which departure from the parameters may be appropriate, and specifies the procedure for a provider to notify the insurer of a requested departure and the procedure for an insurer to respond to a request for departure. Finally, this part also requires providers to notify the insurer before providing non-emergency inpatient hospitalization, surgery, medical equipment, or for a departure from a parameter. Subparts 1 and 9 are amended to add cross-references.

- Part 5221.6100 identifies general principals that must be adhered to when ordering medical imaging studies. Specific imaging procedures and their indications for low back pain are delineated. Proposed amendments to this section clarify terminology.

- The new proposed part 5221.6105 governs the use of medications in the treatment of workers' compensation injuries. Specifically, subpart 2 governs the use of nonsteroidal anti-inflammatory drugs in the treatment of acute and chronic musculoskeletal pain; subpart 3 governs the use of opioid analgesics (sometimes referred to as narcotics) in the treatment of acute and chronic pain; and subpart 4 governs the use of muscle relaxants in the treatment of acute and chronic musculoskeletal pain.

- Part 5221.6200 (low back pain); 5221.6205 (neck pain); and 5221.6210 (thoracic back pain) provide parameters for the diagnosis and treatment of back injuries according to the following standards of medical care:

  A provider must first perform an appropriate history and physical and assign the employee to a diagnostic category before ordering further tests or treatment. Generally accepted diagnostic procedures for back pain are identified. As discussed in more detail later in this SONAR, the proposed amendments update the ICD-9 codes to reflect current diagnostic categories and terminology for back conditions, and amend the rules governing functional capacity evaluations.

  Once a diagnostic category is identified, parameters for three phases of treatment are identified: The first phase is initial nonsurgical treatment, which may include

7. Minn. R. 5221.6030 provides in part: "The ICD-9-CM diagnostic codes referenced in parts 5221.6010 to 5221.6600 are contained in the fourth edition of the International Classification of Diseases, Clinical Modification, 1994, and corresponding annual updates. For information see http://www.cms.hhs.gov/ICD9ProviderDiagnosticCodes/

any combination of passive, active, injection and medication treatment modalities. The second phase is re-evaluation of the diagnosis, treatment and surgery where the injured worker's symptoms persist. The third phase is chronic management, when the injured worker is not a candidate for surgery or when there has not been complete resolution of symptoms following surgery. The proposed amendments update some of the passive modality parameters to reflect changes in terminology, technology and health care provider techniques and practices; and revise the parameters governing medications to reflect the new proposed part 5221.6105.

- Part 5221.6300 addresses diagnosis and treatment of upper extremity disorders, again using the three phases of treatment discussed above. The proposed amendments update the ICD-9 codes to reflect current diagnostic categories and terminology for upper extremity disorders. As with back pain conditions, the proposed amendments revise the parameters for medications to reflect the new proposed part 5221.6105; update some of the passive modality parameters; and revise the functional capacity rule.

- Part 5221.6305. This section describes parameters for complex regional pain syndrome and related conditions (also known as reflex sympathetic dystrophy and causalgia), which is a complication of injuries to upper and lower extremities. The proposed amendments revise these parameters to reflect current medical terminology and ICD-9 codes, respond to case law, and add a subpart on medications consistent with the new proposed part 5221.6105.

- Part 5221.6400. This section provides parameters for inpatient hospitalization. No amendments are proposed to this part.

- Part 5221.6500. This section provides parameters for surgical procedures. No amendments are proposed to this part.

- Part 5221.6600. This section provides parameters for the third phase of treatment, chronic management. No amendments are proposed to this part.

REGULATORY ANALYSIS

Minnesota Statutes, section 14.131, sets out seven factors for a regulatory analysis that must be included in the SONAR. Paragraphs (1) through (7) below quote these factors and then give the agency's response.

"(1) a description of the classes of persons who probably will be affected by the proposed rule, including classes that will bear the costs of the proposed rule and classes that will benefit from the proposed rule"

The proposed amendments to the rules would likely primarily affect injured workers and health care providers who treat injured workers, including physicians, chiropractors, physical therapists, and hospitals. The amendments would also affect workers' compensation employers and insurers;

certified workers' compensation managed care plans; and, less directly, others involved in the workers' compensation system, such as attorneys and pharmacies.

All of the named classes of persons will benefit from the rules because they reflect the current standard of medical care for injured workers, and should reduce disputes and costs related to unnecessary or inappropriate treatment. Because the proposed amendments reflect the current standard of care, additional cost is not anticipated. There may be reduced revenue for providers who do not currently comply with the standard, but that cannot reasonably be measured, because there are too many unknown variables, including how many health care providers do not currently adhere to the standards of care reflected in the proposed rules; the extent to which each health care provider delivers nonstandard care; the number of injured workers treated by the provider; and the extent to which insurers are currently paying for nonstandard treatment. The potential costs or savings to payers will depend on the same variables. There will be savings to the extent payers no longer pay for nonstandard care; there may be additional costs to the extent payers were previously not paying for appropriate care.

"(2) the probable costs to the agency and to any other agency of the implementation and enforcement of the proposed rule and any anticipated effect on state revenues"

No costs to this Department or any other agency are anticipated for the implementation and enforcement of the proposed rules, because they update existing rules according to accepted medical standards, which payers must already use to determine whether treatment of a work-related injury is appropriate and therefore compensable. The proposed rules should reduce, rather than increase litigation, and therefore there should be no additional costs to other agencies, such as the Department of Finance (Employee Relations division) and the Office of Administrative Hearings. There is no anticipated effect on state revenues.

"(3) a determination of whether there are less costly methods or less intrusive methods for achieving the purpose of the proposed rule"

The purpose of the treatment parameters is as stated in Minn. Stat. § 176.83, subd. 5 (a) and (c): "(a) In consultation with the Medical Services Review Board or the rehabilitation review panel, the commissioner shall adopt rules establishing standards and procedures for health care provider treatment. . . . The rules shall be used to determine whether a provider of health care services and rehabilitation services, including a provider of medical, chiropractic, podiatric, surgical, hospital or other services, is performing procedures or providing services at a level or with a frequency that is excessive, unnecessary, or inappropriate under section 176.135, subdivision 1, based upon accepted medical standards for quality health care and accepted rehabilitation standards." [8] . . . . (c) If it is determined by the payer that the level, frequency, or cost of a procedure or service of a provider is excessive, unnecessary, or inappropriate according to the standards established by the rules, the provider shall not be paid for the procedure, service, or cost . . . .

8. Minn. Stat. § 176.135, subd. 1 (a) provides: "The employer shall furnish any medical, psychological, chiropractic, podiatric, surgical and hospital treatment, including nursing, medicines, medical, chiropractic, podiatric, and surgical supplies, crutches and apparatus, including artificial members, or at the option of the employee, if the employer has not filed notice as hereinafter provided, Christian Science treatment in lieu of medical treatment, chiropractic medicine and medical supplies, as may be reasonably be required at the time of the injury and any time thereafter to cure and relieve from the effects of the injury. This treatment shall include treatments necessary to physical rehabilitation."

unless the commissioner or compensation judge determines at a hearing or administrative conference that the level, frequency, or cost was not excessive under the rules in which case the insurer, self-insurer, or group self-insurer shall make the payment deemed reasonable."

Following consultation with the MSRB, the proposed rules update the parameters to reflect current, accepted medical standards for providing quality, cost effective health care to cure and relieve injured workers of the effects of their injuries. No less costly or less intrusive method for achieving this purpose has been identified.

"(4) a description of any alternative methods for achieving the purpose of the proposed rule that were seriously considered by the agency and the reasons why they were rejected in favor of the proposed rule"

As noted above, under Minn. Stat. § 176.83, subd. 5, the purpose of the proposed rule amendments is to update the treatment parameters, in consultation with the MSRB, to reflect accepted medical standards for providing quality and cost effective health care to cure and relieve injured workers of the effects of their injuries. The Department has widely distributed the draft rules as they were revised to interested persons, providers and payers, and received comments in response. At its meetings the MSRB extensively reviewed medical research to assist the Department in determining the accepted medical standards upon which the amendments are based, as more fully discussed later in this SONAR. The MSRB also reviewed the proposed medical standards developed by the Department, and the recommendations submitted by interested persons, providers and payers. The Department seriously considered all of the comments, and incorporated all of the recommendations of the MSRB made in response to the comments. The Department did not seriously consider any amendments that were not supported by applicable medical research and the MSRB.

"(5) the probable costs of complying with the proposed rule, including the portion of the total costs that will be borne by identifiable categories of affected parties, such as separate classes of governmental units, businesses, or individuals"

The Department has not identified any costs of complying with the proposed rules for any of the classes of affected parties. The proposed rules reflect accepted medical standards for quality and cost effective health care as recommended by the MSRB. There are no costs of compliance to providers or payers in that the rules do not require either group to spend money to comply. However, depending on the variables discussed under question 1, the proposed rules may reduce or increase revenue for providers, depending on whether or not they currently meet the standards of practice reflected in the proposed amendments. They may require additional payment by insurers that are not currently paying for accepted medical treatment, and save costs for insurers who are currently paying for treatment that does not meet the standards. The rules should reduce costs for providers, injured workers, and workers' compensation payers to the extent that they reduce litigation and inappropriate denials of treatment. The cost analysis would be no different for governmental units because governmental units either act in the capacity of an employer, insurer or provider. The Department solicited input on the cost of complying with the proposed amendments from members of the Medical Services Review Board and the Workers'

Compensation Insurers Task Force. [9] No costs of compliance were identified in response to the Department's inquiry.

"(6) the probable costs or consequences of not adopting the proposed rule, including those costs or consequences borne by identifiable categories of affected parties, such as separate classes of government units, businesses, or individuals"

The probable costs or consequences of not adopting the proposed rules are that injured workers may not receive treatment that is consistent with accepted medical practice for quality health care, and payers may pay for treatment that does not meet that standard, or may deny payment for treatment that does meet the standard. Additionally, there would be no reduction in the number of workers' compensation disputes related to the treatment governed by the proposed rules.

"(7) an assessment of any differences between the proposed rule and existing federal regulations and a specific analysis of the need for and reasonableness of each difference"

There are no federal regulations governing Minnesota workers' compensation treatment.

PERFORMANCE-BASED RULES

Minnesota Statutes, sections 14.002 and 14.131, require that the SONAR describe how the agency, in developing the rules, considered and implemented performance-based standards that emphasize superior achievement in meeting the agency's regulatory objectives and maximum flexibility for the regulated party and the agency in meeting those goals.

According to Minn. Stat. § 176.83, subd. 5: "The rules shall be used to determine whether a provider of health care services . . . . is performing procedures or providing services at a level or with a frequency that is excessive, unnecessary, or inappropriate under section 176.135, subdivision 1, based upon accepted medical standards for quality health care and accepted rehabilitation standards." As is evident by this statute, the treatment parameters are performance-based rules. The treatment parameters provide health care providers with flexibility to determine what treatment to provide based on the unique needs of each injured worker, within the guidelines set forth in the treatment parameters; they do not rigidly proscribe or prescribe specific treatment, but rather reflect what the medical research and the Medical Services Review Board have identified as acceptable standards of quality health care.

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9. The Workers' Compensation Insurers' Task Force is an organized body of representatives of workers' compensation payers, including insurance companies, and employers who self-insure for their workers' compensation coverage (including government entities). The WCITF meets up to four times a year to facilitate the exchange of information about current workers' compensation issues between payers and with the Department. The WCITF is not created by statute.

The bases for departing from the parameters also apply to the proposed amendments.[10] As stated by the Minnesota Supreme Court in the Jacka case, ". . . the treatment parameters are flexible and yielding and, therefore, ensure that reasonably priced, appropriate medical care will not be denied simply because of a time-line or rigid categories. At the same time, the rules are substantial enough to establish standards and procedures based on good medical practice that can be used to regulate provider abuses and reduce litigation over compensable treatment." *Jacka v. Coca Cola Bottling Co., 580 N.W.2d, 27 at 36 (Minn. 1998)*

ADDITIONAL NOTICE

Minnesota Statutes, sections 14.131 and 14.23, require that the SONAR contain a description of the Department's efforts to provide additional notice to persons who may be affected by the proposed rules or explain why these efforts were not made. This Additional Notice Plan was reviewed by the Office of Administrative Hearings and approved in a September 25, 2009 letter by Administrative Law Judge Eric Lipman.

The department has identified persons and organizations that represent those most likely to be affected by or interested in the rule amendments. The Notice of Intent to Adopt the proposed amendment will be mailed or e-mailed to all of the following:

1. The members of the Workers' Compensation Advisory Council, which consists of labor, employer, and legislative representatives, established pursuant to Minn. Stat. § 176.007, and persons who have requested to receive notice of WCAC meetings.

2. Members of the Workers' Compensation Insurers Task Force, an ad hoc group of workers' compensation payers who meet at the Department of Labor and Industry several times a year to learn about and discuss workers' compensation issues with the Department. The WCITF consists of 19 representatives of workers' compensation insurers, self-insured employers, and third-party administrators. Persons who have requested to receive notice of the WCTIF meetings will also be provided with the Notice;

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10. Minn. R. 5221.6050, Subp. 8. **Departures from parameters.** A departure from a parameter that limits the duration or type of treatment in parts 5221.6050 to 5221.6600 may be appropriate in any one of the circumstances specified in items A to E. The health care provider must provide prior notification of the departure as required by subpart 9. A. Where there is a documented medical complication. B. Where previous treatment did not meet the accepted standard of practice and the requirements of parts 5221.6050 to 5221.6600 for the health care provider who ordered the treatment. C. Where the treatment is necessary to assist the employee in the initial return to work where the employee's work activities place stress on the part of the body affected by the work injury. The health care provider must document in the medical record the specific work activities that place stress on the affected body part, the details of the treatment plan and treatment delivered on each visit, the employee's response to the treatment, and efforts to promote employee independence in the employee's own care to the extent possible so that prolonged or repeated use of health care providers and medical facilities is minimized. D. Where the treatment continues to meet two of the following three criteria, as documented in the medical record: (1) the employee's subjective complaints of pain are progressively improving as evidenced by documentation in the medical record of decreased distribution, frequency, or intensity of symptoms; (2) the employee's objective clinical findings are progressively improving, as evidenced by documentation in the medical record of resolution or objectively measured improvement in physical signs of injury; and (3) the employee's functional status, especially vocational activity, is objectively improving as evidenced by documentation in the medical record, or successive reports of work ability, of less restrictive limitations on activity. E. Where there is an incapacitating exacerbation of the employee's condition. However, additional treatment for the incapacitating exacerbation may not exceed, and must comply with, the parameters in parts 5221.6050 to 5221.6600.

3. Members of the Workers' Compensation Medical Services Review Board, which consists of persons representing health care providers, labor and payers, as specified in Minn. Stat. § 176.103; and persons who have requested to receive notice of MSRB meetings;

4. Persons and organizations who have requested to be on the electronic mailing list for *CompAct*, the department's quarterly workers' compensation publication;

5. Persons and organizations who are on the Department's e-mail list for health care providers;

6. Persons and organizations who are on the Department's e-mail list for workers' compensation insurers;

7. Attorneys on the Office of Administrative Hearing's e-mail list for workers' compensation attorneys;

8 The Minnesota Medical Association, the Minnesota Chiropractic Association, the Minnesota Nurses Association, the Minnesota Chapter of the American Physical Therapy Association, the Minnesota Occupational Therapy Association, and the Minnesota Pharmacy Association;

9. The three workers' compensation managed care plans certified under Minn. Stat. § 176.1351;

10. The League of Minnesota Cities; the Association of Minnesota Counties; the University of Minnesota workers' compensation department; and the Minnesota Department of Finance, Employee Relations division.

11. Those who have commented on the draft amendments since the Request for Comment was published on August 18, 2008;

12. In addition, the department will place the Notice of Intent to Adopt the proposed rules, the proposed rule amendments, and the Statement of Need and Reasonableness on the department's rule docket Web site: http://www.dli.mn.gov/RulemakingWC.asp

The Department's Notice Plan also includes giving notice required by statute. The proposed rules and Notice of Intent to Adopt will be mailed to everyone who has registered to be on the Department's workers' compensation and "all agency" rulemaking mailing lists under Minnesota Statutes, section 14.14, subdivision 1a. Notice will also be given to the Legislature as required by Minnesota Statutes, section 14.116.

CONSULT WITH FINANCE ON LOCAL GOVERNMENT IMPACT

Minnesota Statutes, section 14.131, requires the agency to consult with the Department of Finance to help evaluate the fiscal impact and benefits of proposed rules on local governments. As required by Minnesota Statutes, section 14.131, the Department has consulted with the

Commissioner of Finance. In a memo dated July 24, 2009, Ryan Baumtrog, Executive Budget Officer at the Office of Management and Budget, opined that the proposed changes will not impose a significant cost on local governments.

DETERMINATION FOR RULES REQUIRING LOCAL IMPLEMENTATION.

Under 2009 Minnesota Laws, chapter 152, § 1 (to be codified as Minn. Stat. § 14.128) agencies must determine if a town, county, or home rule charter or statutory city will be required to adopt or amend an ordinance or other regulation to comply with a proposed agency rule. The Department has determined that no local government will be required to adopt or amend an ordinance or other regulation to comply with the proposed amendments because local governments are required to comply with the workers compensation law as set forth in Minn. Stat. chapter 176, including the treatment parameters adopted under Minn. Stat. § 176.83, subd. 5.[11] Therefore, no ordinance or regulation is required to implement these rules.

