New MHRA drug safety advice: February to April 2013

Document as included in MAW

The MHRA and CHM publish the monthly newsletter Drug Safety Update highlighting important information and advice to support the safer use of medicines. To subscribe to Drug Safety Updates from the MHRA, please visit this link to register.

The MHRA has provided the following synopsis of the key drug safety issues from the February, March and April 2013 Drug Safety Updates:

Denosumab 60 mg (Prolia▼)¹
Atypical femoral fractures have been reported rarely in patients with postmenopausal osteoporosis receiving long-term (≥2.5 years) treatment with denosumab 60 mg (Prolia▼) in a clinical trial.

During denosumab treatment, patients presenting with new or unusual thigh, hip or groin pain should be evaluated for an incomplete femur fracture. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated.

Sprayable fibrin sealants (Evicel, Tisseel and Artiss)²
Life-threatening and fatal cases of air embolism have been reported with incorrect use of sprayable fibrin sealants administered using a pressure regulator device.

To avoid potentially fatal air embolism, do not exceed the maximum recommended pressure for the regulator device, and do not spray the product closer than the minimum recommended distance from the tissue surface. Ensure that fibrin sealants are only sprayed using the appropriate gas.

Dabigatran (Pradaxa)³
Dabigatran (Pradaxa) is now contraindicated in patients with prosthetic heart valves requiring anticoagulant treatment related to their valve surgery, regardless of the length of time elapsed since valve replacement took place.
The contraindication is based on new clinical trial data in this population, which showed an increased frequency of thromboembolic and bleeding events in the group of patients treated with dabigatran, compared with warfarin.

**Aqueous cream**

Aqueous cream may cause local skin reactions, such as stinging, burning, itching, and redness, when it is used as a leave-on emollient, particularly in children with atopic eczema. The reactions, which are not generally serious, often occur within 20 minutes of application but can occur later. Reactions may be due to the presence of sodium lauryl sulfate or other ingredients.

If a patient reports or shows signs of skin irritation with the use of aqueous cream, treatment should be discontinued and an alternative emollient that does not contain sodium lauryl sulfate should be tried.

**Botulinum toxin type B (Neurobloc)**

Botulinum toxin type B (Neurobloc) is indicated only for the treatment of cervical dystonia (torticollis) in adults. The MHRA recommend that prescribers adhere to the licensed indication as its safety outside these circumstances has not been established. Cases of the known rare risk of toxin spread have been reported with all botulinum toxin products. Importantly, the cases with botulinum toxin type B were mostly reported with its off-label use.

All patients receiving any product containing botulinum toxin should be warned of the signs and symptoms of toxin spread, such as muscle weakness and breathing difficulties, and advised to seek medical attention immediately if they experience breathing difficulties, choking, or any new or worsening swallowing difficulties, as such side effects may be life-threatening.

**Insulin degludec (Tresiba▼): available in additional higher strength than existing insulins**

Insulin degludec (Tresiba▼) is available in prefilled pen devices (known as FlexTouch) in two strengths: 100 units/mL; and 200 units/mL. The 100 units/mL strength is also available in cartridge form (called Penfill). The 200 units/mL strength is higher than that of other existing basal insulin products in the UK. Ensure the correct insulin product and strength is prescribed and dispensed.

The dose-counter window of the Tresiba FlexTouch pen device shows the number of units that will be injected, irrespective of strength. Therefore no dose conversion is needed when transferring a patient from one strength of Tresiba to a different strength.

People with diabetes should be trained on the correct use of Tresiba products, and always visually verify the dialled units on the dose counter of the prefilled pen device (irrespective of strength). Advise people with diabetes to seek medical advice immediately if they think they have administered an incorrect dose of Tresiba.

**Cilostazol (Pletal): risks of cardiovascular and bleeding events**

Cilostazol (Pletal) is restricted to second-line use in patients for whom lifestyle modifications and other appropriate interventions have failed to sufficiently improve their symptoms.

Furthermore, cilostazol is now contraindicated in patients with any of the following:
- unstable angina, recent myocardial infarction or coronary intervention (within 6 months)
- a history of severe tachyarrhythmia
- those receiving two or more other antiplatelet or anticoagulant treatments.

For patients starting cilostazol, prescribers should assess benefit after 3 months of treatment, and should stop treatment if patients have not made clinically relevant improvements in walking distance. All patients who are currently receiving long-term treatment should be reassessed at a routine appointment, in light of the new advice.

Strontium ranelate (Protelos)
A review of available safety data for strontium ranelate (Protelos) has raised concern about its cardiovascular safety beyond the already recognised risk of venous thromboembolism. An analysis of randomised controlled trial data has identified an increased risk of serious cardiac disorders, including myocardial infarction (relative risk compared with placebo was 1.6 [95% confidence interval 1.07 to 2.38]).

In order to help minimise these risks, updated advice is available.

Other topics
Other topics covered for which further details can be found on the Drug Safety Update page of the MHRA website include:

Learning about reducing risks associated with medicines – Benzodiazepines

Recent drug-name confusion: please be vigilant as life-threatening errors may occur.

The process used to produce Drug Safety Update is NICE accredited.

References
1. Drug Safety Update February 2013, vol 6, issue 7: A1
2. Drug Safety Update February 2013, vol 6, issue 7: A2
3. Drug Safety Update March 2013, vol 6, issue 8: A1
4. Drug Safety Update March 2013, vol 6, issue 8: A2
5. Drug Safety Update March 2013, vol 6, issue 8: A3
8. Drug Safety Update April 2013, vol 6, issue 9: S1
9. Drug Safety Update March 2013, vol 6, issue 8: O1
10. Drug Safety Update April 2013, vol 6, issue 9: H1
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