Chart Review: Jane

BACKGROUND

Personal Information: 48-year-old Caucasian female

Background: New patient.

Neuropsychiatric History : Prior episode of anxiety and depression in college and postpartum.

Medical History : Presents with widespread musculoskeletal pain. Exhausted, not sleeping well (wakes often in the night, sometimes from the pain, exhausted by mid-afternoon, unable to concentrate on classes). Daily headaches radiating from neck. History of severe migraines in teens and 20s; frequency has decreased in last 10 years. Chronic constipation. Serious MVA at 27 with fractured leg and concussion.

Social History : Married school teacher with 2 children ages 15 and 18. Drinks socially on weekends. Has never smoked, no history of illicit drug use.

Family History : No history of chronic musculoskeletal or rheumatic diseases. Reports mother hospitalized 10 years ago with major depressive disorder.

continued on next page

Chart Review: Jane

TODAY'S VISIT

Chief Complaint: Started 2 years ago after a viral illness. Began in the neck and shoulders—patient believed she had strained a muscle in exercise class. Pain became generalized in the month after. Pain has worsened in the past 6 months. Joints feel swollen, but no visible swelling. Ceased going to gym after onset of chronic widespread pain. Gained about 15 pounds.

Evaluation/Treatment to Date: Visited 2 MDs who could find nothing wrong. Lab tests and X-rays were unremarkable. Referred to neurologist and psychiatrist.
Past medication: 20mg fluoxetine daily for 1 week (experienced agitation/jittery and discontinued)
Current medication: Ibuprofen, 2 or 3 every 6-8 hours with minimal relief; also states she is taking numerous supplements recommended by personal trainer
Mood evaluation: Denies feeling anxious or depressed; husband states she has become irritable

Physical Exam: BMI 25.7. Unremarkable findings for skin, head and neck, heart and lungs. Joint swelling and deformities absent. Joint range of motion and muscle strength within normal limits. No focal neurologic abnormalities. Excessive tenderness on palpitation (paraspinal muscles of the neck and shoulders, around the elbows, outer aspect of the hips, inside of the knees).

Management Plan:

- Education to patient and family
- Resume exercise slowly
- Discussed referral to mental health professional for comorbid mood and anxiety evaluation
- Discussed appropriate use of NSAIDS (limited evidence for efficacy)
- Patient instructed to provide further information regarding supplements
- Pharmacologic therapy: Begin with FDA-approved monotherapy
  - Agents approved: duloxitene, milnacipran, pregabalin.
  - Due to past history of agitation with SSRI and significant sleep disruption suggest pregabalin as starting medication.
  - Discuss risks and benefits of all treatment options with patient including education to patient about lack of evidence for use of opioids in fibromylagia.

This continuing education activity is co-sponsored by Indiana University School of Medicine and by CME Outfitters, LLC.

Indiana University School of Medicine and CME Outfitters, LLC, gratefully acknowledge an educational grant from Pfizer Inc. in support of this CE activity.

This CME/CE-certified activity is funded in part by CME Outfitters, LLC.

A Case of Connecting the Dots: Improving Diagnosis and Management of Fibromyalgia

Lesley M. Arnold, MD
Don L. Goldenberg, MD

Moderator

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Professor of Psychiatry
Director, Women's Health Research Program
University of Cincinnati College of Medicine
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Lesley M. Arnold, MD
Disclosures

- ***Research/Grants:*** Allergan, Inc.; Boehringer Ingelheim Pharamceuticals, Inc.; Cypress Bioscience, Inc.; Eli Lilly and Company; Forest Laboratories, Inc.; Pfizer Inc.; Wyeth Pharmaceuticals
- ***Consultant:*** Allergan, Inc.; AstraZeneca Pharmaceuticals LP; Boehringer Ingelheim Pharamceuticals, Inc.; Cypress Bioscience, Inc.; Eli Lilly and Company; Forest Laboratories, Inc.; Pfizer Inc.; Sanofi-aventis; Takeda Pharmaceuticals North America, Inc.; Theravance, Inc.; UCB Pharma; Wyeth Pharmaceuticals

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Disclosures

- ***Consultant:*** Eli Lilly and Company; Forest Laboratories, Inc.; Pfizer Inc.