COST OF COMPLYING FOR SMALL BUSINESS OR CITY

Agency Determination of Cost

As required by Minnesota Statutes, § 14.127, the Department has considered whether the cost of complying with the proposed rules in the first year after the rules take effect will exceed $25,000 for any small business or small city. The Department has determined that the cost of complying with the proposed rules in the first year after the rules take effect will not exceed $25,000 for any small business or small city. Small businesses would most likely be small health care provider offices or small pharmacies. Small cities would most likely be affected as employers of injured workers. As discussed above in the regulatory analysis section, the proposed rules do not require small business health care providers to provide any particular treatment or spend money to comply; they simply describe what is accepted medical practice in evaluating what is appropriate treatment for injured workers for purposes of payment by workers' compensation insurers and self-insured employers. Since workers' compensation health care is a relatively small (about 1.5%) percentage of the cost of general medical care, it is unlikely that the proposed rules will result in reduction in revenue of greater than $25,000 for any small health care provider who is currently providing nonstandard treatment. [12] Small cities (with ten or fewer full time employees) typically do not pay workers' compensation claims directly and therefore there will be no cost of compliance that will exceed $25,000 in the first (or any) year.

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11. Minn. Stat. § 176.021, subd. 1 provides that the workers' compensation law applies to all employers unless excluded by chapter 176. Under Minn. Stat. § 176.011, subd. 10, the definition of "employer" includes counties, towns, cities, school districts, and governmental subdivisions. Minn. Stat. § 176.021, subd. 6 requires home rule charter cities to pay the compensation provided under Minn. Stat. chapter 176, although the charter may provide for compensation that exceeds the amount an employee is entitled to under chapter 176.

12. Workers' compensation total medical expenditures were 493 million in 2007. (Department of Labor and Industry, Policy Development and Research Section.) Total state health expenditures in 2007 in Minnesota were estimated at 33.7 billion (public and private) by the MN Department of Health (in Health Economics Program Issue Brief April 2009 available at: http://www.health.state.mn.us/divs/hpsc/hep/publications/costs/spendingprojections.pdf.

FARMING OPERATIONS; EFFECT ON CHICANO/LATINO PEOPLE

Minnesota Statutes § 14.11imposes additional requirements if the proposed rules affect farming operations. These proposed amendments will not have any significant impact on farming operations, and therefore the requirements of Minn. Stat. §14.11 do not apply. The requirements of Minn. Stat. § 3.9223 do not apply because the rules do not have their primary effect on Chicano/Latino people.

LIST OF WITNESSES

If these rules go to a public hearing, the Department may have the following witnesses testify in support of the need for and reasonableness of the rules, in addition to Department staff:

1. Dr. William Lohman, M.D., the Department's Medical Consultant.
2. Member(s) of the Medical Services Review Board

RULE-BY-RULE ANALYSIS

Part 5221.6040. Definitions.

Subpart 8a. Medical contraindication. This definition is needed because the phrase "medical contraindication" is used in the new part 5221.6105, governing the parameters for appropriate use of medication in the treatment of workers' compensation musculoskeletal conditions. The proposed parameters in part 5221.6105 contain exceptions for when the health care provider determines that the medication is medically contraindicated. This definition is based on information from The American Heritage Stedman's Medical Dictionary, Second Edition, and Dorland's Medical Dictionary for Health Care Consumers.

5221.6050 General Treatment Parameters; Excessive Treatment; Prior Notification.

Subpart 1. General.

Item B of this subpart requires the health care provider to continually evaluate whether the treatment is effective within the response times specified in the parameters. A cross reference to part 5221.6305, governing reflex sympathetic dystrophy and cognate conditions (also sometimes referred to as complex regional pain syndrome and causalgia), was inadvertently omitted from this subpart when the rules were initially adopted. Part 5221.6305 also includes treatment response times and therefore a health care provider should evaluate whether the treatment being provided for these conditions is effective within the treatment response times in the same manner as treatment for the other conditions in this subpart is evaluated.

Subpart 9. Prior notification; health care provider and insurer responsibilities.

The proposed amendments to subitem (5) of this subpart adds a cross-reference that was inadvertently omitted when the rules were initially adopted. Item C provides that a health care provider may elect to provide surgery if the insurer has denied authorization following receipt of a second opinion (subject to a determination of compensability by the commissioner or

compensation judge), except as provided in the cross-referenced rules, where a second opinion is required for repeat surgery, dorsal column stimulators and morphine pumps. The second opinion language in part 5221.6210, subpart 6, items B and C is identical to the language in the referenced parts 5221.6200 and 5221.6205. The missing cross-reference to part 5221.6210, subpart 6 is therefore added.

5221.6100 PARAMETERS FOR MEDICAL IMAGING.

Subpart 2. Specific imaging procedures for low back pain. The proposed amendments to this part change wording for consistency from item to item. In some cases, the rules refer to "spinal surgery to the lumbar spine." In other cases, it refers to just "spinal" surgery. The amendments change the wording to "surgery to the lumbar spine" throughout subpart 2 for ease of readability and to avoid confusion with other types of spinal surgery, such as surgery to the cervical or thoracic spine.

The amendments to items (C) (2) and (D) (4) of this subpart also change wording from progressive neurologic "deficit or changes" and "symptoms or changes" to progressive neurologic "deficit." This provides consistency with the use of the phrase in item B (2), which uses the more standard medical term "deficit."

5221.6105 Medications

Note on sources cited in footnotes.
A number of articles and documents are cited in footnotes throughout this SONAR. Some of the footnotes reference Appendices at the end of this SONAR:

- Appendix A contains Summary Tables of Medical Evidence on NSAIDs (non-steroidal anti-inflammatory drugs) (starting on page 40).
- Appendix B contains Summary Tables of Medical Evidence on Opioid Analgesics (starting on page 46).
- Appendix C contains Summary Tables of Medical Evidence on Muscle Relaxers (starting on page 52).
- Appendix D, starting on page 55, is a Glossary of Terms used in the discussion of this part.

Unless a footnote expressly states otherwise, the documents and articles cited, including MSRB minutes and Reports to the MSRB, are available for review at the Department by contacting by contacting Carrie Rohling, Rule Coordinator, by phone at 651-284-5006 or by e-mail at: Carrie.Rohling@state.mn.us.

Background and rule development process for part 5221.6105.

This part provides parameters for the appropriate use of nonsteroidal anti-inflammatory, opioid (narcotic) and muscle relaxant medications in the outpatient treatment of workers' compensation injuries. Providing treatment parameters for the most commonly used medications in workers' compensation, based on a review of medical research, is necessary to ensure that injured workers receive the most appropriate medication for the relief of pain based on accepted medical standards, and to prevent the use of medication that is ineffective or more costly than other, equally effective, medication.

Since 1990, spending in the United States for prescription drugs has grown from about ~$40 billion per year to more than $200 billion per year in 2005[13]. Costs have increased so rapidly because more drugs are being prescribed, more prescriptions are being written for newer, more expensive brand-name drugs, and generic drug costs have also risen. [14]

By 2003, expenditures per claim for outpatient pharmacy in Minnesota workers' compensation had gone up 142% since 1997[15]. These expenditures dropped with the introduction of pharmacy networks in 2005[16] and 2006 amendments to a fee schedule that provides for a reduced maximum fee when charges for prescription drugs are submitted and paid by electronic transactions. [17] However, in 2006 expenditures were still 41% higher than in 1997, after adjustment for inflation.[18]

There is good evidence that the same factors underlie the increase in drug costs in workers' compensation as explain the growth in drug costs in general medical care: more injured employees are being prescribed medications, more pills are being dispensed when medications are being prescribed, the cost per pill has increased, and newer, more expensive brand-name medications are being substituted for older medications available in generic formulations.[19]

In November 2002, the Department convened a public informational meeting of members of the WCAC and the MSRB and other interested persons to explore whether the pharmacy cost controls used in general health care could be applied to the workers' compensation system.

In 2003, the Department convened a Workers' Compensation Medical Costs Task-Force that met seven times between Aug. 26 and Dec. 2, 2003. Twelve representatives from labor, business, and health care, insurance, hospital and pharmacy industries considered the nature and scope of medical costs in the Minnesota workers' compensation system, including pharmacy costs. In particular, three cost control strategies for pharmacy costs were presented to, and reviewed by, the Medical Cost Task Force:

- Pharmacy networks
- Fee Schedules
- Drug formularies

As noted above, in 2005 the legislature allowed workers' compensation payers to establish pharmacy networks, in Minn. Stat. § 176.135, subd. 1(g) and (h). In April, 2006 the Department amended the workers' compensation fee schedule to provide for a lower maximum fee when charges for prescription drugs are submitted and paid by electronic transactions. Minn. R. 5221.4070.

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13. Kaiser Family Foundation "Prescription Drug Trends" Washington, DC; May 2007. Available at: http://www.kff.org/rxdrugs/upload/3057_06.pdf
14. Ibid
15. David Berry, Brian Zaidman "Minnesota Workers' Compensation System Report, 2003" St. Paul, MN; Research & Statistics, Minnesota Department of Labor & Industry; March 2005. Details available at: http://www.doli.state.mn.us/pdf/wcfact03.pdf
16. See, Minn. Laws 2005, chapter 90, sec. 11
17. See, Minn. R. 5221.4070.
18. David Berry, Brian Zaidman "Minnesota Workers' Compensation System Report, 2006" St. Paul, MN; Research & Statistics, Minnesota Department of Labor & Industry; June 2008. Details available at: http://www.doli.state.mn.us/pdf/wcfact06.pdf
19. "Pharmacy Costs in MN WC" A presentation to the Workers' Compensation Medical Costs Task Force; September 9, 2003. St. Paul, MN; Research & Statistics, Minnesota Department of Labor & Industry,

The Department and the Task Force considered the use of a formulary to supplement pharmacy networks and an updated fee schedule. Formularies limit the specific drugs that may be dispensed to a patient by the pharmacist. In general health care plans, drugs not included in the formulary are either not reimbursed or require a higher co-pay.

While there was no support for the development of a workers' compensation formulary as used in general health care plans, there was interest in some of the benefits of a formulary. It was noted that the many of the benefits of a closed formulary can be achieved by changing the way physicians prescribe medications rather than by interfering with the dispensing of medications by the pharmacist. Specifically:

- Encouragement of generic substitution (when a generic, less costly version of a drug is dispensed instead of the brand-name form that may have been prescribed; e.g. a patient would receive generic ibuprofen instead of Motrin™)
- Support of therapeutic substitution, if appropriate (when the patient receives an equivalent, alternative drug to the one actually prescribed; e.g. a patient would receive ibuprofen instead of Celebrex™)
- Prior Authorization (used to limit access to particularly expensive medications, drugs with misuse potential, or prescription of drugs for "off-label" uses)
- Quantity Limitation (used to limit the number of doses that can be dispensed per prescription or the number of refills allowed; targets drugs used for short-term therapy to prevent excessive or inappropriate use)

Because just a few classes of drugs - nonsteroidal anti-inflammatories, muscle relaxants, and opioid (narcotic) analgesics -account for at least two thirds of the pharmacy costs in workers' compensation in 2005,[20] the Department developed treatment parameters for these classes of drugs to realize the potential benefits of a formulary without creating a formulary.

The Department has developed these rules based on recommendations made by the Medical Services Review Board (MSRB) pursuant to Minn. Stat. § 176.103 and 176.83, subd. 5. The MSRB made their recommendations after considering the results of scientific studies, comments from interested parties in the community, and their own experience with the treatment of work related injuries. The scientific studies reviewed by the MSRB were identified by the Department's medical consultant, Dr. William Lohman, M.D., using an evidence-based medicine approach defined by the MSRB. [21]

For each class of medication – nonsteroidal anti-inflammatories, muscle relaxants, and narcotic analgesics, The MSRB requested that the Department identify scientific studies that addressed three specific clinical questions of relevance:

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20 Lipton B, King B, Laws C, and Stevens J "Workers Compensation Prescription Drug Study - 2007 Update" NCCI Research Brief; November 2007. Available at: https://www.ncci.com/documents/research-RX-Study-2007.pdf

21 Minn. Stat. § 176.103, subd. 1 states: "The commissioner shall hire a medical consultant to assist the in administration oft his section. The medical consultant shall be a doctor of medicine licensed under the laws of Minnesota. The medical consultant shall perform all duties assigned by the commissioner relating to the supervision of the total continuum of care of injured employees and shall also advise the department on matters on which the commissioner requires the consultant's advice or if the consultant deems it appropriate."

1. Are there clinically important differences in effectiveness between specific agents in the same class of medications? (Effectiveness)
2. Are there clinically important differences in safety or adverse effects between different agents in the same class of medications? (Safety)
3. Are there subgroups of patients based on demographics, concurrent use of other medications, or presence of co-morbidities for which one agent is more effective than others in the same class of medications or is associated with fewer adverse effects than others in the same class of medications? (Subgroups)

In identifying the scientific literature that addressed these three clinical questions, the Department used the evidence-based medicine approach defined by the MSRB's Medications Task Force[22]. Evidence-based medicine (EBM) "is the process of systematically reviewing, appraising and using clinical research findings to aid the delivery of optimum clinical care to patients."[23] EBM replaces clinical intuition, observations from personal clinical experience, and hypothetical arguments based on pathophysiological principles as the bases for clinical decision-making. Instead, evidence from systematic surveys and critical appraisals of peer-reviewed, methodologically sound clinical research is gathered, reviewed and synthesized using standardized, objective protocols based on rules of evidence.

Key components of the evidence-based medicine approach used by the Department at the direction of the MSRB are:

a) the systematic search for, and retrieval of, all the relevant medical literature regarding the use of these medications for musculoskeletal disorders, which addresses one or more of the specific clinical questions listed above;
b) sorting the retrieved literature by level of evidence;
c) critical appraisal of that literature to systematically examine its validity, results and relevance; and,
d) synthesis of the findings, with a grade of recommendation.

The search and retrieval of the medical literature was done using computerized search engines and on-line bibliographical databases of the medical literature. In order to maximize the efficient use of time and resources, a number of strategies were adopted to target the searches to the best and most recent evidence by using a step-wise search process.

First, the Department searched the medical literature by "level of evidence." The levels of evidence (Table 1) are a hierarchy representing the strength of the conclusion that can be drawn from a study of that type. Level I evidence is the most compelling, while Level VI evidence is the weakest. The Department restricted the initial search of the medical literature to Level I evidence – systematic reviews and meta-analyses. Not only is this the strongest evidence available but it also has the additional property of representing the other levels of evidence. A systematic review is itself a review of the medical literature conducted using methods (including systematic search

22. For details on the development of the MSRB process, see the memos referenced in Appendix 1[page 18] of the "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005."
23. Rosenberg W, Donald A. "Evidence-based medicine: an approach to clinical problem solving" BMJ 1995; 310(6987): 1122–1126;
Strauss SE, Richardson WS, Glasziou P, Haynes RB Evidence-based Medicine: How to Practice and Teach EBM Edinburgh; Churchill Livingstone, 2005.

and retrieval of all the relevant primary source evidence and critical appraisal of the evidence found using standardized techniques) designed to minimize the likelihood of bias in the results. A meta-analysis is a systematic review in which quantitative methods are used to summarize the results of the review.[24]

Table 1: Levels of Evidence[25]

I	systematic reviews/meta-analyses of multiple randomized, controlled trials
II	randomized, controlled trials
IIIA	controlled studies without randomization
IIIB	other types of quasi-experimental study
IV	non-experimental descriptive studies
V	case series
VI	expert committee reports or opinions/clinical experience of respected authorities, or both

Using Level I evidence meant that the MSRB could review efforts by researchers who had already searched the medical literature for Level III and higher evidence, retrieved and reviewed these studies to determine their relevance and methodological quality, abstracted and evaluated their findings, synthesized the results, and submitted their findings to a peer-review process for publication in a scientific journal. This allowed the MSRB to leverage its resources to review a much larger body of evidence.

Second, the Department focused the search on the most recent studies, so as to best represent the most current information. The initial search was limited to articles from 1990 to the present and then extended back in time as needed, if there were an insufficient number of studies found in the first search.

Prior to beginning the literature search, the Department adopted a set of guidelines for determining when and how the searches would be extended. If at least 10 valid and unrelated references to systematic reviews were not found, the search was extended to look for all articles in category II (randomized controlled trials) from 1990 to the present and for all articles in category I (systematic reviews) in the entire database regardless of date.

The Department conducted the literature searches in two electronic bibliographic databases:

1. Medline through the PubMed portal at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi ; and,
2. The Cochrane Library (The Cochrane Database of Systematic Reviews, Database of Abstracts of reviews of Effects, and The Cochrane Central Register of Controlled Trials) through the Lumina portal of the University of Minnesota Libraries at http://tc.liblink.umn.edu/sfx_local/a-z/default.

PubMed is a service of the National Library of Medicine (NLM) available via the National Center

24. Guyatt G, Rennie D Users' Guides to the Medical Literature. Essentials of Evidence-Based Clinical Practice AMA Press, 2002; FOCUS "Critical Appraisal Tool". Available at: http://www.focusproject.org.uk/
25. Adapted from Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M "Levels of Evidence and Grades of Recommendation" Oxford Centre for Evidence-based Medicine, 1998. Available at: http://www.cebm.net/levels_of_evidence.asp

of Biotechnology's Entrez retrieval system. PubMed is a public access search engine for MEDLINE, NLM's premier bibliographic database for medical literature. MEDLINE contains bibliographic citations and author abstracts from more than 4,800 biomedical journals published in the United States and 70 other countries. The database contains over 12 million citations dating back to mid-1960.

The PubMed search for systematic reviews used a search string published in the medical literature that has been validated as both sensitive and specific for retrieving systematic reviews.[26] The search string was combined with key words identifying the medications as a group (e.g. "nonsteroidal anti-inflammatory") or individually (e.g. "ibuprofen"). The PubMed Search for randomized controlled trials used the PubMed limit terms "randomized controlled trial" and "controlled trial" in combination with key words identifying the medications as a group or individually.

The Cochrane Library consists of a regularly updated collection of evidence-based-medicine databases created by the Cochrane Collaboration, an international non-profit independent organization of health care providers and health care researchers. The Cochrane Library is a collection of evidence-based-medicine databases, which is up-dated quarterly from the best available information about healthcare interventions found in both published and unpublished medical studies from around the world. The Cochrane Database of Systematic Reviews (CDSR) is the collection of systematic reviews done by Cochrane Collaboration work groups. The Database of Abstracts of Reviews of Effects (DARE) contains summaries of systematic reviews done by others, which have met strict quality criteria established by the Cochrane Collaboration. Included reviews have to be about the effects of interventions. The Cochrane Central Register of Controlled Trials (CENTRAL) includes details of clinical trials found in bibliographic databases (notably MEDLINE and EMBASE), and other published and unpublished sources.

