

# SPS Medication Safety Update November 2023

## Recent critical patient safety alerts, reports, and publications

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# Patient Safety Alerts



  
UK Health  
Security  
Agency

Serial number: 2023/045 Date: 21/11/2023

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Event: *Burkholderia cenocepacia* novel cluster with suspected association with carbomer containing lubricating eye gel

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- UKHSA investigating 20 cases of infection – potential association with carbomer containing lubricating eye gel.
- Precautionary measure – avoid carbomer containing lubricating eye gels for dry eyes where possible by: individuals with cystic fibrosis, critical care inpatients, severely immunocompromised inpatients and patients awaiting lung transplantation.
- Submit any isolate from a new infection with *Burkholderia cepacia* complex to the AMRHAI reference laboratory for identification and typing.
- Contact for queries: [HCAIAMR.IOS@ukhsa.gov.uk](mailto:HCAIAMR.IOS@ukhsa.gov.uk).

# Recent regulator and statutory body activity



Medicines & Healthcare products  
Regulatory Agency

- [Isotretinoin \(Roaccutane ▼\): introduction of new safety measures](#)

2 independent prescribers to initiate treatment in <18yrs, new counselling requirements for mental health and sexual function side effects, mental health and sexual function assessment and monitoring, new RMM, new roles & responsibilities.

- [MedSafetyWeek November 2023: your Yellow Card report helps to improve patient safety](#)

Information on the 8<sup>th</sup> annual safety event.

- [Valproate: full pack dispensing guidance](#)

Requirement for full pack dispensing from 11<sup>th</sup> October 2023 unless exceptional circumstances.

- [MHRA to consider European Medicines Agency recommendation to avoid topiramate in pregnancy](#)

The European PRAC recently recommended that topiramate not be used during pregnancy unless no other suitable treatment for epilepsy is available. The MHRA will consider these recommendations as part of its ongoing safety review into the use of topiramate during pregnancy.

- [Falsified Ozempic \(semaglutide\) pens identified at two wholesalers in the UK](#)

MHRA has confirmed that pre-filled pens falsely labelled as Ozempic (semaglutide, 1 mg, solution for injection) have been identified at two UK wholesalers. All affected pens have been recalled and accounted for, and none of the pens have been supplied to UK patients

# Recent regulator and statutory body activity



Medicines & Healthcare products  
Regulatory Agency

## Class 4 Medicines Defect Information

- [Class 4 Medicines Defect Information: Sandoz Limited, Zinacef \[cefuroxime sodium\] powder for solution for injection or infusion vials \(all strengths, including stock in GSK livery\), EL \(23\)A/38](#)

The PIL and SPC state cefuroxime sodium is compatible with aqueous solutions containing up to 1% lidocaine hydrochloride. Dilution with lidocaine is however intended only for IM use, which is not explicitly mentioned. This is not a recall as there is no risk to product quality.

## Health Services Safety Investigations Body (HSSIB)

- [Risks to medication delivery using ambulatory infusion pumps: design and usability in inpatient settings](#)

An investigation was carried out to explore factors that can affect the ability of patients to reliably receive their medication via an ambulatory infusion pump. The focus was on this specific type of device as they are used widely across healthcare providers in England for patients receiving palliative care.

**Some take away points:** alarm not heard, lack of access to PCF, training staff on use

# Recent regulator and statutory body activity

## Healthcare Safety Investigation Branch

- [Health Services Safety Investigation Body \(HSSIB\) officially launches with aim to drive radical change in patient safety](#)

The newly formed HSSIB will look to tackle the biggest risks to patient safety. The focus in the coming year will be in areas of mental health inpatient services, workforce, fatigue and staff wellbeing, health inequalities, and transitions of care between different settings.

- [Investigation report: Caring for adults with a learning disability in acute hospitals](#)

This report found that, 'persistent and widespread' safety risks remain and the current systems and processes within the NHS are not always designed to enable staff to deliver effective care to people with a learning disability.

