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

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Medicines & Healthcare products Regulatory Agency

Specialist Pharmacy Service

NHS England

# Patient Safety Alerts

NHS England

National Patient Safety Alert

**National Patient Safety Alert – risk of oxytocin overdose during labour and childbirth 24.09.24**

An oxytocin infusion can be administered to augment contractions during labour or in a much higher dose to treat postpartum haemorrhage. The inadvertent administration of a postnatal dose of oxytocin prior to the birth of the baby can lead to significant harm to mother and baby.

Review and update local clinical procedures (or equivalent documents) to ensure:

1. Oxytocin infusions for any indication are not pre-prepared at ward level in any clinical area (including delivery suites and theatres).

2. Post-partum haemorrhage (PPH) kits/ trolleys are immediately available in all clinical areas/theatres where it may be required.

3. Where a woman is identified to be at high risk of PPH:
    a. the PPH kit/trolley should be brought into the labour/delivery room/theatre during the second stage of labour
    b. the postpartum oxytocin infusion should be prepared at the time of birth and not before
    c. a second midwife should be available to support the administration of the postpartum oxytocin infusion.

4. Roles and responsibilities of staff groups in the labour setting, including theatres, are clearly defined in terms of prescribing, preparation, administration and disposal of oxytocin infusions.

All actions should be completed by 31 March 2025

See SPS: Managing risks associated with oxytocin infusions during labour

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# Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Valproate use in men: as a precaution, men and their partners should use effective contraception

- Link reported between valproate use by men around time of conception & increased risk of neurodevelopmental disorders in their children. They and female partner should be informed of risk & advised to use effective contraception during and for ≥3 months after stopping valproate.

# Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Class 4 Medicines Defect Information: Chemidex Pharma Ltd, Ponstan 250mg Capsules & 500mg Tablets (mefenamic acid), EL(24)A/

- The PIL in the cartons of the listed batches is out of date. The latest PIL includes updated information about use during pregnancy, which is not mentioned in the out of date PILs. HCPs should ensure patients are aware of the missing information when supplying affected batches.

Class 3 Medicines Recall: Theramex HQ UK Ltd, Evorel Sequi, EL (24)A/41

- An error at packaging site means that a limited number of packs have the incorrect combination of Evorel 50 and Evorel Conti patches. Only the batch listed in this notification is affected. The remainder of the batch is being recalled as a precautionary measure.

Class 3 Medicines Recall: Orion Pharma (UK) Ltd, Eldepryl 5mg Tablets (selegiline), EL(24)A/42

- Orion Pharma (UK) Ltd is recalling this batch as a precautionary measure due to an out of specification result in the assay result during the follow up stability study of the batch.

MHRA finds evidence does not support a link between Glucagon-Like Peptide-1 (GLP-1) receptor agonists and suicidal and self-injurious thoughts and actions

- In July 2023, a new potential safety risk was identified associated with GLP-1 RAs and risk of suicidal thoughts and self-harm following an initial review of post-marketing reports. The MHRA evaluation of the data aligns with the conclusions of a European regulatory review.

# Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Philips Respironics BiPAP A series ventilators: alarm malfunction and risk of therapy interruptions in ventilators not intended for life-support, DSI/2024/006

- Philips Respironics has issued a Field Safety Notice (SN) relating to the Bilevel Positive Airway Pressure (BiPAP) A series ventilators. This relates to a Ventilator Inoperative alarm which could result in the potential loss of therapy to patients without warning.

Pharmacovigilance following agreement of the Windsor Framework

- This guidance is designed to provide information on the implementation of changes to pharmacovigilance for medicines authorised in the UK following the agreement of the Windsor Framework from 1 January 2025. It should be used in conjunction with MHRA's guidance on the Framework.

# Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

PRAC conclude that hydroxycarbamide can cause falsely high CGM sensor readings

- PRAC has announced that it considers there to be a causal relationship between hydroxycarbamide and falsely high CGM sensor glucose readings leading to hypoglycaemia. It has recommended that product information should be amended accordingly.

