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**

Volume 3, Issue 11 **June 2010**

Contents

Click on text to go to page

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.

NHS Evidence accredited provider
NHS Evidence - provided by NICE
www.evidence.nhs.uk

For full details on our accreditation visit http://www.evidence.nhs.uk/Accreditation/

We wish to make you aware of case reports of medication error and inappropriate use of rivastigmine transdermal patches in the treatment of Alzheimer's dementia. The most frequently reported causes have been lack of patch removal and use of more than one patch at the same time. Our advice on p 2 reminds you of some important measures to help ensure safer use. Importantly, this advice should be given to patients and caregivers before starting treatment.

Also this month, we would like to advise you that quinine should not be considered a routine treatment for nocturnal leg cramps, and should only be considered when cramps cause regular disruption of sleep. Although quinine tablets are generally well tolerated at the doses used for treatment of leg cramps, overall efficacy is modest and there is a rare risk of serious thrombocytopenia. It also has significant toxicity in overdose, which can result in death or permanent visual loss (p 3).

Claire Tilstone, Editor

drugsafetyupdate@mhra.gsi.gov.uk

Rivastigmine (Exelon) transdermal patch: risk of medication errors

Keywords: rivastigmine transdermal patch, Exelon transdermal patch

Medication errors and inappropriate use of the rivastigmine transdermal patch have been reported, some of which resulted in overdose. Healthcare professionals should be aware of the correct use of rivastigmine, and should advise patients and caregivers as outlined below

Rivastigmine (Exelon) transdermal patch is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia. The patch is available in two doses: 4·6 mg/24 hours; and 9·5 mg/24 hours. Treatment is started with one 4·6 mg/24 hour patch. After a minimum of 4 weeks and if tolerated well, the daily dose should be increased to the recommended effective dose of 9·5 mg/24 hours.

Risk of medication errors and inappropriate use

Case reports of medication errors and inappropriate use of the rivastigmine transdermal patch have been reported, some of which resulted in overdose and required admission to hospital. The most frequently reported causes were lack of patch removal and application of more than one patch at the same time. Other causes were: application of the patch to non-recommended sites; patch application to the same area for several weeks; cutting the patch into several pieces; and dose errors in prescribing or dispensing.

This article aims to remind healthcare professionals about the correct use and administration of rivastigmine transdermal patches as outlined in the Summary of Product Characteristics. Health professionals should also advise patients and caregivers before starting treatment; similar to any treatment initiated in patients with dementia, rivastigmine should only be started if a caregiver is able to regularly give and monitor treatment.

Further information for patients can be found in the Exelon transdermal patch Patient Information Leaflet.

Advice for healthcare professionals:

- Symptoms of rivastigmine overdose include nausea, vomiting, diarrhoea, hypertension, and hallucinations; bradycardia and/or syncope, associated with malaise or falls, may also occur
- In case of suspected overdose, all rivastigmine patches should be removed immediately and no further patch should be applied for the next 24 hours
- It is important to instruct patients and caregivers on the proper use of the transdermal patch, particularly that:
  - Only one patch should be applied per day to healthy skin on the upper or lower back, upper arm, or chest
  - The patch should be replaced by a new one after 24 hours, and the previous day's patch must be removed before application of a new patch to a different skin location
  - Application to the same skin location within 14 days should be avoided to minimise skin irritation
  - The patch should not be cut into pieces

Continues...

...continued

Access the letter at http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/Monthlylistsofinformationforhealthcareprofessionalsonthesafetyofmedicines/CON081746

A letter has been sent to healthcare professionals in April 2010 with information on this risk.

Reporting of suspected adverse reactions

Please report suspected adverse reactions associated with the use of the rivastigmine patch to us on a Yellow Card (www.yellowcard.gov.uk). Patients and caregivers can also report any suspected reactions to us via the Yellow Card Scheme.

Quinine: not to be used routinely for nocturnal leg cramps

Keywords: Quinine, nocturnal leg cramps

Quinine is not a routine treatment for nocturnal leg cramps, and should only be considered when cramps cause regular disruption of sleep. Quinine should only be considered: when cramps are very painful or frequent; when other treatable causes of cramp have been ruled out; and when non-pharmacological measures have not worked (eg, passive stretching exercises). After an initial trial of 4 weeks, treatment should be stopped if there is no benefit