The Cochrane Library search for systematic reviews used the Cochrane Database of Systematic Reviews with key words identifying the medications as a group (e.g. "nonsteroidal anti-inflammatory") or individually (e.g. "ibuprofen").

A sufficient number of studies were obtained for each group of medications using these strategies that further extensions of the search were not needed. For each group of medications, the results of each search were saved as Word documents identifying the parameters of the search and displaying the title of the articles retrieved, their authors, and their journal citations.

The Department used the inclusion criteria developed by the MSRB's Medications Task Force to determine which of the studies found in the automated searches would be retrieved for further analysis. First, the title of the article was reviewed to confirm that the article was about the therapeutic use of the medication in humans. References for all the articles chosen for further review based on their titles were combined in an Excel database. The abstracts and bibliographical data were then retrieved for articles meeting the first screening, hyperlinked to the Excel database, and reviewed to determine if:

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26. Shojania KG, Bero LA. "Taking advantage of the explosion of systematic reviews: an efficient MEDLINE search strategy" Eff Clin Pract 2001; 4(4): 157-62.

- the article addressed one of the clinical questions of relevance;
- the article represented a study of the appropriate level of evidence;
- it was a study published during the search time frame;
- the article was published in English; and,
- the article was available on-line through the University of Minnesota Bio-Medical Library.

Articles selected for inclusion after a review of the article abstract were retrieved in electronic format from the University of Minnesota Bio-Medical Library through the Lumina portal. An electronic database was created listing the authors, the title of the article, and the journal reference. Each article's full text was then hyperlinked to its citation in the Department database. Retrieved articles were evaluated for quality using criteria that were appropriate to the study type.

For systematic reviews (Level I evidence), the criteria were adapted from recommendations for critical appraisal of systematic reviews, found in the peer-reviewed literature and textbooks of evidence-based medicine.[27] The chosen criteria represent the key quality issues in systematic reviews:

Was there a comprehensive search for studies using appropriate sources?
Were studies chosen based on explicit and appropriate criteria?
Was there a systematic evaluation of the evidence using appropriate methods?
Was the data analyzed appropriately?

For randomized controlled trials (Level II evidence), the quality criteria were adapted from recommendations for critical appraisal of randomized controlled trials, found in the peer-reviewed literature and textbooks of evidence-based medicine.[28] The chosen criteria represent the key quality issues in randomized controlled trials:

Were adequate steps taken to minimize any bias in the results of the trial?
Were the results appropriately analyzed for the relevant outcomes?
Were the patients and treatments well-enough described to allow full comparisons with other trials?

Articles were scored "yes", "no", "can't tell" on each item. A summary score was determined by adding together the "yes" responses, divided by the total number of criteria (22 in the case of systematic reviews and 12 in the case of randomized controlled trials) and then expressed as a percentage. This scoring system is a short hand way of indicating overall study quality and is similar to systems used in many systematic reviews for evaluating primary source literature.

In addition, the author's conclusions regarding the medication were abstracted, along with the

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27. Oxman AD, Cook DJ, Guyatt GH "Users' guides to the medical literature. VI How to use an overview" Journal of the American Medical Association 1994; 272(17): 1367-1371;
FOCUS "Critical Appraisal Tool" Available at: http://www.focusproject.org.uk/;
Crombie IK The Pocket Guide to Critical Appraisal: A Handbook for Healthcare Professionals London; BMJ Publishing Group, 1996. Available at the University of Minnesota Biomedical Library.

28. Oxman AD, Cook DJ, Guyatt GH "Users' guides to the medical literature. VI How to use an overview" Journal of the American Medical Association 1994; 272(17): 1367-1371;
Guyatt GH, Sackett DL, Cook DJ "Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid?" Journal of the American Medical Association 1993; 270(21): 2598-601;
Crombie IK The Pocket Guide to Critical Appraisal: A Handbook for Healthcare Professionals London; BMJ Publishing Group, 1996. Available at the University of Minnesota Biomedical Library.

primary literature relied upon by the author(s) of the systematic review in reaching their conclusions. The results of the quality review, the author's conclusions – along with the number of studies supporting each conclusion –, and the bibliography of the primary source literature were entered into a "Summary Sheet" for each article. These Summary Sheets were then also hyperlinked to the Department database.

The abstracted conclusions from each systematic review, with the number of supporting studies, were also transferred to spreadsheets. There the conclusions were arranged thematically into columns for comparison across systematic reviews. The primary source articles obtained from each systematic review were combined in a separate database, cross-referenced by review article.

Finally, the findings made by each article's author(s) were abstracted, along with the number of primary source studies relied on by the author(s), and arranged by article in another database. These findings were then arranged by themes from the abstracted findings by arranging them into the fewest mutually exclusive categories.

Draft conclusions and recommendations were then derived from the findings and set out in a report to the MSRB. The report, as well as all of the work products of the process, was submitted to the MSRB for review. After the MSRB approved the conclusions and recommendations for a group of medications, draft rules were prepared and circulated to the members of the MSRB and interested parties in the community. All of the comments and suggestions received were collated and presented to the MSRB for consideration. Based on these deliberations the MSRB made further recommendations that were incorporated into subsequent rule drafts. These were then circulated and the process of comment and reconsideration by the MSRB repeated. The rules as proposed in this part are the result of this extensive review of literature and deliberations by the department's medical consultant and the MSRB.

Need and Reasonableness of the Medication Rule Subparts:

Subpart 1. Scope. This subpart first limits application of the medication rules to the use of medication in an outpatient setting. Medication management in an inpatient setting is more complex since the patients tend to be sicker and more likely to receive additional medication while hospitalized. This subpart also provides that subparts 2 to 4 do not require a health care provider to prescribe any class of drugs in the treatment of any patient. This is necessary to ensure that the parameters do not interfere with the judgment of a health care provider in determining what class of medication (NSAID, opioid or muscle relaxant) is needed for the relief of pain. Instead, the parameters reflect what the scientific research says about how to use each class of drug once the provider has made the decision to use it.

Subpart 2. Nonsteroidal anti-inflammatory drugs (NSAIDs). This subpart defines non-steroidal anti-inflammatory drugs, which are drugs with analgesic, antipyretic and anti-inflammatory effects. The term "non-steroidal" is used to distinguish these drugs from steroids. NSAIDs act as inhibitors of the enzyme cyclooxygenase. This definition is based on information from The American Heritage Stedman's Medical Dictionary, Second Edition, 2004, [29] and Dorland's

29. Also see, http://encyclopedia.thefreedictionary.com/Nonsteroidal+anti+inflammatory+drug

Medical Dictionary for Health Care Consumers.[30] This definition is necessary to clearly identify the type of drugs this subpart applies to.

Subpart 2 also provides that, for the purposes of this rule, NSAIDs include diflunisal but not other salicylates or acetaminophen. Acetaminophen and salicylates other than diflunisal are rarely used in prescription strength and have different side-effect profiles. The analyses done as the basis for subpart 2 did not include these drugs and so they are excluded from the rule.

Subpart 2 next describes that NSAIDS can be divided into two groups, nonselective NSAIDs and COX-2 inhibitors.. This definition is based on information from The American Heritage Stedman's Medical Dictionary, Second Edition, and Dorland's Medical Dictionary for Health Care Consumers. Examples of nonselective NSAIDs and a COX-2 inhibitor are listed. The examples include all of the commonly prescribed NSAIDs of both classes.

Item A. This item explains that NSAIDs are indicated for the symptomatic relief of acute and chronic musculoskeletal pain, and that they must be prescribed at the lowest clinically effective dose, as determined by the prescribing health care provider, but not to exceed the manufacturer's maximum daily dosage. This item is based on the Recommendation made by the MSRB to DLI that:

> **I. NSAIDs are indicated for the relief of musculoskeletal pain.** [31]

This recommendation was based on the conclusions drawn by the MSRB from its review of the available medical evidence that:

> *"There is extensive evidence that NSAIDs (both nonselective and COX-2 inhibitors) are more effective than placebo in relieving symptoms of musculoskeletal pain, at least in the short term."* [32]

This item defers to the prescribing provider's professional judgment in determining the proper dose based on the clinical examination and consultation with the patient, so long as the manufacturer's maximum daily dosage is not exceeded.

Item B provides that when treating musculoskeletal pain, a generic nonselective-NSAID is indicated unless a COX-2 inhibitor is indicated as specified in item C. The rule is based on the Recommendation made by the MSRB to DLI that:

> **II. Except in certain patients, a nonselective-NSAID is indicated if an NSAID is prescribed.**[33]

This recommendation was based on the conclusions drawn by the MSRB from its review of the

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30. Available online at: http://www.mercksource.com/pp/us/cns/cns_hl_dorlands_split.jsp?pg=/ppdocs/us/common/dorlands/dorland/nine/000955149.htm
31. "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" Recommendation #I [page 16]
32. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #1, page 10).
33. "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" Recommendation #II [page 16]

medical and scientific literature that:

> *There is extensive evidence that there are no clinically significant differences in efficacy between non-selective NSAIDs and COX-2 inhibitors at equipotent doses.*[34]

There are differences in safety between nonselective NSAIDs and COX-2 inhibitors, but these are clinically important only for certain subgroups of patients as described in item C. As there is no difference in effectiveness between NSAIDs (both nonselective and COX-2 inhibitors) other factors can be used to determine which particular drugs are preferred. The other factors of importance are availability and price. Generic nonselective-NSAIDs are widely available and overall have the lowest cost.

Subitem (1) provides that, when a nonselective NSAID is used, treatment must begin with generic ibuprofen or generic naproxen, unless there is a medical contraindication documented by the prescribing health care provider to each of the medications in this item. As there is no difference in effectiveness between nonselective NSAIDs, other factors can be used to determine which particular drugs are preferred. The other factors of importance are safety, availability and price. Ibuprofen and naproxen are associated with the lowest risk of gastrointestinal side effects among nonselective-NSAIDs, at commonly prescribed doses. Generic ibuprofen and generic naproxen are the least expensive and of roughly equal price based on the maximum allowable cost (MAC/FUL) list for the drugs established by the Minnesota Department of Human Services for state health care programs under Minnesota Statutes, section 256B.0625, subdivision 13e.[35] If there is a medical contraindication, treatment may begin with any other generic nonselective NSAID. This item is based on the Recommendations made by the MSRB to DLI that:

> **II. Except in certain patients, a nonselective-NSAID is indicated if an NSAID is prescribed.**[36]
>
> **IV. Among the nonselective-NSAIDs, ibuprofen and naproxen are preferred at the lowest clinically effective dose but not to exceed the manufacturer's maximum daily dosage, and for the shortest duration needed.**[37]

These recommendations were based on the conclusions drawn by the MSRB from its review of the medical and scientific literature that:

> *There is extensive evidence that there are no clinically significant differences in efficacy among non-selective NSAIDs at equipotent doses;* [38] and

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34. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #3, page 11).
35. Available at: http://www.dhs.state.mn.us/main/idcplg?IdcService=GET_DYNAMIC_CONVERSION&RevisionSelectionMethod=LatestReleased&dDocName=dhs16_138248 (Click on the "State MAC/FUL link.)
36. "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" Recommendation #II [page 16]
37. "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" Recommendation #IV [page 17]
38. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #2, page 11).

There is extensive evidence that there are increased gastrointestinal adverse effects with NSAID use but the risk varies dramatically by agent and dose.[39]

i. Risk is lower at lower doses.

ii. Among nonselective NSAIDs, risk is lowest for ibuprofen and diclofenac;[40] intermediate for naproxen, sulindac, and indomethacin; highest for piroxicam, tolmetin, and ketoprofen.

iii. Risk is highest for patients > 60 years old and patients with a history of gastrointestinal disease.

Subitem (2) provides that other generic nonselective-NSAIDs are not indicated unless one-week trials of each of ibuprofen and naproxen have been ineffective in reducing the patient's pain by at least 50% as determined by the prescribing health care provider. Again, it is the health care provider's judgment about the effectiveness of the medication that determines whether other generic nonselective-NSAIDs are indicated. The rule reflects the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications. Medication trials are typically at least a week in duration as this would be the typical follow-up period in the treatment of acute musculoskeletal injury. Pain relief of 50% is the standard used in scientific studies of analgesics to determine efficacy of pain relief.

Subitem (3) provides that nonselective-NSAIDs that are not available as generics are not indicated. This reflects the same evidence-based recommendation of the MSRB that was used as the basis of subitem (1).

Item C provides that a COX-2 inhibitor may be indicated instead of a nonselective NSAID for (1) patients over 60 years of age; (2) patients with a history of gastrointestinal bleed or peptic ulcer disease; or, (3) patients with a history of gastrointestinal side effects with nonselective-NSAID use. There is good evidence that both COX-2 inhibitors and concurrent gastroprotective medications reduce the risk of gastrointestinal side effects. There is no evidence that COX-2 inhibitors or concurrent gastroprotective medication is superior in reducing the risk of gastrointestinal side effects, in general. Therefore, the choice can be based on other factors. The other factors that may be considered are ease of administration, effects on patient compliance, availability and price. However, for any patient meeting any of the criteria of subitems 1 through 3 who is taking aspirin or who is at an increased risk of cardiovascular disease, a COX-2 inhibitor is not indicated and a nonselective NSAID is indicated as allowed in items A and B, together with gastroprotective medication. This item is based on the Recommendations made by the MSRB to DLI:

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39. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusions #4, page 12).

40. This conclusion was modified at the February 2009 MSRB meeting on the basis of new high quality evidence submitted by an interested party that showed diclofenac to have a substantially higher cardiovascular risk than ibuprofen. The MSRB recommended removing diclofenac as one of the preferred starting medications in subitem (1). See, MRSB Minutes February 12, 2009.

III. COX-2 inhibitors or concurrent gastroprotective medication are indicated for patients over 60 years of age, patients with a history of gastrointestinal disease, or patients with a history of gastrointestinal side effects with nonselective-NSAID use.

BUT for persons in this category – based on the available evidence – gastroprotective medication is preferred, if:

i. the patient is taking aspirin; or,

ii. the patient is at increased risk of cardiovascular disease.[41]

The above recommendations were based on the conclusions drawn by the MSRB from its review of the medical and scientific literature that:

There is extensive evidence that there are increased gastrointestinal adverse effects with NSAID use but the risk varies dramatically by agent and dose. [42]

i. Risk is lower at lower doses.

ii. Among nonselective NSAIDs, risk is lowest for ibuprofen and diclofenac; intermediate for naproxen, sulindac, and indomethacin; highest for piroxicam, tolmetin, and ketoprofen.

iii. Risk is highest for patients > 60 years old and patients with a history of gastrointestinal disease.

There is extensive evidence that the risk of gastrointestinal side effects is lower with COX-2 inhibitors than with all non-selective NSAIDs but still higher than placebo.

i. There is limited evidence that the gastrointestinal benefit of COX-2 inhibitors is reduced in patients using aspirin.[43]

ii. There is good evidence that gastrointestinal side effects attributed to nonselective NSAIDs can be significantly reduced by the use of misoprostol, H2 receptor agonists, and proton pump inhibitors.

There is limited but uncontradicted evidence that there is no difference between nonselective-NSAIDs and COX-2 inhibitors in the rate of total adverse side effects.[44]

There is limited evidence of an increased risk of severe cardiovascular side effects with

41. "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" Recommendation #III [pages 16 to 17]
42. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #4, page 12).
43. See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #5, page 13).
44 See "Summary Tables of Medical Evidence on NSAIDs" in Appendix A; and in "REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005" (Conclusion #6, page 14).

COX-2 inhibitors.[45]

There is good evidence that NSAIDs increase blood pressure in patients treated with anti-hypertensive medications.[46]

Item D provides that NSAIDs are indicated only for the shortest duration needed as determined by the prescribing health care provider, and that:

(1) NSAIDs prescribed within the first four weeks after the date of injury are limited to no more than 2 weeks of medication per prescription or refill.
(2) NSAIDs prescribed more than 4 weeks after the date of injury may not be for more than one month of medication per prescription or refill.
(3) NSAIDs prescribed more than 12 months after the date of injury may not be for more than three months of medication per prescription or refill.

This rule reflects the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications and in consideration of the natural history of musculoskeletal disorders. The majority of musculoskeletal injuries are resolved in a few weeks, so early prescriptions should be limited in time, with frequent reevaluation. Conditions that persist are not likely to resolve quickly, and so prescriptions for longer periods of time are reasonable.

Subpart 3. Opioid Analgesics.

This subpart governs the use of opioid analgesics, sometimes referred to as narcotics. An opioid is any agent that binds to opioid receptors. There are three broad classes of opioids: opium alkaloids, such as morphine and codeine; semi-synthetic opioids such as heroin and oxycodone; and fully synthetic opioids such as pethidine and methadone. Opioid analgesics include codeine, hydrocodone, levorphanol, methadone, morphine, hydromorphone, and oxycodone. This definition is based on information from The American Heritage Stedman's Medical Dictionary, Second Edition, and Dorland's Medical Dictionary for Health Care Consumers. It is necessary to define “opioid” to clearly identify the medication to which this subpart applies.

