SPS Medication Safety Update
July 2024
Recent critical patient safety alerts, reports, and publications

Presented by

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Medicines & Healthcare products Regulatory Agency
Specialist Pharmacy Service
NHS England

Patient Safety Alerts

NHS England

National Patient Safety Alert

Action category: Action

Title: Shortage of Kay-Cee-L (potassium chloride 375mg/5ml) (potassium chloride 5mmol/5ml) syrup

Broadcast content: Kay-Cee-L® (potassium chloride 5mmol/5ml) syrup will be out of stock from late September 2024. The resupply date is to be confirmed.
The supply disruption is caused by an amendment to the manufacturing process, requiring re-formulation, and revalidation of the product.
Sando-K® (potassium bicarbonate 400mg and potassium chloride 600mg) effervescent tablets remain available and can support a full increase in demand. One effervescent tablet contains 12mmol potassium.
Unlicensed potassium chloride oral solutions manufactured within the UK are available via Specials manufacturers.
Remaining supplies of Kay-Cee-L® syrup should be prioritised for patients requiring doses of less than 12mmol of potassium and where other preparations are not suitable (see Notes).
Care is needed to ensure selection of the most appropriate oral potassium supplement and delivery of the correct dosage.
This National Patient Safety Alert provides further background, clinical information and actions for providers.

Additional information: NHS England regions: please cascade this alert to community pharmacy.

Alert reference: NatPSA/2024/008/DHSC

Action underway deadline: 30-Jul-2024

Action complete deadline: 12-Aug-2024

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Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Epimax Ointment and Epimax Paraffin-Free Ointment: reports of ocular surface toxicity and ocular chemical injury

- Healthcare professionals must not prescribe or advise use of these products on the face as contact with eyes may result in pain, swelling, redness or watering of eyes, sensitivity to light, blurred vision, burning or grittiness. These should resolve after stopping use around eyes

Class 2 Medicines Recall: Glaxo Wellcome UK Limited (trading as GlaxoSmithKline UK), Flolan 1.5 mg Powder and Solvent for Solution for Infusion, EL(24)A/30

- Notification that a specific batch of Flolan 1.5mg powder may have been damaged during packaging which may have compromised the integrity of the vial and the quality of the medicine. As a precaution GSK are recalling the batch affected.

Class 2 Medicines Recall: Kent Pharma UK, Itraconazole 10mg/ml Oral Solution, EL(24)A/26

- Certain batches being recalled as precautionary measure due to out of specification in the appearance of the solution, particularly presence of suspended particles or clusters of crystals. Initial investigations indicate this is a solubilisation issue of the active ingredient.

Class 2 Medicines Recall: Sun Pharma UK Limited, Gemcitabine PPF 1800mg/180mL Infusion; Gemcitabine PPF 1600mg/160mL Infusion; Irinotecan PPF 360mg/240mL Infusion, EL(24)A/28

- Sun Pharma UK Ltd is recalling certain batches as a precautionary measure due to a small number of leaks found intermittently in the infusion bags.

Class 2 Medicines Recall: Sun Pharma UK Limited, Pemetrexed 1000MG/100ML (10mg/ml) & 1100MG/100ML (11mg/ml) Infusion Bag, EL(24)A/29

- Sun Pharmaceutical Industries Europe B.V. is recalling the listed batches as a precautionary measure due to visible particulate matter during stability testing.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Class 3 Medicines Recall: Atomoxetine 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg Hard Capsules (Accord Healthcare Ltd)

- The manufacturer is recalling specific batches as a precautionary measure after testing showed variability of the capsule contents beyond permitted levels. Healthcare professionals should stop supplying and quarantine affected batches to return to suppliers.