Disclosures of faculty financial relationships and biographical profiles can be found at neuroscienceCME.com/460

The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational uses (any use not approved by the FDA) of products or devices.

Learning Objectives

- Identify assessment and diagnostic indicators that differentiate fibromyalgia from other pain disorders
- Define the role of multimodal and multidisciplinary approaches to the management of fibromyalgia

Presentation slides and the patient chart from this activity can be found at neuroscienceCME.com/460

To receive CME/CE credits for this activity, participants must complete the post-test and evaluation online at neuroscienceCME.com/test

A Case of Connecting the Dots: Improving Diagnosis and Management of Fibromyalgia

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Learning Objective 1

Identify assessment and diagnostic indicators that differentiate fibromyalgia from other pain disorders

Learning Objective 2

Define the role of multimodal and multidisciplinary approaches to the management of fibromyalgia

Jane
Case Overview

- 48-year-old Caucasian female
- Married school teacher with children aged 15 and 18
- Presents with widespread musculoskeletal pain
- Exhausted and does not sleep well
  - Wakes up a number of times during the night, sometimes from the pain
  - Exhausted by mid-afternoon and often unable to concentrate on her remaining classes
- Headaches daily
  - "Seem to be coming from the neck" and involve the frontal and occipital region
- Chronic constipation

Pain Evaluation

- Pain started 2 years ago after a viral illness
- Pain began in the neck and shoulders
  - Strained muscles in an exercise class and then pain became generalized in the month after
- Past 6 months pain worsened
  - "I am always in pain all over my body"
- Joints feel swollen but no sign of visible swelling
  - Muscles are "sore and achy and it feels like I've been beaten up"
- Ceased going to gym after onset of chronic, widespread pain
  - Gained 15 pounds in past 18 months
  - "Every time I go to the gym I feel worse so I just stopped going"

Medical History

- Prior episodes of anxiety and depression in college and postpartum
- Serious MVA at age 27 with fractured leg and concussion
  - Completely recovered after 6 weeks in rehabilitation center
- Severe migraines in teens and 20s
  - Frequency decreased to once a year last 10 years

Mood Evaluation

- Denies feeling anxious or depressed
- Patient reports "I am just frustrated and worried"
- Husband reports patient irritability
  - "I think she feels overwhelmed"
- No history of drug use and never smoked
- Drinks socially on weekends

Evaluation/Treatment to Date

- Visited 2 physicians who found nothing wrong
- Lab tests and X-ray were unremarkable per the patient
- Referred to neurologist and psychiatrist
- Past medications:
  - 20 mg fluoxetine daily for 1 week
  - Felt agitated, jittery and discontinued
- Current medications:
  - Ibuprofen, 2-3 every 8 hours with minimal relief
  - Numerous supplements recommended by personal trainer

Family History

- No history of chronic musculoskeletal or rheumatic diseases
- History of major depressive disorder (MDD) in mother
  - Hospitalized 10 years ago

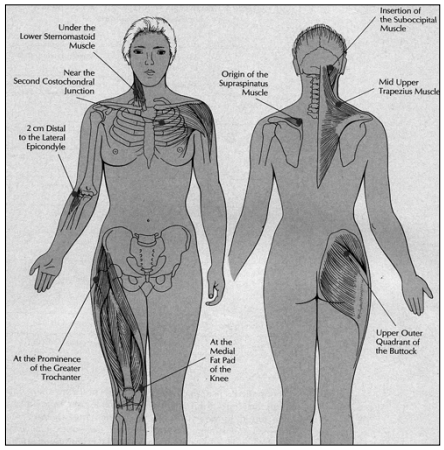
Physical Examination

- BMI 25.7
- Unremarkable findings for skin, head and neck, heart and lungs
- Joint swelling and deformities absent
- Joint range of motion and muscle strength within normal limits
- No focal neurologic abnormalities
- Excessive tenderness on palpation
  - Paraspinal muscles of the neck and shoulders
  - Around the elbows
  - Outer aspect of the hips
  - Inside of the knees

1990 ACR Fibromyalgia Classification Criteria

- History of chronic widespread pain ≥ 3 months
- ≥ 11 of 18 tender points

These criteria were sensitive (88.4%) and specific (81.1%) in comparing FM to other pain disorders



Goldenberg DL. *Hosp Pract* 1989;24:39-52.