Item A provides that opioid analgesics are indicated for the symptomatic relief of acute and chronic pain that has been inadequately relieved by non- opioid medications. Opioid analgesics must be prescribed at the lowest clinically effective dose, as determined by the prescribing health care provider. This item is based on the following Recommendations made by the MSRB to DLI:

I. Narcotic analgesics are indicated for the relief of moderate to severe pain not adequately treated by non-narcotic analgesics. [47]

III. Narcotics should be used at the lowest effective dose to minimize adverse effects and avoid paradoxical increases in pain.[48]

45 See “Summary Tables of Medical Evidence on NSAIDs” in Appendix A; and in “REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005” (Conclusions #7, page 15).
46 See “Summary Tables of Medical Evidence on NSAIDs” in Appendix A; and in “REPORT TO THE MSRB. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS. October 13, 2005” (Conclusions #8, page 15).
47. “REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006” Recommendations #I [page 16]
48. “REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006” Recommendations #III [page 16]

The recommendations were based on the conclusions drawn by the MSRB from its review of the medical and scientific literature:

> *There is extensive evidence that narcotic analgesics are more effective than placebo in relieving both acute and chronic pain.*[49]
>
> *There is extensive evidence that adverse effects - dizziness, drowsiness, nausea, vomiting, headache, and constipation - occur frequently with the use of narcotics to treat both acute and chronic pain. Meperidine has unique adverse effects in excess of other narcotics.*[50]
>
> *There is extensive evidence that the adverse effects of narcotics are dose dependent.*[51]

Again, this item provides that the provider has the discretion, in consultation with the patient, to determine the lowest clinically effective dose. The rule does not reference a maximum manufacturer's dose because opioid analgesics do not have maximum dosages, due to the nature of opioid drugs.

Item B provides that when treating pain, a generic oral opioid analgesic is indicated. While administration by way of intramuscular or intravenous injection may also be indicated, these rules do no address those routes of administration.

Subitem (1) provides that when an oral opioid analgesic is used for the symptomatic relief of acute or chronic pain, treatment must begin with one of the following: generic codeine, generic hydrocodone, generic oxycodone, or generic morphine, unless there is a medical contraindication documented by the prescribing health care provider. However, if there is a medical contraindication documented by the prescribing health care provider to each of the medications in this item, then treatment may begin with any other generic oral opioid analgesic. The prescribing doctor must determine and document when there is a medical contraindication to the use of one of the listed generic drugs. The rule is based on the following Recommendations made by the MSRB to DLI:

> **II. All narcotics and narcotic formulations are equally effective in relieving both acute and chronic pain at equipotent dosing schedules.**[52]

As there is no difference in effectiveness between various oral opioids, other factors can be used to determine which particular drugs are preferred. The other factors of importance considered by the MSRB were availability and price. The most widely available and least expensive generics are indicated. Generic codeine, generic hydrocodone, generic oxycodone, and generic morphine are widely available at the lowest costs based on the state maximum allowable cost (MAC/FUL) list for the drugs established by the Minnesota Department of Human Services for state health care

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49. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006"(Conclusion #1, pages 9-10).
50. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006"(Conclusion #4,[pages 12-14).
51. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006"(Conclusion #5, pages 12-14).
52. "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006" Recommendation #II [page 16]

programs under Minnesota Statutes, section 256B.0625, subdivision 13e. [53]

The recommendations were based on the following conclusions drawn by the MSRB from its review of the medical and scientific literature:

> *There is no evidence that there are any clinically significant differences in effectiveness among narcotics in the treatment of either acute or chronic pain at equipotent doses.*[54]
>
> *There is no evidence that there are any clinically significant differences in effectiveness between immediate-release and sustained-release narcotic formulations in the treatment of either acute or chronic pain at equipotent dosing schedules.*[55]

Subitem (2) provides that other generic opioid analgesics are not indicated for oral use for the symptomatic relief of acute or chronic pain unless one-week trials of each of hydrocodone, oxycodone, and morphine have been ineffective in reducing the patient's pain by at least 50% as determined by the prescribing health care provider. This reflects the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications. Medication trials are typically at least a week in duration as this would be the typical follow-up period in the treatment of acute musculoskeletal injury. Pain relief of 50% is the standard used in the scientific studies of analgesics to determine efficacy of pain relief.

Subitem (3) provides that generically available combinations of an oral opioid and a non-opioid analgesic may be prescribed instead of the opioid analgesic as otherwise allowed under subitems 1 and 2. The rule reflects the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications. Since evidence supports the use of both opioid and non-opioid analgesics in the treatment of musculoskeletal pain, combinations of opioid and non-opioid analgesics are not only effective but clinical experience indicates that a combination allows the use of both medications in lower doses than might be needed if either were used alone.

Subitem (4) provides that oral opioid analgesics that are not available as generics and combinations of an oral opioid analgesic and a non-opioid analgesic that are not available as generics are not indicated. This reflects the same evidence-based recommendation from the MSRB that was used as the basis of subitem (1).

Item C provides that a course of oral opioid analgesics or combination of an oral opioid and a non-opioid analgesic is limited as follows:

(1) Oral opioid analgesics prescribed within the first four weeks after the date of injury are limited to no more than 2 weeks of medication per prescription.

(2) Oral opioid analgesics prescribed more than 4 weeks after the date of injury may not be

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53. Available at: http://www.dhs.state.mn.us/main/idcplg?IdcService=GET_DYNAMIC_CONVERSION&RevisionSelectionMethod=LatestReleased&dDocName=dhs16_138248; and click on the "State MAC/FUL link

54. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006" (Conclusion #2, page 10).

55. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006"(Conclusion #3, page12).

for more than one month of medication per prescription.
(3) Oral opioid analgesics prescribed more than 12 weeks after the injury may be for more than one month of medication per prescription if there has been a clinical evaluation to confirm the need for and efficacy of the prescription and a clinical evaluation at least every six months thereafter during continued use of opiate analgesics.

This rule reflects the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications and the natural history of musculoskeletal disorders. The majority of musculoskeletal injuries are resolved in a few weeks and so prescriptions should be limited in duration. Conditions that persist are not likely to resolve quickly, and so longer prescriptions may be appropriate.

Item D provides that meperidine is not indicated in the treatment of acute or chronic pain. This item is based on the following Recommendation made by the MSRB to DLI:

> **IV. Meperidine has unique adverse risks that make it an undesirable treatment option.**[56]

The recommendations were based on the following conclusion drawn by the MSRB from its review of the medical and scientific literature:

> *There is extensive evidence that adverse effects - dizziness, drowsiness, nausea, vomiting, headache, and constipation - occur frequently with the use of narcotics to treat both acute and chronic pain. Meperidine has unique adverse effects in excess of other narcotics.*[57]

Item E provides that transcutaneous (skin patch) opioid analgesics are only indicated in patients with a documented disorder that prevents adequate oral dosing. This item is based on the following conclusions drawn by the MSRB from its review of the medical and scientific literature:

> *There is no evidence that there are any clinically significant differences in effectiveness among narcotics in the treatment of either acute or chronic pain at equipotent doses.*[58]

> *There is no evidence that the adverse effects of narcotics [other than meperidine] vary by agent or formulation at equipotent dosing schedules.*[59]

As there is no difference in effectiveness between various opioid formulations (oral, transcutaneous, oral transmucosal, and buccal) at equivalent doses, other factors can be used to determine which particular drugs are preferred. The other factors of importance considered by the MSRB in regard to transcutaneous formulations were availability and price. The most widely available and least expensive generics are indicated in item B subitem (1). Generic oral codeine, hydrocodone, oxycodone, and morphine are widely available at a lower cost than the

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56. "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006" Recommendation #IV [page 16]
57. "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006" Conclusion #4 [pages 12-14]
58. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006" (Conclusion #2, page 10).
59. See "Summary Tables of Medical Evidence on Opioid Analgesics" in Appendix B; and in "REPORT TO THE MSRB. NARCOTIC ANALGESICS June 20, 2006"(Conclusion #6, page 14).

transcutaneous preparation based on the state maximum allowable cost (MAC/FUL) list for the drugs established by the Minnesota Department of Human Services for state health care programs under Minnesota Statutes, section 256B.0625, subdivision 13e.[60] Therefore, transcutaneous formulations are only indicated in patients with a disorder that prevents adequate oral dosing.

Item F provides that oral transmucosal (skin patch) preparations and buccal preparations (which dissolve under the tongue, in the cheek or as a lollipop) are only indicated for the treatment of breakthrough pain and only in patients with a documented disorder that prevents adequate dosing with swallowed medications. This reflects the same evidence-based recommendation from the MSRB that was used as the basis of item E.

Subpart 4. Muscle Relaxants. This subpart provides that a muscle relaxant is a drug which decreases the tone of a muscle. This definition is based on information from The American Heritage Stedman's Medical Dictionary, Second Edition, and Dorland's Medical Dictionary for Health Care Consumers. This subpart also states that muscle relaxants include carisoprodol, chlorzoxazone, cyclobenzaprine, metaxalone, methocarbamol, orphenadrine, and tizanide. These examples include all of the muscle relaxants commonly prescribed in the treatment of musculoskeletal injuries. These are the drugs which were included in the analyses reviewed by the MSRB upon which their recommendations are based. The definition, corresponding examples of muscle relaxants, and the exclusion of medication used to treat spasticity, are necessary to identify the drugs to which the subpart applies.

Item A provides that muscle relaxants are indicated for the symptomatic relief of acute and chronic musculoskeletal pain. Muscle relaxants must be prescribed at the lowest clinically effective dose, as determined by the prescribing health care provider, but not to exceed the manufacturer's maximum daily dosage. This item is based on the following Recommendations made by the MSRB to DLI:

> **I. Muscle relaxers are indicated for the relief of musculoskeletal pain.**[61]

There is sufficient evidence of the efficacy of muscle relaxants in the published literature. High quality systematic reviews almost unanimously come to the same conclusion. The only dissenting review [of the seven analyzed by the MSRB] based its conclusion on a single RCT.
This recommendation was based on the following conclusions drawn by the MSRB from its review of the medical and scientific literature:

> *There is sufficient high quality evidence that muscle relaxers are more effective than placebo in relieving symptoms of musculoskeletal pain, at least in the short term.*[62]
>
> *The clinical benefit of muscle relaxers is modest.*[63]

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60. Available at: http://www.dhs.state.mn.us/main/idcplg?IdcService=GET_DYNAMIC_CONVERSION&RevisionSelectionMethod=LatestReleased&dDocName=dhs16_138248; and click on the "State MAC/FUL link.
61. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" Recommendation #I [page 16]
62. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006"(Conclusion #1, page 12).
63. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006"(Conclusion #2, page 13).

A substantial proportion of patients taking muscle relaxers have side effects, most often drowsiness, and most often mild.[64]

i. Side effects are dose-related.

ii. Some muscle relaxers have a potential for addiction at doses higher than those typically used in treatment of musculoskeletal pain.

Item B provides that, when treating musculoskeletal pain, a generic muscle relaxant is indicated.

Subitem (1) provides that, when a muscle relaxant is used, treatment must begin with one of the listed generic drugs, unless there is a medical contraindication documented by the prescribing health care provider to each of the medications in this item. Generic carisoprodol, generic chlorzoxazone, generic cyclobenzaprine, generic methocarbamol, and generic tizanide are the least expensive and of roughly equal price based on the state maximum allowable cost (MAC/FUL) list for the drugs established by the Minnesota Department of Human Services for state health care programs under Minnesota Statutes, section 256B.0625, subdivision 13e. [65] This subitem is based on the following Recommendation made by the MSRB to DLI:

II. All of the muscle relaxers studied are equally effective; the least expensive generic preparation should be prescribed unless the patient is, or proves to be, intolerant of that medication.[66]

This recommendation was based on the following conclusion drawn by the MSRB from its review of the medical and scientific literature:

There is no evidence that any one of the muscle relaxers studied is any more effective than the others. In head-to-head trials, different muscle relaxers have been found to be equally effective.[67]

As there is no demonstrated difference in effectiveness or safety between muscle relaxers other factors can be used to determine which particular drugs are preferred. The other factors of importance considered by the MSRB were availability and price. Generic carisoprodol, generic chlorzoxazone, generic cyclobenzaprine, generic methocarbamol, and generic tizanide are widely available, the least expensive and of roughly equal price based on the state maximum allowable cost (MAC/FUL) list for the drugs established by the Minnesota Department of Human Services for state health care programs under Minnesota Statutes, section 256B.0625, subdivision 13e. [68]

Subitem (2) provides that metaxolone and orphenadrine (the more expensive muscle relaxants) are

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64. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006"(Conclusion #5, page 14).
65. Available at:
http://www.dhs.state.mn.us/main/idcplg?IdcService=GET_DYNAMIC_CONVERSION&RevisionSelectionMethod=LatestReleased&dDocName=dhs16_138248
66. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" Recommendation #II [page 16]
67. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" (Conclusion #3, page 13).
68. Available at:
http://www.dhs.state.mn.us/main/idcplg?IdcService=GET_DYNAMIC_CONVERSION&RevisionSelectionMethod=LatestReleased&dDocName=dhs16_138248

not indicated unless one-week trials of each of other specified drugs have been ineffective in reducing the patient's pain by at least 50% as determined by the prescribing health care provider. This rule reflects the consensus recommendation of the MSRB after carefully considering athe practice experience of its health care provider members in treating injured workers with medications. Medication trials are typically at least a week in duration as this would be the typical follow-up period in the treatment of acute musculoskeletal injury. Pain relief of 50% is the standard used in scientific studies of analgesics to determine efficacy of pain relief.

Subitem (3) provides that generically available combinations of a muscle relaxant and an analgesic may be prescribed instead of the muscle relaxant as otherwise allowed under subitems 1 and 2. This subitem is based on the following recommendation made by the MSRB to DLI:

III. Muscle relaxers can be used in combination with other analgesics.[69]

This recommendation was based on the following conclusion drawn by the MSRB from its review of the medical and scientific literature:

> *Muscle relaxers in combination with an analgesic is more effective than analgesic alone.*[70]

There was only one high quality RCT (of the 2 systematic reviews, 4 RCTs and 2 controlled trials considered by the MSRB) that found no benefit of combined treatment over NSAID alone.

Subitem (4) provides that muscle relaxants, and combinations of a muscle relaxant and an analgesic, that are not available as generics are not indicated. This reflects the same evidence-based recommendation from the MSRB that was used as the basis of subitem (1).

Item C provides that a course of muscle relaxants or combination of a muscle relaxant and an analgesic is limited as follows:

(1) Muscle relaxants prescribed within the first four weeks after the date of injury are limited to no more than 2 weeks of medication per prescription or refill.
(2) Muscle relaxants prescribed more than 4 weeks after the date of injury may not be for more than one month's worth of medication per prescription or refill.
(3) Treatment with muscle relaxants for more than three consecutive months is not indicated.

Subitems (1) and (2) reflect the consensus recommendation of the MSRB after carefully considering the practice experience of its health care provider members in treating injured workers with medications, and in consideration of the natural history of musculoskeletal disorders. The majority of musculoskeletal injuries are resolved in a few weeks, and so shorter prescription durations are appropriate. The limitation of treatment with muscle relaxants to three consecutive months or less in subitem (3) is based on the following recommendation made by the MSRB to DLI:

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69. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" Recommendation #III [page 16]
70. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" (Conclusion #6, page 15).

IV. Muscle relaxers are only indicated for short courses of therapy.[71]

The available evidence suggests that the duration of benefit is limited. The recommendation was based on the following conclusions drawn by the MSRB from its review of the medical and scientific literature:

> *There is sufficient high quality evidence that muscle relaxers are more effective than placebo in relieving symptoms of musculoskeletal pain, at least in the short term.*[72]

Item D provides that benzodiazepines are not indicated as muscle relaxants for the symptomatic relief of acute and chronic musculoskeletal pain. The rule is based on the following recommendation made by the MSRB to DLI:

V. There is no evidence to support the use of benzodiazepines as a muscle relaxant.[73]

The available evidence does not show any clinical superiority of benzodiazepines over the muscle relaxers studied. Given the more significant safety issues and addiction problems with benzodiazepines they are not recommended for use as muscle relaxants.

The recommendation was based on the following conclusion drawn by the MSRB from its review of the medical and scientific literature:

> *There is no evidence that muscle relaxers are any more or less effective than benzodiazepines.* [74]

Part 5221.6200 Low back pain

Subpart 1. Diagnostic procedures for treatment of low back injury.

Item A. Subitem (1) is amended to add new ICD-9 codes to the list of codes that reflect the narrative description of regional low back pain.[75] This is necessary to reflect updates to the ICD-9 codes that may be used to describe regional low back pain. Existing ICD-9 codes in the 722 listing describe intervetebral disc disorders. The additional codes are: 722.8: postlaminectomy syndrome; 722.80: postlaminectomy syndrome unspecified; and 722.83: postlaminectomy syndrome, lumbar region. ICD-9 codes in the 846 category are for sprains and strains of ligaments and adjacent muscles; the new 846.0 is the diagnostic code for sprains and strains of the lumbrosacral joint or ligament. Diagnostic code 922.31 is for contusion of the back.

Subitem (2) is also amended to add new ICD-9 codes that reflect the narrative description of radicular pain. Code 722.11 is for thoracic intervetebral disc without myelopathy; 722.8: postlaminectomy syndrome; 722.80: postlaminectomy syndrome unspecified; and 722.83:

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71. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" Recommendation #IV [page 16]
72. See "Summary Tables of Medical Evidence on Muscle Relaxers" in Appendix C; and in "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006"(Conclusion #1, page 12).
73. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006" Recommendations #V [page 16]
74. "REPORT TO THE MSRB. MUSCLE RELAXERS April 20, 2006"Conclusion #4 [page 13]
75. See footnote 7. ICD-9 codes can also be viewed online at http://eicd9.com/index.php?action=contents

postlaminectomy syndrome, lumbar region. The additional codes in the 722 category appear in both subitems (1) and (2) because the codes refer to a pathology that can result in either clinical condition.

Item I. This item is revised to more clearly describe type of functional capacity assessment or evaluation (FCE) that is governed by the rule, at the recommendation of a physical therapist member of the MSRB. There has been confusion about what type of FCE is governed by the existing rule, and because the existing subitem 4 of the rule provides that only one FCE is indicated per injury, clarification is necessary.