Class 4 Medicines Defect Information: Chelonia Healthcare Limited, Propantheline Tablets 15mg (Genesis Pharmaceuticals livery), EL(24)A/27

- Manufacturers are alerting healthcare professionals of an error in the Patient Information Leaflet (PIL) for specific batches noted in the alert. PIL states the tablets are “pale pink in colour”, whereas they are actually orange

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New EU recommendations for GLP-1 receptor agonists to minimise risk of aspiration and pneumonia aspiration during general anaesthesia or deep sedation

- Although a causal association could not be established, the PRAC has recommended that because of delayed gastric emptying with these drugs, risk of residual gastric content being present should be considered before performing procedures with general anaesthesia or deep sedation.

Glatiramer acetate: anaphylactic reactions may occur months up to years after treatment initiation

- The PRAC has agreed a direct healthcare professional communication to inform healthcare professionals about the risk of anaphylactic reactions, which may occur shortly following administration of glatiramer acetate even after months up to years after initiation of treatment.

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Direct HCP communication

VABYSMO® ▼ (faricimab): tear in primary packaging of Transfer Filter Needle (TFN) co-packaged with vial; localised in Northern Ireland

- Roche identified individual instances of a tear in the primary packaging of the Transfer Filter Needle (TFN) copackaged with VABYSMO (faricimab) vials; this issue is believed to be localised in stock provided in Northern Ireland.

VERORAB, powder and solvent for suspension for injection - PLGB 46602/0029 Interim Supply of UK Stock in Standard Export Packaging (Standard Export Packs) to Mitigate Supply Disruption

- There is currently supply disruption of Rabies vaccines in the UK. In order to ensure some continuity of supply of a rabies vaccine to GP surgeries and travel clinics in the UK, Sanofi has obtained approval from the MHRA to supply its product Verorab, which is expected to be available to the UK market from June/July 2024

SPC changes or Manufacturer RMM

Revised SPC: Tegretol (carbamazepine) 100 mg/5ml Liquid

- In section 4.2 changes have been made to limit the maximum daily dose to 1200 mg per day for Tegretol Liquid.

SPS commentary:

- A Direct healthcare professional letter sent in April had advised that this formulation contains sorbitol, and Novartis is struggling to source sorbitol batches compliant with appropriate spec of by-products. Reduction of maximum daily dose for liquid from 2000 mg to 1200 mg per day is to limit amount of sorbitol intake in order to adhere to the spec.

Revised SPC: Eczmol 1% w/w Cream / Cetraben Protect Antimicrobial 1% (chlorhexidine) Cream

- Updated to warn it must not come into contact with eye as serious cases of persistent corneal injury, potentially requiring corneal transplant, have been reported following accidental ocular exposure to chlorhexidine containing medicinal products, despite eye protective measures.

Revised SPC: Cefotaxime 500mg powder for solution for injection vials

- Drug reaction with eosinophilia and systemic symptoms (DRESS) added as adverse reaction. Section 4.4 updated to include information on severe skin reactions, and advises to withdraw cefotaxime immediately if signs and symptoms of these reactions appear

Revised SPC: Mintreleq (quetiapine) XL prolonged-release tablets- all strengths

- Subsection relating to serotonin syndrome has been added, warning that concomitant administration with other serotonergic agents such as MAO inhibitors, SSRIs, SNRIs or tricyclic antidepressants may result in this potentially life-threatening condition, so caution to be exercised

Revised SPC: Prostap (leuprorelin) DCS Powder and Solvent for Prolonged-release Suspension for Injection in Pre-filled Syringe- all presentations

- SPC now warns severe cutaneous adverse reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (unknown frequency), which can be life-threatening or fatal, have been reported, & metabolic changes linked to GnRH agonist may also include fatty liver disease.

SPC changes or Manufacturer RMM

Revised SPC: Xromi (hydroxycarbamide) 100 mg/ml oral solution

- SPC updated to now include the recommended duration of contraception in male & female patients following the end of treatment with hydroxycarbamide, which should be 3 & 6 months, respectively. Both should be advised to use contraceptive measures before, during & after treatment.

Revised SPC: Topamax (topiramate) products

- The SPC has been updated in line with MHRA guidance on introduction of new safety measures, including a Pregnancy Prevention Programme, which must be fulfilled in women of childbearing potential, otherwise use would be contraindicated in this patient group.

Revised SPC: Buvidal (buprenorphine) prolonged-release solution for injection

- SPC notes opioids can cause sleep-related breathing disorders, and dose reduction can be considered should this occur. Also, presence of traces of natural rubber & latex in product cannot be excluded, and there is a potential risk of allergic reaction in latex sensitive patients.

Revised SPC: Phenergan (promethazine) 25 mg tablets

- SPC now notes that promethazine must not be used in children <6 years of age due to potential for fatal respiratory depression, psychiatric & central nervous system events. Also highlights that phenothiazines may potentiate the action of other depressants (e.g. opiates, alcohol).

Risk minimisation materials for topiramate products: Pregnancy Prevention Programme

- A number of resources are now available as part of the topiramate Pregnancy Prevention Programme, which is aimed at minimising pregnancy exposure during treatment with topiramate. Educational materials for patients include a patient guide, risk awareness form and patient card.

SPC changes or Manufacturer RMM

Revised SPC: Hydrea (hydroxycarbamide) 500 mg Hard Capsules

- SPC updated to note hydroxyurea may falsely elevate sensor glucose results from certain continuous glucose monitoring systems, which may lead to missed hypoglycaemic episodes and can also cause hypoglycaemia if sensor glucose results are relied upon to dose insulin.

Revised SPCs: Yentreve and Cymbalta (duloxetine) hard gastro-resistant capsules

- SPC updated to note neuroleptic malignant syndrome (NMS) may occur with duloxetine treatment, and that in its most severe form, serotonin syndrome can resemble NMS. Stress cardiomyopathy (Takotsubo cardiomyopathy) has been added as an adverse effect.

Revised SPC: Mirapexin (pramipexole) tablets- all strengths

- Spontaneous penile erection has been added to SPC as a rare adverse drug reaction

Drug shortages and discontinuations

Recent medicine shortages and discontinuations are available via: the SPS Medicines Supply Tool (registration required to access)

Shortage of Kay-Cee-L (potassium chloride 375mg/5ml) (potassium chloride 5mmol/5ml) syrup

- A National Patient Safety Alert was issued on 26 July 2024.

Prescribing and ordering available pancreatic enzyme replacement therapies

- A National Patient Safety Alert was issued on 24th May 2024.
- SPS article - Prescribing and ordering available pancreatic enzyme replacement therapies

Shortage of Shortage of Mannitol 100g/500ml (20%) infusion polyfuser bottles

- Anticipated re-supply date 6 September 2024

Shortage of Disopyramide 250mg (Rythmodan Retard) modified-release tablets and disopyramide (Rythmodan) 100mg capsules

- Disopyramide 250mg MR tablets issue has resolved
- Anticipated resupply date of disopyramide 100mg capsules has been brought forward to November 2024

Shortage of Carbamazepine 100mg/5ml oral suspension sugar free (Accord)

- Anticipated re-supply date 16 August 2024
- For patients who are unable to swallow solid dosage forms and are on a dose that is equivalent to a whole tablet, consider on a case-by-case basis the off-label crushing and dispersing in water for oral administration of Tegretol immediate release tablets

This is not a comprehensive list. Only critical safety medication shortages have been highlighted.

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Clinical considerations for patients prescribed clozapine

This resource covers clinical use, patient harm, prescribing (initiation, formulations), monitoring, clozapine toxicity, adverse effects, interactions, missed doses, swallowing difficulties, pregnancy and breastfeeding, and patient and carer engagement.

Prescribing and ordering available pancreatic enzyme replacement therapies

The availability of pancreatic enzyme replacement therapies (PERTs) varies currently. Use our resources and mini-tool to find matches for licensed products.

Purchasing for safety

Using principles of purchasing for safety when making purchasing decisions supports the safe clinical use of medicines and can minimise inadvertent harm.

Using NSAIDs in asthma

Safety and prescribing scenarios for using nonsteroidal anti-inflammatory drugs (NSAIDs) in adults with asthma are outlined.

Managing complexities of medication use across care boundaries

A discussion of factors that add complexities to the prescribing and supply of medicines, with a focus on liquid medicines.

National guidance, publications and resources

Drug and Therapeutics Bulletin

DTB select: Safety update: tramadol-warfarin interaction

An article providing an overview and clinical context for a recently issued MHRA warning about an increased risk of major bleeding when warfarin and tramadol are used concomitantly.

Safety update: more on topical steroid severe adverse effects

Article discusses and provides context on the recent announcement by the MHRA (May 2024 Drug Safety Update) that topical steroids will be labelled with their potency, and reminding healthcare professionals of the risk of severe adverse effects including withdrawal reactions.

Professional Record Standards Body

New transfer of care toolkit

New toolkit aims to improve patient safety, reduce medication errors, and improve efficiencies. It is designed to support health and care systems to achieve successful implementation of the eDischarge Summary Standard with focus on data sharing between secondary and primary care.

National guidance, publications and resources

Homecare Association

Expecting the Unexpected: Homecare providers' views of hospital discharge

Report from the UK's membership body for providers of care services at home suggests widespread problems with hospital discharge & despite guidance, funding & national taskforce, many ICSs are not getting basics right, putting safety & wellbeing of people leaving hospital at risk.

Findings include:

- 55% of care providers said hospital discharge paperwork does not reflect knowledge of the person being supported, including their needs and views.
- 35% said most hospital discharges they are involved with are not safe. Issues include lack of equipment, medication errors, and poor communication.

British Medical Journal

Patient safety commissioner: "A relentless focus on NHS finance and productivity is failing patient safety"

Interview with England's first patient safety commissioner covers developing a safety management system, including an overhaul of complaints process & clinical negligence; embedding patient safety & patient voice throughout healthcare system; & ensuring patients' voices are heard

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0322: Prevention of future deaths report

Date of report: 12/06/2024.

Patient died following an unintentional overdose of morphine and bromazolam, and therapeutic use of codeine, diazepam, zopiclone and quetiapine.

Patient suffered a complex medical history for which they were prescribed a variety of CNS depressant drugs. After admission to hospital they were prescribed oramorph by the hospital. This prescription was continued by her GP together with other CNS depressant drugs.

The **MATTERS OF CONCERN** are as follows.

- There was no agreement before starting opioids, regarding a treatment strategy and plan for end of treatment as recommended by NICE. There was no practice policy requiring such an agreement.
- There was no policy in place at the GP practice regarding long term (longer than 3 months) prescription of opioids.
- There were no warning flags in place at the practice at the 3-month stage of morphine prescription, to reflect the MHRA/CHM advice referred to in NICE guidance, regarding the increased risk of addiction beyond this period.
- There was no policy in place at the GP practice regarding co-prescription of opioids and benzodiazepines, to reflect the MHRA/CHM advice referred to in NICE guidance regarding the increased risk of respiratory depression and death.

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Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0319: Prevention of future deaths report

Date of report: 17/06/2024

Whilst receiving in-patient psychiatric treatment there were concerns they had consumed illicit substances and was displaying symptoms of being physically unwell. He was found unresponsive in his room and attempts were made by staff to resuscitate him. Naloxone and flumazenil were both administered by a junior doctor and the ward pharmacist with the assistance of the paramedics when they arrived – the flumazenil only because it was kept on the ward. It was not carried by the paramedics, and I was told that it is not carried by paramedics. Toxicology after his death revealed the presence of both buprenorphine (strong opioid analgesic) and flualprazolam (novel designer benzodiazepine).

The **MATTERS OF CONCERN** are as follows.

Noted that paramedics and ambulance crew do not carry flumazenil (but often do carry naloxone). The availability of flumazenil was happenstance in this case because he was on an acute psychiatric ward where the said antagonist was being kept and could be prescribed by the ward pharmacist and administered by the doctors.

I am concerned that there may be other acute circumstances when the use of this particular antagonist (flumazenil) could make a difference (say in the case of the collapse of person on the street or otherwise in the community) but will not be available since paramedics do not it.

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Primary research- Medication Safety

Remote prescribing consultations: exploring the principles of effective practice

Chilvers H, Bates. Nursing Standard

This article considers some of the benefits and challenges of remote prescribing and discusses the main principles of effective practice in relation to patient safety, informed consent and documentation.

Medication-related incidents in acute care hospitals among different age groups: An analysis of national patient safety report data

Han JM, Heo KN, Kim AJ, et al. Pharmacoepidemiology and Drug Safety

This study aimed to perform a nationwide analysis of medication errors from hospitals to compare the patterns among different age groups. The proportion of medication-related incidents that resulted in harm was the highest among the <1-year-old age group (67 cases, 51.5%), followed by the elderly (≥ 65 years) (828 cases, 40.9%). The cases leading to patient death were most frequently reported in patients aged ≥65 years.

Improving Compliance with a Nurse-Driven Protocol for Unfractionated Heparin Infusions in Patients with Venous Thromboembolism

Toale KM, Butler G, Richardson G, Beno J, Jawe N. American Journal of Nursing

Unfractionated heparin (UFH) is a high-risk medication. A multidisciplinary workgroup implemented order set changes, nursing communication orders, UFH infusion reports, and a nursing education module to promote compliance with the protocol. The overall rate of compliance with the VTE UFH infusion protocol increased and the median time to first therapeutic aPTT decreased from 831.5 minutes to 808 minutes over the same period.

Primary research- Medication Safety

Is Penicillin Allergy a Clinical Problem? A Systematic Review of Total Joint Arthroplasty Procedures With Implications for Patient Safety and Antibiotic Stewardship

Porto JR, Lavu MS, Hecht CJ 2nd, McNassor R, Burkhart RJ, Kamath AF. Journal Arthroplasty

Patients undergoing total joint arthroplasty (TJA) who report penicillin allergy (PA) are frequently administered second-line antibiotics, although recent evidence suggests that this may be unnecessary and could increase infection risk. Using penicillin allergy (PA) screening and testing can promote antibiotic stewardship by safely increasing the use of first-line antibiotics in patients who have a reported PA.

Evolution of Intravenous Medication Errors and Preventive Systemic Defenses in Hospital Settings-A Narrative Review of Recent Evidence

Kuitunen S, Airaksinen M, Holmstrom AR. Journal of Patient Safety

This narrative review demonstrates a growing interest in systems-based risk management for intravenous drug therapy and in introducing new technology, particularly smart infusion pumps and preparation systems, as systemic defenses.

Drug-Drug Interactions and Actual Harm to Hospitalized Patients: A Multicentre Study Examining the Prevalence Pre- and Post-Electronic Medication System Implementation

Li L, Baker J, Quirk R, et al. Drug Safety

This study aimed to and determine the prevalence of potential drug-drug interactions (pDDIs) verus clinically relevant DDIs (cDDIs) and examine the impact of transitioning from paper-based medication charts to electronic medication management on DDIs and patient harms. Although most patients experienced a pDDI during their hospital stay, less than one-third were cDDIs. The low prevalence of harm identified raises questions about the value of incorporating DDI decision support into systems given the potential negative impacts of DDI alerts.

Primary research- Medication Safety

Look-alike/sound-alike medication errors: An in-depth examination through a hospital case study

Supapaan T.S., Songmuang A., Napaporn J., et al. Pharmacy Practice

The findings of the present study highlight the multifaceted nature of LASA medication errors, with particular attention to complexities arising from similarities in drug names, appearance, and packaging. The authors implemented tailored strategies, such as Tall Man letters, movable LASA signage, augmentation of the workforce and careful management of high-risk medication pairs to address these issues.