

# Drug Safety Update



## Latest advice for all medicines users

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

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| <b>Contents</b>                        |   | Click on text to go to page |
|--|---|-----------------------------|
| <b>Drug safety advice</b>              | Fibrates: new prescribing advice  | 2                           |
|  | Lumiracoxib: hepatotoxicity   | 3                           |
|  | Ceftriaxone: incompatibility with calcium-containing solutions                    | 5                           |
|  | Codeine: very rare risk of side-effects in breastfed babies                       | 6                           |
|  | St John's wort: interactions with all antiepileptics                              | 7                           |
| <b>Yellow Card scheme update</b>       | Please report suspected reactions with herbal medicines                           | 8                           |
| <b>Hot topics</b>                      | Illegal herbal remedies that contain Aristolochia: vigilance needed               | 8                           |
|  | Nasal decongestants that contain pseudoephedrine or ephedrine: sales restrictions | 9                           |
| <b>Stop press</b>                      | Moxifloxacin: hepatotoxicity and serious skin reactions—prescribing update        | 10                          |
|  | Co-proxamol withdrawal: reminder to prescribers                                   | 10                          |
|  | Ecoflac infusion solutions: risk of air embolism                                  | 10                          |
| <b>Other information from the MHRA</b> | Optometrists: independent prescribing   | 11                          |
|  | Patient Information Leaflets: improving quality                                   | 11                          |
|  | MHRA conference: 'Combating Counterfeit Medicines'                                | 11                          |

**A** key part of the MHRA's work is to monitor the continually changing balance of benefits and risks for medicines. This month, we present new advice about the benefit-risk balance for fibrates, which should now be used as first-line therapy only in patients with isolated severe hypertriglyceridaemia (page 2).

Herbal medicines are also an important part of our vigilance activities. This month, we wish to inform healthcare professionals that St John's wort—a herbal ingredient with various uses that is commonly available in the UK in unlicensed products—might interact with any antiepileptic medicines, and patients on antiepileptics should be advised not to use St John's wort (page 7).

Furthermore, Aristolochia—a herbal ingredient whose use was prohibited in 1999 because of its toxicity—continues to be found on the market illegally (page 8). We ask healthcare professionals to be vigilant and report any concerns about products that may contain this ingredient. Please continue to report via the Yellow Card scheme ([www.yellowcard.gov.uk](http://www.yellowcard.gov.uk), page 8) any suspected adverse drug reactions associated with herbal medicines.

On page 11, I am pleased to highlight the efforts to improve the quality of information for patients through the user-testing of Patient Information Leaflets.

Finally, thank you to everyone who has provided feedback about Drug Safety Update. I greatly appreciate your comments, and we will use them to continuously improve the bulletin.

**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 safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

**Claire Tilstone**, Editor  
[drugsafetyupdate@mhra.gsi.gov.uk](mailto:drugsafetyupdate@mhra.gsi.gov.uk)

# Drug safety advice

## Fibrates: new prescribing advice

**Keywords:** bezafibrate, fenofibrate, gemfibrozil, ciprofibrate, statins, lipids, triglycerides, cholesterol, cardiovascular disease, risk-benefit

**Key message:** Fibrates should be used as first-line therapy **only** in patients with isolated severe hypertriglyceridaemia. In patients who also have raised cholesterol, fibrates may be considered only when a statin or other effective treatments are contraindicated or not tolerated

Fibrates (bezafibrate, fenofibrate, gemfibrozil, and ciprofibrate) are one of the oldest classes of drugs that are used to reduce blood lipids. They decrease plasma triglycerides by 30–50% and raise the level of high density lipoprotein cholesterol (HDL-C) by 2–20%. Their effect on total cholesterol and low density lipoprotein cholesterol (LDL-C) ranges from no effect to a small decrease (about 10%).

Fibrates have long been used for treatment of dyslipidaemia, but in recent years a newer class of lipid-lowering drugs—the HMG-CoA reductase inhibitors commonly known as statins—has become the treatment of choice for this indication.

In view of the established role of statins in the primary and secondary prevention of cardiovascular disease, and because of concerns arising from trial data for fibrates, the MHRA has conducted a risk-benefit review of fibrates in the treatment of cardiovascular and dyslipidaemic diseases. This review considered published and unpublished data and relevant clinical guidelines.