2010 Fibromyalgia Clinical Diagnostic Criteria

- Widespread pain index (WPI)
  - How many areas has patient had pain in last week? (Score = 0-19)
    - Shoulder: Lt., Rt.; Upper arm: Lt., Rt.; Lower arm: Lt., Rt.; Jaw: Lt., Rt.; Neck
    - Buttock, hip trochanter: Lt., Rt.; Upper leg: Lt., Rt.; Lower leg: Lt., Rt.
    - Upper back; Lower back; Chest; Abdomen

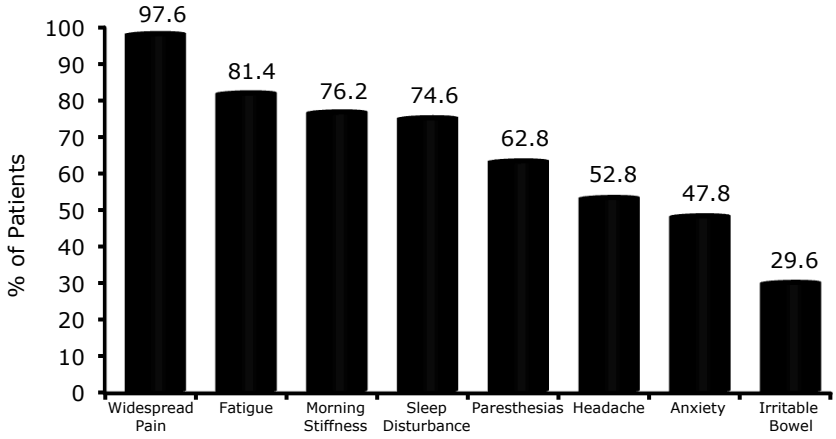
Wolfe F. *Arthritis Care Res (Hoboken)* 2010;62:583-584.

2010 Fibromyalgia Clinical Diagnostic Criteria, cont.

- Symptom severity scale (SS)
  - What is level of severity in last week? (Score = 0-12)
  - 0 = no problem, 1 = slight problem, 2 = moderate, 3 = severe
  - Fatigue
  - Waking unrefreshed
  - Cognitive disturbances
  - General somatic symptoms
- A patient satisfies the 2010 fibromyalgia clinical diagnostic criteria if a) WPI ≥ 7 and SS score ≥ 5 OR b) WPI between 3-6 and SS score ≥ 9

Wolfe F. *Arthritis Care Res (Hoboken)* 2010;62:583-584.

Frequency of Common Symptoms in Primary FM



N = 158

Wolfe F, et al. *Arthritis Rheum* 1990;33:160-172.

Diagnostic Workup for Fibromyalgia

History of chronic, widespread pain for ≥ 3 months
Associated symptoms, including fatigue, headaches, sleep and mood disturbances

Exclude other conditions that may present with chronic widespread pain (very much "clinician-dependent")

General physical exam, neurologic exam, selected laboratory testing (ESR, thyroid tests, avoid screening serologic tests)
Sleep and mood evaluation

Confirm presence of tender points, absence of synovitis

Presumptive diagnosis of fibromyalgia

Wolfe F, et al. *Arthritis Rheum* 1990;33:160-172.
Jain A, et al*. J Musculoskel Pain* 2003*;*11:3-107.