Medroxyprogesterone: increased risk of meningioma with high doses and after prolonged use

- The PRAC has agreed a communication to inform healthcare professionals of this risk with all injectable and ≥100 mg oral formulations, primarily after prolonged use (several years). It will contain information on new contraindications, stopping treatment and monitoring.

Medicines for chemotherapy containing 5-fluorouracil: in patients with moderate or severe renal impairment, phenotyping for dihydropyrimidine dehydrogenase (DPD) deficiency by measuring blood uracil levels should be interpreted with caution

- The PRAC has agreed a communication to inform healthcare professionals that renal impairment can lead to increased blood uracil levels, resulting in an incorrect diagnosis of DPD deficiency and consequently under dosing of 5-FU or other fluoropyrimidines in these patients.

# SPC changes or Manufacturer RMM

Revised SPC: Esbriet (pirfenidone) 267 mg and 801 mg Film-coated Tablets

- SPC updated to warn that 'drug reaction with eosinophilia and systemic symptoms' (DRESS), which can be life-threatening or fatal, have been reported post-marketing in association with pirfenidone treatment.

Revised SPC: Mirena (levonorgestrel) 20 micrograms/24 hours intrauterine delivery system
Revised SPC: Jaydess (levonorgestrel) 13.5 mg intrauterine delivery system

- SPC updated with information to make healthcare professionals aware that the use of excessive force during removal of intrauterine delivery system might lead to device breakage, and with detailed information on the onset of contraceptive efficacy.

Revised SPC: Lemsip Max (paracetamol, phenylephrine) products

- Diabetes mellitus and closed-angle glaucoma added as contraindications (due to presence of phenylephrine), warning added about increased risk of high anion gap metabolic acidosis with concomitant use of flucloxacillin & paracetamol, and use with caution in patients with porphyria.

Revised SPC: Tecentriq (atezolizumab) solution for infusion or injection- all strengths

- Hypophysitis (acute/chronic inflammation pituitary gland) now classified as an uncommon ADR (previously rare) of treatment with atezolizumab as monotherapy and in combination therapy; and qualified to include reports of hypopituitarism & secondary adrenocortical insufficiency.

Revised SPC: Mavenclad (cladribine) 10 mg tablets

- SPC updated to warn that serious, severe, and opportunistic infections, including events with fatal outcome, have been observed with Mavenclad treatment.

# SPC changes or Manufacturer RMM

Revised SPC: Aubagio (teriflunomide) 7mg and 14mg film-coated tablets

- Herpes virus infections added as possible “common” adverse effect. Cases of herpes virus infections, including oral herpes and herpes zoster, have been reported with teriflunomide, with some of them being serious. They may occur at any time during treatment.

Revised SPC: Rystiggo (rozanolixizumab) 140 mg/ml solution for injection

- SPC updated to include information about cases of drug induced aseptic meningitis from spontaneous post-marketing reporting in generalised myasthenia gravis.

Revised SPC: Imfinzi (durvalumab) 50 mg/mL concentrate for solution for infusion

- Coeliac disease and pancreatitis have been added to the SPC as potential adverse effects seen with this medicine when used either as a monotherapy or in combination with other medicines.

Revised SPC: Saxenda (liraglutide) 6 mg/mL solution for injection in pre-filled pen

- Intestinal obstruction added to SPC as an adverse effect of unknown frequency.

Revised SPC: ChloraPrep (chlorhexidine gluconate, isopropyl alcohol) products

- In line with PRAC recommended wording, the previous warning on eyes and mucous membranes has been updated, and details on eyes toxicity added.

Revised SPC: Ninlaro (ixazomib) hard capsules- all strengths

- Pyrexia and arthralgia added as very common adverse reactions (all grades).

Revised SPC: Dobutamine 5 mg/ml and 12.5mg solution for infusion (Hameln)

- Patients with asthma with hypersensitivity to sulfites and phaeochromocytoma have been added as contraindications. It is recommended that hypovolaemia is corrected before dobutamine is administered and it is noted that entacapone may potentiate the effects of dobutamine.