The long-term efficacy and safety of fibrates were assessed in five large randomised, placebo controlled trials: two with gemfibrozil (HHS<sup>1</sup> and VA-HIT<sup>2</sup>); two with bezafibrate (BIP<sup>3</sup> and LEADER<sup>4</sup>); and one with fenofibrate (FIELD<sup>5</sup>). No data from randomised controlled trials are available for ciprofibrate. In most trials, fibrate treatment led to significant lipid-modifying action, but this did not always translate into a clear clinical benefit. All trials showed a trend in the reduction of non-fatal cardiovascular events in patients given fibrates; however, results reached significance only in HHS<sup>1</sup> and VA-HIT<sup>2</sup> with gemfibrozil. For mortality, most trials showed an overall negative trend, with slightly more deaths in patients given fibrates compared with controls. Only VA-HIT<sup>2</sup> with gemfibrozil recorded a favourable effect on mortality, although this was not statistically significant. The most recent study—FIELD<sup>5</sup> which assessed patients with diabetes mellitus—showed no significant benefit of fenofibrate treatment in this population.

On the basis of these trials, current clinical guidelines<sup>6–8</sup> recognise the limited role of fibrates in the treatment of dyslipidaemias and in the prevention of cardiovascular disease. Because fibrates significantly reduce triglycerides, most guidelines agree that fibrates are the treatment of choice for severe hypertriglyceridaemia. However, LDL-C reduction is the primary objective for those with raised cholesterol, and statins should always be used first to reduce it to target levels. This recommendation includes patients with mixed hyperlipidaemia (both raised cholesterol and high triglycerides) and patients with diabetes.

In some cases, clinical guidelines recommend a combination of a statin with a fibrate when statin therapy alone has not reduced triglycerides (or increased HDL-C, or both) to target levels. However, a lack of robust evidence for long-term

- 1 Frick MH, et al. *N Engl J Med* 1987; **317**: 1237–45.
- 2 Rubins HB, et al. *N Engl J Med* 1999; **341**: 410–18.
- 3 BIP Study Group. *Circulation* 2000; **102**: 21–27.
- 4 Meade T, et al. *BMJ* 2002; **325**: 1139–43.
- 5 Keech AC, et al. *Lancet* 2005; **366**: 1849–61.
- 6 Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. *Heart* 2005; **91** (suppl V): 1–52.
- 7 European Society of Cardiology and European Association for the Study of Diabetes guidelines on diabetes, pre-diabetes, and cardiovascular diseases. *Eur Heart J* 2007; **28**: 88–136.
- 8 US National Education Program Adult Treatment Panel III guidelines. *Circulation* 2004; **110**: 227–39.

clinical benefit from such a strategy—and the increased risk of myopathy and rhabdomyolysis associated with concomitant use of these drugs—suggest that this combination should be used with caution, and only when expected benefits outweigh potential risks. Gemfibrozil combined with a statin should be avoided because of potential pharmacokinetic or pharmacodynamic interactions, which further increase the risk of myotoxic adverse reactions.

The benefit-risk review of fibrates concluded that only limited data support a long-term clinical benefit from their use in the primary or secondary prevention of cardiovascular disease. Given the robust evidence for statins in these indications, the use of fibrates as a first-line treatment is no longer justified. However, the effects of fibrates mainly on triglycerides and to a smaller extent on other lipid parameters suggest that some subgroups of patients may still benefit from this therapy. In these subgroups, the overall benefit-risk balance of fibrates for specific indications remains positive.

Has your  
colleague seen  
this bulletin?