Tests Not Recommended Routinely in FM

- ANA, Rheumatoid factor
  - Only if clinical suspicion of SLE or RA
  - High false positivity
- Vitamin D
  - Most studies find no association with low levels
  - No evidence for benefit with Vit D
- Extensive thyroid testing
  - Exclude hypothyroidism
  - TSH, T4 are sufficient
- EBV, other viral titers
- Lyme serology

Differential Diagnosis of Fibromyalgia (FM)

Condition	Distinguishing Features from FM	Special Diagnostic Issues
Viral illness	Fever, rash, abnormal labs	Self-limited
RA	Small joint polyarthritis, ESR elevated	Often concurrent with FM
SLE	Rash, multisystem inflammation, elevated ESR, ANA, anti-DNA	Often concurrent with FM
Polymyalgic rheumatica	60 or older, severe stiffness, less pain, elevated ESR	Normal exam, may use short trial of prednisone
Myositis	Weakness rather than pain elevated muscle enzymes	Enzymes normal in some
Spondyloarthropathies (Seronegative spondyloarthropathies, including ankylosing spondylitis)	Back, neck immobility, elevated ESR, abnormal X-ray, imaging	No obvious synovitis
Neuropathies	Weakness, loss of sensation, abnormal EMG, NCV	Neurologic abnormalities in FM (??)

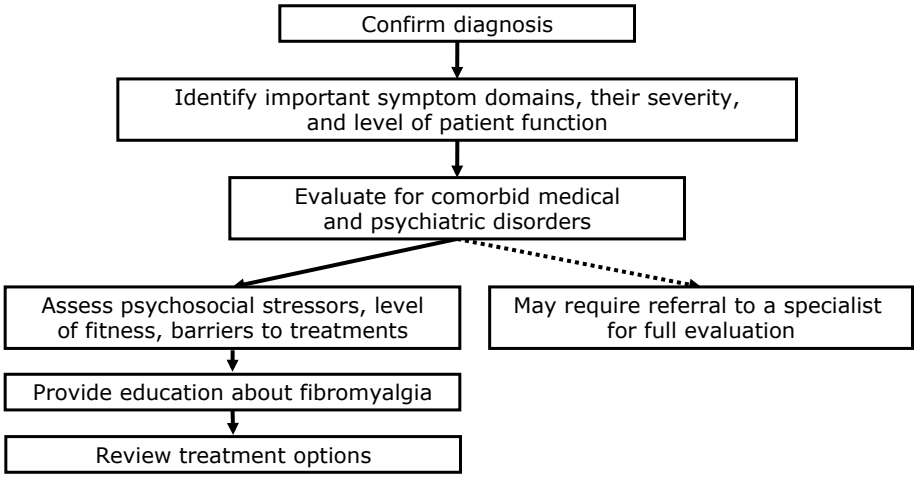
Making an Earlier Diagnosis in Fibromyalgia

- Characteristic symptoms
  - "I hurt all over"
  - "It feels like I always have the flu"
  - Fatigue, sleep and mood disturbances
  - Unremarkable examination
- Exclude rheumatic illness
  - Systemic CTD (RA, myositis, SLE, PMR)
    - Remember: False + ANA very misleading
  - Seronegative spondyloarthropathies may be confusing
  - Fibromyalgia common in RA and SLE

REMEMBER: Exclusion of structural or systemic disease

- Not a "fishing" expedition
- Avoid "screening" rheumatology tests
- Most efficient with early subspecialty referral

Stepwise Treatment of Fibromyalgia (1)



Arnold LM. *Arthritis Research and Therapy* 2006;8:212.

