Drug Safety Update

MHRA

Latest advice for medicines users

The monthly newsletter from the **Medicines and Healthcare products Regulatory Agency** and its independent advisor the **Commission on Human Medicines**

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The safety of non-steroidal anti-inflammatory drugs (NSAIDs) has been under close scrutiny recently. This month, we have several articles that highlight updated safety information for some NSAIDs.

For piroxicam, we explain new restrictions on the use of this medicine, which should now be initiated only by specialists as a second-line treatment for arthritis (page 2). For ketorolac and ketoprofen, we advise healthcare professionals to follow the prescribing advice carefully because these medicines are associated with a higher gastrointestinal risk than most other NSAIDs in the class (page 3). And changes to the prescribing information for lumiracoxib are being implemented after a European review of reports of liver toxicity (page 11).

Also this month, we wish to remind healthcare professionals about the association between bisphosphonate treatment and osteonecrosis of the jaw (page 7).

Finally, please report suspected adverse drug reactions to us via the Yellow Card scheme (www.yellowcard.gov.uk, page 9)—every report we receive can help protect public health.

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The Medicines and Healthcare products Regulatory Agency is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

Drug safety advice

Piroxicam: new restrictions, including specialist initiation

Keywords: Piroxicam, non-steroidal anti-inflammatory drug, NSAID, gastrointestinal toxicity, haemorrhage, ulceration, perforation, skin reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis, arthritis, specialist, risk-benefit

Systemic piroxicam should be initiated only by specialists as a second-line treatment for arthritis. Patients who currently take piroxicam should be reassessed at a routine appointment

Piroxicam is a non-steroidal anti-inflammatory drug (NSAID). Prescribing advice for systemic formulations of piroxicam is being amended in view of its safety profile (particularly the risk of serious gastrointestinal and skin reactions) compared with other NSAIDs.

New restrictions and general prescribing advice:

- Licensed indications for adults are restricted to osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Systemic piroxicam is no longer indicated for **any** acute indications
- Existing indications for paediatric use are unchanged
- Only specialists (ie, consultants in rheumatology, rehabilitation medicine, medical orthopaedics, and general practitioners with a special interest [GPSIs] in rheumatology) should start new patients on piroxicam only as a second-line NSAID
- Maximum daily dose is 20 mg; review the need for continued treatment after 14 days, and frequently thereafter
- Consider the possible need for combination therapy with gastroprotective agents (eg, misoprostol or proton pump inhibitors), especially in the elderly; avoid use of piroxicam in patients older than 80 years

Revised contraindications include:

- History of, or active, gastrointestinal ulceration, bleeding, or perforation
- History of, or active, gastrointestinal disorders that predispose to bleeding abnormalities such as ulcerative colitis, Crohn's disease, gastrointestinal cancers, and diverticulitis
- Concomitant use with other NSAIDs, including COX-2 selective NSAIDs, aspirin at analgesic doses, and anticoagulants such as warfarin
- History of previous serious allergic drug reaction of any type, especially cutaneous reactions such as erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis
- Previous hypersensitivity to piroxicam; skin reaction (irrespective of severity) associated with piroxicam, other NSAIDs, or other medicines

Revised warnings also highlight the need for caution when piroxicam is used with other drugs that may increase gastrointestinal risk (eg, selective serotonin reuptake inhibitors class of antidepressants and low-dose aspirin). Patients should stop taking piroxicam and seek medical advice at the first occurrence of gastrointestinal symptoms.

Assessment of patients who currently take piroxicam

Any patient who currently takes systemic piroxicam should be reviewed at a routine appointment. Patients who are receiving intermittent piroxicam treatment (eg, for flares of inflammatory arthritis) should be considered as a 'new' patient at the time of their next prescription, and either switched to an alternative treatment or referred to a specialist if piroxicam is still considered necessary. Patients who are receiving continuous long-term piroxicam treatment should be reassessed carefully in light of the increased risks of this treatment. If after full consideration of the risks and benefits there seems to be no alternative to piroxicam, specialist referral may be considered.

Topical formulations

The above recommendations apply only to systemic formulations of piroxicam: there are no new restrictions on topical use.