**Advice for healthcare professionals:**

- Fibrates should be considered as first-line therapy only in patients with isolated severe hypertriglyceridaemia
- For patients with mixed hyperlipidaemia, fibrates may be used only when a statin or other effective treatments are contraindicated or not tolerated
- In patients with primary hypercholesterolaemia, the use of gemfibrozil may be considered, but only when a statin or other effective treatments are contraindicated or not tolerated
- Combination therapy with a statin and a fibrate should be used with caution and only when the benefits are expected to outweigh potential risks. Avoid concomitant use of gemfibrozil with a statin

**Lumiracoxib: hepatotoxicity**

**Keywords:** lumiracoxib, osteoarthritis, hepatic, liver, aminotransferase, transaminases, jaundice, failure, fulminant, transplantation, osteoarthritis, contraindications, monitoring

**Key message:** Lumiracoxib should not be used in patients with current or past liver disease, those taking other hepatotoxic medicines, or those who have a history of drug-induced liver reactions. Monitoring of liver function is needed at baseline and at monthly intervals during treatment. Do not exceed 100 mg once daily and use only for the shortest duration necessary to control symptoms

Lumiracoxib is a selective inhibitor of COX-2, and is indicated for the symptomatic treatment of osteoarthritis of the knee and hip at a single daily dose of 100 mg.

Worldwide, there have been about 8.5 million prescriptions of lumiracoxib since July 2005. Concomitantly, 19 cases of severe hepatic reactions, including 13 hepatic failure, 2 deaths and 3 liver transplantations, have been reported spontaneously in patients who had taken lumiracoxib. In most cases, liver injury occurred after several months of use, but a few occurred within a few days of starting treatment with lumiracoxib. Although most cases were associated with doses higher than 100 mg

Severe hepatic reaction is defined as hepatic failure; Hy's case (ie, transaminases >3xULN and bilirubin >2xULN); fatal outcome; or liver transplantation. See: Temple R. *Pharmacoepidemiol Drug Saf* 2006; **15**: 241-43.

daily, eight cases of severe liver injury were reported with 100 mg daily.

Clinical studies of up to 1-year duration that compared lumiracoxib with placebo or active comparator identified elevated alanine aminotransferase (ALT), aspartate aminotransferase (AST), or both, greater than three-times the upper limit of normal ( $>3\times\text{ULN}$ ) in about 1.0% of patients given lumiracoxib 100 mg once daily. These studies recorded marked elevations (ie,  $>8\times\text{ULN}$ ) in 0.2% of patients given 100 mg once daily. Furthermore, cholecystitis, cholelithiasis, and acute hepatitis (with or without jaundice) were reported in more than 1 in 10 000 patients, but in fewer than 1 in 1000 patients, in clinical studies that mostly used doses higher than 100 mg once daily.

Patients must be advised not to exceed the daily dose of 100 mg, and must use lumiracoxib for the shortest duration possible to control symptoms. Patients and prescribers must remain vigilant for symptoms of liver damage, which might occur at any time during treatment. All patients should have liver-function tests before starting treatment with lumiracoxib, and these tests should be repeated at monthly intervals for the duration of treatment.

This issue is under continual review and further advice will be issued as necessary.

For the latest safety information on lumiracoxib, see <http://www.mhra.gov.uk/mhra/safetywarningsandmessagesformedicines>

#### Advice for healthcare professionals:

1. The following patients should **not** be prescribed lumiracoxib:

- Patients with any current or past hepatic disease
- Patients with previous drug-induced substantial elevations (ie,  $>3\times\text{ULN}$ ) of transaminases
- Patients with liver transaminases  $>1.5\times\text{ULN}$  before treatment, or  $>3\times\text{ULN}$  during treatment
- Patients who are taking other drugs known to cause clinically significant hepatotoxicity

2. Liver function should be monitored:

**Baseline monitoring**—all patients should have baseline liver-function tests before starting treatment. Patients with transaminases  $>1.5\times\text{ULN}$  should not commence treatment with lumiracoxib

**Periodic monitoring**—treatment duration should be kept to a minimum; however, if treatment for more than 30 days is needed, then liver-function tests should be repeated at monthly intervals (see action to take below)

**Intercurrent illness**—any patient who reports symptoms of liver disease during lumiracoxib treatment should have liver-function testing (see action to take below)

*Action to take in the event of elevated liver transaminase (AST or ALT) during treatment:*

Withdraw lumiracoxib immediately in the event of any elevation of transaminases  $>3\times\text{ULN}$ . Lumiracoxib may be continued on identification of transaminase levels  $>2\times\text{ULN}$ , but liver-function tests should be repeated in 7 days

