SPS Medication Safety Update
February 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

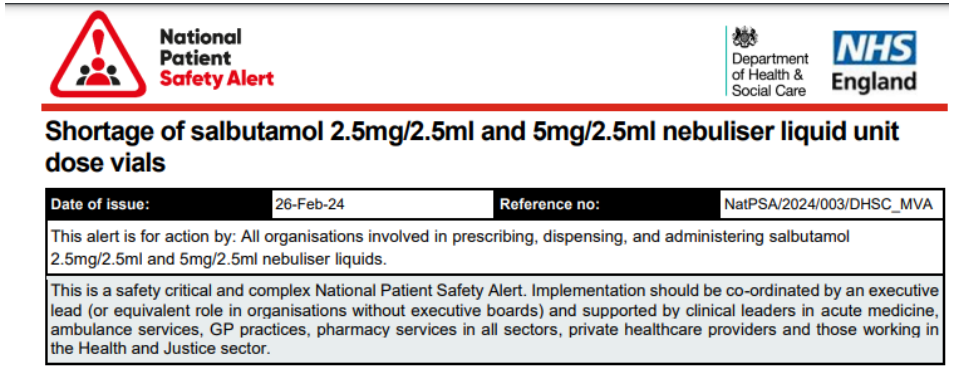
Shortage of salbutamol 2.5mg/2.5ml and 5mg/2.5ml nebuliser liquid unitdose vials

(26/2/24)

Actions:

All providers MUST:

- Liaise with local pharmacy teams and place urgent orders for unlicensed imports of salbutamol nebuliser liquid - do not wait for supplies to be exhausted before placing orders for imports.
- Wean all patients off nebulisers as soon as their condition has stabilised.
- Consider use of high-dose salbutamol pressurised metered-dose inhaler (pMDI) via a large volume spacer in patients with mild to moderate asthma attacks or COPD (see clinical information) ensuring the patient is issued with a new inhaler to avoid risk of using a near empty device and can administer it effectively if not being administered by a healthcare professional.



National Patient Safety Alert

Department of Health & Social Care

NHS England

Shortage of salbutamol 2.5mg/2.5ml and 5mg/2.5ml nebuliser liquid unit dose vials

Date of issue:	26-Feb-24	Reference no:	NatPSA/2024/003/DHSC_MVA

This alert is for action by: All organisations involved in prescribing, dispensing, and administering salbutamol 2.5mg/2.5ml and 5mg/2.5ml nebuliser liquids.

This is a safety critical and complex National Patient Safety Alert. Implementation should be co-ordinated by an executive lead (or equivalent role in organisations without executive boards) and supported by clinical leaders in acute medicine, ambulance services, GP practices, pharmacy services in all sectors, private healthcare providers and those working in the Health and Justice sector.

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National Patient Safety Alert

CAS Alerts

Valproate: important new regulatory measures for oversight of prescribing to new patients and existing female patients

As there continues to be cases of valproate being prescribed during pregnancy, the Commission on Human Medicines has recommended further restrictions to valproate use to reduce avoidable harm, which were introduced by the MHRA in January.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

[Codeine linctus (codeine oral solutions): reclassification to prescription-only medicine]

Reclassification from a pharmacy-only medicine (P) to a prescription only medicine (POM) is owing to the risk of dependence, addiction, and overdose. It is licensed only for the treatment of dry cough in adults and children aged 12 to 18 years without breathing difficulties.

[Pseudoephedrine: very rare risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)]

Patients and caregivers should be advised to be alert to the symptoms for PRES and RCVS, to stop the medication immediately and to seek urgent medical attention if these occur. Pseudoephedrine-containing medicines should be used for short-term, symptomatic use only and avoided in hypertension.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

[New valproate safety measures apply from 31 January]
MHRA highlight that from 31 Jan, new regulatory measures are in place to reduce the harms to the baby if valproate taken during pregnancy. It must not be started in new patients (male or female) <55yrs unless 2 specialists consider there is no effective or tolerated alternative. original alert for the new regulatory measures was sent on 28th November 2023 detailing actions required

[Paclitaxel coated devices (PCD) used in the treatment of peripheral arterial disease]
The MHRA has updated its previous guidance on the use of paclitaxel coated devices (PCD). Where indicated, PCD can be considered a treatment option in patients with critical limb ischaemia or intermittent claudication.