Evidence of increased risk for piroxicam versus other NSAIDs

For further epidemiological evidence, see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2031549&ssTargetNodeId=221

Available epidemiological evidence suggests that systemic piroxicam poses a significantly greater risk of serious gastrointestinal toxicity than other NSAIDs, including gastrointestinal haemorrhage, ulceration, and perforation.[1-3]

Serious skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with NSAID use. Evidence from observational studies suggests that piroxicam may be associated with a higher risk of these reactions than other non-oxicam NSAIDs. Patients seem to be at highest risk of these reactions early in the course of therapy: most cases occur within the first month.

There is no apparent efficacy advantage for systemic formulations of piroxicam versus other NSAIDs.

1 Henry D, et al. *Int J Clin Pract 2003*; **135** (Suppl): 43–49.
2 Laporte JR, et al. *Drug Saf 2004*; **27:** 411–20.
3 Lanas A, et al. *Gut 2006*; **55:** 1731–38.

Ketoprofen and ketorolac: gastrointestinal risk

Keywords: ketoprofen, ketorolac, non-steroidal anti-inflammatory drug, NSAID, gastrointestinal toxicity, haemorrhage, ulceration, perforation

Ketorolac and ketoprofen have been associated with a higher gastrointestinal risk than most other NSAIDs in the class; prescribing advice should be followed carefully, particularly recommended upper dose limits

Although epidemiological studies have suggested that piroxicam (see page 2) is associated with a higher gastrointestinal risk than most non-steroidal anti-inflammatory drugs (NSAIDs), these studies have also raised concern about the relative gastrointestinal safety of ketorolac[1-8] and ketoprofen.[5,9,10] Prescribers are reminded of the following restrictions:

1 Traversa G, et al. *Epidemiology* 1995; **6:** 49–54.
2 Strom B, et al. *JAMA* 1996; **275:** 376–82.
3 Garcia-Rodriguez LA, et al. *Arch Intern Med* 1998: **158:** 33–39.
4 Menniti-Ippolito F, et al. *Eur J Clin Pharmacol* 1998; **54:** 393–97.
5 Laporte JR, et al. *Drug Saf* 2004; **27:** 411–20.
6 Lanas A, et al. *Eur J Gastroenterol Hepatol* 2003; **15:** 173–78.
7 Gallerani M, et al. *J Clin Epidemiol* 2004; **57:** 103–10.
8 Llorente-Melero MJ, et al. *Rev Esp Enferm Dig* 2002; **94:** 7–12.
9 Henry D, et al. *Int J Clin Pract* 2003; **135** (Suppl): 43–49.
10 Lanas A, et al. *Gut* 2006; **55:** 1731–38.

Dose

For information about dosing of ketorolac, see the Summary of Product Characteristics at http://emc.medicines.org.uk/

- **Ketorolac:** treatment should be initiated only in hospital. Maximum duration of treatment should not exceed 7 days for tablets, or 2 days for continuous daily dosing with intravenous or intramuscular formulations
- **Ketoprofen:** recommended maximum daily dose range is 100–200 mg in divided doses. The balance of risks and benefits should be considered carefully before commencing treatment with 200 mg daily

Contraindications

Ketoprofen and ketorolac are contraindicated in patients with active peptic ulcer, or with any history of gastrointestinal bleeding, ulceration, or perforation.

General advice on gastrointestinal safety for all NSAIDs:

- Use the lowest dose and shortest duration of treatment necessary to control symptoms
- Avoid use with other concomitant NSAIDs (including COX-2 selective inhibitors)
- Consider combination therapy with protective agents (eg, misoprostol or a proton pump inhibitor) for high-risk patients (eg, elderly people and patients who need concomitant low-dose aspirin)
- Patients with a history of any gastrointestinal toxicity, particularly those who are elderly, should report any unusual abdominal symptoms, particularly in the initial stages of treatment. If gastrointestinal bleeding or ulceration occurs, withdraw treatment immediately
- Give NSAIDs with care to patients who have a history of gastrointestinal disease (eg, ulcerative colitis, Crohn's disease) because these conditions may be exacerbated

Interactions and gastrointestinal risk

Corticosteroids, antiplatelet agents, and selective serotonin reuptake inhibitors (SSRIs) may increase the risk of gastrointestinal ulceration or bleeding. NSAIDs may enhance the effects of anticoagulants, such as warfarin.