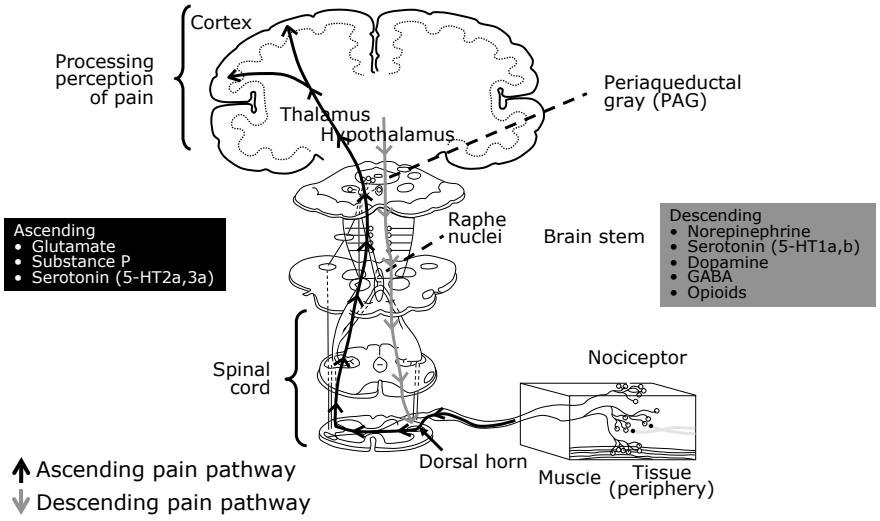
Overall Management Strategy in Fibromyalgia

Goldenberg DL, et al. *JAMA* 2004;292:2388-2395.

Steps to Management of Jane

- Start with education to patient and family
- Non-pharmacologic management
  - Exercise and nutrition counseling
- Assess for comorbid mood disorder and sleep-wake disturbance
- Pharmacologic management
  - Currently three FDA-approved medications
  - Ask about other current medications or supplements
  - Assess past medication history and response

Ascending and Descending Pain Pathways



Steps to Management of Jane

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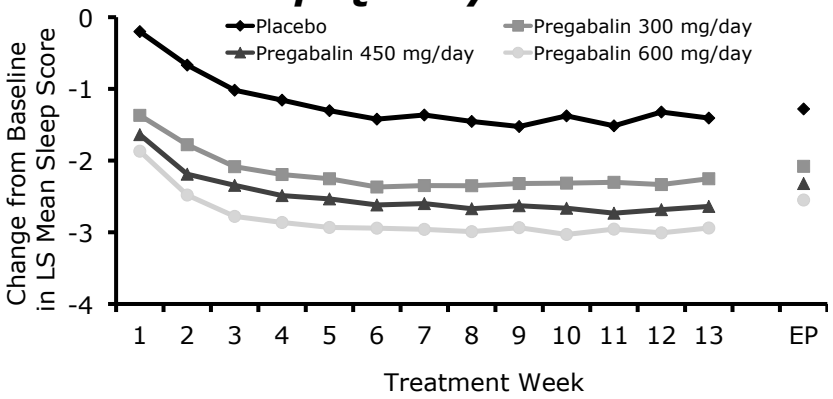
  - Currently three FDA-approved medications
  - Ask about other current medications or supplements
  - Assess past medication history and response

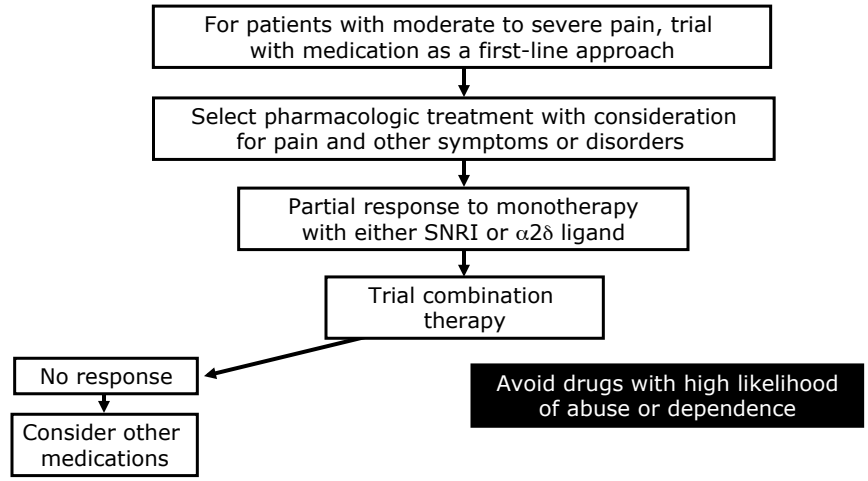
Pregabalin
Improvement in Weekly Mean Sleep-Quality Scores



$p < .0001$ for all comparisons of pregabalin vs. placebo; LS = least squares; EP = endpoint; FDA-recommended doses are 300 mg/day and 450 mg/day

Arnold LM, et al. Abstract presented at the Annual European Congress of Rheumatology, EULAR 2007; June 13-16, 2007; Barcelona, Spain. Abstract #OP0036; Arnold LM, et al. *J Pain* 2008 9:792-805; Mease PJ, et al. *J Rheumatol* 2008;35:502-514.