[Yellow Card Biobank to investigate how a patient's genetic makeup can impact the safety of Direct Oral Anticoagulants (DOACs)]
MHRA is asking anyone with excessive bleeding due to DOAC to report it to Yellow Card scheme, after which they may be contacted for consent to provide further information & submit a blood sample to explore if they are at higher risk of excessive bleeding due to genetic makeup.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Class 2 Medicines Recall Information

Class 2 Medicines Recall: Novartis Pharmaceuticals UK Limited, Adakveo 10 mg/ml concentrate for solution for infusion, EL(24)A/06

Recall of Adakveo (crizanlizumab) is due to the benefit-risk balance of Adakveo no longer being considered favourable by the MHRA and the revoking of the UK conditional marketing authorisation.

Class 3 Medicines Recall Information

Torrent Pharma (UK) Limited, Ramipril 1.25mg tablets, EL(24)A/05

Torrent Pharma (UK) Limited is recalling specific batches of Ramipril 1.25mg tablets as a precautionary measure due to these batches having a low assay and high related substances test results after their release to the market.

Class 4 Medicines Defect Information

Cadila Pharmaceuticals (UK) Limited, Pantoprazole 40 mg Gastro-Resistant Tablets, EL (24)A/03

Manufacturers have informed MHRA of an error with the barcode of certain batches, which identify the incorrect product, though other details on the carton are correct. Batches are not being recalled, and HCPs are advised to carry out manual rather than automated dispensing.

Exeltis UK Limited, Gepretix (progesterone) 100mg Capsules, EL (24)A/04

There is an inconsistency in the PIL packaged in cartons of the affected batches. In the ‘How much to take’ subsection, PIL states: ‘Take one capsule at bedtime on days 15 to 26 of your 28 day cycle’ instead of ‘Take two capsules at bedtime on days 15 to 26 of your 28- day cycle’

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

[European Medicines Agency confirms measures to minimise the risk of serious side effects with medicines containing pseudoephedrine]

New measures to minimise risks of posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome include avoiding use in patients with patients with severe or uncontrolled hypertension or severe acute or chronic kidney disease or renal failure.

[PRAC reminds healthcare professionals of risk of serious and potential fatal adverse reactions with Paxlovid]

Following evidence review of interactions between Paxlovid and calcineurin inhibitors (tacrolimus, ciclosporin) or mTOR inhibitors (everolimus, sirolimus), the PRAC agreed on a direct healthcare professional communication warning of risk of these interactions, which is known and already described in the product information.

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Direct HCP communication

In January 2024, the following letters were sent or provided to relevant healthcare professionals:

Omega-3-acid ethyl ester medicines (Omacor/Teromeg 1000 mg capsules): dose-dependent increased risk of atrial fibrillation in patients

Lagevrio® (molnupiravir) 200 mg hard capsules ▼ – Extended Use Beyond Labelled Expiry Date

Artiss 2ml Fibrin Sealant [Human] (product code: 5500649): Interim supply of Nordic Stock (Norway/Denmark) to Mitigate Supply Disruption

EXKIVITY▼ (mobocertinib) 40 mg hard capsules – Conditional Marketing Authorisation Withdrawal

Veltassa 16.8 g powder for oral suspension (Patiromer): Interim Supply of Northern Ireland Stock to Mitigate Supply Disruption

ADAKVEO (crizanlizumab): revocation of UK marketing authorisation due to lack of therapeutic efficacy as determined by MHRA

Plasma-Lyte 148 and Glucose 5% w/v Discolouration

Tostran (Testosterone, 2% gel): priming instructions in the current PIL require updating

Tamiflu® (oseltamivir) 45 mg Hard Capsules: Different colour ink used on blister pack

SPC changes or Manufacturer RMM

Brufen (ibuprofen) 100 mg/5 ml Syrup and Calprofen (ibuprofen) 100mg/5ml oral suspension

SPCs updated to note cases of Kounis syndrome (KS) have been reported in patients treated with ibuprofen. KS is defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to MI.

Lopinavir/Ritonavir Mylan 200 mg/50 mg film-coated tablets

Information about interaction with DOACs added to SPC. Clinical monitoring and/or dose reduction of the DOAC should be considered when a DOAC transported by P-gp but not metabolised by CYP3A4, including dabigatran and edoxaban, is co-administered with lopinavir/ritonavir.

Maxtrex (methotrexate) 10 mg Tablets

SPC updated to include a warning that photosensitivity has been observed in some patients using methotrexate. Exposure to intense sunlight or UV rays should be avoided and patients should use a sun-protection product with a high protection factor.