- [Investigation report: Safety management systems - an introduction for healthcare](#)

Investigation identified 3 key opportunities for an organised approach to safety management (SM) in the healthcare system: safety accountability frameworks across healthcare, SM systems development in healthcare, and safety maturity assessments across healthcare.

# Pharmacovigilance Risk Assessment Committee (PRAC)



Nil of note this month.

## Direct HCP communication

- **Azathioprine 75 mg & 100 mg tablets: Risk of overdose if wrong dose prescribed or dispensed**  
New strengths of azathioprine launched in the UK. Cautions with prescribing and dispensing to ensure the patient receives the intended dose.
- **Paracetamol 10mg/ml solution for infusion PL 46788/0008 - Blushing of PVC bags**  
Products may appear opalescent rather than transparent. Aesthetic phenomenon, no affect on quality, efficacy or safety.
- **Vaxneuvance ▼ (pneumococcal polysaccharide conjugate vaccine (15-valent, adsorbed)) suspension for injection in pre-filled syringe: potential for breakage.**  
Inspect for breakage before use and avoid exerting excessive force on the syringe.
- **Letters and medicine recalls sent to healthcare professionals in September 2023**  
(retrospective checklist)

## SPC changes

- **Revised SPC: Flolan (epoprostenol) 0.5 mg Powder and Solvent for Solution for Infusion (with pH 12 solvent & Vented Vial Adaptor)**

The maximum in-use period for the reconstituted solution, when used to treat pulmonary arterial hypertension, has been amended.

- **Revised SPCs: Numeta G19%E emulsion for infusion (parenteral nutrition)**

SPC now notes that use of a 1.2 micron filter is recommended for administration of Numeta G19%E. The same information has also been added to Numeta G13%E Preterm.

- **Revised SPC: Azocan-P (fluconazole) Capsules 150mg**

SPC updated to advise a washout period of ~ 1 week (5-6 half-lives) before becoming pregnant. Fluconazole increases exposure of abrocitinib active moiety by 155%, so if co-administered, the dose of abrocitinib needs to be adjusted in line with its prescribing information.

- **Revised SPC: Phenobarbital Elixir**

The SPC has been updated in several sections to advise that phenobarbital should not be used in women of childbearing potential unless the clinical benefit is judged to outweigh the potential risk of increasing the risk of congenital malformations by a factor of 2-3.



# SPC changes

- **[Revised SPC: Arikayce \(amikacin\) liposomal nebuliser dispersion](#)**

SPC now warns of increased risk of ototoxicity in patients with mitochondrial DNA mutations (particularly nucleotide 1555 A to G substitution in 12S rRNA gene), even if levels are in recommended range. Alternative options should be considered in such patients.

- **[Revised SPC: Vantobra \(tobramycin\) 170mg nebuliser solution](#)**

Updated to note increased risk of ototoxicity in patients with mitochondrial DNA mutations (nucleotide 1555 A to G substitution in the 12S rRNA gene) even if aminoglycoside serum levels are within range during treatment. Alternative options should be considered in these patients.

- **[Revised SPC: Lamictal \(lamotrigine\) preparations](#)**

SPC updated to highlight presence of the HLA B\*1502 allele in individuals of Asian (primarily Han Chinese & Thai) origin is associated with a risk of Stevens Johnson Syndrome with lamotrigine treatment. Potential use of lamotrigine should be carefully considered in such patients.

- **[Revised SPC: Iomeron \(iomeprol\) preparations](#)**

SPC now notes that the small amount of free inorganic iodide that may be present in contrast media might have some effects on thyroid function, and these effects appear more evident in patients with latent or overt hyperthyroidism or goitre. Thyroid storm has even been reported.

# SPC changes

- **Revised SPCs: Flucloxacillin products**

Product SPCs now note flucloxacillin (a CYP450 inducer) has been reported to significantly decrease plasma voriconazole concentrations. Monitoring for potential loss of voriconazole effectiveness (e.g. therapeutic drug monitoring) is recommended, and increasing dose if required.