Quinine has been used in the UK for the treatment of nocturnal leg cramps for many years. Although patient response may vary, overall efficacy is modest. A meta-analysis of eight randomised placebo controlled trials reported that the mean number of cramps in a 4-week period while taking placebo was 17·08 and the absolute reduction in cramps while taking quinine was 3·6 (95% CI 2·2–5·1). Hence patients had around 20% fewer cramps in this period—around one episode a week difference—when taking quinine compared with placebo.[1]

1 Man-Son-Hing M, et al. *J Gen Intern Med* 1998; **13:** 600–06.

Recommended dose

The licensed dose for the treatment and prevention of nocturnal leg cramps in adults is 200–300 mg at night for quinine sulphate (recommended starting dose 200 mg), and is 300 mg at night for the bisulphate. The quinine salt should always be stated when prescribing because 200 mg quinine sulphate is equivalent to around 300 mg quinine bisulphate.

Patient selection and clinical monitoring

Quinine should not be considered a routine treatment for nocturnal leg cramps, and should only be considered when cramps cause regular disruption of sleep. Before use for nocturnal leg cramps, the risks should be carefully considered relative to the potential benefits. Quinine should only be considered: when cramps are very painful or frequent; when other treatable causes of cramp have been ruled out; and when non-pharmacological measures have not worked (eg, passive stretching exercises).

A reduction in frequency of leg cramps may take up to 4 weeks to become apparent. Patients should be monitored closely during the early stages of treatment for adverse effects. After an initial trial of 4 weeks, treatment should be stopped if there is no benefit. Treatment should be interrupted approximately every 3 months to reassess the benefit. In patients taking quinine long term, a trial discontinuation may be considered.

Summaries of Product Characteristics and Patient Information Leaflets are being updated, and should be consulted for safety information.

Continues...

...continued

Safety summary

Quinine tablets are generally well tolerated at the doses used for treatment of leg cramps. However, adverse events may include tinnitus, impaired hearing, headache, nausea, disturbed vision, confusion, flushing, and abdominal pain. Treatment should be stopped if these occur.

A rarer but more serious adverse reaction is thrombocytopenia, thought to be a hypersensitivity reaction. A small number of deaths linked to thrombocytopenia have been reported in patients taking quinine for the treatment of leg cramps, including two cases in the UK Yellow Card database. Quinine should not be prescribed to patients who have previously experienced any adverse reaction to quinine, including that found in tonic water or other beverages. Patients should be instructed to stop treatment and consult a physician if signs of thrombocytopenia occur, such as unexplained petechiae, bruising, or bleeding.

Quinine has a number of potentially significant drug interactions, including with digoxin and warfarin. It also has significant toxicity in overdose, which can result in death or permanent visual loss.

Advice healthcare professionals:

- Quinine is not a routine treatment for nocturnal leg cramps, and should only be used when cramps regularly disrupt sleep
- Before use of quinine for nocturnal leg cramps, the risks should be carefully considered relative to the potential benefits
- After a trial of at least 4 weeks, treatment should be stopped if there is no benefit. If treatment continues, the benefits should be assessed around every 3 months
- Patients should be warned not to exceed the recommended dose. Serious side effects including irreversible blindness and death may occur with overdose
- Thrombocytopenia is a rare but potentially life-threatening adverse reaction associated with quinine. Patients should be instructed to stop treatment and consult a physician if signs of thrombocytopenia occur, such as unexplained petechiae, bruising, or bleeding
- Quinine should not be prescribed or given to patients who have previously experienced any adverse reaction to quinine, including that found in beverages

Stop press

Bevacizumab (Avastin): hypersensitivity and infusion reactions

Bevacizumab (Avastin) is a monoclonal antibody, which inhibits vascular endothelial growth factor and is authorised for the treatment of various metastatic cancers.

Healthcare professionals are advised to be aware that infusion reactions and hypersensitivity reactions have been reported commonly (≥1/100–<1/10) during treatment with Avastin. The incidence of such reactions is estimated to be up to 5% in clinical trials. Symptoms reported have included dyspnoea, flushing, rash, hypotension or hypertension, oxygen desaturation, chest pain, rigors, and nausea or vomiting. These reactions normally resolve quickly if the infusion is stopped immediately. Treatment with corticosteroids, antihistamines, oxygen, and intravenous fluids may also be administered as clinically indicated.

Further information is available in a letter for healthcare professionals sent in April 2010.

See http://www.mhra.gov.uk/Safetyinformation/Safetywarningsalertsandrecalls/Safetywarningsandmessagesformedicines/Monthlylistsofinformationforhealthcareprofessionalsonthesafetyofmedicines/CON081746

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

Sign up to receive an email alert when a new issue is published: email registration@mhradrugsafety.org.uk

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