Morphine sulfate products: MST Continus prolonged release tablets, MXL prolonged release tablets and Sevredol tablets

SPCs include acute generalised exanthematous pustulosis, central sleep apnoea syndrome, pancreatitis and spasm of the sphincter of Oddi as adverse reactions of unknown frequency. Also notes interaction with gabapentin/ pregabalin which increases risk of respiratory depression.

Linezolid 2mg/ml solution for infusion

SPC updated to note hyponatraemia and/or SIADH have been observed in some patients treated with linezolid. Serum sodium levels should be monitored regularly in patients at risk of hyponatraemia (e.g. elderly patients; those taking medicines that may lower blood sodium levels).

SPC changes or Manufacturer RMM

Revised SPCs: Finasteride oral tablets - all products

Suicidal ideation has been added as a potential adverse effect of treatment (frequency unknown).

Telfast (fexofenadine) Film-coated Tablets - all strengths

Blurred vision as adverse effect of unknown frequency. The interaction section has information added on risk of concomitant use with P-gp inhibitors or inducers, which can affect exposure to fexofenadine, a P-gp substrate.

Entocort CR (budesonide) 3 mg Capsules

Hypersensitivity reactions such as angioedema added as known possible adverse effect of unknown frequency.

Zithromax (azithromycin) all formulations

SPC updated to highlight that, following the use of azithromycin in neonates (treatment up to 42 days of life), infantile hypertrophic pyloric stenosis has been reported. Parents/caregivers should be informed to contact a physician if vomiting or irritability with feeding occurs.

Tysabri (natalizumab) 300 mg concentrate for solution for infusion

In this revised SPC, the shelf life of the diluted solution has changed from 8 to 24 hours. The diluted product should be used as soon as possible and within 24 hours if stored at 2°C to 8°C. It should be allowed to warm to room temperature prior to infusion.

OPDIVO (nivolumab) 10 mg/mL concentrate for solution for infusion

SPC updated to include cytokine release syndrome as possible “common” adverse effect.

SPC changes or Manufacturer RMM

Ketalar (ketamine) injection – all strengths

SPC updated to note that hepatotoxicity (such as mixed liver injury, cholestatic liver injury and biliary dilation) has also been reported in patients with extended use (>3 days). Ketamine, therefore, is not indicated nor recommended for long-term use.

Affenid (methylphenidate) prolonged release tablets – all strengths

SPC updated to include more information about possible effects of methylphenidate on ability to drive and operate machines.

Froben (flubiprofen) 100mg tablets

SPC now carries a warning that flurbiprofen can mask symptoms of infection with advice for caution if a patient currently has an infection.

Yervoy (ipilimumab) 5mg/ml concentrate for solution for infusion

Cytokine Release Syndrome has been added to this update as an adverse effect occurring at a frequency of <1%. It has been reported as an infusion reaction (possibly resulting from a rapid injection rate).

Naseptin (neomycin, chlorhexidine) Nasal Cream

SPC updated to note the product contains cetostearyl alcohol which may cause local skin reactions (e.g., contact dermatitis).

Neupro (rotigotine) transdermal patches – all strengths

SPC warns of occasional reports of dystonic reactions including dystonia, abnormal posture, torticollis & pleurothotonus (Pisa Syndrome) in patients with Parkinson's disease after initiation/incremental dose increase.

Manufacturer Educational RMM

RMM - Elfabrio (pegunigalsidase alfa)

The information for healthcare professionals, for patients and caregivers, and an infusion diary booklet are available to help minimise the risk of hypersensitivity reactions and medication errors for patients in the home infusion setting.

RMM – Fibrovein (sodium tetradecyl sulphate)

Article discusses key safety concerns associated with this product and measures to be taken prior to treatment, including consideration of contra-indications, practitioner training, correct preparation and administration, and follow-up.

RMM – Enspryng (satralizumab) – Patient card

Card provides information on the increased susceptibility to infection, including a list of signs of infection for which medical attention should be sought, and actions for the treating healthcare professional to take if infection is suspected.

RMM – Aclasta (zoledronic acid monohydrate 5mg) – Patient card

Card discusses the risk of osteonecrosis of the jaw which has been reported very rarely in patients receiving this medicine for osteoporosis, the possible need for dental examination prior to treatment, and measures to take to reduce the risk whilst receiving treatment.

RMM – Lemtrada (alemtuzumab)

Guide for healthcare professionals provides information about potential serious risks associated with the use of alemtuzumab and recommendations on risk mitigation through patient counselling, monitoring and management. Patient guide and alert card are also available.

