



Treatment of Fibromyalgia Syndrome (FMS)

Fibromyalgia Syndrome (FMS) is characterized by chronic, widespread, non-inflammatory pain, fatigue, stiffness, sleep disturbances, and mood changes.¹⁻³ Women are more commonly affected than men and an exact cause is largely unknown.³ Onset of fibromyalgia has been associated with physical and emotional events such as injury, stress, infection or illness, and can be exacerbated by various stressors.¹⁻⁴

In the absence of musculoskeletal abnormalities, the underlying pathology of FMS is hypothesized to involve neurotransmitter imbalance, therefore manifesting as a disorder of pain regulation.⁴ Diagnosis is contingent on a 3-month history of widespread, bilateral, axial pain above and below the waist, accompanied by pain on palpation at 11 or more of 18 tender points.¹⁻³ In addition to fatigue and stiffness, other diagnostic symptoms include neurological and neurocognitive dysfunction, sleep disturbances, and possible autonomic abnormalities.¹ Debate exists as to whether depression is a risk factor, co-morbidity, or a complication of fibromyalgia.^{1,2,5}

The neuropathic etiology of fibromyalgia pain makes FMS difficult to fully treat. Therapy aims to reduce pain, stiffness, and fatigue while improving physical and mental stamina, functionality, and quality of life.^{1,2,6,7} No single pharmacological agent addresses all symptoms of FMS. Rather, treatment options aim at attenuating various symptoms, rarely resolving them entirely.^{6,7} The following is an evidence-based summary of available therapies for FMS. Generally, the evidence from clinical trials with these agents is limited by the relatively short duration of study and low subject count.

Tricyclic Medications

Literature supports the use of tricyclic medications as first-line therapy for FMS.

- Amitriptyline (Elavil®) has the strongest evidence for the treatment of fibromyalgia. Two meta-analyses found amitriptyline to have modest efficacy over placebo at improving pain severity, fatigue, sleep, and overall well-being.^{2,8-10} It has also been shown to improve tender point pain, although some studies included in the analysis were limited by small sample size.^{2,8,10} Typical doses start at 5-10 mg HS, titrated to 25-50 mg HS as tolerated.^{9,10} Secondary tricyclic antidepressants such as desipramine may be better tolerated but studies are lacking.^{6,7}
- Cyclobenzaprine (Flexeril®) in various doses resulted in more self-reports of improvement over placebo in a meta-analysis.^{6,8,9} Efficacy and treatment effect were found to be comparable to that of amitriptyline, although improvements in pain severity were not significant beyond 8 or 12 weeks of therapy.⁶ Doses of cyclobenzaprine range from 10-40 mg divided daily or HS as tolerated.⁶⁻⁸

Reuptake Inhibitors: SSRIs and SNRIs

Evidence suggests that reuptake inhibitors may be an appropriate first-line therapy if further trials show efficacy in patients with a significant depressive component.

- Fluoxetine (Prozac®) has shown improvement in pain, fatigue, and depression at doses from 20 mg up to 80 mg daily in a placebo-controlled trial.^{1,5-7} A crossover trial showed that combination therapy of fluoxetine 20 mg AM & amitriptyline 25 mg HS was better than either antidepressant alone in a number of outcome measures, noting similar results with fluoxetine 20 mg AM & cyclobenzaprine 10 mg HS.⁵⁻⁷
- Escalating doses of controlled-release paroxetine (Paxil CR®) have shown benefit in a large placebo-controlled trial. Significantly more subjects receiving controlled-release paroxetine 12.5-62.5 mg daily achieved ≥ 25% improvement in symptom scores than those receiving placebo.⁵⁻⁶
- Duloxetine (Cymbalta®), a potent dual reuptake inhibitor, has shown significant improvement over placebo in two multicenter trials.^{6,10-11} Sixty milligrams given once or twice daily improved pain threshold, functionality, and quality of life scores. Duloxetine did not significantly improve pain severity.¹⁰⁻¹¹
- Venlafaxine (Effexor®) was found to be efficacious in two small open-label studies but a large clinical trial found no significant improvement over placebo.¹¹⁻¹²

