

# Wyoming Drug Utilization Review

## Fibromyalgia: The Misunderstood Syndrome

Kerri Powell, Pharm.D. Candidate

Fibromyalgia (FM) is often a misunderstood and misdiagnosed musculoskeletal syndrome characterized by widespread muscle/joint pain and tenderness.<sup>1</sup> Although FM is considered a rheumatic condition, it is not a form of arthritis as it does not cause inflammation or damage joints, muscles, or other tissues. Approximately 3-6% of the population is affected by FM, predominantly women. It is commonly diagnosed in individuals between 30-50 years of age; however, onset can occur during childhood.<sup>1</sup> The exact cause is unknown and is thought to be related to the central nervous system's processing of pain, an imbalance of neurotransmitters, and/or dysfunction of skeletal muscle nociception.<sup>4,5</sup> FM may be triggered by physical trauma such as an accident, surgery, or illness.<sup>3</sup> Patients often present with

profound, widespread, chronic pain and fatigue that interferes with daily activities. Sleep disturbances and other associated complications, such as irritable bowel and bladder, headaches/migraines, restless leg syndrome, impaired memory and concentration, anxiety, depression, and other neurological complications may occur and fluctuate over time.<sup>2</sup>

No laboratory or diagnostic test exists for FM. Diagnosis is based on patient symptoms, physical examination, and exclusion of other disorders.<sup>1</sup> The American College of Rheumatology has developed FM diagnostic criteria consisting of widespread musculoskeletal pain (bilateral, above and below the waist, and axial skeleton) for at least three months and tenderness in 11 of 18 identified tender point sites, shown in Figure 1 on page 3.<sup>1,4,6</sup> The management of FM is complex as there is no cure or single most-effective treatment, requiring both pharmacologic and non-pharmacologic treatments to manage symptoms.

### Non-Pharmacologic Treatments

The goal of treating FM is to enhance overall health. Studies indicate patients enrolled in FM treatment programs comprised of patient education, physical activity, and self-management

strategies demonstrated an improved quality of life and overall well-being.<sup>13</sup> Education enables patients to understand their illness, learn how to avoid triggers (stress, excessive physical exertion, lack of slow-wave sleep, and changes in humidity and barometric pressure), and learn self-management strategies.<sup>7,8,9</sup> Self-management strategies include adequate sleep, exercise, a well-balanced diet, and involvement in FM support groups (National Fibromyalgia Partnership [www.fmpartnership.org](http://www.fmpartnership.org), Fibromyalgia Network [www.fimnetnews.com](http://www.fimnetnews.com), and the National Fibromyalgia Association [www.fmaware.org](http://www.fmaware.org)).<sup>7,8,9</sup> Exercise improves physical function, mood, and symptom severity, as well as increasing the threshold for tender-point pain.<sup>10,11,12</sup>

### Pharmacologic Treatments

Many different pharmacological treatments are employed to control symptoms, but Pregabalin (*Lyrica*) is the only FDA-approved agent for the treatment of FM.<sup>28</sup>

**Anti-Convulsants** improve pain, physical function, slow-wave sleep, and overall well-being. Common side effects include dizziness, drowsiness, and peripheral edema.<sup>23,24</sup>

- **Pregabalin** (*Lyrica*) is an analogue of GABA and selectively binds to the alpha-2-delta subunit of the voltage-gated calcium channel; however, the exact mechanism is unknown. Pregabalin at 450mg per day has shown to significantly reduce the pain severity (29% vs. 13%, P=0.003), improve sleep, fatigue, and health-related quality of life.<sup>16,27</sup> The recommended daily dose for FM is 300mg to 450mg per day. Doses greater than 450mg per day have not proven to be more effective and are associated with a higher incidence of adverse effects. The starting dose is typically 75mg twice a day increasing to 150mg twice a day within a week based on efficacy and tolerability.<sup>28</sup> Pregabalin is a Schedule V controlled substance with an increased potential for dependence, misuse, and/or abuse.<sup>25</sup> Discontinuation of pregabalin should be gradual over a minimum of one week.<sup>24</sup>
- **Gabapentin** (*Neurontin*) is structurally similar to pregabalin, and patients treated with doses of 1,200 to 2,400mg per day showed significant reduction in brief pain inventory (BPI  $\geq$  30%; P=0.015), sleep, and fatigue. Gabapentin study results were consistent with pregabalin results.<sup>22</sup>