Manufacturer Educational RMM

RMM – Cerezyme (imiglucerase)

A home infusion manual for healthcare professionals provides guidance on managing patients receiving this medicine at home. There is also a manual for patients, which discusses Gaucher disease, the treatment, and how it is prepared and administered in the home setting.

RMM – Fabrazyme (agalsidase beta)

A home infusion manual for healthcare professionals provides guidance on managing patients receiving this medicine at home. There is also a manual for patients, which discusses organisation of treatment and how it is prepared and administered at home, and a log book.

Drug shortages and discontinuations

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

Medicine Supply Notification: Methadone 5mg tablets (MSN/2024/011)

DHSC has issued a medicine supply notification for methadone 5mg tablets which states: tablets are out of stock until late May 2024, supplies will remain available in hospitals throughout this period and methadone 1mg/ml oral liquid is available and can support increased demand.

Medicine Supply Notification: Activated charcoal (Charcodote) 200mg/ml oral suspension (MSN/2024/013)

Charcodote is out of stock till May 2024. Carbomix (Activated Charcoal) 81.3% (50g) granules for oral solution remain available and can support increased demand.

Medicine Supply Notification: Oxcarbazepine 150mg and 300mg tablets MSN/2024/016

Oxcarbazepine 150mg tablets (Viatris) are out of stock until late March 2024. Trileptal® 150mg tablets remain available, however, cannot support the full increase in demand. The 60mg/ml oral suspension also remains available but cannot support the increase in demand.

Medicine Supply Notification: Lisdexamfetamine (Elvanse) capsules MSN/2024/019

Supplies of different strengths will be intermittent until April 2024. Generic dexamfetamine 5mg and Amfexa (various strengths) supplies are unable to meet large increases in demand.

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

Drug shortages and discontinuations

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Medicine Supply Notification: Gastrografin (meglumine amidotrizoate 3.3g/5ml/sodium amidotrizoate 500mg/5ml) (MSN/2024/017)

Gastrografin® gastroenteral solution is out of stock until the end of June 2024. Omnipaque® and Visipaque® remain available and can support the increased demand across their portfolio. Where these are not suitable, unlicensed supplies of Gastrografin® gastroenteral solution may be sourced.

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

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[Using heparins during breastfeeding]
Low molecular weight heparin and unfractionated heparin can be used during breastfeeding. Recommendations apply to full term, healthy infants only.

[Using NSAIDS during breastfeeding]
There is very limited published information; however, ibuprofen and diclofenac are the preferred choices due to their shorter half-lives and extensive use during breastfeeding in clinical practice.

[Using nitrofurantoin during breastfeeding]
Article advises that nitrofurantoin can be used with caution during breastfeeding. This includes modified release preparations and when used for longer term prophylaxis.

[Using benzodiazepines during breastfeeding]
Lorazepam and oxazepam are the preferred benzodiazepines during breast feeding, if clinically appropriate. Recommendations apply to full term, healthy infants.

[Using penicillin antibiotics during breastfeeding]
All penicillin antibiotics can be used during breastfeeding with precautionary infant monitoring. Flucloxacillin, phenoxymethylpenicillin and the broad-spectrum penicillins (amoxicillin, ampicillin) are preferred, as there is more evidence and experience to support their use.

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[The licence and supporting evidence for natalizumab biosimilar]
This page discusses the licensed natalizumab biosimilar, Tyruko, and provides information about its licensed indications, evidence supporting safety and efficacy and NICE recommendations.

[Preparing to use natalizumab biosimilar]
Page aims to support pharmacy teams and individuals planning on using the natalizumab biosimilar. It signposts to key information including the relevant national guidance and commissioning policy for multiple sclerosis and gives advice on developing an implementation plan.

[Good governance when implementing natalizumab biosimilar]
Governance should consider processes for approval, procurement and supply, prescribing and administration, monitoring and pharmacovigilance.

[Introduction to PGDs]
Article discusses what a Patient Group Direction (PGD) is and how it is used in clinical practice. It forms part of a series covering when PGDs can be used, when not to use a PGD, and P and GSL medicines with PGDs

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[Using St Mark's electrolyte solution]

This webpage contains information on the preparation and use of St Mark's solution (also known as St Mark's Electrolyte mix or E-mix), an oral rehydration solution which maintains fluid balance in conditions like short bowel syndrome and intestinal failure.

[Requirements for Governance and Preparation of Gene Therapy]

Gene therapies are an important class of advanced therapy medicinal product. This webpage contains practical advice for centres implementing gene therapies, detailing governance requirements and optimal preparation location decision making support.