Inhaled corticosteroids: pneumonia

Keywords: fluticasone, salmeterol, TORCH, chronic obstructive pulmonary disease, COPD, Seretide, pneumonia, bronchitis, lower respiratory tract infection, exacerbation, inhaled corticosteroid

Physicians should remain vigilant for pneumonia and other infections of the lower respiratory tract (ie, bronchitis) in patients with chronic obstructive pulmonary disease who are treated with inhaled products that contain steroids

Long-acting beta$_2$ agonists (salmeterol or formoterol) and combination products that contain salmeterol with fluticasone (Seretide Accuhaler) or formoterol with budesonide (Symbicort Turbohaler) are indicated for the management of chronic obstructive pulmonary disease (COPD). Although inhaled corticosteroids are not indicated for monotherapy in COPD, treatment guidelines (including those issued by the Global initiative on Obstructive Lung Disease, GOLD)[1] recommend that inhaled steroids may be added to ongoing bronchodilator therapy in COPD management.

The TORCH study

TOwards a Revolution in COPD Health (TORCH)[2] compared Seretide Accuhaler (50 µg salmeterol/500 µg fluticasone twice a day), 50 µg salmeterol twice a day, and 500 µg fluticasone twice a day with placebo over a 3-year period. The primary endpoint was all-cause mortality within 3 years. The absolute risk for all-cause mortality was reduced by 2·6% for Seretide compared with placebo, and was increased by 0·8% for fluticasone compared with placebo (both non-significant).

The table summarises the absolute and relative risks of pneumonia for groups in the TORCH study:

	Placebo (n=1544)	Salmeterol (n=1542)	Fluticasone (n=1552)	Seretide (n=1546)
Number of events	139 (9%)	162 (11%)	224 (14%)	248 (16%)
Events per 1000 treatment-years	51·9	51·5	84·4	87·6
Probability of event by 3 years* (95% CI)	12·3% (10·4–14·3)	13·3% (11·4–15·2)	18·3% (16·1–20·4)	19·6% (17·4–21·9)
Active treatment *vs* placebo				
Hazard ratio (95% CI)		1·09 (0·87–1·37)	1·53† (1·24–1·89)	1·64† (1·33–2·02)
Seretide *vs* components				
Hazard ratio (95%CI)		1·51† (1·24–1·84)	1·07 (0·89–1·28)	

Note: Log-Rank test stratified by smoking status. *Kaplan-Meier estimate. †p<0·001.

In TORCH, older patients, patients with a lower body mass index (ie, <25 kg/m^2), and patients with very severe disease (FEV$_1$<30% predicted) were at highest risk of pneumonia, irrespective of treatment.

1 Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2006. See http://www.goldcopd.org

2 Calverley PM, et al. *N Engl J Med* 2007; **356:** 775–89.

Other data

A recent case-control study[3] of 175 906 elderly patients with COPD suggested that current use of inhaled corticosteroids was associated with a significant increase of 70% in the frequency of hospitalisation for pneumonia compared with non-use in the last year. For patients with pneumonia who died within 30 days of hospitalisation, current use of inhaled corticosteroids significantly increased the frequency by 53%. The risks of hospitalisations for pneumonia and for subsequent death within 30 days were dose-dependent.

3 Ernst P, et al. *Am J Respir Crit Care Med* 2007; **176:** 162–66.

Advice for healthcare professionals:

- Physicians should remain vigilant for the development of pneumonia and other infections of the lower respiratory tract (ie, bronchitis) in patients with COPD who are treated with inhaled drugs that contain steroids because the clinical features of such infections and exacerbation frequently overlap
- Any patient with severe COPD who has had pneumonia during treatment with inhaled drugs that contain steroids should have their treatment reconsidered

Pneumovax II: tolerability of re-vaccination

Keywords: Pneumovax II, pneumococcal polysaccharide vaccine, re-vaccination, local reactions, systemic reactions

Healthcare professionals should advise patients who need re-vaccination with Pneumovax II to expect a more intense reaction than after their first vaccination

Pneumovax II pneumococcal polysaccharide vaccine is recommended for immunisation against disease caused by pneumococcal serotypes contained in the vaccine. Pneumovax II is not effective for prevention of acute otitis media, sinusitis, or other common infections of the upper respiratory tract.