The only type of FCE that the proposed rules govern is the extensive evaluation performed when it is necessary to develop permanent restrictions. These are referred to throughout item I as "comprehensive" FCEs to distinguish them from other types, which either have CPT codes assigned because they are part of a physical therapy treatment modality, or because they are part of work hardening (both of which are already governed by other parts of the treatment parameters). Because the rule governs only "comprehensive" FCEs, and not the more limited type performed as part of ongoing physical therapy treatment or work hardening, the description of the FCE is amended to more clearly describe the activities that are part of the evaluation. A comprehensive FCE is designed to measure permanent restrictions or determine ability to perform a specific job, and so the new language refers to the patient's current level of function and work-related tasks as well as the ability to sustain the tasks over time.

Subitem 1 is amended to reflect that the comprehensive FCE is not indicated during the period of initial nonsurgical management, because continued improvement can be expected.

Subitem 2 is also amended to reflect that a comprehensive FCE is indicated when permanent, rather than temporary, restrictions must be identified.

Subitem 3 is amended to standardize language for consistency throughout the rule by using "indicated" rather than "appropriate." The other changes to this subitem are intended to use language that more clearly describes when a comprehensive FCE should not be used - to evaluate change in performance during a course of treatment, when continued improvement is anticipated and therefore permanent restrictions would be premature.
Subitem 4 is amended to clarify that it is the extensive comprehensive FCE that is limited to once per injury.

Subitem 5 is added to describe what services are not considered part of a comprehensive FCE. These evaluations may be performed by a therapist during treatment or during a work hardening program, and therefore it may be appropriate to evaluate functional status on a more limited basis, more often than once per injury before permanent restrictions are needed.

Subpart 3. Passive treatment modalities. This subpart is amended to include additional types of modalities that are used to provide the passive treatment listed. These descriptions and examples were developed in consultation with the MSRB and reflect changes in terminology, technology and health care provider techniques and practices in order to clarify application of the rule. The examples given are not exhaustive because technology continues to evolve.

Item E. The amendments to item E update the additional types of modalities that provide electrical muscle stimulation. Muscle stimulation, low-volt therapy, sine wave therapy, and stimulation of peripheral nerves are examples of additional techniques and technology used to provide electrical muscle stimulation.

Item F. This item is amended to provide a description of mechanical traction and a list of examples of types of mechanical traction. The description is needed because there have been questions about whether the listed technologies and methods are all forms of traction.

Item G. Acupressure is removed from the definition of acupuncture because acupressure is now considered part of manual therapy. The deleted language related to endorphin-mediation was a hypothesis about the mechanism of action and is not needed to describe the service.

Item H. The examples of manual therapy are expanded to include myofascial release, joint mobilization and manipulation, manual lymphatic drainage, soft-tissue mobilization and manipulation, trigger point therapy, acupressure, muscle stimulation -manual (nonelectrical), and any form of massage.

Subpart 8. Durable medical equipment.

The amendment to item D of this subpart adds a cross reference to the low back conditions described in subpart 1, item A because these are the conditions to which this subpart specifically applies.

Subpart 10. Scheduled and nonscheduled medication.

The amendments to this subpart delete language related to controlled substances because prescription of opiods (narcotics) and muscle relaxants are now governed by the new medication treatment parameters in part 5221.6105. The amendments also require the provider to document the rationale for the use of all medication prescribed as required by Minn. State. § 176.135, subd. 7 and Minn. R. 5221.0700, subp. 2. Finally, the amendment cross references the new part 5221.6105.

Part 5221.6205. Neck pain

Subpart 1. Diagnostic procedures for treatment of neck injury.

Item A. Subitem (1) is amended to add new ICD-9 codes to the list of codes that reflect the narrative description of regional neck pain. This is necessary to reflect updates to the ICD-9 codes since the rules were initially adopted in 1995. Existing ICD-9 codes in the 722 listing describe intervetebral disc disorders. The additional codes are: 722.0: Displacement of cervical intervertebral disc without myelopathy; 722.2: Displacement of intervertebral disc, site unspecified, without myelopathy; 722.39: Schmorl's nodes, other; 722.8: postlaminectomy syndrome; 722.80: postlaminectomy syndrome unspecified; and 722.81: postlaminectomy syndrome, cervical region; 738.2: acquired deformity of neck; and 847.9: sprains and strains of joints and adjacent muscles; unspecified site of back. Code 926.12 (the erroneously included crushing injury of buttock) is replaced by 926.11 (crushing injury of back).

Subitem 2, governing radicular pain, is amended to add the following ICD-9 codes: 722.8: postlaminectomy syndrome; 722.80: postlaminectomy syndrome unspecified; and 722.81: postlaminectomy syndrome, cervical region; and 724.9: other unspecified back disorders. (Code 724.9 is deleted because it is for spinal stenosis "other than cervical," unspecified region.)

Subitem 4, governing cervical compressive myleopathy, is amended to add ICD-9 code 336.9: (Hereditary and degenerative diseases of the central nervous system; unspecified disease of spinal cord).

Item I. This item, governing comprehensive functional capacity evaluations, is amended so that it is identical to item I of part 5221.6200 for low back pain and part 5221.6210 for thoracic back pain because the purpose and indications for comprehensive FCEs does not vary by the type or location of the injury. The language in subitems (3) and (4) is new language because the concepts were inadvertently omitted from this part when it was initially adopted in 1995.

Subpart 3. Passive treatment modalities.

Items E, F, G and H include the same amendments as those for low back pain, because the descriptions and examples of the types of modalities listed are consistent regardless of the location or type of injury.

Subpart 8. Durable medical equipment.

The amendment to item D of this subpart adds a cross reference to the neck pain conditions described in subpart 1, item A, because those are the conditions to which this subpart specifically applies.

Subpart 10. Scheduled and nonscheduled medication.

As in the corresponding subpart 10 in part 5221.6200 for low back pain, the amendments in this subpart delete language related to controlled substances because prescription of opiods (narcotics) and muscle relaxants are now governed by the new medication treatment parameters in part 5221.6105. The amendments also require the provider to document the rationale for the use of all medication prescribed as required by Minn. State. § 176.135, subd. 7 and Minn. R. 5221.0700, subp. 2. Finally, the amendment cross references the new part 5221.6105 to provide easier navigation of the rules.

Part 5221.6210. Thoracic back pain

Subpart 1. Diagnostic procedures for treatment of thoracic back injury.
Item A, subitem (4) is amended to add the ICD-9 code 336.9, which reflects the narrative description of thoracic compressive myleopathy: "Hereditary and degenerative diseases of the central nervous system; unspecified disease of spinal cord."

Item I. This item, governing comprehensive functional capacity evaluations, is amended so that it is identical to item I of part 5221.6200 for low back pain and part 5221.6205 for neck pain because the purpose and indications for comprehensive FCEs does not vary by the type or location of the

injury. The language in subitems (3) and (4) is new language because the concepts were inadvertently omitted from this part when it was initially adopted in 1995.

Subpart 3. Passive treatment modalities.

Items E, F, G and H include the same amendments as those for low back pain in part 5221.6200 and neck pain in part 5221.6205, because the descriptions and examples of the types of modalities listed are consistent regardless of the location or type of injury.

Subpart 8. Durable medical equipment.

Item D. The amendment to item D of this subpart adds a cross reference to the thoracic back pain conditions described in subpart 1, item A, because those are the conditions to which this subpart specifically applies.

Subpart 10. Scheduled and nonscheduled medication.

As in the corresponding subpart 10 in part 5221.6200 for low back pain, and part 5221.6205 for neck pain, the amendments in this subpart delete language related to controlled substances because prescription of opiods (narcotics) and muscle relaxants are now governed by the new medication treatment parameters in part 5221.6105. The amendments also require the provider to document the rationale for the use of all medication prescribed as required by Minn. State. § 176.135, subd. 7 and Minn. R. 5221.0700, subp. 2. Finally, the amendment cross references the new part 5221.6105 to provide easier navigation of the rules.

Part 5221.6300 Upper extremity disorders

Subpart 1. Diagnostic procedures for treatment of upper extremity disorders (UED).

Item A. Subitem (2) is amended to update the rule with additional ICD-9 codes that reflect the narrative description of tendonitis of the forearm, wrist and hand.[76] This is necessary to reflect updates to the ICD-9 codes since the rules were initially adopted in 1995. The additional codes are in the 727 category governing: "Diseases of the musculoskeletal system and connective tissue; rheumatism, excluding the back; other disorders of synovium, tendon, and bursa." Specific additional codes are 727.09: synovitis and tenosynovitis, other; 727.3: other bursitis (with exclusions); 727.4 to 727.49: ganglion and cyst of synovium, tendon and bursa; 727.8 to 727.82: other disorders of synovium, tendon, and bursa; contracture of tendon (sheath) and calcium deposits in tendon and bursa; 727.89: other, abscess of bursa or tendon; and 727.9: unspecified disorder of synovium, tendon and bursa. ICD-9 code 726.5 "unspecified enthesopathy" is deleted because that code is used with conditions affecting the hips.

Subitem (5) is updated with additional ICD-9 codes to reflect the narrative description of shoulder impingement syndromes: Category 840 describes "sprains and strains of shoulder and upper arms follows: Code 840.7: superior glenoid labrum lesion; the existing 840.8 (other specified sites of

76. See footnote 7. An online list of ICD-9 codes is also at: http://icd9.chrisendres.com/index.php?action=contents

shoulder and upper arm; and 840.9: unspecified site of shoulder and upper arm.

Item E. The amendment to this item adds a cross reference to the specific clinical conditions covered by this part, as described in item A. This language appears in the corresponding items of other parts of the rules, but was inadvertently omitted from this item.

Item J. This item, governing comprehensive functional capacity evaluations, is amended so that it is identical to item I of part 5221.6200 for low back pain, part 5221.6205 for neck pain, and part 5221.6210 for thoracic back pain because the purpose and indications for comprehensive FCEs does not vary by the type or location of the injury.

Subpart 3. Passive treatment modalities.

Items E, F, G and H include the same amendments as those for low back pain in part 5221.6200, neck pain in part 5221.6205, and thoracic back pain in part 5221.6210 because the descriptions and examples of the types of modalities listed are consistent regardless of the location or type of injury.

Subpart 8. Durable medical equipment.

Item D. The amendment to item D of this subpart corrects a cross reference to the upper extremity conditions to those described in subpart 1, item A, because those are the conditions to which this subpart specifically applies.

Subpart 10. Scheduled and nonscheduled medication.

As in the corresponding subpart 10 in part 5221.6200 for low back pain, and part 5221.6205 for neck pain, the amendments in this subpart delete language related to controlled substances because prescription of opiods (narcotics) and muscle relaxants are now governed by the new medication treatment parameters in part 5221.6105. The amendments also require the provider to document the rationale for the use of all medication prescribed as required by Minn. State. § 176.135, subd. 7 and Minn. R. 5221.0700, subp. 2. Finally, the amendment cross references the new part 5221.6105 to provide easier navigation of the rules.

Part 5221.6305. Reflex sympathetic dystrophy.

Subpart 1. Scope.

This subpart amends the clinical categories that are covered by this part. Clinicians and others use different names to describe the same or similar constellation of symptoms and clinical findings, and therefore it is necessary to include other terminology used so that the name of the condition does not preclude application of the appropriate treatment parameter. The Workers' Compensation Court of Appeals has stated that the "five out of eight" criteria are not to be used as diagnostic criteria for purposes of establishing an insurer's liability for a condition. Darvell v.

Wherley Motors, (WCCA 2005).[77] The amendments to this part address this concern by providing that the parameters apply to any of the names, conditions or ICD-9 codes identified in item A. The intent of the amendments is to minimize disputes about whether the parameters in this part apply because of the label applied by health care providers to describe a similar set of symptoms and clinical findings.

Item A, subitem (1) replaces the deleted language in subitem 2. It provides that this clinical category encompasses any condition that is diagnosed as complex regional pain syndrome, reflex sympathetic dystrophy, or causalgia or any other condition encompassed in the listed ICD-9 codes. The ICD-9 codes using these terms (expanded from the deleted codes in subitem 2) are as follows:

- 337.20 Reflex sympathetic dystrophy, unspecified; Complex regional pain syndrome type I, unspecified;
- 337.21 Reflex sympathetic dystrophy of the upper limb; Complex regional pain syndrome type I of the upper limb;
- 337.22 Reflex sympathetic dystrophy of the lower limb; Complex regional pain syndrome type I of the lower limb;
- 337.29 Reflex sympathetic dystrophy of other specified site; Complex regional pain syndrome type I of other specified site;
- 337.9 Unspecified disorder of autonomic nervous system;
- 354.4 Causalgia of upper limb; Complex regional pain syndrome type II of the upper limb (with exclusions);
- 355.71 Causalgia of lower limb (with exclusions);
- 355.9 Mononeuritis of unspecified site; Causalgia NOS; Complex regional pain syndrome NOS; (with exclusions); and
- 733.3 Algoneurodystrophy; Disuse atrophy of bone; Sudeck's atrophy.

Subitem (2) retains the original description of reflex sympathetic dystrophy, based on the clinical symptoms that are presented. The conditions initially listed in the rule are retained under this subitem to ensure proper application of the parameter if a provider for some reason fails to diagnose the condition under subitems 1 or 3.

Subitem (3) provides the description of the condition based on the criteria developed by the International Association for the Study of Pain.[78] This is included because some practitioners use this description to diagnose the conditions.

Subpart 2. Initial nonsurgical management.

Item A, subitem (b) is amended to refer to injections to a limb, rather than a "site." This is necessary because the term "site" is too vague and could be interpreted to permit multiple injections to the affected arm or leg, which is not the standard of care. RSD only affects limbs.

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77. See a similar analysis with respect to the use of the eight criteria in establishing a rating under the Permanent Partial Disability schedule in Minn. R. chapter 5223 in Stone v. Harold Chevrolet; 65 W.C.D. 102 (WCCA 2004); S. A'ffd., 692 N.W.2d 888 (Minn. 2005); and Mundy v. American Red Cross, 66 W.C.D. 99 (WCCA 2005).

78. Merskey H, Bogduk N. Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms. Seattle, WA: IASP Press; 1994. Available from the University of Minnesota Biomedical Library.

Item D is amended to require the same practices and standard of care required for the use of medications in other parts of the treatment parameters. The language is the same as found in parts 5221.6200, subpart 10; 5221.6205, subpart 10; and 5221.6300, subpart 10.

CONCLUSION: Based on the foregoing, the proposed rules are both needed and reasonable.

October 13, 2009 /s/

Patricia Todd, Assistant Commissioner

This Statement of Need and Reasonableness was made available for public review on 10/14/2009.

Appendix A: Summary Tables of Medical Evidence on NSAIDs

1. There is extensive evidence that NSAIDs (both nonselective and COX-2 inhibitors) are more effective than placebo in relieving symptoms of musculoskeletal pain, at least in the short term.

Article and citation	***NSAID efficacy vs. placebo***
Med Sci Sport Exercise 1998; 30(8): 1183-1190	Improved pain scores for NSAIDs [*diclofenac, oxaprozin, phenylbutazone, fentiazac, flurbiprofen, tenoxicam*] vs. placebo during short term (7-28d) follow-up.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD004768	A single dose of diclofenac 50 mg has an NNT of 2.3 (2.0 to 2.7) for at least 50% pain relief compared with placebo. The NNTs for diclofenac 25 mg and 100 mg were 2.8 (2.1 to 4.3) and 1.9 (1.6 to 2.2) respectively, indicative of a dose-response relationship with increasing dose provide better pain relief.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD004604	When compared with placebo, the NNT for at least 50% pain relief over 6 hours with rofecoxib 50 mg was 2.2 (2.0 to 2.5).
Clin Ther. 2003 Mar;25(3):817-51.	rheumatoid arthritis: valdecoxid 10, 20, 40 more effective than placebo; dysmenorrhea: valdecoxib more effective than placebo
Cochrane Database of Systematic Reviews 2004 Issue 4: CD001548	In postoperative pain the NNTs for ibuprofen 200 mg were 3.3 (95% confidence interval 2.8 to 4.0) compared with placebo, for ibuprofen 400 mg 2.7 (2.5 to 3.0), for ibuprofen 600 mg 2.4 (1.9 to 3.3). In postoperative pain the NNTs for diclofenac 50 mg were 2.3 (2.0 to 2.7) and for diclofenac 100 mg 1.8 (1.5 to 2.1).
Cochrane Database of Systematic Reviews 2004 Issue 4: CD002762	For single doses of piroxicam 20 mg and 40 mg the respective numbers-needed-to-treat for at least 50% pain relief were 2.7 (2.1 to 3.8) [95% confidence interval] and 1.9 (1.2 to 4.3) [95% confidence interval] compared with placebo over 4-6 hours in moderate to severe postoperative pain.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003831	Celecoxib significantly better than placebo in treatment of RA.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003685	Rofecoxib significantly more effective than placebo in treating RA.
Anesthesiology 2003; 99(5): 1198-1208	Rofecoxib superior to placebo in perioperative pain control Celecoxib superior to placebo in perioperative pain control Parecoxib (3 studies), valdecoxib (3 studies), nimesulide (1 study), and meloxicam (1 study) superior to placebo
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003686	There is some evidence for short term benefit with respect to pain and function from oral NSAIDs, but this benefit is not sustained.
Ann Pharmacother. 1999 Sep;33(9):979-88. x	meloxicam more effective than placebo in OA, RA;
Cochrane Database of Systematic Reviews 2004 Issue 4: CD000232	Weak evidence of a modest benefit of NSAIDs for the alleviation of acute symptoms.
J Clin Oncol. 2004 May 15;22(10):1975-92.	NSAID more effective than placebo
Spine. 2000 Oct 1;25(19):2501-13.	NSAIDs more effective than placebo
J Spinal Disorders 2000; 13(6): 463-469	No evidence that NSAIDs are effective in treatment of sciatica
Clin Ther. 2001 Sep;23(9):1323-38.	dental surgery: rofecoxib more effective than placebo ortho surgery: rofecoxib more effective than placebo OA/RA: rofecoxib more effective than placebo
Drugs 2002; 62 (14): 2059-2071	knee OA: valdecoxib superior to placebo hip OA: valdecoxib superior to placebo RA: valdecoxib superior to placebo post hip arthroplasty: valdecoxib superior to placebo post foot surgery: valdecoxib superior to placebo dental surgery: valdecoxib superior to placebo dysmenorrhea: valdecoxib superior to placebo
BMJ 2004; 329: 1317-1320	knee OA: NSAIDS superior to placebo
Semin Arthritis Rheum. 1997 Apr;26(5):755-70.	NSAIDs were superior to placebo in all short-term trials
Ann Pharmacother. 1993 Apr;27(4):456-63	nabumetone superior to placebo in OA & RA
J Clin Oncol. 1994 Dec;12(12):2756-65.	NSAID studies found greater analgesic efficacy than placebo
Clin J Sport Med. 1995 Jul;5(3):175-86.	the literature would substantiate active mobilization following ankle sprains with judicious early use of nonsteroidal anti-inflammatory drugs
J Am Pharm Assoc (Wash). 2002 Jan-Feb;42(1):74-82.	the most appropriate pharmacologic treatments are acetaminophen or nonsteroidal anti-inflammatory drugs for mild-to-moderate pain
J Clin Epidemiol 1995: 48(5): 691-704	superior short-term efficacy of NSAIDs in comparison with placebo

2. There is extensive evidence that there are no clinically significant differences in efficacy among non-selective NSAIDs at equipotent doses.

