Observatory
November 2016
Observatory of recent safe medication practice research, reports, and publications

Presented by Ben Rehman
UKMI
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Recent regulator and statutory body activity

Classification: Official

NHS Improvement

Patient Safety Alert

Risk of severe harm and death due to withdrawing insulin from pen devices
16 November 2016

1. Identify whether incidents involving inappropriate use of insulin pen devices could occur in your organisation.

2. Consider if immediate action needs to be taken locally and ensure that an action plan is underway, if required, to reduce the risk of incidents, including ensuring access to appropriate equipment and training wherever insulin is administered.

3. Share this alert, or its key messages in alternative formats (such as posters or revised local safety advice), to all clinical staff who prescribe, dispense or administer insulin.

4. Share any learning from local investigations or locally developed good practice by emailing: patientsafety.enquiries@nhs.net

UKMii
UK Medicines Information
Recent regulator and statutory body activity

**Patient Safety Alert**

Risk of death and severe harm from error with injectable phenytoin
9 November 2016

1. Identify if the issues in this alert could occur in your organisation.

2. Consider if immediate action needs to be taken locally to improve the safe use of injectable phenytoin, and ensure an action plan to embed further improvement to patient safety is underway if required.

3. Circulate this alert to all relevant staff, including those with responsibilities for developing protocols, procedures, training and equipment required for the safe use of injectable phenytoin.

4. Share any learning from local investigations or locally developed resources via the Medication Safety Officers network or by emailing: patientsafety.enquiries@nhs.net

NHS Improvement

UKMi
How can we minimise the risks to patients when using intravenous phenytoin in status epilepticus (SE)?

Published 7th November 2016, updated 18th November 2016

Phenytoin is prone to errors in its prescribing, dose calculation, preparation and administration and, as it is relatively rarely used, a lack of familiarity when managing a medical emergency such as SE may lead to patient risk and harm.

Ensuring that the teams who may be called upon to use IV phenytoin in SE are familiar with the risks and are supported by training, protocols and equipment will help to reduce the risk of patient harm.

NHS Improvement have issued an alert on this topic (see link below).
Recent regulatory and statutory body activity

Drug Safety Update

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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Brimonidene gel (Mirvasco): risk of exacerbation of rosacea

Some patients may have exacerbation or rebound symptoms of rosacea. It is important to initiate treatment with a small amount of gel and increase the dose gradually, based on tolerability and treatment response.

**Advice for healthcare professionals:**

- exacerbation of rosacea symptoms occurred in up to 16% of patients treated with brimonidene gel in clinical studies; in most cases, erythema and flushing resolve after stopping treatment.
- initiate treatment with a small amount of gel (less than the maximum dose) for at least 1 week and increase the dose gradually, based on tolerability and response to treatment.
- advise patients carefully on how to apply the gel and on the importance of not exceeding the maximum daily dose (which is 1 g of gel in total weight, approximately 5 pea-sized amounts).
- advise patients to stop treatment and consult a doctor if their symptoms worsen during treatment (increased redness or burning).
Social media campaign to support drug reaction reporting

Show your support for reporting suspected adverse drug reactions

From: Medicines and Healthcare products Regulatory Agency

We are running a social media campaign to promote the reporting of suspected adverse drug reactions to the Yellow Card Scheme in support of an awareness week from 7 to 11 November 2016. The main message of the campaign is that reporting helps make medicines safer and saves lives.
Recent regulator and statutory body activity

Letters sent to healthcare professionals in October 2016

From: Medicines and Healthcare products Regulatory Agency
Therapeutic area: Cancer, Endocrinology, diabetology and metabolism, Haematology, Respiratory disease and allergy, and Urology and nephrology

A summary of recent safety letters sent to relevant healthcare professionals

In October 2016, the following letters were sent to relevant healthcare professionals:

• Flolan (epoprostenol): new thermostable formulation (solvent pH 12) available from October 2016, with differences in storage and administration from previous formulation (pH 10.5)
• Teva levothyroxine: reintroduction to market and introduction of new tablet strengths (letter for Clinical Commissioning Groups, and for pharmacists and dispensers); see also further information here
• Blincyto▼ (blinatumomab): cases of pancreatitis

Flolan letter

GLAXOSMITHKLINE SAFETY ADVISORY

Date: September 2016

- Flolan® 0.5 mg Powder and Solvent for Solution for Infusion (PL 10949/0310)
- Flolan® 1.5 mg Powder and Solvent for Solution for Infusion (PL 10949/0312)
- Flolan® (epoprostenol) – Introduction of new sterile solvent with different pH; temporary availability of two different formulations.