Who should be vaccinated?

Pneumovax II is recommended for all individuals aged 65 years or older and those aged 2 years or older who are at increased risk of serious or fatal pneumococcal disease.

Who should be re-vaccinated and when?

For current at-risk groups, see http://www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Greenbook/DH_4097254; in 2006, a pneumococcal conjugate vaccine (Prevenar) was added to the routine childhood immunisation programme

- Healthy adults and children should not be routinely re-vaccinated with Pneumovax II
- Re-vaccination may be considered for individuals older than 10 years of age who are at increased risk of serious pneumococcal infection, and who have not been vaccinated in the past 5 years, or for those known to have had a rapid drop in pneumococcal antibody levels
- For populations who are known to be at high risk of fatal pneumococcal infection (eg, asplenics), re-vaccination at 3 years may be considered
- For children aged 2–10 years, re-vaccination after 3 years should be considered only for those at high risk of pneumococcal infection

Tolerability of re-vaccination

Re-vaccination within 3 years of primary vaccination is not recommended because of an increased risk of adverse reactions. A clinical trial recorded an increased frequency and intensity of local reactions after re-vaccination at 3–5 years after primary vaccination. This effect was most marked in people aged 65 years or older. Injection-site reactions occurred within 3 days of vaccination and typically resolved within 5 days. Systemic adverse experiences such as chills, asthenia, and myalgia were more common after re-vaccination than after primary immunisation in those aged 65 years or older. Most people recovered completely after symptomatic treatment.

Healthcare professionals should avoid antibiotic therapy as symptomatic treatment unless specifically indicated.

Adverse reactions

Spontaneous data and clinical trial data suggest that more than one in ten vaccinees will experience pyrexia and injection-site redness, pain, induration, and swelling. Pain and swelling of the vaccinated limb, which may result in its reduced mobility, have also been reported. Very rarely, injection-site cellulitis has developed shortly after vaccination.

Bisphosphonates: osteonecrosis of the jaw

Keywords: osteonecrosis, jaw, bisphosphonates, dental examination, benefit-risk assessment, cancer treatment

Dental surgery may exacerbate osteonecrosis of the jaw in patients who develop this disorder during bisphosphonate treatment

Bisphosphonates are used for: prophylaxis and treatment of osteoporosis; treatment of Paget's disease; and as part of some anticancer regimens. Osteonecrosis of the jaw has been reported in association with bisphosphonates.[1,2] Most reports have been in patients treated with intravenous bisphosphonates; however, reports have also been received in those taking oral bisphosphonates.

Advice for healthcare professionals:

- Dental examination, with appropriate preventive dentistry, should be considered before bisphosphonate treatment in patients with concomitant risk factors (eg, cancer, chemotherapy, corticosteroids, and poor oral hygiene)
- During bisphosphonate treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop osteonecrosis of the jaw during bisphosphonate treatment, dental surgery may exacerbate the condition
- Whether discontinuation of bisphosphonate treatment in patients who need dental procedures reduces the risk of osteonecrosis of the jaw is not known. Clinical judgment should guide the management of every patient on the basis of an individual benefit-risk assessment

1 *Current Problems in Pharmacovigilance* 2006; **31:** 4. http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2023859&ssTargetNodeId=368

2 Migliorati CA, et al. *Lancet Oncol* 2006; **7:** 508–14.

Lorazepam: reduction of recommended maximum daily dose

Keywords: lorazepam, benzodiazepines, short-term use, anxiety, insomnia

Maximum dose of lorazepam for short term, symptomatic treatment is 4 mg per day for severe, disabling anxiety, and 2 mg per day for severe, disabling insomnia

Lorazepam is a benzodiazepine anxiolytic; its indications include short-term use in anxiety or insomnia.

