Observatory
25th January 2017
Observatory of recent safe medication practice research, reports, and publications

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Recent regulator and statutory body activity

Drug Safety Update – December 2016

www.gov.uk/drug-safety-update

- **Cobicistat, ritonavir and coadministration with a steroid: risk of systemic corticosteroid adverse effects**

  - Coadministration of a corticosteroid with an HIV-treatment-boosting agent may increase the risk of adrenal suppression due to a pharmacokinetic interaction.
    - There is potential for this interaction to occur even with non-systemically administered steroid formulations, including intranasal, inhaled, and intra-articular routes.
    - If co-administration of an inhaled/nasal preparation is necessary, consider using beclomethasone where possible - particularly for long-term use.

- **Spironolactone and renin-angiotensin system drugs in heart failure: risk of potentially fatal hyperkalaemia—clarification, December 2016**

  - In light of feedback the MHRA have clarified that:
    - **Concomitant use of spironolactone with ACEi or ARB increases the risk of severe hyperkalaemia**, particularly in patients with marked renal impairment, and should be **used with caution**.
    - The same advice applies for concomitant use of the aldosterone antagonist eplerenone with ACEi or ARB in heart failure.
Recent regulator and statutory body activity

Drug Safety Update – January 2017
www.gov.uk/drug-safety-update

• Direct-acting antiviral interferon-free regimens to treat chronic hepatitis C: risk of hepatitis B reactivation
  • All patients should be screened for hepatitis B before starting treatment for chronic hepatitis C with direct-acting antiviral interferon-free regimens.

• Direct-acting antivirals to treat chronic hepatitis C: risk of interaction with vitamin K antagonists and changes in INR
  • INR should be monitored closely during treatment of chronic hepatitis C with direct-acting antivirals in patients also receiving vitamin K antagonists (eg, warfarin), because of possible changes in liver function during treatment.

• Apremilast (Otezla ▼): risk of suicidal thoughts and behaviour
  • There is an increased risk that some patients may experience psychiatric symptoms with apremilast, including depression and suicidal thoughts.

• Intravenous N-acetylcysteine (NAC) for paracetamol overdose: reminder of authorised dose regimen; possible need for continued treatment with NAC
  • The authorised dose regimen for N-acetylcyesteine (NAC) in paracetamol overdose is 3 consecutive bags given intravenously over 21 hours.
Recent regulator and statutory body activity

Letters sent to healthcare professionals in November 2016

- **Apremilast (Otezla▼)**: risk of **suicidal ideation and behaviour**
  - Assess benefits vs. risks of treatment for patients with a history of psychiatric symptoms or taking medicines likely to cause psychiatric symptoms
  - If patients suffer new or worsening psychiatric symptoms, suicidal ideation or if suicidal behaviour is identified, discontinue treatment with apremilast

- **Lenalidomide (Revlimid▼)**: new advice about **viral reactivation**
  - Some patients previously infected with varicella zoster or hepatitis B viruses (HBV) have had HBV reactivation progressing to acute hepatic failure and death
  - Establish HBV status before initiating treatment with lenalidomide
  - Consult a physician with expertise in the treatment of hepatitis B for patients who test positive for HBV infection.
  - Monitor patients previously infected for signs and symptoms of viral reactivation.
Recent regulator and statutory body activity

Letters sent to healthcare professionals in December 2016

- **Levetiracetam (Keppra) 100 mg/mL**: risk of medication errors
  - Cases of an up to 10-fold accidental overdose with Keppra (levetiracetam) oral solution have been reported. The majority of cases occurred in children aged between 6 months and 11 years.

- **Ammonaps (sodium phenylbutyrate)**: only for use when there is no alternative treatment
  - The manufacturing site has shortcomings in relation to good manufacturing practice.
  - There is no indication of risk to patients.
  - While corrective measures are being implemented, Ammonaps tablets and granules should only be used when other sodium or glycerol phenylbutyrate-containing medicines cannot be used.
  - If the alternative phenylbutyrate medicine is not suitable for patients with nasogastric tube or gastrostomy, Ammonaps granules can continue to be used.
Alerts and recalls for drugs December/January
https://www.gov.uk/drug-device-alerts

- **Mirena 20 micrograms / 24 hours intrauterine delivery system** (EL17(A)02)
  - Mirena inserters with an insertion tube which is mounted inversely to the handle (Class 4) (5/1/17)
- **Arava 10mg film-coated tablets (Leflunomide)** (EL (17)A/01)
  - Error in the Braille on some batches of Arava 10mg film-coated tablets (Class 4) (3/1/17)
- **Evacal D3 1500mg/400iu Chewable Tablets - metal contamination in a very small number of tablets**
  - Precautionary batch recall
Alerts and recalls for devices  [https://www.gov.uk/drug-device-alerts](https://www.gov.uk/drug-device-alerts)

- **Alaris® syringe pumps (all models) – risk of uncontrolled bolus of medicine with non-recommended syringes**
  - Using non-recommended syringes in Alaris syringe pumps that have a broken spring in the plunger assembly may cause unintended bolus of medication. (22/12/16)
Pharmacovigilance Risk Assessment Committee (PRAC)

- **December 2016**
  - Risk of hepatitis B re-activation with direct acting antivirals for hepatitis C
    - Recommendation - before starting treatment, all patients should be screened for hepatitis B virus; those patients co-infected with hepatitis B and C viruses must then be monitored and managed according to current clinical guidelines (Confirmed by CHMP December meeting)
    - Five assessments under evaluation.

