September 21, 2007 — The European League Against Rheumatism (EULAR) has issued the first guidelines for the treatment of fibromyalgia syndrome (FMS) and published them in the September 17 Online First issue of the *Annals of the Rheumatic Diseases*.

"Although effective treatments are available no guidelines exist for management of FMS," write Serena F. Carville, from King's College London, United Kingdom, and colleagues. "The objectives were to ascertain the strength of the research evidence on effectiveness of treatment of FMS and develop recommendations for its management based on the best available evidence and expert opinion to inform healthcare professionals."

The authors of these guidelines consisted of a multidisciplinary task force from 11 European countries. This panel defined the study design a priori, using standard operating procedures published by EULAR. These included search strategy, which was a systematic review using the keywords "fibromyalgia," "treatment or management," and "trial"; "participants"; "interventions"; "outcome measures"; "data collection"; and "analytical method."

Exclusion criteria for identified studies were failure to use classification criteria from the American College of Rheumatology (ACR), studies that were not clinical trials or studies comprising inclusion of patients with chronic fatigue syndrome or myalgic encephalomyelitis. The main endpoints were change in pain measured by the visual analog scale (VAS), and the fibromyalgia impact questionnaire (FIQ).
The panel categorized the studies by quality, based on whether they were randomized, blinded, and concealed allocation, and they used only the highest-quality studies as a basis for their recommendations. The panel used a Delphi process to provide a basis for recommendation when evidence from the literature was inadequate.

Of 146 studies eligible for review, 39 pharmacologic intervention studies and 59 nonpharmacologic studies were used to create the final recommendation summary tables, after those of lower quality or with insufficient data were excluded. Identified categories of treatment were antidepressants, analgesics and "other pharmacological," and exercise, cognitive behavioral therapy, education, dietary interventions, and "other nonpharmacological interventions."

Using this systematic review process and expert consensus, the panel developed 9 recommendations for the management of FMS. However, many studies reviewed had insufficient sample size and study quality to allow the panel to issue strong recommendations. EULAR plans to update the guidelines every 5 years and incorporate findings from good-quality clinical trials that will add to currently available evidence.

"These recommendations are the first to be commissioned for FMS, although previous reviews have addressed the area," the review authors conclude. "These recommendations should assist health care providers, with a secondary intention to incorporate information into materials for patients. The 9 recommendations included 8 management categories, 3 of which had strong evidence from the current literature, and 3 were based on expert opinion."

Specific recommendations in these guidelines regarding general considerations for management of FMS are as follows:

- Comprehensive evaluation of pain, function, and psychosocial context is needed to understand FMS completely, because it is a complex, heterogeneous condition involving abnormal pain processing and other secondary features (level of evidence, IV D).
- Optimal treatment of FMS mandates a multidisciplinary approach, which should include a combination of nonpharmacologic and pharmacologic interventions. After discussion with the patient, treatment modalities should be specifically tailored based on pain intensity, function, and associated features such as depression, fatigue, and sleep disturbance (level of evidence, IV D).

Specific recommendations on nonpharmacologic management of FMS are as follows:

- Heated pool treatment, with or without exercise, is effective (level of evidence, IIA B).
- For some patients with FMS, individually tailored exercise programs can be helpful. These may include aerobic exercise and strength training (level of evidence, IIB C).
- For certain patients with FMS, cognitive behavioral therapy may be beneficial (level of evidence, IV D).
- Based on the specific needs of the patient, relaxation, rehabilitation, physiotherapy, psychological support, and other modalities may be indicated (level of evidence, IIB C).

Specific recommendations on pharmacologic management are as follows:

- Tramadol is recommended for management of pain (level of evidence, Ib A). Although other treatment options may include simple analgesics (eg, paracetamol) and other weak opioids, corticosteroids and strong opioids are not recommended (level of evidence, IV D).
- Antidepressants are recommended for the treatment of FMS because they decrease pain and often improve function (level of evidence, Ib A). Appropriate options may include amitriptyline, fluoxetine, duloxetine, milnacipran, moclobemide, and pirlindole.
- Tropisetron, pramipexole, and pregabalin are recommended for the treatment of FMS because they reduce pain (level of evidence, Ib A).

Limitations of these recommendations are that some are based only on expert opinion; basis from clinical trial data limited to changes in pain measured by the VAS and function evaluated with the FIQ; failure to consider positive effects on other outcome measures of pain or on function evaluated with different instruments; and high variability in outcome measures used, results reporting, and poor methodologic quality precluding meta-analysis.