# SPC changes or Manufacturer RMM

Revised SPC: QVAR (beclometasone dipropionate) products

- Cushing's syndrome and Cushingoid features added to SPC as a very rare adverse effect of treatment.

Revised SPC: Kymriah cells dispersion for infusion (tisagenlecleucel)

- The SPC has updated to state that T-cell malignancies have been reported following treatment with CAR-T cell therapy. It is advised that patients should be monitored life-long for secondary malignancies following treatment.

Revised SPC: Propofol 10mg/mL and 20mg/mL emulsion for injection or infusion (Baxter)

- The SPC has been updated to include hepatomegaly as a potential adverse event of unknown frequency.

Revised SPC: Nutriflex peri and plus Solution for Infusion

- SPC updated with warning that administration of glucose to patients with a preexisting Thiamin (vitamin B1) deficiency may be associated with the development of severe lactic acidosis and/or a Wernicke encephalopathy. Pre-existing thiamine (Vitamin B1) deficiency must be corrected before infusion of glucose containing solutions.

Revised SPC: Relevtec (buprenorphine) transdermal patch – all strengths

- SPC updated to note concomitant use with gabapentinoids (gabapentin and pregabalin) may result in respiratory depression, hypotension, profound sedation, coma or death, and to include advice on drug dependence

Revised SPC: Remsima (infliximab) 120 mg solution for injection in pre-filled pen

- Posology information updated to include three IV induction doses for Crohn's disease (CD) and ulcerative colitis, and the possibility for dose adjustment from 120mg to 240mg (subcutaneous) for patients with CD with loss of response.

# SPC changes or Manufacturer RMM

Revised SPC: Velcade (bortezomib) 3.5mg powder for solution for injection

- SPC now notes due to its genotoxic potential, women of childbearing potential must use effective contraception & avoid pregnancy during & for 8 months after treatment. Male patients should use effective contraception & not father a child during & for 5 months after treatment.

Revised SPC: Li-Liquid (lithium citrate) 509 mg/5ml Oral Syrup

- SPC updated to include information about an interaction between lithium and topiramate.

Revised SPC: Tioguanine 40 mg Tablets (Mylan)

- The SPC has been updated to include warnings that patients treated with this medicine, in combination with other immunosuppressive or chemotherapeutic agents, are at increased risk of severe or atypical viral, fungal or bacterial infections.

Revised SPC: Retsevmo (selpercatinib) capsules

- The SPC has been updated to note that epiphysiolysis of the femoral head has been reported in up to 6.4% of paediatric patients that have received this medicine.

Risk Minimisation Materials for Fabhalta (iptacopan hydrochloride monohydrate)

- The healthcare professionals brochure aims to provide guidance and mitigate possible risk of infections during iptacopan treatment, and haemolysis after discontinuation. A patient and caregiver guide and patient safety card are also available.

Healthcare Professional Guide to the risk of progressive multifocal leukoencephalopathy (PML) associated with Tysabri™ (natalizumab)

- This healthcare professional (HCP) guide and a related administration checklist are for use by HCPs administering subcutaneous natalizumab outside a clinical setting. The guide discusses the risk factors for PML, its diagnosis, patient monitoring, and important considerations.

# Drug shortages and discontinuations

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

Management information on medicines supply issue notifications

- Analysis of total number of monthly medicine supply issue notifications in UK, reported to DHSC, sourced from the DaSH portal, found just over 5,600 notifications have been reported since October 2020, with around 1,600 in both 2022 and 2023.

Medicine Supply Notification: Methylphenidate prolonged-release tablets

- These are in limited supply and intermittent regional supply disruptions expected to continue until Oct 2024. Unlicensed supplies of methylphenidate prolonged-release tablets can be sourced, lead times vary. Lisdexamfetamine (Elvanse®, Elvanse Adult®) capsules remain available.