[SPS publishes suite of 23 new and 2 updated PGDs and a new protocol for 7 conditions]

SPS have published, with support from RCGP, ARPHAI, UKHSA, NHSE & specialist stakeholders, a suite of 25 (23 new & 2 updated) PGDs and a new protocol for 7 conditions: sore throat, otitis media, sinusitis, shingles, impetigo, infected insect bites and uncomplicated UTI in women.

National guidance, publications and resources

Prescribing and dispensing/supply/administration by the same healthcare professional

Position statement from RPS updates previous position and clarifies that the same healthcare professional can be responsible for the prescribing, dispensing and/or supply/administration of medicines, where clinical circumstances make it necessary and in interest of the patient.

Source: Royal Pharmaceutical Society

Legislative changes to enable the prescribing supply and administering of controlled drugs by certain healthcare professionals

The Home Office has made changes to the Misuse of Drugs Regulations 2001 to enable the prescribing, supply and administering of controlled drugs by certain healthcare professionals, including paramedic, podiatrist, chiropodist, and radiographer independent prescribers.

Source: Royal Pharmaceutical Society

National measles guidelines

How to manage cases of suspected measles: what patient details to take, who to notify and assessing risk of disease spreading in close contacts.

Source: UK Health Security Agency

Hepatitis A infection: prevention and control guidance - update

The main updates are: clearer criteria for feasibility of anti-hepatitis A virus immunoglobulin testing prior to human normal immunoglobulin issue, and more detailed assessment of susceptibility of close contacts including definition of immune, primed & fully susceptible

Source: UK Health Security Agency

National guidance, publications and resources

Suspected sepsis: recognition, diagnosis and early management – updated guidance (NG51)

Updated guidance makes new recommendations on risk evaluation & management, covering the population and settings in which the national early warning score (NEWS2) applies. Also includes recommendations on when GPs & ambulances should have mechanisms in place to give antibiotics.

Source: National Institute for Health and Care Excellence

National learning report: Positive patient identification

Report aims to help reduce the risk of patient misidentification, makes safety recommendations and safety observations aimed at healthcare organisations and policymakers to help improve patient safety.

Source: HSIB

Never event framework consultation

The consultation is being held following the findings of reports from the CQC and HSIB that highlighted for several types and sub-types of Never Events the barriers are not strong enough to make an incident wholly preventable. The consultation will run until 5th May 2024.

Source: NHS England

The Hughes Report: Options for redress for those harmed by valproate and pelvic mesh

Report aims to help government understand options for providing redress to those patients harmed, has made 10 recommendations. Commissioner thinks there is clear case for redress based on systemic healthcare & regulatory failures revealed by First Do No Harm review in 2020.

Source: Patient Safety Commissioner

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0061 – Alcohol and self-medication for PTSD (7th February 2024)

- Died from health complications arising from use of alcohol and prescription medication to try to deal with the complications of severe post-traumatic stress disorder. Names of prescription medication not documented.

Ref: 2024-0085 – Clozapine and alcohol (15th February 2024)

- Death resulted from the combined toxic effect of alcohol and clozapine (individually not at toxic levels) acting to suppress his central nervous system.
- Warnings relating to alcohol and clozapine are noted in the PIL, however does not mention death as a possibility.

Ref: 2024-0081 - Inadvertently overdosed on Fentanyl (14th February 2024)

- Inadvertently overdosed on Fentanyl (3 patches worn at the same time), and that, in combination with other medicines (unknown), several of which possessed the ability to depress the nervous system, led to her death.

Ref: 2024-0094 – Overprescribing of zopiclone (23rd February 2024)

- Fatal level of zopiclone in blood at the time of his collapse from which never recovered. Over twice the appropriate amount of zopiclone was issued over a period of 57 days.
- Consideration of a different prescribing period and very careful monitoring of the online requests for repeat prescriptions were recommended.

Primary research- Medication Safety

Medication errors involving intravenous paracetamol in children: experience from enquiries to the National Poisons Information Service

Analysis of enquiries concerning 266 children (55% <1 year) found common error themes included 10-fold overdose (16.9%) and inadvertent concomitant oral and IV dosing (24.1%). Most were asymptomatic, with many calls regarding overdoses below the treatable dose of 60 mg/kg.

Source: Archives of Disease in Childhood

Exploring the Role of Guidelines in Contributing to Medication Errors: A Descriptive Analysis of National Patient Safety Incident Data

Difficulties finding and using information from clinical guidelines contribute to thousands of prescribing and medication administration incidents, some of which are associated with substantial patient harm.

Source: Drug Safety