Anticonvulsants

- Pregabalin (Lyrica®) is currently the only medication with an FDA-labeled indication for the treatment of fibromyalgia in the U.S.^{7,11} A 14-week RCT found 77.8% of patients taking Lyrica® 450 mg and 66.1% taking Lyrica® 600 mg reported improvement of symptoms versus 47.6% of those receiving placebo.¹¹ Mean reduction in pain severity was 0.93 points on a 10-point visual analog scale.⁶ An 8-week trial found that Lyrica® 450 mg daily more than doubled the likelihood of achieving ≥ 50% improvement in symptoms over placebo.^{7,11} Pregabalin displays dose-dependent improvement in pain, fatigue, sleep, and quality of life.¹¹
- Gabapentin (Neurontin®) has displayed similar efficacy and tolerability as pregabalin at doses ranging from 1200 – 2400 mg daily.^{6,7,11}

Analgesics and Anti-Inflammatory Drugs

- Tramacet® (tramadol 37.5 mg / acetaminophen 325 mg) showed modest improvement in pain and associated symptom scores versus placebo. A randomized trial found 35% of Tramacet®-treated subjects achieved ≥ 50% reduction in pain scores versus 18% with placebo.^{7,13} The dose was titrated to a maximum of 2 tablets QID, and may be effective initial therapy in patients previously untreated with tricyclics or anticonvulsants.¹³
- NSAIDs and corticosteroids have no evidence supporting their use due to the non-inflammatory pathogenesis of fibromyalgia.^{6,7} Opioid analgesics have not yet been investigated in controlled trials.¹¹

Sedative-Hypnotics

- Zopiclone, clonazepam, and other sedatives may help with fatigue by aiding sleep onset, but no evidence is currently available on outcomes in fibromyalgia.^{2,7,11}

Non-Pharmacologic Therapy

There is strong evidence to support multi-disciplinary treatment of fibromyalgia. Sustained improvement on outcomes has been reported with:^{1,2,7}

- Cognitive Behavioural Therapy (CBT) - beliefs about pain control
- Aerobic exercise - cardiovascular & strength training
- Patient Education – real diagnosis, condition waxes & wanes, expectations of therapy
- Sleep hygiene

- Stress management

Investigational Drugs & Natural Health Products

Inadequately controlled fibromyalgia pain may lead patients to seek alternative treatment modalities. Evidence supporting the use of these products is weak, requiring further evaluation.

- Natural Health Products¹ – SAMe, 5-HTP, melatonin, malic acid, magnesium, zinc, essential fatty acids, B-complex, ginkgo biloba, valerian
- Others¹¹ – pramipexole (Mirapex®), ropinirole (Requip®), human growth hormone, lidocaine injections, modafinil (Alertec®), sodium oxybate

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Frequently Asked Questions Regarding Guaifenesin for Treatment of Fibromyalgia

Is guaifenesin effective for fibromyalgia?

There is no solid evidence. There is only one unpublished study using guaifenesin 600mg b.i.d. versus placebo which showed no difference between the groups(1).

What is the “guaifenesin protocol”?

A physician in the US, Dr. St. Amand, has promoted a treatment protocol using guaifenesin for fibromyalgia. The protocol, detailed on his website, includes instructions for the titration of guaifenesin along with instructions to avoid products that contain salicylate which will negate the effect of guaifenesin(2). According to the protocol, the dose of guaifenesin used is 300mg b.i.d. titrated up to 1200mg b.i.d.. Titration is based on worsening of symptoms. In other words, if symptoms do not worsen, dose is increased.

Does the “guaifenesin protocol” work?

Evidence is based on the experience of Dr. St. Amand as opposed to large, randomized, placebo controlled trials. The one unpublished study mentioned above is refuted on Dr. St. Amand's website citing poor study design as participants may have been exposed to salicylates(3). This may be so but still leaves us with no published, clinical evidence.

What type of guaifenesin is used?

There are three specific brands promoted on Dr. St. Amand's website including Mucinex, Sologuai Six by Cleure, and a compounded product called FibroFree none of which are available in Canada(4). In fact, there are no commercial solid dosage forms of guaifenesin available in Canada(5), although a powder is available from Medisca. It is not recommended to use cough syrups containing guaifenesin.

Is guaifenesin safe?

According to published data the following adverse reactions are possible: rash, nausea, vomiting, dizziness, and headache . Kidney stones have been reported only in those abusing medications containing guaifenesin(6).

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