**Central Nervous System Active Agents** are also successful pharmacotherapy agents used to treat FM as they affect the neurotransmitters (serotonin, norepinephrine, and Substance P) and may act on the brain and spinal cord to modulate pain sensation and tolerance.<sup>4</sup>

- **Low-dose tricyclic antidepressants (I.e. Amitriptyline) and cyclobenzaprine** have the largest supporting evidence for use in FM patients and are typically considered first-line

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# WY-DUR Board Meeting Update

The DUR Board met for its bimonthly business meeting on September 27, 2007. Highlights of this meeting include:

- The Department of Health gave an update on the regulation requiring the use of tamper resistant prescription pads effective October 1, 2007 for all Medicaid prescriptions. Implementation of the regulation has been postponed for six months.
- The Department of Health announced that GHS has been selected to negotiate supplemental drug rebates for Wyoming Medicaid.
- A new draft of antidepressant criteria was approved by the Board. The criteria can be viewed at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR). The DUR program is asking for public comment through November 9, 2007. Public comment can be emailed to [alewis13@uwyo.edu](mailto:alewis13@uwyo.edu) or [lgm@uwyo.edu](mailto:lgm@uwyo.edu) or can be mailed to:

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- Draft prior authorization criteria for Invega were approved by the Board and can be viewed at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR). Public comment will be accepted through November 9, 2007 and may be provided via the mechanisms listed above.
- The Preferred Drug List Advisory Committee will be meeting October 10, 2007 in Cheyenne to review beta blockers and newer insomnia medications. The agenda may be viewed online at [www.uwyo.edu/PDL](http://www.uwyo.edu/PDL).

The next DUR Board meeting will be held November 30, 2007 in Casper. Topics for discussion will include the antidepressant and Invega criteria. An agenda will be posted approximately two weeks prior to the meeting.

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therapy.<sup>11</sup> Tricyclic agents inhibit the re-uptake of serotonin and norepinephrine, improve pain, stiffness, fatigue, quality of sleep, and global well-being. Unfortunately, these agents have a high frequency of side effects including anticholinergic effects (dry mouth and eyes, urinary retention, and constipation) and sedation. These side effects and potential cardiotoxicity limit tricyclic use in the elderly.<sup>4,12,14</sup> Amitriptyline doses range from 5mg to 50mg per day at bedtime (titrated doses). Cyclobenzaprine doses typically start at 10mg at bedtime and are increased as tolerated to 40 mg per day, either at night or divided during the day.<sup>28</sup>

- **Selective Serotonin Reuptake Inhibitors (SSRI)** have shown mixed results with only moderate improvement in FM related symptoms.<sup>12</sup> Fluoxetine in combination with amitriptyline has shown to be better than either drug alone. Amitriptyline counteracts the potential negative impact of the SSRI on sleep. In turn, fluoxetine inhibits the metabolism of amitriptyline increasing the levels of amitriptyline.<sup>3,4,12,15,28</sup>
- **Serotonin Norepinephrine Reuptake Inhibitors (SNRI)** enhance serotonin and norepinephrine neurotransmission and lack the adverse side effects associated with tricyclic medications. Duloxetine is effective in the management of pain and depression symptoms but has no effect on sleep dysfunction or tender point pain. Male patients treated with duloxetine did not see any significant improvement.<sup>4,11,20</sup> Venlafaxine has shown mixed results.<sup>21</sup>

**Analgesics** have shown some benefit as adjunctive therapy to control pain in FM patients.<sup>28</sup>

- **Tramadol**, with or without acetaminophen, has been shown to improve pain and physical function, but with risk of potential abuse with long term use. In patients also taking

antidepressants, neuroleptics, or other agents that decrease the seizure threshold, an increased risk of seizures exists.<sup>3,4,20</sup>

- **Non-Steroidal Anti-inflammatory (NSAID)** agents are useful adjuncts for analgesia when combined with tricyclic medications; however, when used alone they are ineffective.<sup>4,20,28</sup>
- **Opioids** are used to treat many chronic pain syndromes, but controlled clinical trials have not been conducted for use in FM patients. Due to the potential for abuse, opioids should be considered only after all pharmacologic and non-pharmacologic therapies have failed.<sup>3,4,16,28</sup>