- **January 2017**
  - Six assessments under evaluation. No recommendations or warnings issued
  - New assessment
    - Medicinal products containing lactose of bovine origin for IV/IM use in acute allergic reactions (methylprednisolone)
14/12/16
The FDA warn that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children’s brains.

Advice
Health care professionals should balance the benefits of appropriate anesthesia in young children and pregnant women against the potential risks, especially for procedures that may last longer than 3 hours or if multiple procedures are required in children under 3 years.
Drug shortages and discontinuations

- **Drug shortage memo: topotecan capsules**
  - Topotecan capsules (Hycamtin, 0.25mg and 1mg), have been out of stock since November due to pan-European manufacturing issues.
  - The memo discusses possible relevant alternatives.
  - January update – Novartis advised that they are not expecting supplies to be available until the end of February 2017
National guidance, publications and resources

• **Specimen High Risk Injectable Medicines List**
  • Produced using the NPSA’s risk assessment tool. It is intended to assist NHS organisations to generate their own list of high risk injectable medicines prepared in clinical areas and to provide a basis for this local risk assessment.

• This is not intended to be a comprehensive list of all potential high risk injectables and does not obviate the need for assessment of local practice.

• **Resources to support answering medicines-related questions in primary care**
Primary research presented at MSO Observatories 2016

- A summary of safe medication primary research presented at the Medication Safety Monthly WebEx The Observatory 2016
This month’s papers - overview

• Medication errors room: a simulation to assess the medical, nursing and pharmacy staffs' ability to identify errors related to the medication-use system

• Learning from the design, development and implementation of the Medication Safety Thermometer
  http://intqhc.oxfordjournals.org/content/early/2016/12/28/intqhc.mzw149.full.pdf

• Identification of priorities for improvement of medication safety in primary care: a PRIORITIZE study
  BMC Family Practice 16 Nov 2016 17: 160

• Provider risk factors for medication administration error alerts: analyses of a large-scale closed-loop medication administration system using RFID and barcode
  Pharmacoepidemiology and Drug Safety, December 2016; 25: 1387-1396
This month’s papers - overview

• A description of medication errors reported by pharmacists in a neonatal intensive care unit
  International Journal of Clinical Pharmacy, November 2016(1-7)

• Iatrogenic medication errors in a paediatric intensive care unit in Durban, South Africa
  South African Medical Journal Dec 2016;106(12):1222-1229

• Systematic review of the prevalence of medication errors resulting in hospitalization and death of nursing home residents

• Carers' Medication Administration Errors in the Domiciliary Setting: A Systematic Review
  PLOS One 1 Dec 2016; 11(12): e0167204. doi:10.1371/journal.pone.0167204
  http://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0167204&type=printable

• Trends in emergency hospital admissions in England due to adverse drug reactions: 2008-2015
This month’s paper - details

Patient Safety Incidents Involving Sick Children in Primary Care in England and Wales: A Mixed Methods Analysis

Philippa Rees, Adrian Edwards, Colin Powell et al.
http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002217

AIMS

• to characterise the nature and severity of patient safety incidents involving sick children in primary care
• to identify potential priority areas requiring action, and
• to make recommendations for improvement.
This month’s papers - details

Study design
• Retrospective cross-sectional mixed methods study
• All incident reports submitted to the NRLS between 1\textsuperscript{st} January 2005 and 1\textsuperscript{st} December 2013 (8 years) from primary care and involving sick children less than 18 years old were included

Results
• 2,191 safety incidents identified from 2,178 reports
• 30\% were harmful including 12 deaths and 41 cases of severe harm
• Incident source:
  – the UK national telephone triage service, NHS 111\((n = 646; 30\%)\),
  – out-of-hours health centers \((n = 604; 28\%)\),
  – community pharmacies \((n = 401; 18\%)\),
  – general practices \((n = 218; 10\%)\)
• Population age:
  – 22\% involved infants <1 year old
  – 25\% involved pre-school children < 5 years old
This month’s papers - details

• **674 medication-related incidents were described**

• **Source**
  – 57% were related to dispensing errors in community pharmacies
  – 18% were administration errors typically in the home setting
  – 10% were prescribing errors in general practice
  – 10% were clinical treatment decision-making incidents in the general practice or out-of-hours setting

• **32% of medication-related incidents resulted in harm including**
  – 2 deaths
  – 6 reports of severe harm
  – 64 reports of moderate harm
  – 143 reports of low harm

• **Children involved in medication-related incidents had:**
  – respiratory conditions (18%)
  – injuries (13%)
  – nonspecific signs and symptoms e.g. fever (13%)
  – gastrointestinal or genitourinary conditions (12%)
Other results
• 63% dispensing errors described contributory factors
  – confusing medications with similar names or appearances
  – different formulations of the same medication having similar packaging
  – organizational factors such as busy or distracting work conditions
  – staff failing to follow protocols
  – patient age-specific factors such as weight-based dose calculation errors

Recommendations for Improvement
• Community pharmacy dispensing errors could be reduced through electronic transmission of prescriptions from general practice to the dispensing community pharmacy
• implementing a bar coding system for all medications
• education and training of all pharmacy staff in human factors