Prescribers are reminded of previous advice:

- Benzodiazepines are indicated for the short-term relief (2–4 weeks only) of anxiety that is severe, disabling, or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic, or psychotic illness
- The use of benzodiazepines to treat short-term mild anxiety is inappropriate and unsuitable
- Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or subjecting the individual to extreme distress

See British National Formulary. 53rd edn (March 2007): **178**.

Doses of lorazepam above 4 mg per day are not considered appropriate in view of the recommended maximum treatment duration of 4 weeks, which includes a dose-reduction period. Prescribing information, which previously contained posology for up to 10 mg per day for lorazepam (equivalent to 100 mg per day of diazepam), is being updated for relevant products.

Advice for healthcare professionals:

- The maximum dose of lorazepam is 4 mg per day for the short-term treatment of anxiety and phobia, and is 2 mg per day for the treatment of insomnia

Yellow Card scheme update

The Yellow Card scheme collects information on suspected adverse drug reactions. See www.yellowcard.gov.uk

For details of what to report, see *Drug Safety Update* 2007; **1**(2): 10. http://www.mhra.gov.uk/mhra/drugsafetyupdate

For further information about the strategy to strengthen Yellow Card reporting, see annex B of the summary minutes of the meeting of the Pharmacovigilance Expert Advisory Group, June 13, 2007: http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=896

For further information about the MHRA consultation, see page 11 and also http://www.mhra.gov.uk/mhra/Consultations: we are asking, "How can the Agency encourage you to report problems you experience with medicines and medical devices?"

Since establishment of the Yellow Card scheme in 1964, we have received more than half a million reports. Up to 1997, GPs, hospital doctors, dentists, and coroners were able to send us Yellow Cards. Reporting by hospital pharmacists was introduced in 1997, community pharmacist reporting in 1999, and nurse reporting formally in 2002. Since 2005, patients have been able to send Yellow Cards. Although the types of healthcare professionals that can report has expanded, the level of reports received has not changed substantially over the past few years.

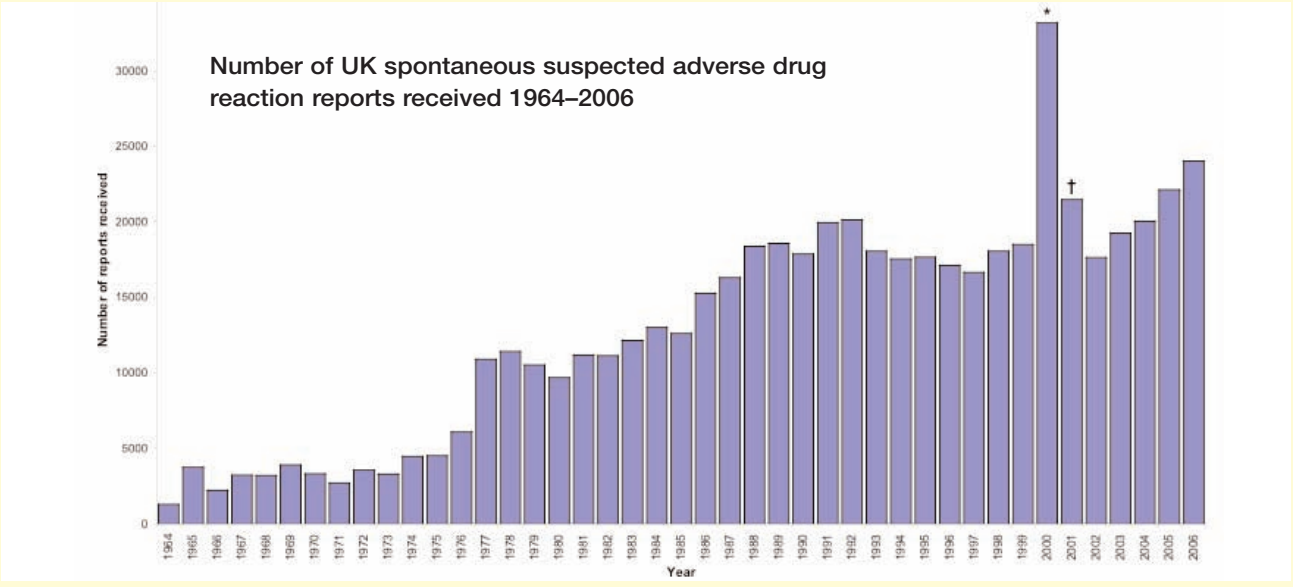
Please continue to send us Yellow Cards of suspected adverse drug reactions—every report can help protect public health.