Article and citation	***Comparisons among nonselective NSAIDs***
Cochrane Database of Systematic Reviews 2004 Issue 4: CD001548	Direct comparisons of diclofenac 50 mg with ibuprofen 400 mg showed no significant difference between the two
Clin Ther. 2003 Jun;25(6):1593-617.	Efficacy of indomethacin, naproxen, sulindac etodolac, flurbiprofen, and meclofenamate is similar
J Clin Oncol. 2004 May 15;22(10):1975-92.	No consistent evidence of increased efficacy of one NSAID compared with another
Cochrane Database of Systematic Reviews 2004 Issue 4: CD000517	No consistent evidence of differences in efficacy among NSAIDs in treatment of OA
Spine. 2000 Oct 1;25(19):2501-13.	Strong evidence that NSAIDs are equally effective
Cochrane Database of Systematic Reviews 2004 Issue 4: CD000142	No evidence of differences in efficacy between etodolac, piroxicam, naproxen, diclofenac, indomethacin, and, nabumetone
J Rheumatol. 1997 Feb;24(2):349-57.	Only 5 of the 29 (17%) NSAID comparisons found statistically significant differences in efficacy.
Rheumatol Int. 1993;13(2 Suppl):S19-24.	No significant differences in outcome between etodolac and comparators
Semin Arthritis Rheum. 1997 Apr;26(5):755-70.	In the 32 comparative NSAID trials, only five (16%) found significant differences in efficacy
Ann Pharmacother. 1993 Apr;27(4):456-63	No significant difference compared to other NSAIDs
Scand J Rheumatol. 1993;22(6):255-60.	No differences between drugs
J Clin Epidemiol 1995: 48(5): 691-704	No conclusive evidence in favor of a particular NSAID with respect to efficacy or tolerability

3. There is extensive evidence that there are no clinically significant differences in efficacy between non-selective NSAIDs and COX-2 inhibitors at equipotent doses.

Article and citation	***Coxib vs. nonselective NSAID***
Clin Ther. 2003 Mar;25(3):817-51.	rheumatoid arthritis: valdecoxid 10, 20, 40 no more effective than naproxen 500 BID; osteoarthritis: no difference in outcomes between valdecoxib and naproxen dysmenorrhea: valdecoxib no more effective than naproxen
Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004 Feb;97(2):139-46.	celecoxib 200, 400 less effective than naproxen 550 or ibuprofen 400 (single dose studies); rofecoxib 50 equivalent to naproxen 550 (single dose studies)
BMJ 2002; 325: 619-623	Celecoxib and NSAIDS were equally effective for all efficacy outcomes.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003831	Celecoxib controls the symptoms of RA to a similar degree to that of naproxen, diclofenac and ibuprofen.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003685	Rofecoxib at a dosage of 50 mg/day demonstrated similar efficacy to naproxen at a dosage of 500 mg twice daily.
Anesthesiology 2003; 99(5): 1198-1208	COX-2I no more effective than other NSAIDs; Rofecoxib, parecoxib, and valdecoxib, have a postoperative analgesic dosage ceiling similar to that of traditional NSAIDs
Ann Pharmacother. 1999 Sep;33(9):979-88.	no difference in outcome with meloxicam compared to piroxicam, diclofenac, naproxen;
Clin Ther. 2003 Jun;25(6):1593-617.	Etoricoxib no more effective than indomethacin
Clin Ther. 2001 Sep;23(9):1323-38.	dysmenorrhea: rofecoxib equivalent to naproxen dental surgery: rofecoxib equivalent to ibuprofen and naproxen ortho surgery: rofecoxib equivalent to naproxen OA/RA: rofecoxib equivalent to diclofenac, ibuprofen, nabumetone
Drugs 2002; 62 (14): 2059-2071	knee OA: valdecoxib equivalent to naproxen hip OA: valdecoxib equivalent to naproxen RA: valdecoxib equivalent to naproxen dysmenorrhea: valdecoxib superior to naproxen

4. There is extensive evidence that there are increased gastrointestinal adverse effects with NSAID use but the risk varies dramatically by agent and dose.

i. Risk is lower at lower doses.

ii. Among nonselective NSAIDs, risk is lowest for ibuprofen and diclofenac; intermediate for naproxen, sulindac, and indomethacin; highest for piroxicam, tolmetin, and ketoprofen.

iii. Risk is highest for patients > 60 years old and patients with a history of gastrointestinal disease.

Article and citation	***GI: nonselective NSAIDS***
Am J Med. 1998 Mar 30;104(3A):30S-34S	Ibuprofen and diclofenac were found to be associated with the lowest relative risk; indomethacin, naproxen, sulindac, and aspirin were associated with intermediate risk; and azapropazone, tolmetin, ketoprofen, and piroxicam were associated with higher risk. Some of these apparent differences in toxicity may, however, be dose related. The low risk of gastrointestinal complications associated with ibuprofen appears to be attributable to the low doses that are prescribed routinely in clinical practice. Higher doses of ibuprofen were associated with relative risks similar to those of naproxen and indomethacin.
Arch Intern Med. 2000 Jul 24; 160(14): 2093-9.	Risk of upper gastrointestinal bleed during NSAID treatment increases least with ibuprofen (RR=1.9); then diclofenac and sulindac (RR=3.3); naproxen, indomethacin, and ketoprofen (RR=4-5); and piroxicam (RR=6.3). Risk of upper gastrointestinal bleed during NSAID treatment increases with dose.
Am J Med 1999; 107(6A): 55S-64S	Perforation, obstruction, bleeding significantly less frequent in nabumetone users. Endoscopically-confirmed perforation, obstruction, bleeding significantly less frequent in nabumetone users.
J Clin Pharmacol 1999: 39(5): 520-532	No difference in rate of gastrointestinal adverse events between nonprescription ibuprofen and placebo
Br J Clin Pharmacol. 2002 Sep;54(3):320-6.	The risk of upper gastrointestinal bleeding with NSAIDs varies twenty-fold depending on the drug. (ibuprofen OR = 1.7; diclofenac OR = 4.9; indomethacin OR = 6.0; naproxen OR = 9.1; piroxicam OR = 13.1; ketoprofen OR = 34.9). The risk of upper gastrointestinal bleeding with NSAIDs varies by three to seven-fold depending on the dose chosen (increasing with increasing dose). Risk is maximal during the first week and decreases thereafter.
Arthritis Rheum. 2003 Aug 15;49(4):508-18.	High dosages (e.g., ibuprofen 3200 mg/d, naproxen 1500 mg/d) of any NSAID increase the risk of dyspepsia by about 3-fold, but no increased risk with medium or low doses (e.g., ibuprofen 1600 mg/d, naproxen 500 mg/d). Any dosage of indomethacin, meclofenamate, or piroxicam increases the risk of dyspepsia by about 3-fold.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD002296	Misoprostol significantly reduces the risk of duodenal and gastric ulcers, but significantly increases the risk of diarrhea. Double dose H2 receptor agonists reduce the risk of duodenal and gastric ulcers, and symptoms of abdominal pain. Proton pump inhibitors reduce the risk of duodenal and gastric ulcers, and symptoms of dyspepsia.
Am J Gastroenterol. 2002 Aug;97(8):1951-8.	Pooled risk ratio of dyspepsia for NSAIDs compared with placebo is 1.36 (95% CI _ 1.11–1.67). (With a loose definition of dyspepsia, the pooled risk ratio was 1.13). In the placebo-treated control groups, the percent of patients reporting dyspepsia ranged from 2.3% (strict definition) to 4.2% (loose definition) vs. 4.8% and 9.6% in the NSAID-treated groups.
J Rheumatol. 1997 Feb;24(2):349-57.	Indomethacin was more toxic in 7 of 12 comparisons
Semin Arthritis Rheum. 1997 Apr;26(5):755-70.	Indomethacin was most toxic
Ann Intern Med. 1991 Nov 15;115(10):787-96.	Users of NSAIDs are at approximately three times greater relative risk for developing serious adverse gastrointestinal events than are nonusers.
Ann Pharmacother. 1993 Apr;27(4):456-63	Nabumetone shows same risk of gastrointestinal adverse events as other ns-NSAIDs

Arch Intern Med. 1996 Nov 11;156(20):2321-32.	The use of misoprostol, but no that of H2 blockers, was beneficial in the prevention of NSAID-induced gastric ulcers. The number of patients to be treated to prevent 1 gastric ulcer with short- and long-term NSAID treatment is 11 and 15, respectively, for an intermediate baseline risk of 10%. Misoprostol and H2 blockers were beneficial in the long-term prevention of duodenal ulcers; misoprostol or H2 blockers in the short-term prevention of duodenal ulcers remains to be confirmed.
Drugs. 1993;46 Suppl 1:243-8.	NSAIDs are associated with serious upper gastrointestinal disorders, with a relative risk of 2.7 in patients receiving NSAIDs compared with subjects not receiving NSAIDs. An increase in the dose and duration of NSAIDs are associated with an increase in the risk of upper gastrointestinal toxicity
J Clin Gastroenterol. 1993 Oct;17(3):238-43.	During short-term NSAID use, 37% of the subjects developed severe gastric mucosal damage as compared to 12% of subjects given some protective agent. The figures for the duodenum are 13% and 4%, respectively. Owing to the small number of studies on prevention of chronic NSAID-induced gastroduodenal damage, results were not pooled together; misoprostol was shown to be highly effective in reducing the prevalence of gastric ulcer, and ranitidine prevented the occurrence of duodenal but not gastric ulcer
J Rheumatol. 2000 Sep;27(9):2203-14.	Misoprostol, PPI, and double dose H2RA are effective in preventing chronic NSAID related endoscopic gastric and duodenal ulcers. Lower doses of misoprostol are less effective and are still associated with diarrhea. Only misoprostol 800 micrograms/day has been directly shown to reduce the risk of ulcer complications
Semin Arthritis Rheum. 1997 Aug;27(1):1-16.	Wide variations in relative risk among NSAIDs were observed with piroxicam and azapropazone being the most toxic. Ibuprofen was associated with the least risk, probably because of its widespread use as a low-dose analgesic. Five studies provided comparative data on NSAIDs at "high" and "low" doses (as defined in the original reports), showing that the risk of toxicity was dose related. Furthermore, at full anti-inflammatory doses, the risk associated with ibuprofen was similar to that of naproxen and diclofenac
J Clin Oncol. 1994 Dec;12(12):2756-65.	The incidence of gastrointestinal side effects showed a trend to increase with dose, without a ceiling effect, and to increase with multiple doses

5. There is extensive evidence that the risk of gastrointestinal side effects is lower with COX-2 inhibitors than with all non-selective NSAIDs but still higher than placebo.

i. There is limited evidence that the gastrointestinal benefit of COX-2 inhibitors is reduced in patients using aspirin.

ii. There is good evidence that gastrointestinal side effects attributed to nonselective NSAIDs can be significantly reduced by the use of misoprostol, H2 receptor agonists, and proton pump inhibitors.

Article and citation	***GI: nonselective NSAID vs. COX-2i***
Ann Pharmacother 2001; 35(7-8): 829-834	Celecoxib 200 mg twice daily was associated with a significantly lower rate of gastroduodenal ulcers than was naproxen 500 mg twice daily at 12 weeks (RR 0.24; 95% CI 0.17 to 0.33). Celecoxib 200 mg twice daily had a significantly lower risk of endoscopic ulcers than did modified-release diclofenac 75 mg twice daily at 24 weeks (RR 0.24; 95% CI 0.11 to 0.52). Celecoxib 200 mg twice daily had a significantly lower risk of endoscopic ulcers than ibuprofen 800 mg three times daily at 12 weeks (RR 0.30; 95% CI 0.20 to 0.46).
Clin Ther. 2003 Mar;25(3):817-51.	In RA: more gastrointestinal adverse events for naproxen 500 BID than valdecoxib 10, 20 but not 40. In OA: 2/3 studies no difference in adverse events between valdecoxib and naproxen; 1/3 studies fewer gastrointestinal adverse events with valdecoxib 5, 10 than naproxen 500 BID. Fewer ulcers than with valdecoxib naproxen, ibuprofen, diclofenac

Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004 Feb;97(2):139-46.	Lower rates of ulcers with COX-2i than naproxen, ibuprofen, diclofenac
BMJ 2002; 325: 619-623	In patients taking celecoxib the rate of withdrawals due to adverse gastrointestinal events was 46% lower (95% confidence interval 29% to 58%; NNT 35 at three months). In patients taking celecoxib the incidence of ulcers detectable by endoscopy was 71% lower (59% to 79%; NNT 6 at three months). In patients taking celecoxib the incidence of symptoms of ulcers, perforations, bleeds, and obstructions was 39% lower (4% to 61%; NNT 208 at six months). Subgroup analysis of patients taking aspirin showed that the incidence of ulcers detected by endoscopy was reduced by 51% (14% to 72%) in those given celecoxib compared with other NSAIDs. The reduction was greater (73%, 52% to 84%) in those not taking aspirin.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003831	There is a reduced rate of UGI complications with celecoxib but there is also evidence to suggest that these benefits may not be evident in the long-term. Celecoxib offers no additional benefit in patients who are also receiving cardio-prophylactic low dose aspirin.
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003685	The combined rate of clinically significant gastrointestinal ulcers, and bleeds was lower with rofecoxib than with naproxen
Eur J Clin Pharmacol 2003; 59(2): 169-175	Perforation, obstruction, ulcers, and bleeding significantly reduced in patients receiving COX-2I
Ann Pharmacother. 1999 Sep;33(9):979-88.	Fewer gastrointestinal adverse events with meloxicam than piroxicam. Fewer endoscopically-confirmed ulcers with celecoxib than ibuprofen, diclofenac. Fewer gastrointestinal adverse events with rofecoxib than ibuprofen.
Am J Med. 1999 Dec 13;107(6A):48S-54S.	Patients using meloxicam experienced less dyspepsia (odds ratio = 0.73; 95% CI, 0.64–0.84), compared with piroxicam, diclofenac, naproxen. Patients using meloxicam experienced fewer perforations, ulcers, bleeding (odds ratio = 0.52; 95% CI, 0.28–0.96), compared with piroxicam, diclofenac, naproxen. Patients using meloxicam experienced less frequent discontinuation of NSAID because of adverse gastrointestinal events (odds ratio = 0.59; 95% CI, 0.52–0.67) compared with piroxicam, diclofenac, naproxen.
Arch Intern Med. 2000 Oct 23;160(19):2998-3003.	The number of discontinuations due to gastrointestinal adverse events is lower with rofecoxib than ibuprofen, diclofenac, nabumetone. The incidence of dyspeptic adverse events lower with rofecoxib than ibuprofen, diclofenac, nabumetone.
Clin Ther. 2001 Sep;23(9):1323-38.	Fewer gastrointestinal adverse events with rofecoxib than ibuprofen, naproxen, diclofenac, nabumetone

6. There is limited but uncontradicted evidence that there is no difference between nonselective-NSAIDs and COX-2 inhibitors in the rate of total adverse side effects.

Article and citation	***Total AEs: nonselective vs. COX-2i***
Clin Ther. 2003 Mar;25(3):817-51.	In RA: no difference between valdecoxib 20, 40 and naproxen 500 BID in total adverse events
Eur J Clin Pharmacol 2003; 59(2): 169-175	Total serious adverse effects no different

7. There is limited evidence of an increased risk of severe cardiovascular side effects with COX-2 inhibitors.

Article and citation	***Cardiovascular effects***
Cochrane Database of Systematic Reviews 2004 Issue 4: CD003685	Compared to patients taking naproxen, patients taking rofecoxib had a greater risk of having any cardiovascular event and had greater risk of having a non-fatal myocardial infarction.
Circulation. 2001 Nov 6;104(19):2280-8.	The relative risk for cardiovascular, hemorrhagic, and unknown deaths nonfatal myocardial infarctions and nonfatal strokes was 0.84 (95% CI: 0.51, 1.38) when comparing rofecoxib with placebo; 0.79 (95% CI: 0.40, 1.55) when comparing rofecoxib with non-naproxen NSAIDs; and 1.69 (95% CI: 1.07, 2.69) when comparing rofecoxib with naproxen.
JAMA. 2001 Aug 22-29;286(8):954-9.	Risk of cardiovascular event greater with rofecoxib than naproxen. No difference in risk of cardiovascular event with celecoxib compared to diclofenac, ibuprofen

8. There is good evidence that NSAIDs increase blood pressure in patients treated with anti-hypertensive medications.

Article and citation	***Cardiovascular effects***
Ann Intern Med. 1994 Aug 15;121(4):289-300.	NSAIDs elevate mean blood pressure by approximately 5.0 mm Hg, at least over a period of several weeks. (A 5 to 6 mm Hg increase in diastolic blood pressure over a few years may be associated with a 67% increase in total stroke occurrence and a 15% increase in coronary heart disease.)
Ann Pharmacother. 2003 Mar;37(3):442-6.	COX-2I drugs raised blood pressure more than placebo and similarly to other NSAIDs
Arch Intern Med. 2005;165:490-496	Coxibs cause equivalent increases in blood pressure to nonselective-NSAIDs Coxibs cause equivalent increases in blood pressure to placebo
Arch Intern Med. 1993 Feb 22;153(4):477-84.	In short-term use, NSAIDs vary considerably in their effect on blood pressure. Of the drugs studied, indomethacin and naproxen were associated with the largest increases in blood pressure. The average effects of piroxicam, aspirin, ibuprofen, and sulindac were negligible.
Can J Cardiol. 2002 Dec; 18(12):1301-8.	If there are differences between traditional NSAIDs and coxibs in the blood pressure-raising potential of these drugs, these differences do not appear to be clinically significant.