- **MHRA extends licence of cystic fibrosis drugs Kaftrio (ivacaftor, tezacaftor and elexacaftor) and Kalydeco (ivacaftor) to include patients aged two to five years old**

These medicines were already authorised for use in treating cystic fibrosis with a common gene mutation in patients aged  $\geq$ six years. The licence extension is supported by evidence from 24-week, phase 3 study in 75 patients aged 2-5 years, with at least one F508del mutation.

- **Revised SPC: Cutaquig (human normal immunoglobulin)**

Infusion rate information has been updated. For those already on immunoglobulin therapy, use previously used rates for the initial infusions. Then gradually increase rate by approx. 10ml/h/site every 2-4 wks in adults ( $\geq$ 40kg) and up to 10mL/h/site every 4 wks for paediatrics.

# Manufacturer RMM

- [Columvi \(glofitamab\) Healthcare Professional Guide](#)

Guide and patient card to help minimise the risk of cytokine release syndrome when this medicine is used to treat relapsed or refractory diffuse large B-cell lymphoma.

- [Risk Minimisation Materials: Produodopa \(foslevodopa/foscarbidopa\) patient guide](#)

Guidance on preventing and managing the risk of infusion site skin infection and skin reactions, which are very common side-effects of this treatment.

- [Risk Minimisation Materials for Libtayo \(cemiplimab\)](#)

Resources providing important safety information to minimise complications from immune-mediated adverse reactions.

- [Risk Minimisation Materials: Columvi \(glofitamab\) patient card](#)

Patient card discusses cytokine release syndrome and the symptoms for which immediate medical attention should be sought. It also includes information for other healthcare professionals and space for details of the treatment schedule and prescribing haematologist to be added.

- [Risk Minimisation Materials for Talvey™ \(talquetamab\)](#)

Booklet for healthcare professionals raises awareness of the risk of neurological toxicity and provides recommendations to minimise the risk, and to facilitate management and monitoring if it does occur. A patient card lists symptoms which warrant immediate medical attention.

# Drug shortages and discontinuations

Recent medicine shortages and discontinuations are available via the [SPS Medicines Supply Tool](#) (registration required to access). This is not a comprehensive list. Only critical safety medication shortages have been highlighted.

## Drug Shortages

- [Etoposide 50mg and 100 capsules](#)
- [Prilocaine 100mg/5ml solution for injection amps](#)
- [Rasagiline 1mg tablets](#)
- [Rifampicin 150mg capsules](#)
- [Mivacurium chloride \(Mivacron\) 10mg/5ml and 20mg/10ml solution for injection amps](#)
- [Co-trimoxazole 40mg/200mg/5ml oral suspension sugar free](#)
- [Bisacodyl \(Dulcolax\) 5mg suppositories](#)
- [Lamotrigine 5mg dispersible tablets](#)
- [Dinoprostone \(Prostin E2\) 3mg pessaries](#)

## Discontinuations

- [Ethanol 100% solution for injection amps](#)
- [Eptifibatide 75mg/100ml and 20mg/10ml solution for infusion vials \(Integrilin\)](#)
- [Oxybutynin 3mg tablets](#)

# Specialist Pharmacy Service



## Interactions

- [Considering drug interactions with smoking](#)
- [Managing specific interactions with smoking](#)
- [Managing interactions between macrolides and statins](#)

## Breast feeding:

- [Paracetamol](#) (including combination products)
- [Specific antidepressants](#)
- [Vaccines](#)
- [Laxatives](#)

**Genomics:** [Implementing pharmacogenomics testing for aminoglycosides](#)

**Risk minimisation:** [Managing the risks of using liquid oral phenobarbital](#)

**Reminder:** [ADHD pages](#)

## PGDs:

- [Patient Group Direction use in Hospital at Home, including virtual ward services](#)
- [Patient Group Direction use by temporary professional registrants](#)

## Webinars:

- [Health and Justice Meds Op: 2023-25 strategic priorities](#) 05/12/23, 1-2pm
- [Reviewing medicines for people at risk of falls](#) 09/01/24, 1-2pm

# National guidance, publications and resources

- [Provisional publication of Never Events reported as occurring between 1 April and 30 September 2023](#)

**NHS England:** A total of 179 serious incidents were identified of which there were 7 reports of oral medication given IV, 1 of oral medication given subcut, 2 of overdose of insulin due to incorrect device and 2 of methotrexate prescribed & administered more than the intended weekly dose.

