## European Group Issues Fibromyalgia Guidelines

BY NANCY WALSH New York Bureau

ibromyalgia guidelines issued by the ↓ European League Against Rheumatism represent a work in progress on a field "that is very much in evolution," Dr. Philip J. Mease said in an interview.

The recommendations were formulated by a European working group that included specialists from various fields including rheumatology, pain medicine, and neurology, who reviewed all the available trials through 2005.

They have done a good job with a difficult challenge, because the trials are so different, both in terms of the outcome measures used and the treatment approaches tried," said Dr. Mease, a rheumatologist who is clinical professor of medicine, University of Washington, Seattle, and chief of rheumatology clinical research, Swedish Hospital Medical Center, Seattle.

'Moreover, they used a balanced way of looking at both pharmacologic and nonpharmacologic approaches, to give the managing physician a choice of therapeutic approaches," he said.

Among the general recommendations of the EULAR investigators were the concepts that fibromyalgia requires a comprehensive assessment of pain, function, and psychosocial context, and that treatment should be multidisciplinary, combining various modalities tailored to pain intensity, function, and associated features such as depression and fatigue. While recommendations were evidence based whenever possible, these general recommendations regarding the heterogeneity of fibromyalgia and the need for multidisciplinary treatment were based on expert opinion.

Among the recommendations for nonpharmacologic measures were for the use of heated pool treatment, with or without exercise. This modality was found to be effective in improving pain and function in several "fairly high quality" trials, according to the investigators.

They also suggested that cognitive-behavioral therapy may be beneficial for some patients. This recommendation was based on expert opinion, but the only two studies identified that evaluated this approach were of poor quality. However, they wrote, "This is another area in which the poor quality of trials has masked what experts believe to be a realistic reflection of possible benefits," and cited potential improvements in pain and function (Ann. Rheum. Dis. July 20, 2007 [Epub doi:10.1136/ard.2007.071522]).

With regard to pharmacologic treatments, the working group recommended tramadol for the management of pain, based on two randomized controlled trials. They also favored the use of acetaminophen and other weak opioids.

However, they advised against the use of corticosteroids and strong opioids, because of their potential for significant long-term side effects and a scarcity of clinical trial data.

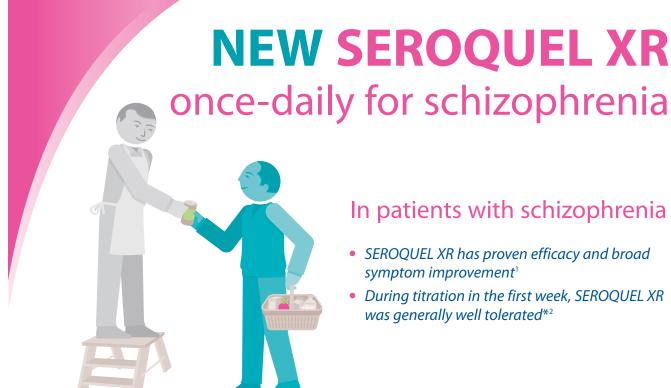
Antidepressants should be considered, the recommendations state, because of their ability to reduce pain and often to improve function. Amitriptyline, for example, was found to be beneficial in four of five trials that assessed pain according to a visual analogue scale (VAS).

The amitriptyline data exemplify a difficulty the investigators faced in their analysis when there were multiple trials evaluating the same drug, in that they averaged the effect sizes in these trials. With some trials being of high quality and others not, this may have skewed in an adverse way the effect size for amitriptyline, Dr. Mease observed.

Other antidepressants that have shown benefits in varying numbers and sizes of trials were fluoxetine, duloxetine, milnacipran, moclobemide, and pirlindole.

Finally, the investigators stated that tropisetron, pramipexole, and pregabalin reduce pain and should be considered for the treatment of fibromyalgia. This recommendation illustrates a further difficulty faced by EULAR. "Both pregabalin and pramipexole are recommended, but if you look at the specific trials they are vastly different," Dr. Mease said. Pregabalin was evaluated in a multicenter, 500-plus patient trial that was very well controlled and excluded all other drugs that might influence fibromyalgia. In contrast, the pramipexole trial took place in a single center and, importantly, permitted the use of background drugs including opioids, he said.

The recommendations will be updated every 5 years, with the hope that clinical trials of good quality will add to the available evidence, according to the investigators.



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- During titration in the first week, SEROQUEL XR was generally well tolerated\*2

## **Important Safety Information**

- SEROQUEL XR is indicated for the treatment of schizophrenia. Patients should be periodically reassessed to determine the need for treatment beyond the acute response
- Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death, compared to placebo (4.5% vs 2.6%, respectively). SEROQUEL XR is not approved for the treatment of patients with dementia-related psychosis (see Boxed Warning)
- Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics, including quetiapine. The relationship of atypical use and glucose abnormalities is complicated by the possibility of increased risk of diabetes in the schizophrenic population and the increasing incidence of diabetes in the general population. However, epidemiological studies suggest an increased risk of treatment-emergent, hyperglycemia-related adverse events in patients treated with atypical antipsychotics. Patients starting treatment with atypical antipsychotics who have or are at risk for diabetes should undergo fasting blood glucose testing at the beginning of and periodically during treatment. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing
- A potentially fatal symptom complex, sometimes referred to as Neuroleptic Malignant Syndrome (NMS), has been reported in association with administration of antipsychotic drugs, including quetiapine. Rare cases of NMS have been reported with quetiapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include immediate discontinuation of antipsychotic drugs

\*Data combined from 2 multicenter, 6-week, randomized, double-blind, placebo-controlled schizophrenia trials comparing SEROQUEL XR (n=679) to placebo (n=235). During Week 1, incidence of somnolence was 9.0% vs 1.3% for placebo, sedation was 7.4% vs 3.4% for placebo, dizziness was 5.9% vs 2.6% for placebo, dry mouth was 6.8% vs 0.9% for placebo, headache was 3.4% vs 6.4% for placebo, and insomnia was

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