UKMi Observatory
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Observatory of recent safe medication practice research, reports, and publications

Presented by
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Recent regulator and statutory body activity

**Improvement**

**Revised SPC: Actrapid (insulin, human) 100 international units/ml, Solution for Injection in a vial**

Electronic Medicines Compendium

The statement “in case of emergency in current Actrapid users (hospitalisation or insulin pen malfunction), Actrapid can be withdrawn with an U100 insulin syringe from a cartridge or pre-filled pen” has been removed from SPC.

**Revised SPC: Fiasp (insulin aspart) 100 units/mL solution for injection in cartridge (Penfill)**

Electronic Medicines Compendium

The SPC now advises that pre-filled pen is only suitable for subcutaneous injections; and if administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used.

**Confirming removal or flushing of lines and cannulae after procedures**

NHS Improvement

A video has been added to the resources available to support implementation of this safety alert. It features a patient who experienced temporary paralysis and respiratory arrest after residual anaesthetic drugs were not flushed from her lines and cannulae following surgery.

**March BNF/BNFC eNewsletter**

British National Formulary

This issue includes three new monographs (guselkumab, niraparib, tenofovir alafenamide, adalimumab, budesonide, chloroquine, and gentamicin), updated guidance on ADHD and UTI in children, updated MHRA advice, and new NICE guidance.
Mesna 100mg/ml solution for injection/infusion, 5 x 4ml - company led recall
Clarins Lifesciences UK Limited are issuing a company-led drug alert for one batch of Mesna 100mg/ml solution for injection/infusion, 5 x 4ml due to stability issues (CLDA (18)A/01)
Drug alert: company-led. Issued: 28 March 2018

All T34 ambulatory syringe pumps – risk of unintended pump shutdown and delay to treatment
Manufactured by Caesarea Medical Electronics (CME) Ltd – a variation in battery size can cause problems with connections in the battery housing. (MDA/2018/010)
Alert type: Medical device alert. Issued: 28 March 2018

Class 4 medicines defect information: Inhixa solution for injection in pre-filled syringe (EL (18)A/07)
Techdow Europe AB has issued the Direct Healthcare Professional Communication (DHCP) attached due to rare cases of premature self-activation of the safety device in unused, unopened pre-filled Inhixa syringes as shown in the DHCP diagrams. When premature activation has occurred, administration is not possible.
Issued: 18/4/2018
Drug Safety Update

Valproate medicines (Epilim▼, Depakote▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met.
Valproate medicines must no longer be used in women or girls of childbearing potential unless a Pregnancy Prevention Programme is in place.

Obeticholic acid (Ocaliva▼): risk of serious liver injury in patients with pre-existing moderate or severe hepatic impairment; reminder to adjust dosing according to liver function monitoring.
We are aware of reports of serious liver injuries and deaths in patients with primary biliary cholangitis with pre-existing moderate or severe liver impairment who were not adequately dose-adjusted.
Hot off the press!! Taken from the April 18
MHRA DSU

New contraindication: Valproate

- DHPC and educational materials will be sent to pharmacists within weeks
- Pharmacists are asked to:
  - Provide the revised Valproate Patient Card when they dispense a valproate medicine to female patients
  - Discuss risks in pregnancy with female patients each time they dispense valproate medicines and ensure they have the Patient Guide and have seen their GP or specialist to discuss their treatment and the need for contraception
  - If the prescriber has not discussed the risk with the patient or the patient is not using effective contraception, advise them NOT to stop valproate medicines and tell them to contact their GP for an urgent follow-up.
  - Dispense valproate in the original packaging with the outer warning wherever possible. In the situations where this cannot be avoided, always provide a copy of the package leaflet, patient card, and add a warning sticker (available with the educational material) to the outer box.

To highlight April Drug Safety Update article:

- New contraindication for valproate medicines – not to be used in women and girls of childbearing potential unless the conditions of the pregnancy prevention programme are met

Warning for Women and Girls

This medicine can seriously harm an unborn baby. Always use effective contraception during your treatment.
If you are thinking about becoming pregnant, or you become pregnant, talk to your doctor straight away.
Do not stop taking this medicine unless your doctor tells you to.
In March 2018, letters were sent to healthcare professionals about:

Zinbryta▼ (daclizumab beta): Marketing authorisation suspended in the European Union – for more information see here

Recall of specific batches of Lynparza 50 mg capsules – see here

Radium-223-dichloride (Xofigo▼) contraindicated in combination with abiraterone acetate (Zytiga) and prednisolone/prednisone – for more information see here
Risk minimisation materials: Jaydess (levonorgestrel) intrauterine system
Information on how to differentiate between the physical appearances of Jaydess (levonorgestrel) and Mirena (levonorgestrel) and the risks of ectopic pregnancy in women using Jaydess is available for healthcare professionals.

Risk minimisation materials: Neulasta (pegfilgrastim) on body injector patient alert card
The Patient Alert Card contains information regarding the importance of actively monitoring the on body injector device, how to recognize a failure of the device, and actions to take if patients have issues with the device or symptoms of infection.

Risk minimisation materials: Zoledronic acid medac Patient Reminder Cards
This reminder card contains important safety information that patients need to be aware of before and during treatment with Zoledronic acid medac infusions for cancer-related conditions.
**Pharmacovigilance Risk Assessment Committee (PRAC)**

**Colour change for insulin injection Fiasp to avoid mix ups with Tresiba**
The colour of cartridges, pre-filled pens and vials of the rapid-acting insulin Fiasp is changing from yellow to red and yellow following cases where patients have mistakenly injected Fiasp instead of the long-acting insulin Tresiba (available in the EU as light green cartridges and pens) or the other way around. Such mix-ups, due to the similar colour of the products especially in poor lighting, can cause hypo- or hyperglycaemia (low or high blood glucose levels), which can lead to serious health problems. Fiasp is a rapid acting insulin (insulin aspart) intended to be injected at mealtimes and Tresiba is a long acting insulin (insulin degludec) which is injected once a day. Patients may be prescribed the two medicines simultaneously.

**Withdrawal of pain medicine flurtipine endorsed**
This product is not marketed in the UK but has been available in other EU countries so patients travelling to the UK may have had access to it. It is being withdrawn because of the risk of serious liver injury.

**Updated measures for pregnancy prevention during retinoid use**
Retinoids include the active substances acitretin, adapalene, alitretinoin, bexarotene, isotretinoin, tazarotene and tretinoin. They are taken by mouth or applied as creams or gels to treat several conditions mainly affecting the skin, including severe acne and psoriasis. Some retinoids are also used to treat certain forms of cancer. The EMA has concluded its review of retinoids and confirmed that an update of measures for pregnancy prevention is required. In addition, a warning on the possibility that neuropsychiatric disorders (such as depression, anxiety and mood changes) may occur will be included in the prescribing information for oral retinoids (those taken by mouth).

**New measures to avoid valproate exposure in pregnancy endorsed**
Evidence shows that information about the risks of pregnancy whilst taking valproate is still not reaching women in a timely manner, so valproate medicines are now contra-indicated in girls and women able to have children unless the terms of a special pregnancy prevention programme are followed. Educational materials and product information will be updated to reflect this.
Managing medicines shortages in an acute trust: a case study
Published 20th March 2018, updated 28th March 2018
The author, Diane Slater, is a specialist pharmacist dealing with medication shortages. This case study describes the management of one medicines shortage in an anonymised hospital trust, the clinical impact on patient care and the effort and co-ordination required to manage and mitigate the unexpected complexity of the shortage of a single medicine. It highlights the need for considerable amount of investigation and the importance of timely and effective communication with clinical teams as well as the need for clinical advice and Quality Control input in addition to procurement and Pharmacy stock management resources.

Shortage of Xylocaine (lidocaine) 10 mg Spray
Published 1st March 2018, updated 11th April 2018
Aspen, the sole supplier, is out of stock again until some point in May. This memo provides advice on how to manage the shortage and potential alternative treatment options.
Smart pumps with dose-error reduction software (DERS) allow organizations to create a tailored library of medications with dosing guidelines by establishing standard concentrations, dosing limits, and alerts (e.g., clinical advisories, soft stops, hard stops). Smart pumps with enabled DERS can detect dosing and programming errors that may harm patients. They can also provide a great deal of data that is useful in improving safe practices, including compliance with using the drug library, alert types and frequency, action taken in response to an alert (e.g., reprogramming), and the frequency of overridden soft stops. The data can also help investigate pump-related errors and identify good catches as well as risky practices such as unnecessary nurse dilution of intravenous (IV) medications.

This survey collated feedback from 618 respondents including MSOs looking at –

- Error types experienced in the past 12/12/ despite the use of smart infusion pumps
- Most frequent challenges encountered by respondents related to smart infusion pumps
Standardising strengths of high risk, unlicensed oral liquids formulations for anti-TB medicines
The North RMOC issued a statement about standardising strengths of high risk, unlicensed oral liquid formulations for anti-TB medicines used in children. Data shows there is wide variation in strengths and formulations of ethambutol, pyrazinamide and isoniazid liquids. Only rifampicin is available in a licensed oral liquid version.

Which medicines require extra care when switching between liquid and tablet/capsule formulations?
For a small number of medicines, there are differences in equivalent doses of oral formulations of the same medicine. This Q&A considers which licensed medicines may require dose adjustment when switching between oral formulations and presents information on dose adjustment in a summary table. In instances where it may not be possible to achieve a dose that is exactly the same, practical advice such as additional patient monitoring is suggested. Other concerns relating to the suitability of the formulation for the patient are discussed. This topic was raised by the South West MSO network group.

Do stains cause alopecia?
Most UK licensed statins (hydroxymethylglutaryl coenzyme A reductase inhibitors) have been reported by manufacturers to cause hair loss as a side effect. This Medicines Q&A aims to review incidence of alopecia with UK licensed statins. The Q+A discusses hair growth and causes of alopecia as well as looking at the rates of hair loss with individual statins. A useful summary guides clinicians through some of the areas to consider when deciding if hair loss may be due to a statin or not.

NHS Product Quality Assessment: Potassium chloride 0.4mMol/ml for infusion (Ennogen)
Specialist Pharmacy Service
This product has been classified as medium risk. Consideration should be given to using this product to reduce risk in clinical areas that currently use strong potassium chloride injection to prepare concentrated infusions.
This month’s papers - overview

Chemotherapy medication errors
Weingart S.N.; Zhang L.; Sweeney M.; Hassett M. The Lancet Oncology; Apr 2018; vol. 19 (no. 4)

STOMP - time to make more noise

SYSTEMATIC REVIEW: Drug induced liver injury: Alternative causes in case series as confounding variables
Teschke R and Danan G British Journal of Clinical Pharmacology; April 2018
https://doi.org/10.1111/bcp.13593

Impact of a commercial order entry system on prescribing errors amenable to computerised decision support in the hospital setting: a prospective pre-post study.

Safer dispensing labels for prescription medicines
Adam La Caze. Aust Prescr 2018;41:46-93 Apr 2018DOI: 10.18733/austprescr.2018.009

G190 Patient safety incidents in neonatology: a 10-year descriptive analysis of reports from nhs england and wales
Stuttaford L et al. Archives of Disease in Childhood 2018;103:A78.
Pediatric Medication Safety in the Emergency Department
Lee et al. Pediatrics March 2018, VOLUME 141 / ISSUE 3

Direct Observation of Medication Errors in Critical Care Setting: A Systematic Review
Foster M et al. Critical Care Nursing Quarterly: January/March 2018; Vol 41(1): 76–92

An observational feasibility study of a new anaesthesia drug storage tray
Almghairbi DS et al. Anaesthesia; Volume73, Issue3; March 2018: Pages 356-364

*Dispensing errors from look-alike drug trade names

Deprescribing one year on: challenging the first iatrogenic epidemic - editorial

*Large differences in neonatal drug use between NICUs are common practice: time for consensus?
Flint RB et al British Journal of Clinical Pharmacology. Early view. First published: 17 April 2018
https://doi.org/10.1111/bcp.13563

*A review of the growing risk of vitamin D toxicity from inappropriate practice
Taylor PN and Davies JS British Journal of Clinical Pharmacology. Early view. First published: 16 April 2018
https://doi.org/10.1111/bcp.13573
*Dispensing errors from look-alike drug trade names*
EPMA is coming to hospitals in the UK and there needs to be thought about how to prevent LASA (look alike, sound alike) errors and integrate this with EPMA systems.

The authors compare error rates pre- and post- interventions to reduce near miss dispensing errors. The interventions included tall man lettering, enlargement of drug names and highlighting look alike names on drug storage shelves. Tall man lettering was introduced on computer screens, shelf labels and prescriptions. **Limitations** – only considered look-alike and not sound-alike drug errors, did not break down the results to show the impact of individual interventions.

**Comment** – there were still errors, so further work is needed to explore how to reduce those to zero; this was about brand name LASA and not generic name (majority of prescribing/dispensing in the UK is generic – but ?impact of increasing use of branded generics especially in primary care).

*A review of the growing risk of vitamin D toxicity from inappropriate practice*
Taylor PN and Davies JS British Journal of Clinical Pharmacology. Early view. First published: 16 April 2018  [https://doi.org/10.1111/bcp.13573](https://doi.org/10.1111/bcp.13573)
Vitamin D in loading and maintenance doses is widely used across primary and secondary care. There have been and continue to be errors with dosing, particularly the high loading dose schedules. This is exacerbated by the wide range of licensed and unlicensed vitamin D products available. Vitamin D in toxicity can cause a number of serious consequences mediated through hypercalcaemia. The symptoms range from mild, such as thirst and polyuria, to severe, including seizures, coma and death. Errors have occurred in adults and children, and those at greatest risk appear to be those at extremes of age, i.e. children and older adults.

The authors describe the main areas of error leading to vitamin D toxicity including formulation or fortification errors, Inappropriate prescribing or dispensing (including in children and breastfeeding infants) and Inappropriate administration of vitamin D. The authors’ state *The fact that it (vit D) is a vitamin and a frequently used nutritional supplement, may have led to considerable complacency regarding its potential for toxic effects.*