- [National paediatric early warning system \(PEWS\) observation and escalation charts](#)

**NHS England:** To standardise the approach of tracking the deterioration of children in hospital and are to be used on general children's wards.

- [Position statement 2023-03: Use of injection solutions to administer analgesics or sedatives via the intranasal route](#)

**Neonatal & Paediatric Pharmacists Group:** Comprehensive overview of the off-label use of injectable products given via the intranasal route, including dosing and practical recommendations for dose delivery.

- [DTB select - Safety update: methotrexate and photosensitivity reactions](#)

Summary and context is provided on the drug safety update from the MHRA.

- [New RPS interim professional standards for virtual wards](#)

Interim professional standards for pharmacy services for virtual wards to ensure the delivery of high-quality care and optimal outcomes for patients in the 'hospital at home' setting.

# Prevention of Future Death Reports (Regulation 28)



## Courts and Tribunals Judiciary

- [Ref: 2023-0368](#) 05/10/2023

Overdose case. Concern relating to patient having excessive supply of the same medicines (issued from GP and following hospital discharge).

- [Ref: 2023-0411](#) 26/10/2023

Overdose case. Patient discharged with excessive supply of medicines despite warnings that supplies should be restricted to 7 days.

# Primary research- Medication Safety

- [Safety outcomes when switching between biosimilars and reference biologics: A systematic review and meta-analysis](#)

Review of 31 studies of 21 biosimilars found no difference in safety parameters for patients switched to biosimilars after treatment with reference biologic.

- [Janus Kinase Inhibitors and Adverse Events of Acne: A Systematic Review and Meta-Analysis](#)

Review found JAK inhibitors linked to 3.83 times higher odds of acne compared with placebo, with increased odds for abrocitinib, baricitinib, upadacitinib, deucravacitinib and deuruxolitinib. Patients should be counselled on this potential ADR.

- [Posaconazole-ibrutinib interaction cannot be avoided by staggered dosing: How to optimize ibrutinib dose during posaconazole treatment](#)

Study found posaconazole increases ibrutinib (IB) exposure substantially, by ~10-fold. This interaction cannot be avoided by dosing the drugs 12 hours apart. Authors conclude a 70 mg daily dose of IB should not be exceeded during posaconazole treatment to avoid toxic side effects

- [Identification and comparison of sex-specific serious adverse drug reactions in spontaneous reports and systematically collected reports \(ADRED\)](#)

Analysis of two different datasets found some cancer and neurological drugs had a higher adverse drug reaction (ADR) reporting rate in women than men, whereas ADRs of the respiratory system and haemorrhages were described predominantly for males in both datasets.



# Primary research- Medication Safety

- **SGLT2 Inhibitor–Induced Ketoacidosis in a Patient Without Diabetes**

Case is presented of 79 year old who had recently started SGLT2 inhibitor for cardiac failure. Ketoacidosis likely due to combination of reduced glucose availability (dietary and from glycogen stores) and resultant inadequate insulin secretion in the setting of critical illness.

- **Medication prescription profile and hospital admission related to medication administration errors in England and Wales: an ecological study**

Study found hospital admissions related to medication errors increased from 184 per 100,000 in 1999 to 243 in 2020; most commonly in those taking non-opioid analgesics, antipyretics and antirheumatics, psychotropics, and antiepileptic, sedative-hypnotic and Parkinson's drugs.