Please do not assume that another healthcare professional will report the suspected adverse drug reaction: we can identify duplicate reports, and combining them may provide complementary information and a fuller picture about an adverse drug reaction. For instance, reports of the same reaction may cover different periods, informing us of the outcome as well as the event.

In view of our current strategy to strengthen Yellow Card reporting by healthcare professionals and patients, and the MHRA's consultation to seek views from healthcare professionals about how we oversee medicines in the UK (see page 11), we welcome any feedback on reporting to the Yellow Card scheme.

For instance, the figure below shows that there was a sustained increase in reporting in 1986 and subsequent years compared with 1985—an increase that we attribute to the inclusion at that time of Yellow Cards at the back of prescription pads. If you have any ideas about how to enhance Yellow Card reporting, no matter how simple, you can respond to the consultation (see http://www.mhra.gov.uk/mhra/Consultations) or email drugsafetyupdate@mhra.gsi.gov.uk. We will keep healthcare professionals updated as the strategy develops.

Number of UK spontaneous suspected adverse drug reaction reports received 1964–2006



*In 2000, a large number of reports were received because of a nationwide meningitis C vaccination campaign, in which we piloted Yellow Card reporting by nurses, and because of the introduction of bupropion (Zyban) for smoking cessation, which continued into 2001 (†).

Hot topics

Botulinum toxin products: rare but serious risk

Four products that contain botulinium toxin are licensed in the UK: Botox, Dysport, NeuroBloc, and Vistabel. Indications include focal spasticity, some types of spasm, and excessive sweating of the axillae (arm pits). Vistabel is indicated only for treatment of vertical frown lines between the eyebrows, where their severity has an important psychological effect on the patient. Botulinum toxins prevent the release of acetylcholine at neuromuscular or other cholinergic junctions and reversibly denervate muscles or eccrine glands.

Products that contain botulinum toxin are associated with a risk of serious adverse reactions due to distant spread of toxin

- Spread reactions—including muscle weakness, dysphagia, and aspiration—have been reported rarely with all products that contain botulinum toxin
- Extreme caution is needed on administration of products that contain botulinum toxin to patients who have neurological disorders, or a history of dysphagia or aspiration
- Only physicians with appropriate experience (including use of the required equipment) should administer products that contain botulinum toxin
- Patients or caregivers should be informed about the risk of spread of toxin, and should be advised to seek immediate medical care if problems with swallowing or speech develop, or if respiratory symptoms arise
- Units of botulinum toxin are not interchangeable from one product to another
- Recommended administration techniques and specific dosing guidance (including the recommendation to use the minimum effective dose and titrate according to individual need) should be followed

Letter to healthcare professionals sent June, 2007. See http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2031602&ssTargetNodeId=221

Rosiglitazone and pioglitazone: cardiovascular safety and fracture risk

Rosiglitazone (Avandia, Avandamet ▼) and pioglitazone (Actos ▼, Competact ▼) are indicated for the treatment of type 2 diabetes, and belong to the thiazolidinedione class of antidiabetic drugs.

In May, 2007, a meta-analysis[1] suggested that patients who are receiving rosiglitazone may be at an increased risk of myocardial infarction and death from cardiovascular causes compared with comparator treatments.