Dear Healthcare Professional

A new formulation of Flolan (with Solvent pH 12) will be available (from 14\textsuperscript{th} October 2016) with differences in storage and administration from the current formulation (with Solvent pH 10.5). There will be overlap in availability in this new formulation with the current one – until April 2017.

Reconstituted Flolan with pH 12 Solvent (the new formulation) is more thermostable, which eliminates the need for use of a cold pouch/ice pack during administration.
Epoprostenol – Important information about change in formulation of Flolan

Published 26th October 2016, updated 28th October 2016

GlaxoSmithKline (GSK) has reformulated Flolan (epoprostenol). The company issued a notice stating there will be two formulations of Flolan on the market until April 2017 or until stocks are exhausted of the old formulation. The new formulation has a solvent pH of 12, the old one has a solvent pH of 10.5. Both 0.5mg and 1.5mg strengths have been reformulated.

There is also a difference between old and new formulations in their licensed indications, recommended infusion concentrations, shelf life and storage.

The old formulation is thermolabile; it is stable for only 12 hours at 25°C. When used as a continuous infusion over 24 hours, a cold pouch/ice pack is used to prevent/delay degradation. The new formulation is more stable and a cold pack is not needed. The new formulation is also stable for longer once reconstituted.

To increase the stability of epoprostenol it is necessary to increase the pH. However, this introduces other issues that need to be considered notably effects on administration devices.

This briefing document outlines issues that need to be considered, the risks that have been identified and what NHS organisations need to do to minimise risks associated with transition of Flolan pH 10.5 to Flolan pH 12.5.
Teva levothyroxine re-introduction

News story

Teva levothyroxine tablets: re-entry to market and introduction of new tablet strengths

From: Medicines and Healthcare products Regulatory Agency
First published: 17 October 2016

Following extensive changes to the formulation and manufacture of levothyroxine tablets by Teva, the Commission on Human Medicines (CHM) is now reassured that Teva has demonstrated an acceptable level of efficacy and safety to allow their levothyroxine tablets to re-enter the market. Additional tablet strengths have also been introduced, to improve precision of dosing.

A total of five tablet strengths will be available from week commencing 17 October, 2016: 12.5, 25, 50, 75 and 100 micrograms.

These products do not contain lactose
Blincyto and risk of pancreatitis

Dear Health Care Professional,

Amgen in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Cases of pancreatitis, some life-threatening or fatal, have occurred in patients treated with BLINCYTO\textsuperscript{\textregistered} in clinical trials and in the post-marketing setting. High-dose corticosteroid therapy may have contributed, in some cases, to the pancreatitis.
- Patients should be closely monitored for signs and symptoms of pancreatitis, including physical examination, laboratory evaluation for serum amylase and serum lipase and abdominal imaging.
- BLINCYTO\textsuperscript{\textregistered} should be withheld if pancreatitis grade 3 occurs, then restarted at 9 micrograms/day after improvement to grade 1 and escalated to 28 micrograms/day after 7 days if pancreatitis does not recur.
- In the event of pancreatitis grade 4, permanent discontinuation of BLINCYTO\textsuperscript{\textregistered} should be considered.
- Patients should be advised to recognize features of pancreatitis such as upper abdominal tenderness and pain (made worse by eating), nausea and vomiting. They should be instructed to get medical advice if symptoms occur.
Recent regulator and statutory body activity

Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 7-10 November 2016

- Nine medicines recommended for approval, including 3 biosimilars
  - New biosimilar insulin glargine
  - 2 new biosimilar teriparatide

- Five recommendations on extensions to therapeutic indications

- Renewal of conditional marketing authorisation for translarna (ataluren)

- No specific recommendations in relation to safety
Pharmacovigilance Risk Assessment Committee (PRAC)

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 24-27 October 2016

At its monthly meeting, the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) discussed four ongoing safety reviews. More information on all safety reviews currently under evaluation is provided in the table below. The Committee did not initiate or conclude a referral.

**Ongoing referrals**

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<th>Procedure</th>
<th>Status</th>
<th>Update</th>
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<tr>
<td>Article-20 procedure: Direct-acting antivirals for treatment of hepatitis C (interferon-free)</td>
<td>Under evaluation</td>
<td>PRAC adopted a list of outstanding issues to be addressed by the marketing-authorisation holders.</td>
</tr>
<tr>
<td>Article-31 referral: Factor VIII</td>
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</tr>
<tr>
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<td>Under evaluation</td>
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</tr>
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<td>Article-20 procedure: SGLT2 Inhibitors (previously Canagliflozin)</td>
<td>Under evaluation</td>
<td>PRAC adopted a list of outstanding issues to be addressed by the marketing-authorisation holders.</td>
</tr>
<tr>
<td>Article-31 referral: Gadolinium-containing contrast agents</td>
<td>Under evaluation</td>
<td>PRAC continued its assessment</td>
</tr>
<tr>
<td>Article 31-referral: Retinoid-containing medicinal product</td>
<td>Under evaluation</td>
<td>PRAC continued its assessment</td>
</tr>
</tbody>
</table>
Drug shortages and discontinuations

