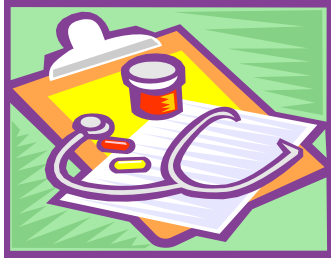




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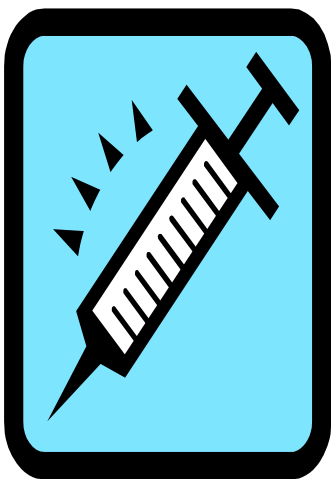


How to manage fibromyalgia. EULAR, a multidisciplinary taskforce of European experts (European League Against Rheumatism) recently published recommendations on the management of **fibromyalgia** syndrome (FMS) (*Ann Rheum Dis* 2008; 67: 536-41). FMS, a common rheumatological condition, is characterised by **chronic widespread pain, combined with pain on palpation at specific tender point sites**, including occiput, low cervical, trapezius, supraspinatus, second rib, gluteal, knee (*see Arthritis Rheum* 1990; 33: 160-72 for full criteria). **Associated features** include fatigue, depression, anxiety, sleep

disturbance, headache, altered bowel habit, diffuse abdominal pain and urinary frequency. Although the precise **pathogenesis** is unknown, peripheral and central hyperexcitability at spinal or brainstem level, altered pain perception and somatisation have been hypothesised and demonstrated in some patients. The EULAR consensus stated that **FMS should be recognised as a complex and heterogeneous condition, where there is abnormal pain processing and other secondary features.** The following recommendations were made:

Pharmacotherapy: Data from 2 randomised controlled trials (RCTs) showed that **tramadol** was effective in the management of FMS pain for up to 13 weeks. However, caution was recommended due to the possibility of typical opiate withdrawal symptoms on discontinuation and risk of dependence and abuse. **Simple analgesics and weak opioids** might also be useful, based on expert opinion but studies were lacking. The use of corticosteroids or strong opioids was not recommended. Studies on **antidepressants** showed benefit (on pain, function or both) in studies lasting 6-12 weeks. The strongest evidence was for **tricyclic antidepressants** (in particular amitriptyline). Tropicisetron, pramipexole and pregabalin were noted to reduce pain in short-term studies (up to 12 weeks) and were recommended for consideration in the treatment of fibromyalgia.

Non-pharmacological interventions that were shown to be beneficial included heated pool treatment, individualised exercise programmes (aerobic exercise and strength training), relaxation, rehabilitation, physiotherapy and psychological support. Cognitive behavioural therapy (CBT) might be of benefit to some FMS patients but studies were of poor quality. Overall, the group concluded that evidence exists for short-term beneficial effects with some medicines but **optimal treatment requires a multidisciplinary approach with a combination of modalities tailored to the specific patient's needs** (in terms of pain intensity, function effects and associated features).



Updated Immunisation Guidelines The 2002 immunisation guidelines for Ireland have recently been updated. The following **changes** to the immunisation schedule are recommended:

- Hepatitis B and pneumococcal vaccines to be added to the routine childhood schedule
- Meningococcal C conjugate vaccine to be given at 4, 6, 13 mths (instead of 2, 4, 6 mths)
- Haemophilus influenzae type B booster to be given at 13 mths (rather than 12 mths)
- Low dose acellular pertussis vaccine to be added to the current tetanus and low-dose diphtheria vaccine given at 11-14 years
- Women of child-bearing age with no history of varicella and negative serology to be vaccinated if no contraindications exist
- People ≥ 50 years to receive annual influenza vaccinations (to be implemented on a phased basis).