Stepwise Treatment of Fibromyalgia (2)



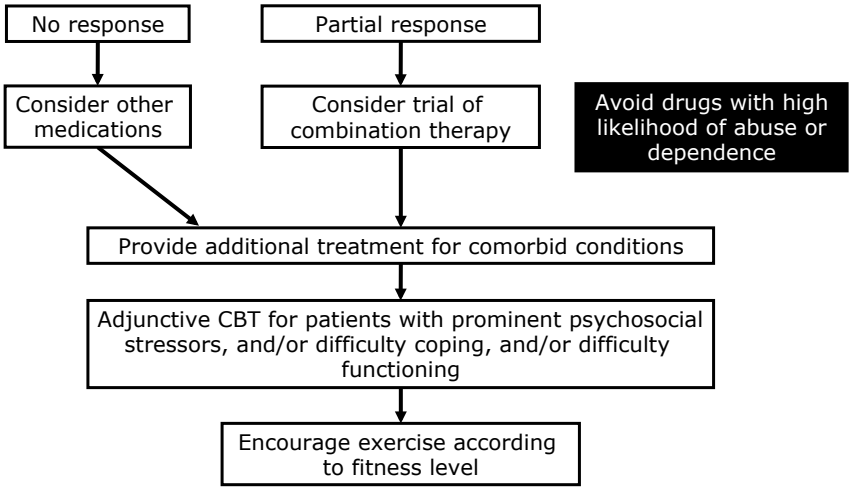
Arnold LM. *Arthritis Research and Therapy* 2006;8:212.

Summary of Medications for Fibromyalgia

- FDA-approved medications
  - Pregabalin 300-450 mg/day
  - Duloxetine 60-120 mg/day (FDA-approved at 60 mg/day)
  - Milnacipran 100-200 mg/day
- Limited evidence: NSAIDs
- No evidence of efficacy: other opioids, steroids, benzodiazepines
- Other medications with controlled trials supporting efficacy but no FDA approval for fibromyalgia
  - Cyclic medications (e.g., amitriptyline 25-50 mg at bedtime or cyclobenzaprine 10-30 mg at bedtime)
  - Gabapentin 1200-2400 mg/day
  - Tramadol 100-300 mg/day
  - SSRI fluoxetine 20-80 mg/day
  - Sodium oxybate (4.5 g/night-6 g/night)
  - NRI esreboxetine (4-8 mg/day)
  - Nonbenzodiazepine hypnotics (for sleep only)

Modified from: Goldenberg DL, et al. JAMA 2004;292:2388-2395.

Stepwise Treatment of Fibromyalgia (3)



Arnold LM. *Arthritis Research and Therapy* 2006;8:212.

Questions?

Type your question in the box at the bottom of this window and click the Submit button to send.

Lesley M. Arnold, MD

Don L. Goldenberg, MD

FDA-Approved Treatments for Fibromyalgia

- Pregabalin – Approved 2007
- Duloxetine – Approved 2008
- Milnacipran – Approved 2009

Pregabalin

- Binds to $\alpha 2\delta$ subunit of voltage-gated calcium channels of neurons
- Reduces calcium influx at nerve terminals and therefore inhibits release of neurotransmitters
  - Glutamate, Substance P
- FDA approvals in the US:
  - Neuropathic pain associated with diabetic peripheral neuropathy (DPN)
  - Post herpetic neuralgia (PHN)
  - Adjunctive therapy for adult patients with partial onset seizures
  - Fibromyalgia

Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed April 30, 2010.