25th November 2016

Dear Colleague

Re: Co-trimoxazole 80mg/400mg/5ml solution for infusion ampoules

As you may be aware Aspen Pharma are currently experiencing supply constraints for the above product. Whilst a shipment of stock is due to be made available on Monday 28th November 2016 this will be insufficient to meet all orders which have been placed.

Aspen will be fulfilling orders in full for their main sites (Southmead, Aberdeen, Sheffield, Nottingham, Cardiff) with remaining customers receiving 50% of their requirement on average.

Please note that any back orders will be cancelled so hospitals should re-order if they do not receive their full order.

Aspen have suggested that any hospital in critical need should contact one of the aforementioned main centres for supply, if spare stock is available. DH/CMU have also confirmed that stocks of unlicensed co-trimoxazole are available from pharmaceutical importers.

DH/CMU recognise the importance of this critical medicine and will remain in regular contact with the company to confirm further anticipated delivery dates and volumes and will communicate further once these are confirmed.

Yours sincerely

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M: 07748 334449
Please note change of phone number
Sodium bicarbonate oral solution is used to treat children aged 0-16 years with hyperacidic states related to chronic renal disease. A 1mmol/ml product (Thamicarb) was licensed in 2016, but the labelling of this product has raised safety concerns and use of unlicensed preparations is currently known to continue. The table summarises details of currently known available products.
How can you minimise the risks of medication errors with buprenorphine patches?

Published 28th October 2016, updated 28th October 2016 · South West Medicines Information and Training

Transdermal buprenorphine patches are widely prescribed and available from a variety of manufacturers. A number of patient safety incidents have occurred in the use of transdermal opiate patches and concerns have been raised nationally about errors seen with these products.

There are two groups of buprenorphine patches, lower strength and higher strength and there are at least 8 different brands and 21 individual preparations in each of the low and high strength categories. This Q&A aims to cover a number of topics in order to improve the safety of buprenorphine patch prescribing and administration, as well as highlighting some of the concerns. This Q&A does not compare the costs of the various transdermal buprenorphine products.
This months’ papers - overview

The revolving door: antibiotic allergy labelling in a tertiary care centre
B Knezevic, D Sprigg, J Seet, M Trevenen, J Trubiano, W Smith, Y Jeelall, S Vale, R Loh, A McLean-Tooke, M Lucas
Internal Medicine Journal Nov 2016;46(11):1276-1283

Paracetamol overdosing in a tertiary care hospital: implementation and outcome analysis of a preventive alert programme
DF Niedrig, G Bucklar, M Fetzer, S Machler, C Gott, S Russmann
This months’ papers - overview

Quality improvement project to reduce paediatric prescribing errors in a teaching hospital
MEH Leach, N Pasha, K McKinnon, L Etheridge
Archives of Disease in Childhood - Education and Practice Dec 2016;101(6):311-315
http://ep.bmj.com/content/101/6/311.abstract
Is the ‘blue’ colour convention for inhaled reliever medications important? A UK-based survey of healthcare professionals and patients with airways disease

Monica Fletcher¹, Jane Scullion², John White³, Bronwen Thompson⁴ and Toby Capstick⁵
Paper - details

• Survey of reliever inhaler blue colour convention between HCPs and patients

• Background
  – safety issues with introduction of non-blue inhalers in the recent past
  – no standardised regulatory approach to colour convention for inhalers
Results

- 596 HCPs responded (39% nurses; 17% drs; 14% physiologists; 13% pharmacists; 8% allied professions; 9% unspecified)
- 45.6% that colour was the most common way to identify reliever inhalers
- 86.8% reported that they usually or often refer to colour with patients
- 95% felt colour important in inhaler identification
- 87%: blue only for relievers
Results

• 2,517 patients (asthma and COPD); results from 2,127 (390 excluded – disease not identified)

• Colour (49.8%) or brand-name (35.4%) most important identifier

• 80% like knowing that blue inhaler for relief

• 90% agree that colour important

• Some variation: asthma vs COPD
Discussion and recommendations

• Patients and HCPs like to use the term “blue inhaler”
• Patients: brand name & colour (brand name more important in COPD)
• Blue for relief is the most common non-formalised colour convention in use
• Case to formalise convention to support safety so not possible for blue inhaler to be licensed that is not a reliever