**Non-benzodiazepines** sleep agents may help improve sleep and reduce fatigue; however, there is no evidence or evaluation of effectiveness in FM patients. Zolpidem only affects the onset of sleep; whereas, eszopiclone is effective in sleep onset, duration, and maintenance of chronic insomnia.<sup>3,28</sup>

## **Conclusion**

Fibromyalgia is a difficult syndrome to treat as symptoms vary among patients; therefore, treatment must be individualized. Upon diagnosis, the patient should be educated about FM and other comorbidities should be evaluated and treated. Although Pregabalin is the only FDA-approved agent for the treatment of fibromyalgia; clinical trials only show modest efficacy in pain relief.<sup>28</sup> Typically, CNS-active medications have been the most effective agents for the treatment of FM. Low-dose tricyclics, amitriptyline and cyclobenzaprine, show strong evidence for efficacy; therefore, initially, a trial of a low-dose tricyclic antidepressant or cyclobenzaprine should be considered.<sup>20,28</sup> If further therapy is required, a trial of other medications (tramadol, SSRI, or SNRI), a combination of medications, or use of anticonvulsants (gabapentin or pregabalin) might be benefi-

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# Medicaid Coverage for Smoking Cessation

Aimee Lewis, Pharm.D.

Wyoming Medicaid began covering tobacco cessation medications on January 1, 2007. This has been a very successful program to date, serving 642 recipients who have received 1,079 claims for a total of \$106,050.

Since coverage of smoking cessation products began, a noticeable trend of using both varenicline (Chantix) and bupropion (Wellbutrin SR, Zyban) together has been observed. A Medline search conducted September 10, 2007 revealed no clinical studies regarding the use of the two products together. No evidence can be found regarding the safety or effectiveness of this practice, however, there is a significant increase in the cost of therapy with the combination versus either agent alone.

Bupropion can be used with any form of nicotine replacement therapy (NRT), although treatment-emergent hypertension has been observed with bupropion and the nicotine patch.<sup>1</sup> Varenicline plus

NRT may result in an increased incidence of adverse effects including nausea, headache, vomiting, dizziness, dyspepsia and fatigue. One study showed a much higher rate of discontinuation with the combination of varenicline and NRT versus NRT alone or placebo.<sup>2</sup>

When using bupropion for smoking cessation alone, please dispense Zyban or its generic equivalent. This will help to identify clients for additional support through case management as well as track utilization of tobacco cessation medications. Appropriate utilization of these agents will ensure continued success of this program by allowing smoking cessation therapy to be provided to as many recipients as possible while working within the confines of a finite budget.

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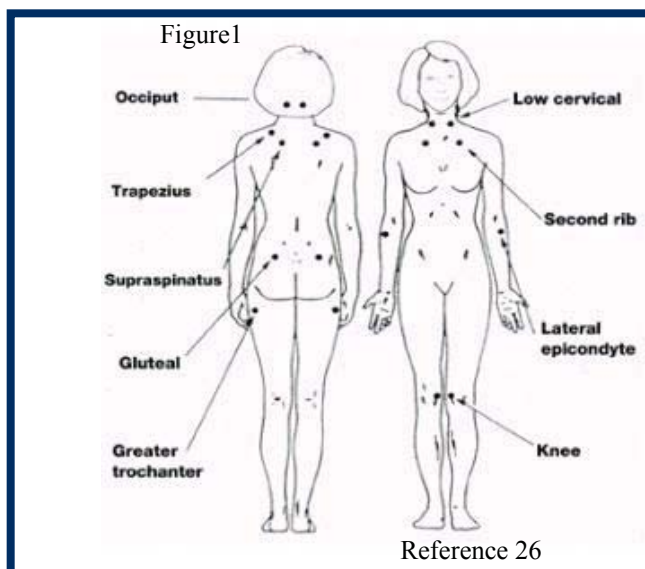
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cial. Pharmacological therapy is most effective when combined with education and exercise. Patients who do not respond to the above therapies should be referred to an appropriate specialist (rheumatologist, psychiatrist, pain management specialist).<sup>20,28</sup>

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