3. Patients who are already taking lumiracoxib should be reviewed at the next convenient appointment, if they have not been reviewed already. If continued treatment is considered appropriate (after consideration of the overall benefit and risks, and after taking new contraindications into account), then liver-function tests should be done

**Advice for patients:**

- Patients should remain vigilant for any symptoms that are compatible with liver injury during treatment with lumiracoxib (eg, anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine, jaundice, or pruritus). These symptoms might occur at any time during treatment. Patients should stop lumiracoxib if any such symptoms occur, and should seek medical advice urgently
- Patients should be reminded of normal limits for safe alcohol consumption while taking lumiracoxib. Excessive alcohol consumption could aggravate any drug-related liver reaction. Patients should use lumiracoxib for the shortest duration necessary to control symptoms, and should **never** exceed 100 mg daily

**Ceftriaxone: incompatibility with calcium-containing solutions**

**Keywords:** ceftriaxone, Ringer's, Hartmann's, incompatibility, precipitation, calcium, neonate, newborns, contraindicated

**Key message:** Ceftriaxone is contraindicated in newborns who need calcium treatment. It should not be mixed with, or given at the same time as, calcium-containing solutions because of a risk of calcium precipitation

Ceftriaxone (Rocephin) is a broad-spectrum cephalosporin antibiotic that is used to treat infections known or likely to be due to one or more susceptible micro-organisms and when parenteral therapy is needed. Ceftriaxone can be given by deep intramuscular injection, slow intravenous injection, or by slow intravenous infusion after reconstitution of the solution.

Ceftriaxone is not compatible with calcium-containing solutions such as Hartmann's solution and Ringer's solution, and should not be mixed with (or added to) such solutions. Several neonatal deaths associated with calcium–ceftriaxone precipitates in the lungs and kidneys have been reported worldwide. In some cases, patients had received ceftriaxone and calcium at different times and through different intravenous lines.

From the data available, there are no reports of intravascular precipitations in patients other than newborns treated with ceftriaxone and calcium-containing solutions or any other calcium-containing products.

**Advice for healthcare professionals:**

- Ceftriaxone is contraindicated in newborns who need calcium treatment because of a risk of precipitation of ceftriaxone–calcium salt
- In all patients, ceftriaxone must not be mixed with calcium-containing solutions, and must not be given to any patient simultaneously with calcium-containing solutions—even via different infusion lines

## Codeine: very rare risk of side-effects in breastfed babies

**Keywords:** codeine, morphine, breastfeeding, neonates, CYP2D6 polymorphisms

**Key message:** Breastfed babies might very rarely develop side-effects due to the presence of morphine in breast milk

Codeine is a widely used analgesic for mild to moderate pain. Codeine is a prodrug, and requires the cytochrome P450 enzyme CYP2D6 for conversion to the active component morphine. Thus, a patient who is deficient in this enzyme will obtain no analgesic effect from codeine. Conversely, some patients have more than two copies of the gene for this enzyme and are ultra-rapid metabolisers. These patients are more likely to have side-effects than extensive metabolisers because they convert codeine to morphine more quickly or in greater quantities.

A Canadian case report<sup>1</sup> described a breastfed neonate who died from morphine poisoning associated with maternal codeine used for episiotomy pain. The mother was an ultra-rapid codeine metaboliser as a result of CYP2D6 polymorphisms.

Some breastfed babies might develop side-effects due to the presence of morphine in breast milk. However, in the UK, only 1–2% of people are CYP2D6 ultra-rapid metabolisers and only the breastfed babies of these mothers may be more prone to these adverse effects. Therefore, most mothers should be able to use codeine-containing analgesics safely during breastfeeding without any side-effects in their baby. If a breastfeeding mother has side-effects associated with codeine use, extra vigilance should be exercised with close observation for these or other side-effects in the baby.

<sup>1</sup> Koren G, et al. *Lancet* 2006; **368**: 704.

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this bulletin with  
your colleagues?