In addition there is information on catch-up schedules (children aged 4 mths -10 years and 10-18 years) and new / expanded chapters on rabies, hepatitis B, pneumococcal infection and varicella-zoster (which includes recommendations on the treatment of neonates, pregnant women and immunosuppressed people exposed to chicken pox and outlines the procedure for vaccinating health-care workers). Get the full updated immunisation guideline in pdf format on www.dohc.ie/publications/immunisation_guidelines.html



New prescribing recommendations for fluoroquinolones. The European Medicines Agency (EMA) recently recommended changes to the prescribing information for 2 oral fluoroquinolones as follows:

Moxifloxacin: Due to concerns regarding hepatic toxicity the EMA recommends that oral moxifloxacin (Avelox®) should **only be prescribed** in the treatment of acute bacterial sinusitis, acute exacerbation of chronic bronchitis and community acquired pneumonia when other antibiotics cannot be used or

have failed. It has also recommended that the **safety warnings of oral moxifloxacin should be strengthened** concerning the risk of diarrhoea, heart failure in women and older patients, severe skin reactions and fatal liver injury.

Norfloxacin: The EMA has recommended that the **marketing authorisation (licence) for oral norfloxacin for its use in the treatment of acute or chronic complicated pyelonephritis should be withdrawn** because the benefits do not outweigh the risks in this specific indication. This is based on the fact that there is not enough clinical data to demonstrate the efficacy of oral norfloxacin for this type of infection. (According to the IMB website, Norflocux® is the only oral norfloxacin product currently authorised in Ireland). Check out www.emea.europa.eu and www.imb.ie for further information, including a press release and a Questions and Answers document on each topic.

[Editor's note: Don't forget that the SPC for all fluoroquinolones notes an **increased risk of tendonitis and tendon rupture** with use. In the US, the FDA has recently added a black box warning in this regard to the labelling for such products. Check out: www.fda.gov/medwatch]



Drugs and QT-prolongation QT-Prolongation (QT-Pr) increases the risk of ventricular fibrillation and torsades de pointes (TdP). **Drug-induced QT-Pr** has been reported with both cardiac and non-cardiac drugs but the frequency of adverse events due to drug-induced QT-Pr is unknown. Additional risk factors include congenital long QT syndrome, heart disease, female sex, elderly, hypokalaemia, hepatic insufficiency and stimulant drug abuse.

The association of antipsychotic and antidepressant drugs with QT-Pr was reviewed recently (*Am J Health-Syst Pharm June 2008; 65:1029-38*). This is more frequently seen with antipsychotic drugs than antidepressants. There is a greater risk with typical compared with atypical antipsychotics. Thioridazine, pimozide and IV haloperidol have all been associated with QT-Pr; the risk with thioridazine was shown to be 5 times greater than other antipsychotics resulting in its withdrawal from the market. Atypical antipsychotics, including sertindole, have also been associated with QT-Pr; case reports of QT-Pr have been seen with risperidone and quetiapine (particularly in overdose). Tricyclic antidepressants (TCA) are more commonly associated with QT-Pr than selective serotonin-reuptake inhibitors, particularly at higher doses and with overdose. Amitriptyline is one of the commonest TCAs implicated in case reports of QT-Pr. **Drug-drug interactions** should be considered when treating patients with antipsychotics or antidepressants as many of these drugs compete with each other for receptor-binding sites. Also, these patients are often subject to polypharmacy and many antidepressants and antipsychotics undergo metabolism by CYP2D6 and CYP3A4 isoenzymes, further increasing the risk of higher levels. The authors conclude that QT-Pr is a concern for prescribers of antidepressants and antipsychotics, due to an increased risk of fatal arrhythmias in some patients, but the risk is minimal in a patient with no apparent risk factors receiving a drug at therapeutic doses.

[Editor's note: Recently 2 cases of QT-Pr have been reported from Ireland. One identified **clarithromycin** (known to cause QT-Pr) as a factor in a 79-year old female who developed ventricular tachycardia / TdP within 24 hours of initiation of clarithromycin and ceftriaxone (*Ir J Med Sci 2008;177:67-68*). She was also found to have a congenitally long QT. The second involved a 34-year old male receiving protease inhibitor antiretroviral therapy, methadone and flurazepam who experienced QT-Pr followed by TdP (*IMJ 2007; 100 (10):631-632*). Methadone is extensively metabolised by the cytochrome P450 system and it is thought that the protease inhibitors (potent inhibitors of CYP3A4) and flurazepam (also metabolised by the same enzyme system) may have resulted in much higher levels of methadone with associated toxicity. Check out the following websites for further information on QT prolonging drugs: <http://www.torsades.org> and www.qtsyndrome.ch]

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH. Tel: Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie