

SPS/UKMi Observatory 26th October 2022

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

Presented by: Christine Randall

Senior MI and Pharmacovigilance pharmacist, NWMIC, Liverpool

Christine.Randall@liverpoolft.nhs.uk

Recent regulator and statutory body activity



Improvement



- No CAS Alerts issued in the last month
- **National Patient Safety Alert: Class 1 Medicines Recall Notification:**
Recall of Targocid 200mg powder for solution for injection/infusion or oral solution, Aventis Pharma Limited t/a Sanofi, due to the presence of bacterial endotoxins
 - Healthcare professionals should be aware of the following clinical symptoms related to the potential risk to patient health: a high temperature (fever) or low body temperature, chills and shivering, cold, clammy and pale or mottled skin, a fast heartbeat, fast breathing, severe breathlessness, severe muscle pain, feeling dizzy or faint, a change in mental state – such as confusion or disorientation, loss of consciousness, slurred speech, nausea and vomiting and/or diarrhoea.
 - In the event the affected batches have been administered to patients, appropriate clinical assessment should be performed, in addition to close monitoring for any adverse reactions.

Recent regulator and statutory body activity



- [Class 2 Medicines Recall: hameln pharma ltd, Ephedrine Hydrochloride 30 mg/ml Solution for Injection](#)
 - out of specification results obtained during routine ongoing stability studies
 - quarantine any remaining stock of the affected batch
- [Class 2 Medicines Recall: hameln pharma ltd, Amiodarone Hydrochloride 50 mg/ml Concentrate for Solution for Injection/Infusion](#)
 - increased presence of visible crystalline particles within the solution
 - quarantine affected stock, other batches – inspect for clarity, particulate matter, discolouration and container integrity
- [Class 2 Medicines Recall: Aventis Pharma Limited \(t/a Sanofi\), Stemetil 5mg/5ml Syrup](#)
 - identification of N-nitrosomethylphenylamine (NMPA) above the acceptable limit
 - Stop supplying the above batches immediately and quarantine all remaining stock.
- [Class 4 Medicines Defect Information: Flamingo Pharma UK Ltd, Ibuprofen 400mg Tablets, Paracetamol 500mg Tablets \(Caplets\)](#)
 - error relating to the ink printing of the batch number and expiry date on the carton for three batches of Ibuprofen 400mg tablets
 - the quality and safety of the product is not impacted
 - check the outer carton before dispensing the affected products

Recent regulator and statutory body activity



Drug Safety Update

- MedSafetyWeek November 2022: Every Yellow Card report helps to improve patient safety
 - 7th annual #MedSafetyWeek social media campaign takes place **7 to 13 November 2022**
 - this year's focus is the importance of reporting suspected adverse reactions to medicines and vaccines
 - Also reporting suspected problems with medical devices or other healthcare products to the Yellow Card scheme.
- Use #MHRAYellowcard, #MedSafetyWeek, #ReportSideEffects, and #patientsafety



Direct HCP communications

Sent September 2022

- Rixathon ▼ (rituximab) – Temporary supply of Rixathon 500mg vials in foreign packaging (Dutch)
- Streptokinase 250,000 IU and 1,500,000 IU vials for injection: supply of non-serialised packs
- Tukysa ▼ 50 mg and 150mg film-coated tablets: interim supply of French or German/Austrian stock (Northern Ireland)
- Spikevax ▼ bivalent Original/Omicron BA.1 COVID-19 mRNA Vaccine (nucleoside modified) (elasomeran/imelasomeran): Temporary supply of product with different product name, carton and multidose vial labels (Northern Ireland)

Pharmacovigilance Risk Assessment Committee (PRAC)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- [PRAC recommendations for terlipressin-containing medicines in the treatment of hepatorenal syndrome](#)
 - a warning to avoid terlipressin-containing medicines in patients with advanced acute-on-chronic liver disease
 - patients with breathing problems should receive treatment to manage their condition before starting terlipressin
 - patients should be monitored for signs and symptoms of respiratory failure and infection.
 - HCPs should give terlipressin-containing medicines as a continuous infusion rather than by bolus injection to reduce the risk of severe side effects
- [PRAC warning - Codeine with ibuprofen: to include warning of serious renal and gastrointestinal harms, particularly when taken for prolonged periods at higher than recommended doses.](#)
- [PRAC recommendation - Ibrutinib: new risk minimisation measures, including dose modifications, due to the increased risk for serious cardiac events](#)

Manufacturer RMM or SPC changes

[Revised SPC: Priadel \(lithium citrate\) liquid and tablets – all strengths](#)

- SPC updated with addition of warning that concomitant administration with dapagliflozin may decrease serum lithium levels due to an increase in lithium renal clearance.

[Revised SPC: Spikevax \(elasomeran\)](#)

- SPC now notes the high-dose quadrivalent influenza vaccine can be concomitantly administered with Spikevax.

[Revised SPC: Cometriq \(cabozantinib\) 20 and 80 mg Hard Capsules](#)

- Pneumothorax has been added to SPC as a common adverse effect and cutaneous vasculitis as an adverse effect of unknown frequency.

[Revised SPC: Dexamfetamine sulfate tablets](#)

- SPC now notes that amphetamines can cause a significant elevation in plasma corticosteroid levels, and that this increase is greatest in the evening. Also, amphetamines may interfere with urinary steroid determinations.

[Revised SPC: Lenzetto \(estradiol\) 1.53 mg/spray, transdermal spray, solution](#)

- SPC updated to reinforce warning that estradiol spray can be accidentally transferred to children from area of skin where it was sprayed on, and to advise on avoidance measures, and to seek medical care if exposed child experiences breast development or other sexual changes.

Manufacturer RMM or SPC changes

[Zavedos \(idarubicin\) Powder for Solution for Injection](#)

- women should be advised not to breastfeed during treatment with idarubicin and for at least 14 days after last dose, and males & females treated with idarubicin are advised to adopt effective contraceptive measures during therapy & for a period after treatment

[RMM: Lamzede® \(Velmanase Alfa\) Home Infusion Therapy](#)

- guidance on how to transfer velmanase alfa infusion therapy in patients with alpha-mannosidosis from the hospital setting to the patient's home

[RMM: Nerlynx \(neratinib\) Patient Alert Card](#)

- To be carried by patients prescribed this medicine, is intended for healthcare professionals who are not involved in their routine care

Drug shortages and discontinuations

Medicines Supply Tool – SPS

Medicine	Out of stock	Alternatives
Aztreonam 1g powder for solution for injection vials	<ul style="list-style-type: none"> Limited supply until week commencing 31st October 2022. 	<ul style="list-style-type: none"> Aztreonam 2g powder for solution for injection
Ceftolozane 1g / Tazobactam 500mg powder for solution for infusion vials	<ul style="list-style-type: none"> Anticipated re-supply date 18 October 2022 prescribers and pharmacists should work together to ensure patients receive appropriate antibiotic therapy based on their clinical needs 	<ul style="list-style-type: none"> Alternative antibiotics are available and choice of agent should be based on indication for treatment, the patients cultures and sensitivities and local formularies
Dioralyte oral rehydration sachets	<ul style="list-style-type: none"> Anticipated re-supply date 30 December 2022 	<ul style="list-style-type: none"> Consider the use of alternative oral rehydration treatments (see clinical information). See MSN A local decision should be taken on the appropriateness of using O.R.S Hydration tablets, which are classified as a food supplement. Diluted apple juice has been reported to be a potential alternative to electrolyte maintenance fluids in children with mild gastroenteritis and minimal dehydration.
Dulaglutide (Trulicity) 0.75mg, 1.5mg, 3mg and 4.5mg solution for injection devices	<ul style="list-style-type: none"> Anticipated re-supply date 27 January 2023 Do not initiate new patients on dulaglutide solution for injection pre-filled pens 	<ul style="list-style-type: none"> Consider initiating patients on an alternative GLP-1 receptor agonists until the shortage has resolved e.g. liraglutide, exenatide seek advice from specialists if there is uncertainty about selecting the most appropriate GLP-1 RA.

Drug shortages and discontinuations

Medicines Supply Tool – SPS

Medicine	Out of stock	Alternatives
Semaglutide (Ozempic) 1mg/0.74ml solution for injection 3ml pre-filled disposable device	<ul style="list-style-type: none"> Anticipated re-supply date 31 January 2023 ensure that Ozempic is being used for licensed indications only Do not initiate new patients 	<ul style="list-style-type: none"> Consider initiating patients on an alternative GLP-1 receptor agonists until the shortage has resolved. seek advice from specialists if there is uncertainty about selecting the most appropriate GLP-1 RA.
Regadenoson (Rapiscan) 400 micrograms in 5ml solution for injection	<ul style="list-style-type: none"> Anticipated re-supply date 31 March 2023 Review stock holdings, note stock exhaustion date of late November 2022 work with Radiology departments to review protocols 	<ul style="list-style-type: none"> Adenosine 30mg in 10ml solution for infusion vials are available and can support a partial uplift in demand. Unlicensed imports of regadenoson 400 micrograms in 5ml solution for injection can be obtained from: Alium, Durbin, Mawdsleys, Target
Prochlorperazine (Stemetil) 12.5mg/ml solution for injection ampoules	<ul style="list-style-type: none"> Anticipated re-supply date 24 October 2022 review local stock holding of prochlorperazine 12.5mg/ml solution for injection ampoules If insufficient stocks request mutual aid Work with appropriate clinical leads and the local MSO 	<ul style="list-style-type: none"> Refer to BNF and local guidelines for choice of alternative antiemetic

Drug shortages and discontinuations

Medicines Supply Tool – SPS

Medicine	Out of stock	Alternatives
Nafarelin 200micrograms/dose nasal spray	<ul style="list-style-type: none"> Anticipated re-supply date 23 December 2022 consider switching to an alternative gonadotropin-releasing hormone (GnRH) analogue in consultation with the appropriate specialist for those switched to or initiated on a SC injection, ensure they can self-administer and are not intolerant to any of the excipients 	<ul style="list-style-type: none"> Available parenteral GnRH analogues approved for licensed indications covered by nafarelin (Synarel) 200microgram/dose nasal spray: buserelin, goserelin, leuprorelin, triptorelin
Calcichew 500mg chewable tablets	<ul style="list-style-type: none"> Anticipated re-supply date 16 December 2022 	<ul style="list-style-type: none"> The following alternatives remain available and can support an uplift in demand: Calcichew-D3 500 mg/200 IU chewable tablets
Carbocisteine (Mucodyne) 250mg/5ml oral solution	<ul style="list-style-type: none"> Anticipated re-supply date 11 November 2022 	<ul style="list-style-type: none"> Generic carbocisteine 250mg/5ml oral solution remains available from other suppliers and can support an uplift in demand.
Naratriptan 2.5mg tablets (Teva)	<ul style="list-style-type: none"> Anticipated re-supply date 16 December 2022 	<ul style="list-style-type: none"> Naramig 2.5mg tablets continue to remain available and can support a full uplift demand.

Drug shortages and discontinuations

Medicines Supply Tool – SPS

Medicine	Discontinued	Alternatives
Piroxicam (Feldene) 0.5% gel	<ul style="list-style-type: none">To be discontinued 1 December 2022	<ul style="list-style-type: none">Generic piroxicam 0.5% gel will continue to remain available.
Prochlorperazine (Stemetil) 5mg/5ml Syrup	<ul style="list-style-type: none">To be discontinued 6 October 2022	<ul style="list-style-type: none">Prochlorperazine 5mg tablets - identical licensed indicationsProchlorperazine 3mg buccal tablets - identical licensed indications but only approved for adults and children aged 12 years and over.The following are antiemetics available as liquid formulations: Promethazine (Phenergan) Elixir 5 mg/5 ml, Ondansetron 4mg/5ml Syrup, Metoclopramide 5mg/5ml Oral Solution
Daktacort 2% / 1% w/w ointment	<ul style="list-style-type: none">To be discontinued December 2022	<ul style="list-style-type: none">Daktacort cream will remain available

Specialist Pharmacy Services

- [Reversing an adult opioid overdose with naloxone in the medical setting](#)

Highlighting the risks of giving inappropriate doses of naloxone and how to select and administer appropriate intravenous doses.

- [Managing constipation in people taking clozapine](#)

Constipation in people taking clozapine can be fatal. Guidance on preventing and managing constipation in these individuals is described.

- [Herbal medicines: safety during pregnancy](#)

Pregnant women often use herbal medicines as alternatives to conventional medicines and a review of the safety of commonly used herbal medicines is provided

- [Managing peripheral oedema caused by calcium channel blockers](#)

All calcium channel blockers may cause peripheral oedema. There are different treatment options and the incidence can be affected by different factors.

National guidance, publications and resources

- [HSIB's local investigation pilot: shared learning for local healthcare systems](#)

HSIB

The final evaluation report shares in-depth findings and learning drawn from investigations done over the last year that may be of benefit to local healthcare systems, individual organisations and recently formed Integrated Care Systems.

- [HSIB launches new 'Spotlight on Safety' newsletter](#)

HSIB

Introduction of the new monthly newsletter follows feedback from people across healthcare sector who would like more information about how HSIB works, their investigations, recommendations, and the positive impacts on patient safety.

- [NRLS national patient safety incident reports: commentary](#)

NHS England

This report covers Apr 2021 to Mar 2022, a period characterised by restoration of services following outbreak of COVID-19 pandemic. NRLS reporting levels increased during this period vs. previous year. Most incidents are reported as causing no harm (70.6%) or low harm (26.0%).

- [Organisation patient safety incident report up to March 2022](#)

NHS England

Reporting levels increased across care settings when compared to the previous year; however nationally the overall profile of incident characteristics was similar for most groups.

- [Appropriate prescribing of antipsychotic medication in dementia](#)

NHS England

Guidance and information on uses, risks and alternatives to antipsychotic medication, risk reduction in antipsychotic prescribing, and support for local systems to deliver best practice in antipsychotic prescribing and de-prescribing.

National guidance, publications and resources

- [NIHR alert: Review finds little evidence to support gabapentinoid use in bipolar disorder or insomnia](#)

NIHR

Commentary on a review of 70 mixed studies which found insufficient evidence to support use in bipolar disorder or insomnia and moderate evidence for anxiety disorders. Given lack of evidence and side effects, prescribers are advised to use gabapentinoids with caution.

- [Consultation on how MHRA communicate with healthcare professionals to improve medicines and medical devices' safety](#)

MHRA

The MHRA is reviewing its approach to engagement with healthcare professionals (HP) to improve safety of medicines and medical devices. Consultation seeks views on how HPs want to receive safety information, how they'd like to be engaged, and feedback on the Yellow Card system.

- [Medicines and Pregnancy Registry - Antiepileptic use in females aged 0 to 54 in England: April 2018 to March 2022](#)

NHS Digital

An analysis of existing administrative data, designed to support the MHRA in monitoring the level of success of the valproate pregnancy prevention plan and to enable further understanding of the outcomes for women prescribed it during pregnancy and their children.

- [BSACI guideline for the set-up of penicillin allergy de-labelling services by non-allergists working in a hospital setting](#)

Clinical and Experimental Allergy 2022;52;1135-1141

Recommendations include a checklist to identify patients at low risk of allergy (AL) & a framework for conduct of drug provocation testing by non-allergists. There are separate sections for adults & paediatrics in light of common differences in history and likelihood of true AL.

National guidance, publications and resources

- [COVID-19 vaccination: women who are pregnant or breastfeeding](#)

UKHSA

The autumn booster is being offered to those at high risk of complications from COVID-19: those with underlying medical conditions; overweight; >35 years; in third trimester pregnancy; of black and Asian minority ethnic background or remain unvaccinated or partially vaccinated.

- [UKHSA is warning parents and guardians of the serious health risks from children missing routine immunisations](#)

UKHSA is urging parents and guardians to ensure their children are up to date with all their routine childhood immunisations including polio and MMR vaccinations. This comes as new data shows vaccination coverage for young children fell last year for virtually all programmes.

- [UKHSA urges people to take up flu and COVID-19 vaccines](#)

UKHSA warns of lower levels of natural immunity to flu this year and increased COVID-19 circulation. It is urging everyone eligible for free flu vaccine & COVID-19 booster to take up offer ASAP ahead of what could be a difficult winter with respiratory viruses circulating widely.

- [HIV testing, PrEP, new HIV diagnoses, and care outcomes for people accessing HIV services: 2022 report](#)

UKHSA

The overall downward trajectory in new HIV diagnoses prior to the pandemic was sustained, although there was a rise in late diagnoses (from 44% in 2020 to 46% in 2021). Comparison with 2019 data suggests there may have been some delay to testing and diagnosis due to the pandemic.

National guidance, publications and resources

- [RightCare Asthma Toolkit](#) and [RightCare Pneumonia Toolkit](#)
NHS England
These toolkits, which reflect priorities in respiratory care (identification of risk factors, prevention, detection and diagnosis, medicines optimisation and reducing inappropriate admissions) will support respiratory clinical services to improve patient care and outcomes.
- [RightCare Stroke Toolkit](#)
NHS RightCare
This toolkit provides Integrated Stroke Delivery Networks and local stroke services with key actions to guide service improvement in a number of pathway specific areas as well as across pathway system improvement priority areas.
- [Where do people keep their household medicines?](#)
Royal Pharmaceutical Society
A survey of 2,199 adults has revealed 19% and 45% of people inappropriate keep their medicines in the bathroom and kitchen respectively, which may cause problems with stability and efficacy. Advice and tips for patients on medicines storage is included.
- [Electronic prescribing system cuts dispensing errors by almost half in one trust](#)
Pharmaceutical Journal
According to data obtained through a freedom of information request, implementation of an electronic prescribing and medicines administration (ePMA) system in the East London NHS Foundation Trust generated cost savings of £916,058 per year.

Material Regulation 28 – to prevent future deaths

- [Ref: 2022-0208](#)
- Patient with psoriatic arthritis was treated by an Ayurvedic practitioner with an array of herbal based medicines (patient concerned about possible effects of conventional medicines)
- Cause of death
 - Idiosyncratic Ayurvedic drug induced liver injury (treated with transplant)
 - Sepsis
 - Recurrent intestinal ischaemia
- Concerns
 - Ayurvedic practitioners are not regulated and do not have the possible complications of their treatments as part of their routine frame of reference
 - Hospital consultant could not identify herbs in the Ayurvedic preparation
 - GP made no physical examination of reported yellow skin and eyes, cessation of Ayurvedic medicines not advised, blood tests ordered but abnormal results, although they had been returned to GP, only picked up at routine rheumatology clinic appointment (10 days after first contact with GP practice) – immediate admission