### Advice for healthcare professionals:

- All patients should be advised about the typical side-effects of opioids because most patients are not aware of their CYP2D6 status
- If any symptoms of opioid toxicity develop in the mother or baby (eg, nausea, vomiting, lack of appetite, and somnolence, with symptoms of circulatory and respiratory depression in severe cases) patients should stop taking all codeine-containing medicines, and alternative analgesics should be prescribed. In severe cases, naloxone may be appropriate to reverse the effects
- These side-effects are very rare and most women will be able to use medicines that contain codeine to obtain adequate analgesia when needed after labour without any problems for them or their baby

## St John's wort: interactions with all antiepileptics

**Keywords:** St John's wort, *Hypericum perforatum*, interactions, antiepileptic medicines

**Key message:** Any antiepileptic medicine may interact with St John's wort: patients with epilepsy should not take products that contain St John's wort

For further information about the regulation and safety of herbal medicines, see <http://www.mhra.gov.uk/mhra/herbalmedicines>

Further information about the Yellow Card scheme is available at <http://www.yellowcard.gov.uk>; see also page 8

For further information about the Herbal Medicines Advisory Committee see <http://www.mhra.gov.uk/mhra/HerbalMedicinesAdvisoryCommittee>

Further information about the Commission on Human Medicines Pharmacovigilance Expert Advisory Group see <http://www.mhra.gov.uk/mhra/CommissiononHumanMedicines>

St John's wort (*Hypericum perforatum*) is a herbal ingredient commonly available in the UK as an unlicensed herbal medicine.

Traditionally, St John's wort has had various uses, including external application as a treatment for wounds and burns; it is also taken orally to treat fevers and conditions such as depression.

In 2000, warnings were issued that some antiepileptic medicines interacted with St John's wort. These warnings were based on the metabolism of these medicines and the known induction and inhibitory effects of St John's wort on various cytochrome P450 enzymes.

The MHRA continues to receive reports of possible interactions with St John's wort through the Yellow Card Scheme. A recent case involved St John's wort and several different antiepileptic medicines, which resulted in an increase in the frequency and severity of the patient's seizures. The antiepileptic medicines the patient was taking (levetiracetam, lamotrigine, and clobazam) were not those previously known to interact with St John's wort.

The Herbal Medicines Advisory Committee and the Commission on Human Medicines Pharmacovigilance Expert Advisory Group have considered the interaction between St John's wort and antiepileptic medicines by routes other than the recognised cytochrome P450 pathway. Both have recommended that the current warnings about interactions should extend to include all antiepileptic medicines.

### Advice for healthcare professionals:

- Concomitant use of St John's wort and antiepileptic medicine is not recommended: healthcare professionals should advise patients with epilepsy not to use products that contain St John's wort
- Please continue to report any suspected adverse reaction with St John's wort, or any other herbal medicines, through the Yellow Card Scheme ([www.yellowcard.gov.uk](http://www.yellowcard.gov.uk))

## Yellow Card scheme update

The Yellow Card scheme collects information on suspected adverse drug reactions. See [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)

Please use the Yellow Card scheme to report any suspected adverse drug reaction associated with a herbal medicine. We would like to remind you that the Yellow Card scheme collects information on unlicensed medicines as well as those that are licensed.

This month's Drug safety advice article on the potential for St John's wort—a herbal ingredient commonly available in the UK as an unlicensed herbal medicine—to interact with any antiepileptic medicine (page 7) illustrates the importance of the Yellow Card scheme in the identification of important safety signals associated with herbal remedies.

**Please continue to send us Yellow Cards reports of suspected adverse drug reactions with St John's wort or any other herbal medicine. Send us a sample of the product if you are not sure what it contains.**

Our Hot topic article on the continued availability of herbal remedies that contain the prohibited ingredient *Aristolochia* (page 8) highlights that people can have very serious reactions after taking a herbal medicine. *Aristolochia* is associated with distinctive renal fibrosis called Chinese Herb Nephropathy, and some patients have developed transitional-cell carcinomas after its use.

However, Yellow Cards that report a reaction to a herbal medicine account for less than 1% of the total Yellow Cards we receive every year. Patients and carers send us a substantial proportion (15%) of the Yellow Cards we receive for reactions to a herbal medicine. We would like to encourage this reporting and keep patients and carers alert for potential side-effects of herbal remedies. The other main sources of Yellow Card reports for herbal medicines are from GPs (28%) and pharmacists (26%).

Remember to ask a patient about the use of herbal medicines and over-the-counter medicines when inquiring about the basis for a potential adverse drug reaction or interaction.