Appendix B: Summary Tables of Medical Evidence on Opioid Analgesics

1. There is extensive evidence that narcotic analgesics are more effective than placebo in relieving both acute and chronic pain.

Article and citation	Acute pain: *efficacy*
Cochrane Database Syst Rev 2000; (2): CD001440	For a single dose of dextropropoxyphene 65 mg in postoperative pain the NNT for at least 50% pain relief was 7.7 (95% confidence interval 4.6 to 22) when compared with placebo over 4-6 hours. For the equivalent dose of dextropropoxyphene combined with paracetamol 650 mg the NNT was 4.4 (3.5 to 5.6) when compared with placebo.
Cochrane Database Syst Rev 2000; (4): CD002763	A significant benefit of active drug over placebo was shown for all doses of oxycodone and oxycodone plus paracetamol, except oxycodone 5 mg.
Pain 1997 Feb; 69(3): 287-94	Tramadol drugs gave significantly more analgesia than placebo. In postsurgical pain tramadol 50, 100 and 150 mg had NNTs for .50%maxTOTPAR of 7.1 (95% confidence intervals 4.6–18), 4.8 (3.4–8.2) and 2.4 (2.0–3.1). With the same dose of drug postsurgical patients had more pain relief than those having dental surgery. Tramadol showed a dose-response for analgesia in both postsurgical and dental pain patients.
Cochrane Database Syst Rev 2002; (1): CD003447	Hydromorphone is a potent analgesic; the effect is dose-dependent.
J Pain Palliat Care Pharmacother 2002; 16(4): 5-18	Morphine, the most widely used mu-opioid analgesic for acute and chronic pain, is the standard against which new analgesics are measured.
J Clin Pharm Ther 1996 Aug; 21(4): 261-82	There is some evidence that codeine 60 mg adds to the analgesic effects of paracetamol 600 mg, using pain relief or pain intensity scores as outcomes, but this is not necessarily translated into an increase in number of patients who obtain moderate to excellent pain relief.
J Clin Pharm Ther 1997 Apr; 22(2): 79-97	Codeine 60 mg may produce a small increase in the analgesic effect of aspirin 650 mg. However, this effect is not clinically meaningful.

Article and citation	Chronic pain: *efficacy*
Cochrane Database Syst Rev 2004; (2): CD003726	All three trials comparing tramadol with placebo showed a significant reduction in neuropathic pain with tramadol. Two of the trials that compared tramadol to placebo (total 161 participants) were combined in a meta-analysis. The number needed to treat with tramadol compared to placebo to reach at least 50% pain relief was 3.5 (95% confidence interval 2.4 to 5.9).
Eur J Pain. 2005 Dec 3	Short-term studies show that opioids can reduce the intensity of dynamic mechanical allodynia and perhaps of cold allodynia in peripheral neuropathic pain. Insufficient evidence precludes drawing conclusions regarding the effect of opioids on other forms of evoked NP. A meta-analysis of intermediate-term studies demonstrates the efficacy of opioids over placebo for evoked NP. These findings are clinically relevant because dynamic mechanical allodynia and cold allodynia are the most prevalent types of evoked pain in NP.
JAMA. 2005 Jun 22;293(24):3043-52.	The 14 short-term trials had contradictory results. In contrast, all 8 intermediate- term trials demonstrated opioid efficacy for spontaneous neuropathic pain. A fixed-effects model meta-analysis of 6 intermediate-term studies showed mean post-treatment visual analog scale scores of pain intensity after opioids to be 14 units lower on a scale from 0 to 100 than after placebo (95% confidence interval [CI], -18 to -10; *P*_.001).
Pain. 2005 Dec 5;118(3):289-305. Epub 2005 Oct 6.	Oral long-term treatment with opioids has only been tested using placebo-controlled designs in peripheral neuropathic pain conditions. Morphine was superior to placebo in patients with postherpetic neuralgia, phantom limb pain, and painful diabetic neuropathy with an NNT of 2.5 (CI 1.9–3.4). Oxycodone has been tested in post-herpetic neuralgia and painful diabetic neuropathy, with a NNT of 2.6 (CI 1.9–4.1), comparable to the effect of morphine. Tramadol studied in two trials in painful polyneuropathy and in one trial in post-herpetic neuralgia had an overall NNT of 3.9 (CI 2.7–6.7).
Pain. 2004 Dec;112(3):372-80.	The short-term efficacy of opioids was good in both neuropathic and musculoskeletal pain conditions. The mean decrease in pain intensity in most studies was at least 30% with opioids and was comparable in

	neuropathic and musculoskeletal pain.
Clin J Pain 2005 Nov-Dec; 21(6): 503-12	Methadone (20 mg/day) demonstrated a statistically significant improvement in pain compared to placebo.
Cochrane Database Syst Rev 2003; (4): CD003868	Morphine was shown to be an effective analgesic.
Cochrane Database Syst Rev 2003; (4): CD004311	Oral transmucosal fentanyl citrate (OTFC) is effective treatment for breakthrough pain.
Prescrire Int 2004 Feb; 13(69): 22-5	Combinations of paracetamol and weak opiates (codeine, dextropropoxyphene and tramadol) have been inadequately studied in chronic noncancer pain and are only second-line options
Curr Med Res Opin 2004 Sep; 20(9): 1419-28	Both transdermal fentanyl and sustained release morphine were effective in improving pain 'right now' scores (0-100 scale) from baseline to Day 28.
Curr Med Res Opin. 2005 Oct;21(10):1555-68.	There is both moderate/high- and low-quality evidence suggesting that long-term treatment with opioids can lead to significant improvements in functional outcomes, including QoL, in patients with chronic, non-malignant pain.
J Pain Palliat Care Pharmacother 2002; 16(1): 29-59	Published studies demonstrate methadone's efficacy in pain management
J Pain Palliat Care Pharmacother 2002; 16(4): 5-18	Morphine, the most widely used mu-opioid analgesic for acute and chronic pain, is the standard against which new analgesics are measured.

2. There is no evidence that there are any clinically significant differences in effectiveness among narcotics in the treatment of either acute or chronic pain at equipotent doses.

Article and citation	**Acute pain: *vs. other narcotics***
Cochrane Database Syst Rev 2000; (2): CD001440	The combination of dextropropoxyphene 65 mg with paracetamol 650 mg shows similar efficacy to tramadol 100 mg for single dose studies in postoperative pain but with a lower incidence of adverse effects. The same dose of paracetamol combined with 60 mg codeine appears more effective but, with the slight overlap in the 95% confidence intervals, this conclusion is not robust.
J Pain Symptom Manage 1998 Dec; 16(6): 388-402	The first, and obvious, conclusion is that the Cmax and Tmax obtained with immediate-release, controlled-release, and once-daily formulations differed in the expected manner, so that the respective Tmax values were 1, 3, and 9 hours [and C_{max} values were 6, 3, and 0.5 nmol/L]. A second clinically important point is that, within formulation, there was little difference between different salts or different brands.
Cochrane Database Syst Rev 2000; (4): CD002763	Single-dose oral oxycodone, with or without paracetamol, appears to be of comparable efficacy to intramuscular morphine and nonsteroidal anti-inflammatory drugs.
Am J Ther 2002 Jan-Feb; 9(1): 53-68	Comparative studies fail to demonstrate any advantages of meperidine over comparable doses of other analgesics. The analgesic effects of meperidine are not pronounced.
Cochrane Database Syst Rev 2002; (1): CD003447	Hyromorphone is not clinically superior to other strong opioids
Prescrire Int 1998 Feb; 7(33): 9-12	There is no proof that tramadol has a better risk-benefit ratio than the paracetamol + codeine combination or other step 2 analgesics in the World Health Organisation classification
J Pain Palliat Care Pharmacother 2004; 18(4): 17-30	Oxycodone is used for the relief of moderate-to-severe pain and is pharmacodynamically comparable to morphine.

Article and citation	**Chronic pain: *vs. other narcotics***
J Pain Symptom Manage. 2003 Nov;26(5):1026-48	There is insufficient evidence to suggest that one long-acting opioid is superior to another in terms of efficacy in adult patients with chronic non-cancer pain. There is insufficient evidence to suggest superior efficacy of long-acting opioids as a class compared to short-acting opioids in adults with chronic non-cancer pain. There is fair evidence to suggest that long-acting oxycodone and short-acting oyxcodone are equally effective for pain control in adult patients with chronic non-cancer pain.
Cochrane Database Syst Rev 2004; (2): CD003726	There were insufficient data to draw conclusions about the effectiveness of tramadol compared to morphine.

Cochrane Database Syst Rev 2004; (2): CD003971	There is evidence to suggest that methadone is an analgesic with similar efficacy to morphine. However, the majority of studies involved single dose comparisons or short-term use.
J Pain Symptom Manage. 2001 Aug;22(2):672-87.	Most of the studies report very wide ranges in EDR (equianalgesic dose ratio). This reflects the marked observed inter- and intra-individual variability among patients' responses to different opioids. Numerous factors contribute to this variability, including the route of administration, a drug's half-life, bioavailability, drug interactions, the pathophysiology of the pain state, clearance by the liver and/or kidneys, accumulation of opioid metabolites, access to the receptors and binding affinity to the receptors. PO oxycodone appears to be 1.5 to 2 times relatively more potent than PO morphine. Wide ranges in EDR are however reported.
Cochrane Database Syst Rev 2002; (1): CD003447	No differences in efficacy between hydromorphone, morphine and oxycodone at equi-analgesic doses. No difference in efficacy between immediate release and sustained release hydromorphone
Arch Intern Med 2006; 166: 837-843	The efficacy of oxycodone is similar to morphine and hydromorphone.
Pharmacotherapy 2002 Jul; 22(7): 898-904	Immediate-release and controlled-release preparations of oxycodone have similar efficacy. Controlled release morphine and methadone appear to be as effective as oxycodone.
Cochrane Database Syst Rev 2003; (4): CD003868	Pain relief did not differ between oral sustained-release morphine [MSR] and oral immediate-release morphine [MIR]. Pain relief did not differ between morphine and other opioids when titrated to effect.
Prescrire Int 1998 Feb; 7(33): 9-12	There is no proof that tramadol has a better risk-benefit ratio than the paracetamol + codeine combination or other step 2 analgesics in the World Health Organisation classification
Curr Med Res Opin 2004 Sep; 20(9): 1419-28	Improvement was significantly more pronounced in the transdermal fentanyl treatment group
J Pain Palliat Care Pharmacother 2004; 18(4): 17-30	Oxycodone is used for the relief of moderate-to-severe pain and is pharmacodynamically comparable to morphine.

3. There is no evidence that there are any clinically significant differences in effectiveness between immediate-release and sustained-release narcotic formulations in the treatment of either acute or chronic pain at equipotent dosing schedules.

Article and citation	**Acute pain: *vs. other narcotics***
J Pain Symptom Manage 1998 Dec; 16(6): 388-402	The first, and obvious, conclusion is that the Cmax and Tmax obtained with immediate-release, controlled-release, and once-daily formulations differed in the expected manner, so that the respective Tmax values were 1, 3, and 9 hours [and C_{max} values were 6, 3, and 0.5 nmol/L]. A second clinically important point is that, within formulation, there was little difference between different salts or different brands.

Article and citation	**Chronic pain: *vs. other narcotics***
J Pain Symptom Manage. 2003 Nov;26(5):1026-48	There is insufficient evidence to suggest that one long-acting opioid is superior to another in terms of efficacy in adult patients with chronic non-cancer pain. There is insufficient evidence to suggest superior efficacy of long-acting opioids as a class compared to short-acting opioids in adults with chronic non-cancer pain. There is fair evidence to suggest that long-acting oxycodone and short-acting oyxcodone are equally effective for pain control in adult patients with chronic non-cancer pain.
Cochrane Database Syst Rev 2002; (1): CD003447	No differences in efficacy between hydromorphone, morphine and oxycodone at equi-analgesic doses. No difference in efficacy between immediate release and sustained

	release hydromorphone
Pharmacotherapy 2002 Jul; 22(7): 898-904	Immediate-release and controlled-release preparations of oxycodone have similar efficacy. Controlled release morphine and methadone appear to be as effective as oxycodone.
Cochrane Database Syst Rev 2003; (4): CD003868	Pain relief did not differ between MSR and MIR. Pain relief did not differ between morphine and other opioids when titrated to effect.

4. There is extensive evidence that adverse effects - dizziness, drowsiness, nausea, vomiting, headache, and constipation - occur frequently with the use of narcotics to treat both acute and chronic pain. Meperidine has unique adverse effects in excess of other narcotics.
5. There is extensive evidence that the adverse effects of narcotics are dose dependent.

Article and citation	**Acute pain: *adverse effects***
Cochrane Database Syst Rev 2000; (2): CD001440	Pooled data showed increased incidence of central nervous system adverse effects for dextropropoxyphene plus paracetamol compared with placebo.
BMJ 1996 Aug 10; 313(7053): 321-5	The cumulative incidence of side effects with each treatment was comparable in the single dose trials. In the multidose studies a significantly higher proportion of side effects occurred with paracetamol-codeine preparations [than with paracetamol alone].
J Pain Symptom Manage 2002 Feb; 23(2): 121-30	Adverse effects were similar for the combination drugs and the opioid component alone. Common adverse effects were dizziness, drowsiness, nausea, vomiting, and headache.
Cochrane Database Syst Rev 2000; (4): CD002763	Significantly more adverse effects with active drug than with placebo were shown for all doses, except oxycodone 5 mg and its combination with paracetamol 325 mg. This was also shown for drowsiness/somnolence. Significantly more nausea, vomiting and dizziness/lightheadedness were reported with oxycodone 10 mg plus paracetamol (650 mg and 1000 mg) than with placebo.
Cochrane Database Syst Rev. 2005;(2):CD004137.	The majority of trials showed a higher incidence of adverse events in patients treated with opioids. There was significantly less vomiting in patients treated with NSAIDs (RR 0.35, 95% CI 0.23 to 0.53, P < 0.00001). In particular, patients receiving pethidine had a much higher rate of vomiting compared with patients receiving NSAIDs.
Am J Ther 2002 Jan-Feb; 9(1): 53-68	Meperidine use is complicated by unique side effects including serotonergic crisis and normeperidine toxicity.
BMJ 1997 Dec 13; 315(7122): 1565-71	Compared with placebo, the combination produced more dizziness (3.1; 1.1 to 8.9) whereas paracetamol resulted in more drowsiness (1.8; 1.1 to 2.9).
Cochrane Database Syst Rev 2000; (2): CD001547	The addition of codeine 60 mg to paracetamol may be accompanied by an increase in drowsiness and dizziness.
Pain 1997 Feb; 69(3): 287-94	Adverse events (headache, nausea, vomiting, dizziness, somnolence) with tramadol 50 mg and 100 mg had a similar incidence to comparator drugs. There was a dose response with tramadol, tending towards higher incidences at higher doses.
Eur J Clin Pharmacol 1998 Jan; 53(5): 303-11	Codeine 60 mg combined with ibuprofen 400 mg increased its adverse effects
Cochrane Database Syst Rev 2002; (1): CD003447	Hydromorphone's side effects are similar to other strong opioids

Article and citation	**Chronic pain: *adverse effects***
J Pain Symptom Manage. 2003 Nov;26(5):1026-48	There is insufficient evidence to suggest that one long-acting opioid is superior in terms of adverse events than any other in adult patients with chronic non-cancer pain.
JAMA. 2005 Jun 22;293(24):3043-52.	According to number needed to harm (NNH), the most common adverse event was nausea (NNH, 3.6; 95% CI, 2.9-4.8), followed by constipation (NNH, 4.6; 95% CI, 3.4-7.1), drowsiness (NNH, 5.3; 95% CI, 3.7-8.3), vomiting (NNH, 6.2; 95% CI, 4.6-11.1), and dizziness (NNH, 6.7; 95% CI, 4.8-10.0).
J Pain Symptom Manage. 2003 Jun;25(6):559-77.	Opioids do not impair driving-related skills in opioid-dependent/tolerant patients.
Pain. 2004 Dec;112(3):372-80.	About 80% of patients experienced at least one adverse event, with constipation (41%), nausea (32%) and somnolence (29%) being most

	common.
Arthritis Res Ther. 2005;7(5):R1046-51	Use of any oral opioid produced higher rates of adverse events than did placebo. Dry mouth (affecting 25% of patients), nausea (21%), and constipation (15%) were the most common adverse events. A substantial proportion of patients on opioids (22%) withdrew because of adverse events. Because most trials were short, less than four weeks, and because few titrated the dose, these results have limited applicability to longer-term use of opioids in clinical practice.
Cochrane Database Syst Rev 2004; (2): CD003971	There is evidence to suggest that methadone has a side effect profile comparable to morphine. However, the majority of studies involved single dose comparisons or short-term use. Therefore there is a very significant danger that the effects of methadone accumulation leading to delayed onset of adverse effects which occurs with chronic administration have not been represented. Fixed interval dosing schedules conducted over several days are associated with a high risk of serious morbidity and mortality.
Cochrane Database Syst Rev 2002; (1): CD003447	No differences in side effects between hydromorphone, morphine and oxycodone at equi-analgesic doses
Arch Intern Med 2006; 166: 837-843	The tolerability of oxycodone is similar to morphine and hydromorphone.
Pharmacotherapy 2002 Jul; 22(7): 898-904	Immediate-release and controlled-release preparations of oxycodone have comparable side effect profiles.