Patients with diabetes have an increased risk of cardiovascular disorders, including heart failure and ischaemic heart disease, because of the underlying condition. An association between rosiglitazone and pioglitazone and cardiac failure has been recognised since they were first licensed, and the cardiovascular safety of these medicines is kept under continuous review. In October, 2006, after a review of clinical trial data, prescribing information for rosiglitazone was updated to include new information about the risks of cardiac failure, cardiac ischaemia, and myocardial infarction. This review considered data from most of the individual studies that were included in the May, 2007, meta-analysis.[1]

The MHRA, together with other regulatory agencies in the European Union, is currently reviewing all available data for the cardiovascular safety of rosiglitazone and pioglitazone. We will inform healthcare professionals of any changes to prescribing advice as soon as these reviews have been completed.

Analysis of clinical trial data has identified an increased risk of fracture (mainly in the foot and upper limb) in women given rosiglitazone or pioglitazone; this analysis did not identify a risk in men. **The risk of fracture should be considered in the care of patients, especially women, treated with pioglitazone or rosiglitazone.**

1 Nissen SE and Wolski K. *N Engl J Med 2007*; **356:** 1–15.

For an MHRA statement on the meta-analysis, see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2031268&ssTargetNodeId=221

Letters to healthcare professionals were sent in March and April, 2007. See http://www.mhra.gov.uk/mhra/HealthcareProfessionalLetters

Stop press

Safety information sent to healthcare professionals by Marketing Authorisation Holders is published and updated monthly on our website. See http://www.mhra.gov.uk/mhra/HealthcareProfessionalLetters

Recent letters to healthcare professionals

In August, 2007, a letter was sent to healthcare professionals to inform them of safety information for **lopinavir** with **ritonavir** (Kaletra) after an administration error in a neonate.

For further information, see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2032098&ssTargetNodeId=221

Lumiracoxib and hepatotoxicity: prescribing update

After a European review of the COX-2 inhibitor lumiracoxib (Prexige ▼) and reports of hepatotoxicity, changes to the prescribing information are being implemented to recommend monitoring of liver function before and during treatment.

Latest safety information

See http://www.npsa.nhs.uk/health/display?contentId=6344

The National Patient Safety Agency has issued an alert to all healthcare professionals who administer intravenous **amphotericin** about the potentially lethal consequences from confusion of lipid and non-lipid forms of the drug. These different formulations, which are used to treat systemic fungal infections have different dosage regimens that must be checked carefully.

Other information from the MHRA

Field safety notices for medical devices

For further information about the regulation of medical devices, see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=48. Field safety notices are published on our website to improve awareness of field safety corrective actions. For the latest field safety notices, see http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=967

For further information, read the field safety notice at http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2031902&ssTargetNodeId=967

In August, 2007, the MHRA placed a field safety notice about the SynchroMed EL Programmable Pump—an implantable, battery-powered device that stores and dispenses drugs. Patients who use this device typically include those who need intrathecal therapy for baclofen or morphine, or chemotherapy for hepatic arterial infusion. Based on an analysis of pumps, the most common cause of failure is stalling of the pump motor because of gear shaft wear. The pump does not have an alarm to alert the patient or clinician to a stalled motor. The manufacturer is not aware of any patient deaths or permanent injuries have been attributable directly to this motor failure. However, potential hazards associated with gear shaft wear are underinfusion, withdrawal symptoms, loss of symptom relief, and additional surgery to replace the pump.

Advice for healthcare professionals:

- Although manufacturing improvements have reduced the likelihood of motor stall due to gear shaft wear, it has not been eliminated completely
- Continue to work closely with patients to ensure they recognise symptoms associated with loss of therapy
- Follow the patient management and system-troubleshooting guidelines that are given in the field safety corrective action

Consultation—MHRA strategy

To access the consultation document and further information, see http://www.mhra.gov.uk/mhra/Consultations

Please tell us how you think the MHRA should respond to the key challenges and priorities for the coming years. The MHRA is approaching the 5th anniversary of its establishment, and we would like to consult you on our future plans for overseeing medicines and medical devices in the UK.

Read more about the Commission on Human Medicines, including summaries of minutes from meetings, at http://www.mhra.gov.uk/mhra/CommissiononHumanMedicines

Report a suspected adverse drug reaction at http://www.yellowcard.gov.uk