**Please remain vigilant for potential reactions associated with herbal medicines—send a Yellow Card if you suspect such a reaction.**

## Hot topics

### Illegal herbal remedies that contain *Aristolochia*: vigilance needed

*Aristolochia* is a plant genus of the family *Aristolochiaceae*. Various *Aristolochia* species have been used in herbal medicines worldwide as anti-inflammatory agents for gout, arthritis, rheumatism, and chronic inflammatory skin diseases.

Use of *Aristolochia* species in herbal medicines was prohibited in the UK in 1999 because of the toxicity of the aristolochic acid constituents, which are nephrotoxic, carcinogenic, and mutagenic—even at very small doses. The UK prohibition order also includes several other plant species that do not cause nephrotoxicity on their own, but which were commonly substituted with *Aristolochia* in the remedies.

Aristolochia is associated with distinctive renal fibrosis, which has been called Chinese Herb Nephropathy. End-stage renal failure in Chinese Herb Nephropathy can be reached 6–24 months after ingestion of Aristolochia. Furthermore, some patients have developed transitional-cell carcinoma in the renal pelvis, ureter, and bladder.

The MHRA continues to identify cases of herbal medicines, particularly traditional Chinese medicines, which contain Aristolochia or aristolochic acids. Commonly, there has been no reference to Aristolochia on the list of ingredients for the products. In recent years, the MHRA has found Aristolochia in the following products:

To contact us, you can email [info@mhra.gsi.gov.uk](mailto:info@mhra.gsi.gov.uk); call 020 7084 2000 (weekdays 0900 h to 1700 h); or write to 10-2 Market Towers, 1 Nine Elms Lane, London SW8 5NQ

For information about Aristolochia and other herbal safety news see [http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2031938&ssTargetNodId=663](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2031938&ssTargetNodId=663)

Read the latest safety warnings and messages for herbal medicines at [http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&nodId=846](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&nodId=846)

- Xie Gan Wan
- Longdan Xie Gan Wan
- Guan Xin Su He
- Longdan Qiegan Wan (Longdan Xie Gan Wan)
- Jingzhi Kesou Tanchuan
- Guanxin Suhe capsules
- Qing Re An Cang Wan



Products that contain Aristolochia are illegal. Anyone with information about the sale or supply of products suspected to contain Aristolochia should contact the MHRA immediately.

Healthcare professionals should ask patients who present with unexplained nephrotoxicity about any herbal products they may have taken, particularly traditional Chinese medicines.

## Nasal decongestants that contain pseudoephedrine or ephedrine: sales restrictions

Nasal decongestants in cold and influenza remedies that contain pseudoephedrine or ephedrine are to have tighter sales restrictions.

New restrictions are being introduced in response to a public consultation by the MHRA earlier this year to reclassify these medicines from pharmacy (P) availability to prescription-only (POM) because of increasing concern about the potential for pseudoephedrine and ephedrine to be extracted from over-the-counter medicines and used in the illegal manufacture of the Class A controlled drug methylamphetamine (crystal meth).

The Commission on Human Medicines has recommended the following to try to ensure that the benefits of these medicines outweigh the potential risk to the public from their illicit use:

- Small 720-mg packs of nasal decongestants that contain pseudoephedrine or ephedrine (the equivalent of 12 tablets or capsules of 60 mg, or 24 tablets or capsules of 30 mg) will replace large packs
- A limit of one pack per customer per purchase

For further information, including the minutes of the Commission's discussion on the outcome of the consultation, see [http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2032216&ssTargetNodId=389](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2032216&ssTargetNodId=389)

A public consultation on proposals to make the sale and supply of products that contain more than 720 mg pseudoephedrine and 180 mg ephedrine subject to a prescription was announced on Oct 2, 2007. To find out more, and to respond to the consultation by Nov 13, see [http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2032570&ssTargetNodId=373](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2032570&ssTargetNodId=373)

The Commission has set-up a working group to advise on the practical introduction of these recommendations and to monitor the effect of these controls. This group will also review the risks and benefits associated with all decongestants in this class compared with alternative treatments.