"Guidance on how to conduct good RCTs [randomized controlled trials] in FMS, including standardised outcome measures and validated, sensitive instruments is important for future research," the review authors conclude. "The assessment of strength of evidence tends to favour pharmacological studies as double blinding and placebo controls are impossible in many non-
pharmacological studies. However, most non-pharmacological interventions are safe and have other health benefits."

EULAR provided financial support for creation of these guidelines. Some of the review authors have disclosed various financial relationships with Procter and Gamble, Sanofi-Aventis, Roche, Bristol Meyers Squibb, Pierre Fabre, Servier, Pfizer, Eli Lilly, Jazz Pharmaceutical, Allergan, and Wyeth.

*Ann Rheum Dis.* Published online September 17, 2007.

**Learning Objectives for This Educational Activity**

Upon completion of this activity, participants will be able to:

1. Describe pharmacologic measures that may be indicated for management of fibromyalgia syndrome.
2. Describe nonpharmacologic measures that may be indicated for management of fibromyalgia syndrome.

**Clinical Context**

The predominant rheumatologic features of FMS include chronic, widespread pain and lowered pain threshold, with hyperalgesia and allodynia. Other features often accompanying FMS include fatigue, depression, anxiety, sleep problems, headache or migraine, bowel irregularity, diffuse abdominal pain, and urinary frequency.

The most frequently used research classification criteria for FMS are those developed by the ACR. However, no previous guidelines have addressed management of FMS, despite the availability of effective treatments. EULAR sought to evaluate the strength of the research evidence on the effectiveness of FMS treatment and to develop management recommendations for healthcare professionals based on the best evidence and expert opinion.

**Study Highlights**

- A multidisciplinary task force from 11 European countries wrote these guidelines using EULAR standard operating procedures.
- Studies were excluded that were not clinical trials, did not use ACR classification criteria, or included patients with chronic fatigue syndrome or myalgic encephalomyelitis.
- Main outcomes studied were change in pain on the VAS and the FIQ.
- The panel based its recommendations on only the highest-quality studies. A Delphi process was used for consensus opinion when evidence from the literature was inadequate.
- Of 146 eligible studies reviewed, those of lower quality or with insufficient data were excluded, and 39 pharmacologic and 59 nonpharmacologic studies were used to create the 9 final recommendations.
- The 9 recommendations included 8 management categories, 3 of which had strong evidence from the current literature, and 3 that were based on expert opinion.
- The 9 recommendations were as follows:
  - Comprehensive evaluation of pain, function, and psychosocial context are needed to understand FMS completely, because of its complex, heterogeneous nature.
  - Optimal treatment of FMS mandates a multidisciplinary approach, including nonpharmacologic and pharmacologic interventions. Treatments should be specifically tailored to patient reports of pain intensity, function, and associated features such as depression, fatigue, and sleep disturbance.
  - Heated pool treatment, with or without exercise, is effective. Individually tailored exercise programs, which may include aerobic exercise and strength training, may be helpful for some patients.
  - Cognitive behavioral therapy, relaxation, rehabilitation, physiotherapy, psychological support, and other modalities may be indicated for certain patients.
  - Tramadol is recommended for management of pain from FMS. Simple analgesics (eg, paracetamol) and other weak opioids may be considered, but corticosteroids and strong opioids are not recommended.
  - Antidepressants are recommended to decrease pain and improve function (eg, amitriptyline, fluoxetine, duloxetine, milnacipran, moclobemide, and pirilindole).
  - Tropisetron, pramipexole, and pregabalin are recommended to reduce pain of FMS.
- EULAR plans to update the guidelines every 5 years and incorporate findings from good-quality clinical trials that will add to currently available evidence.
Pearls for Practice

- Pharmacologic interventions recommended for FMS include tramadol for pain management, with simple analgesics and weak opioids if needed. Corticosteroids and strong opioids are not recommended. Antidepressants are recommended to decrease pain and improve function.
- Nonpharmacologic interventions recommended for FMS include comprehensive evaluation; multidisciplinary, specifically tailored therapy; and heated pool treatment, with or without exercise. Individually designed exercise programs, cognitive behavioral therapy, relaxation, rehabilitation, physiotherapy, psychological support, and other modalities may be helpful for some patients.

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This article is intended for primary care clinicians, rheumatologists, and other specialists who care for patients with fibromyalgia syndrome.

Goal

The goal of this activity is to provide medical news to primary care clinicians and other healthcare professionals in order to enhance patient care.

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