Pregabalin

Side Effects in FM Trials (≥ 5% and Greater than Placebo)

- Dizziness 38%
- Somnolence 20%
- Headache 12%
- Weight gain 11%
- Dry mouth 8%
- Blurred vision 8%
- Constipation 7%
- Fatigue 7%
- Edema 6%
- Euphoric mood 6%
- Peripheral edema 6%
- Increased appetite 5%

Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed April 30, 2010.

Duloxetine

- Primary mechanism of action is dual reuptake inhibition of serotonin and norepinephrine (SNRI)[1,2]
- FDA approvals in the US:
  - Acute and maintenance treatment of major depressive disorder
  - Acute and maintenance treatment of generalized anxiety disorder
  - Diabetic peripheral neuropathic pain
  - Fibromyalgia[3] (FDA-recommended dose: 60 mg once daily)

1. Arnold LM, et al. *Arthritis Rheum* 2004;50:2974-2984.
2. Arnold LM, et al. *Pain* 2005;119:5-15.
3. US Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed May 6, 2010.

Duloxetine

Side Effects in FM Trials (≥ 5% and Greater than Placebo)

- Nausea 29%
- Headache 20%
- Dry mouth 18%
- Insomnia 16%
- Constipation 15%
- Fatigue 15%
- Diarrhea 12%
- Decreased appetite 11%
- Dizziness 11%
- Somnolence 11%
- Hyperhidrosis 7%
- Agitation 6% (defined as jittery, restlessness, tension, psychomotor agitation)
- Dyspepsia 5%
- Musculoskeletal pain 5%

US Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed May 6, 2010.

Milnacipran

- Primary mechanism of action is dual reuptake inhibition of serotonin and norepinephrine (SNRI)[1,2]
- Approvals in the US
  - Fibromyalgia
    - FDA-recommended dose is 50 mg twice daily (BID)[3]; may be increased to 100 mg BID)

1. Clauw DJ, et al. *Clin Ther* 2008;30:1998-2004.
2. Mease P, et al. *J Rheumatol* 2009;36:398-409.
3. US Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed April 30, 2010.

Milnacipran
Side Effects in FM Trials (≥ 5% and Greater than Placebo)

- Nausea 37%
- Headache 18%
- Constipation 16%
- Dizziness 10%
- Insomnia 12%
- Hot flush 12%
- Hyperhidrosis 9%
- Vomiting 7%
- Palpitation 7%
- Heart rate increased 6%
- Dry mouth 5%
- Migraine 5%
- Hypertension 5%

US Food and Drug Administration. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed May 6, 2010.

Additional Resources

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Upcoming Live and On Demand

Pneumococcal Disease in High-Risk Patients: Prevention, Guidelines, and Early Recognition

Faculty: Larry Culpepper, MD, MPH; Keith P. Klugman, MD, PhD; Kristin L. Nichol, MD, MPH, MBA

Wednesday, June 23, 2010
12:00–1:00 p.m. ET

Visit **neuroscienceCME.com/TV483**
for current information

Additional Questions

Faculty will be taking questions via e-mail for the next two weeks at ***questions@cmeoutfitters.com***

Questions and answers will be posted online at ***neurosienceCME.com/460***

Lesley M. Arnold, MD

Don L. Goldenberg, MD

After the live broadcast,
this activity will be available
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Activity Title and Faculty:
A Case of Connecting the Dots: Improving Diagnosis and Management of Fibromyalgia
with Lesley M. Arnold, MD, and Don L. Goldenberg, MD

Site/Institution Name: ______________________________

Practice Setting: ❑ Community Mental Health ❑ State Mental Health ❑ Private Practice ❑ Primary Care ❑ Other: __________

Address: ______________________________

City: ____________________ State: ________ ZIP: __________

Site Coordinator: ____________________ Phone: ____________________

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Completion Date: __________ We participated in a: ❑ ARCHIVE webcast ❑ Podcast/MP3

Attendee Name (please print)	Please Circle Discipline						
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