The Commission advised that nasal decongestants that contain pseudoephedrine or ephedrine should be reclassified from P to POM status in 24 months' time (in 2009), or earlier if necessary, unless the new sales restrictions contain the risk to the public from the misuse of these medicines.

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## Stop press

### **Moxifloxacin: hepatotoxicity and serious skin reactions—prescribing update**

Following a review of recent safety data, changes have been implemented to the prescribing information for moxifloxacin (Avelox ▼) to warn of the risk of potentially fatal liver failure and toxic epidermal necrolysis. Healthcare professionals are reminded to be vigilant of the early signs and symptoms of such disorders, and ask patients to seek medical advice as appropriate.

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### **Co-proxamol withdrawal: reminder to prescribers**

At the end of January 2005, the MHRA announced that the painkiller co-proxamol was to be withdrawn from the market. This decision followed a 12-week consultation exercise to gather further information on the risks and benefits of co-proxamol. A decision was made to withdraw co-proxamol over a phased period—until the end of 2007—to enable patients on co-proxamol to move to suitable alternatives.

Any patients who are still taking co-proxamol should, where possible, be moved to a suitable alternative ahead of the cancellation of the licences at the end of the year. We recognise that there is a small group of patients who are finding it difficult to change, or where there is an identified clinical need when alternatives seem to be ineffective or unsuitable. For this small group of patients, continued provision of co-proxamol through normal prescribing may continue until the cancellation of the licences at the end of 2007. After this time, a provision will remain for the supply of unlicensed co-proxamol on the responsibility of the prescriber, and the Marketing Authorisation holder for the brand leader (Distalgesic) has indicated that they will continue to manufacture co-proxamol to meet clinical demand.

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### **Ecoflac infusion solutions: risk of air embolism**

These semi-rigid plastic containers contain infusion solutions (glucose, KCl, or NaCl) for intravenous administration. They are designed to collapse during use, and they include a substantial volume of air. To avoid the risk of air embolism, these products should not be infused under pressure. It is recommended that they are used under gravity feed with a drip tube or an intravenous infusion pump to minimise the risk of air embolism. Partially used containers should not be reused.

See  
[http://www.mhra.gov.uk/home/idcplg?IdcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON002065&ssTargetNodId=389](http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON002065&ssTargetNodId=389)

For further information, see  
[http://www.mhra.gov.uk/home/idcplg?IdcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2025739&ssTargetNodId=387](http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2025739&ssTargetNodId=387)

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## Other information from the MHRA

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### Optometrists: independent prescribing

Optometrists will be able to train to prescribe medicines. After a public consultation, the Commission on Human Medicines has recommended that suitably qualified optometrists should be able to prescribe any licensed medicine for conditions that affect the eye or the surrounding tissue within the recognised expertise and competence of the optometrist.

Optometrists who wish to have prescribing responsibilities will need to train at a Higher Education Institution and be accredited by the General Optical Council. Continued training and education will be needed to maintain specialty registration as a prescriber.

For further information, see our News Centre  
[http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2032211&ssTargetNodeId=387](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2032211&ssTargetNodeId=387)

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### Patient Information Leaflets: improving quality

Patient information leaflets (PILs) are improving in quality as a result of new legal obligations on manufacturers to test them with potential patients. User-testing makes sure that the presentation of the information enables patients to find and understand key messages for safe and effective use of the medicine. To promote this new initiative, we are publishing a series of examples of best practice on our website. The latest in the series is the PIL for **Andropatch**, a transdermal delivery system of testosterone for androgen deficiency.

To access PIL of the month, click  
[http://www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2032657&ssTargetNodeId=387](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2032657&ssTargetNodeId=387)

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### MHRA conference: 'Combating Counterfeit Medicines'

Register now for the MHRA's conference 'Combating Counterfeit Medicines', November 22, 2007 in London.

Featuring Rt. Hon Dawn Primarolo MP, Minister of State for Public Health, alongside speakers from MHRA, WHO, Chinese Ministry of Public Security, and EU Commission, and HM Revenue and Customs.

For more information on this event, see  
<http://www.mhra.gov.uk/conferences/counterfeits>

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Read more about the Commission on Human Medicines including summaries of minutes from meetings, at

<http://www.mhra.gov.uk/mhra/CommissiononHumanMedicines>

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