Article and citation	**Abstracts**
Prescrire Int 1998 Feb; 7(33): 9-12	Tramadol can have neuropsychological adverse effects, especially a risk of dependence and misuse
Curr Med Res Opin 2004 Sep; 20(9): 1419-28	Significantly fewer patients in the transdermal fentanyl [TDF] than in the sustained-release oral morphine [SRM] group reported any AE (72% vs. 87% respectively; $p < 0.001$), or an AE leading to the study drug being permanently discontinued (16% vs. 23% respectively; $p < 0.001$). Constipation and somnolence occurred considerably less frequently in the TDF than in the SRM treatment group.
J Pain Palliat Care Pharmacother 2002; 16(1): 9-28	The evidence in this review indicates that opioids do not appear to be associated with intoxicated driving, MVA and MVA fatalities, and consistently indicated that opioids are not associated with MVA.
Clin Neuropharmacol 1999 Mar-Apr; 22(2): 87-92	Opiate-induced myoclonus (OIM) is often generalized and is either periodic or associated with rigidity. Opiate-induced myoclonus frequently occurs in the context of underlying medical conditions, D2 antagonist co-administration, or other drugs (nonsteroidal anti-inflammatory agents, antidepressants), and usually responds to either naloxone or benzodiazepines. Opiate withdrawal myoclonus may be stimulus-sensitive, associated with D2 antagonist co-administration, and responsive to benzodiazepines and unresponsive to naloxone.
J Pain Palliat Care Pharmacother 2002; 16(1): 29-59	Inter-patient variability in pharmacokinetic variables of methadone produces difficulties in developing guidelines for methadone use.
J Pain 2003; 4(5): 231-256	The lack of well-designed, randomized controlled trials and the heterogeneity of populations and study designs made the drawing of firm conclusions difficult and precluded performance of meta-analysis. The type, strength, and consistency of evidence for available interventions to manage opioid side effects vary from strong (eg, on the use of naloxone to reverse respiratory depression or constipation) to weak (e.g., changing from the oral to epidural route of morphine administration to manage sedation).

6. There is no evidence that the adverse effects of narcotics [other than meperidine] vary by agent or formulation at equipotent dosing schedules.

Article and citation	**Acute pain: *adverse effects***
Pain 1997 Feb; 69(3): 287-94	Adverse events (headache, nausea, vomiting, dizziness, somnolence) with tramadol 50 mg and 100 mg had a similar incidence to comparator drugs. There was a dose response with tramadol, tending towards higher incidences at higher doses.
Cochrane Database Syst Rev 2002; (1): CD003447	Hydromorphone's side effects are similar to other strong opioids

Article and citation	Chronic pain: *adverse effects*
J Pain Symptom Manage. 2003 Nov;26(5):1026-48	There is insufficient evidence to suggest that one long-acting opioid is superior in terms of adverse events than any other in adult patients with chronic non-cancer pain.
Arthritis Res Ther. 2005;7(5):R1046-51	Use of any oral opioid produced higher rates of adverse events than did placebo. Dry mouth (affecting 25% of patients), nausea (21%), and constipation (15%) were the most common adverse events. A substantial proportion of patients on opioids (22%) withdrew because of adverse events. Because most trials were short, less than four weeks, and because few titrated the dose, these results have limited applicability to longer-term use of opioids in clinical practice.
Cochrane Database Syst Rev 2004; (2): CD003971	There is evidence to suggest that methadone has a side effect profile comparable to morphine. However, the majority of studies involved single dose comparisons or short-term use. Therefore there is a very significant danger that the effects of methadone accumulation leading to delayed onset of adverse effects which occurs with chronic administration have not been represented. Fixed interval dosing schedules conducted over several days are associated with a high risk of serious morbidity and mortality.
Cochrane Database Syst Rev 2002; (1): CD003447	No differences in side effects between hydromorphone, morphine and oxycodone at equi-analgesic doses
Arch Intern Med 2006; 166: 837-843	The tolerability of oxycodone is similar to morphine and hydromorphone.
Pharmacotherapy 2002 Jul; 22(7): 898-904	Immediate-release and controlled-release preparations of oxycodone have comparable side effect profiles.

Appendix C: Summary Tables of Medical Evidence on Muscle Relaxers

1. There is sufficient high quality evidence that muscle relaxers are more effective than placebo in relieving symptoms of musculoskeletal pain, at least in the short term

The only high quality systematic review [of the seven analyzed by the MSRB] that did not find muscle relaxers more effective than placebo based that conclusion on a single randomized controlled trial.

reference	***efficacy***
Arch Intern Med. 2001 Jul 9;161(13):1613-20.	patients given cyclobenzaprine were nearly 5 times more likely to improve than patients given placebo (NNT~3)
Arthritis Rheum. 2004 Feb 15;51(1):9-13.	Patients are about 3 times as likely to report improvement in their symptoms (NNT = 5)
Cochrane Database Syst Rev. 2005 Apr 18;(2):CD000319	Basmajian 1978 showed that cyclobenzaprine was not superior to placebo for subacute mechanical neck disorders [MND] at 14 to 18 days, using a global evaluation of muscle spasm
Cochrane Database Syst Rev. 2003;(2):CD004252.	Muscle relaxants are more effective than placebo for patients with acute low back pain on short-term pain relief
J Pain Symptom Manage. 2004 Aug;28(2):140-75.	17 fair-quality trials consistently found cyclobenzaprine to be more effective than placebo for various measures of efficacy (pain relief, muscle spasms, functional status) in patients with musculoskeletal conditions. A good-quality systematic review of 14 trials reported similar findings. The body of evidence is not as robust for carisoprodol (4 trials), orphenadrine (4 trials), and tizanidine (6 trials), but these medications were also consistently found to be more effective than placebo. There is very limited or inconsistent data regarding the effectiveness of methocarbamol, metaxalone, dantrolene, chlorzoxazone, or baclofen compared to placebo.
Spine. 1996 Dec 15;21(24):2840-9	These drugs are effective in treating acute back pain
Clin Ther. 2004 Sep;26(9):1355-67.	4-7 days carisoprodol more effective than placebo; 7-9 days of metaxalone more effective than placebo 7 days of cyclobenzaprine more effective than placebo;
Clin Ther. 2003 Apr;25(4):1056-73.	2 studies: 7 days of cyclobenzaprine more effective than placebo in acute neck and back pain
Spine 2004;29(12):1346–1351	Patients taking muscle relaxants, after controlling for baseline status, return to self-assessed ability to perform their daily activities more slowly than patients who do not take muscle relaxants.
Best Pract Res Clin Rheumatol. 2003 Feb;17(1):137-50.	The use of skeletal muscle relaxants is only weakly supported by results from controlled clinical trials
Minerva Stomatol. 2004 Jun;53(6):305-13.	The use of muscle relaxants in patients with myofascial pain of masticatory muscles seems to be justifiable
Spine. 1997 Sep 15;22(18):2128-56.	Muscle relaxants effective for acute low back pain
Ann Clin Res. 1975 Apr;7(2):85-8	Orphenadrine more effective than placebo in acute musculoskeletal conditions
Arthritis Rheum. 1994 Jan;37(1):32-40.	1 month of cyclobenzaprine more effective than placebo in fibromyalgia patients
Curr Med Res Opin. 1975;3(6):382-5	Methocarbamol more effective than placebo
J Int Med Res. 1979;7(3):240-6	Orphenadrine more effective than placebo in post-surgical pain
J Rheumatol Suppl. 1989 Nov;19:140-3.	Cyclobenzaprine more effective than placebo in fibromyalgia
J Rheumatol. 1991 Mar;18(3):452-4.	Cyclobenzaprine more effective than placebo in decreasing in evening fatigue and increasing total sleep time but no more effective in improving pain, tender point count, dolorimetry, mood ratings, and alpha non-REM EEG sleep anomaly
JAMA. 1978 Sep 8;240(11):1151-2.	14 days of cyclobenzaprine more effective than placebo in chronic low back pain
Arch Phys Med Rehabil. 1978 Feb;59(2):58-63.	Cyclobenzaprine more effective than placebo in neck and back pain
Arthritis Rheum. 1988 Dec;31(12):1535-42.	Cyclobenzaprine more effective than placebo in relieving pain in fibrositis patients
J Oral Surg. 1975 Sep;33(9):655-8.	Carisoprodol not more effective than placebo in myofascial pain-dsyfunction syndrome

2. The clinical benefit of muscle relaxers is modest.

Reference	***size of benefit***
Arch Intern Med. 2001 Jul 9;161(13):1613-20.	The magnitude of improvement is modest (effect size 0.5)
Arthritis Rheum. 2004 Feb 15;51(1):9-13.	The average treated patient would experience a moderate amount of improvement in sleep at all time points, pain would be modestly improved, but only early on, and patients would experience no improvement in fatigue or tender points.

reference	***duration of benefit***
Arch Intern Med. 2001 Jul 9;161(13):1613-20.	Evidence of a trend toward decreasing efficacy over time, with the greatest benefit in the first few days of treatment
Arthritis Rheum. 2004 Feb 15;51(1):9-13.	The average treated patient would experience a moderate amount of improvement in sleep at all time points, pain would be modestly improved, but only early on, and patients would experience no improvement in fatigue or tender points.
Spine. 1996 Dec 15;21(24):2840-9	Their effectiveness in chronic pain rarely has been studied, and conclusions about their efficacy in this setting are impossible

3. There is no evidence that any one of the muscle relaxers studied is any more effective than the others. In head-to-head trials, different muscle relaxers have been found to be equally effective.

reference	***comparative efficacy***
Cochrane Database Syst Rev. 2003;(2):CD004252.	Various muscle relaxants were found to be similar in performance
J Pain Symptom Manage. 2004 Aug;28(2):140-75.	There was no clear evidence from head-to-head trials that one skeletal muscle relaxant was superior to any other.
Spine. 1996 Dec 15;21(24):2840-9	These drugs are roughly equivalent in efficacy
Clin Ther. 2004 Sep;26(9):1355-67.	7 days of carisoprodol no more effective than cyclobenzaprine

4. There is no evidence that muscle relaxers are any more or less effective than benzodiazepines.

reference	***efficacy vs. others***
J Pain Symptom Manage. 2004 Aug;28(2):140-75.	2 fair-quality head-to-head trials and 1 fair-quality meta-analysis of unpublished trials found that cyclobenzaprine and diazepam are roughly equivalent for various measures of efficacy including pain, spasm, and global response, but 3 other fair-quality trials found that cyclobenzaprine was superior to diazepam for most (2 trials) or some (1 trial) clinical outcomes.
Arthritis Rheum. 1994 Jan;37(1):32-40.	1 month of cyclobenzaprine not more effective than amitriptyline in fibromyalgia patients
J Int Med Res. 1981;9(1):62-8	7 days of tizanide more effective than diazepam in acute spinal pain
J Int Med Res. 1981;9(6):501-5	7 days of tizanide not more effective than diazepam in acute spinal pain
JAMA. 1978 Sep 8;240(11):1151-2.	14 days of cyclobenzaprine no more effective than diazepam in chronic low back pain

5. A substantial proportion of patients taking muscle relaxers have side effects, most often drowsiness, and most often mild.

i. Side effects are dose-related.

ii. Some muscle relaxers have a potential for addiction at doses higher than those typically used in treatment of musculoskeletal pain.

reference	***side effects***
Arch Intern Med. 2001 Jul 9;161(13):1613-20.	more than half of patients experience at least one adverse side effect, most commonly drowsiness
Cochrane Database Syst Rev. 2003;(2):CD004252.	Adverse events were significantly more prevalent in patients receiving muscle relaxants and especially the central nervous system adverse

	effects
J Pain Symptom Manage. 2004 Aug;28(2):140-75.	There is insufficient evidence to accurately judge comparative adverse event rates from skeletal muscle relaxants in patients with musculoskeletal conditions. Direct comparisons of skeletal muscle relaxants in head-to-head trials were too limited in quantity and quality. Placebo-controlled trials showed no pattern of one skeletal muscle relaxant being superior to others and were generally of inferior quality compared to head-to-head trials. There are no data to judge comparative abuse or addiction risk. Tizanidine and chlorzoxazone are associated with usually reversible (rarely serious or fatal) hepatotoxicity, but data to estimate comparative event rates are not available. Other serious adverse events appear to be rare, but no assessment of comparative risk could be made.
Ann Emerg Med. 2003 Jun;41(6):818-26.	2 days of ibuprofen + cyclobenzaprine associated with more side effects than ibuprofen alone in acute myofascial pain
Clin Ther. 2003 Apr;25(4):1056-73	The most common AEs were somnolence and dry mouth, typical anticholinergic side effects that were generally mild in intensity. The incidence of AEs associated with cyclobenzaprine therapy appeared to be dose related, as did the rate of discontinuation due to AEs.
J Int Med Res. 1988 Mar-Apr;16(2):75-82	tizanide + ibuprofen associated with more drowsiness and cns side effects than placebo + ibuprofen
J Int Med Res. 1993 Mar-Apr;21(2):74-80.	side-effects in fibromyalgia patients receiving cyclobenzaprine are more common at higher doses (10 mg./d vs. 30 mg./d)
J Pharmacol Exp Ther. 1992 Aug;262(2):707-20.	Methocarbamol also produced significant increases in subjects' ratings of drug effect and liking and measures of sedation, but it produced only minor impairment of psychomotor and cognitive performance than placebo
Int J Clin Pharmacol Res. 1988;8(2):75-94	Neither the maximal clinical dosage of tizanidine (3 mg) nor twice that dosage (6 mg) induced any marked somatic or psychic symptoms compared with the placebo
J Int Med Res. 1988 Mar-Apr;16(2):83-91	tizanide + ibuprofen associated with more drowsiness and cns side effects than placebo + ibuprofen
J Pharmacol Exp Ther. 1989 Mar;248(3):1146-57	methocarbamol, at doses well above those used therapeutically, has some potential to be abused by persons with histories of sedative/hypnotic abuse

6. Muscle relaxers in combination with an analgesic is more effective than analgesic alone.
There was only one high quality RCT [of the 2 systematic reviews, 4 RCT,s and 2 controlled trials considered by the MSRB] that found no benefit of combined treatment over NSAID alone.

reference	***combination therapy***
Cochrane Database Syst Rev. 2005 Apr 18;(2):CD00031	Nasswetter 1998 showed that cyclobenzaprine plus lysinine cloniximate was superior to lysine cloniximate alone for pain in MND at 14 days.
Cochrane Database Syst Rev. 2003;(2):CD004252.	muscle relaxants + analgesics more effective than analgesics alone
Ann Emerg Med. 2003 Jun;41(6):818-26.	2 days of ibuprofen + cyclobenzaprine not more effective than ibuprofen alone in acute myofascial pain
Curr Med Res Opin. 1983;8(8):531-5.	7 days of orphenadrine + paracetamol more effective than placebo in relieving spinal pain
J Int Med Res. 1983;11(1):42-5.	orphenadrine + paracetamol more effective than paracetamol alone
J Int Med Res. 1988 Mar-Apr;16(2):75-82	tizanide + ibuprofen more effective than placebo + ibuprofen in low back pain patients
Clin Rheumatol. 1989 Jun;8(2):245-50.	combination of carisoprodol and paracetamol (acetaminophen) and caffeine is more effective than placebo in the treatment of fibromyalgia
J Int Med Res. 1988 Mar-Apr;16(2):83-91	tizanide + ibuprofen more effective than placebo + ibuprofen in low back pain patients
Spine. 1989 Apr;14(4):438-9.	cyclobenzaprine + diflunisal more effective than either alone or placebo in acute back pain

Appendix D: Glossary of Terms:

AE: “adverse event”; an unintended negative consequence of taking a medication

buccal: pertaining to the cheek; medications in buccal preparations are absorbed while held in the mouth against the inside of the cheek

CI: “confidence interval”; the range of numerical values in which we can be confident (to a computed probability, such as 90 or 95%) that the population value being estimated will be found.

NNH; “number needed to harm”; the number of patients who must be exposed to an intervention before the an adverse event of interest occurs

NNT: “number needed to treat”; the number of patients who must be exposed to an intervention before the clinical outcome of interest occurs

NSAID: “nonsteroidal anti-inflammatory medication”

OA: “osteoarthritis”

opioid receptor: A membrane protein especially in the brain and gut; they bind opiate peptide neurotransmitters; opiates are potent agonists that occupy these receptors and mimic the action of the natural transmitters.

OR: “odds ratio”; the number of people with the outcome who were exposed to a factor over those with disease who were not exposed divided by those without the outcome who were exposed to the same factor over those without who were not exposed; the odds of exposure among the cases compared with the odds of exposure among the controls

PPI: “proton pump inhibitor”; class of medications used to treat gastritis and peptic ulcer disease

QoL: “quality of life”; refers to the patient’s level of comfort, enjoyment, and ability to pursue daily activities. Often used as a measure of the overall benefit to patients in studies of treatment options.

RA: “rheumatoid arthritis”

RCT: “randomized controlled trial”; study design where treatments, interventions, or enrollment into different study groups are assigned by random allocation rather than by conscious decisions of clinicians or patients. If the sample size is large enough, this study design avoids problems of bias and confounding variables by assuring that both known and unknown determinants of outcome are evenly distributed between treatment and control groups.

RR: “risk ratio” or “relative risk”; the ratio of the probability of developing, in a specified period of time, an outcome among those receiving the treatment of interest or exposed to a risk factor, compared with the probability of developing the outcome if the risk factor or intervention is not present

transcutaneous: Entering the body through the dermis or skin; in medications, the administration of a drug by application to the skin in ointment or patch form.

transmucosal: Entering the body through a mucosal membrane; in medications, the administration of a drug by absorption while through a mucus membrane (buccal, intranasal, rectal).