Medicine Supply Notification: Naltrexone 50mg tablets

- These are in limited supply until early Sept 2024, then out of stock until late Oct 2024. Adepend 50mg tablets out of stock until mid-Sept 2024 & unable to support once back in stock. Naltrexone 50mg tablets (AOP Orphan) remain available & can support increased demand.

Medicine Supply Notification: Norethisterone (Noriday® ) 350microgram tablets

- These will be out of stock from late Aug 2024 until early Dec 2024. Desogestrel 75microgram tablets remain available and can support increased demand. Levonorgestrel (Norgeston®) 30microgram tablets remain available but cannot support an uplift in demand.

# Drug shortages and discontinuations

Temporary ban on prescription and supply of puberty blockers extended.

- Continuation of ban applies to sale or supply of these drugs, prescribed by private UK-registered prescribers for gender incongruence/dysphoria to under 18s not already on them. It also prevents sale & supply from prescribers registered in EEA or Switzerland to those under 18.

Medicine Supply Notification: Creon® Micro Pancreatin 60.12mg gastro-resistant granules (MSN/2024/089)

- Creon Micro Pancreatin 60.12mg gastro-resistant (GR) granules are in limited supply until late 09/2024. Creon 10,000 GR caps are in limited supply into primary care via wholesalers. But, a small amount is in secondary care which may be used for the patient cohort on Creon Micro.

Medicine Supply Notification: Naloxone (Nyxoid® ) 1.8mg/0.1ml nasal spray unit dose

- Naloxone (Nyxoid®) 1.8mg/0.1ml nasal spray is out of stock until w/c 30th September 2024. Naloxone 1.26mg/0.1ml nasal spray unit dose remains available and can support a full increase in demand, as can naloxone (Prenoxad®) 1mg/ml solution for injection pre-filled syringes.

Medicine Supply Notification: Isosorbide mononitrate 60mg modified-release tablets and capsules.

- Chemydur 60XL tablets out of stock until mid-Sept, Monomax XL 60mg tablets until early Oct, Nyzamac SR 60mg capsules until late Oct; & Monomil XL 60mg tablets in limited supply until late Dec. Isotard 60XL, Medomon XL, Relosorb XL & Tardisc XL 60mg tablets remain available

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

# Drug shortages and discontinuations

- Support for medicines shortages

Prescribing and ordering available pancreatic enzyme replacement therapies (Last updated 20 August 2024)

Prescribing available medicines to treat ADHD (Last updated 27 August 2024)

Prescribing and using thiamine to prevent refeeding syndrome (Last updated 30 August 2024)

Using and prescribing thiamine in alcohol dependence (Last updated 30 August 2024 )

# Specialist Pharmacy Service

Specialist Pharmacy Service

Managing risks associated with oxytocin infusions during labour

- This document supports organisations to complete the actions listed in the most recent Patient Safety Alert.

Pharmacy Institutional Readiness for Exagamglogene Autotemcel (Casgevy®)

- This document highlights key areas where Chief Pharmacists should focus pharmaceutical expertise prior to implementation of Exagamglogene Autotemcel.

Using generic liposomal amphotericin B

- This comparison of the new generic liposomal amphotericin B from Tillomed with the original brand AmBisome includes advice on mitigating risks of confusion with non-liposomal Fungizone.

# National guidance, publications and resources

The use of Calcium and Phosphate supplementation in neonates and children: updated position statement

- The position statement (originally published March 2023) has been updated to cover Sando K®.

Source: Neonatal & Paediatric Pharmacists Group

Complete routine immunisation schedule

- The complete routine immunisation schedule has been updated to reflect the introduction of Respiratory syncytial virus (RSV) programmes for pregnant women and older adults.

Adrenal insufficiency: identification and management- guidance (NG243)

- In this clinical guideline, NICE provide recommendations on initial identification and referral, pharmacological management, management during physiological or psychological stress, emergency management of adrenal crises, ongoing care and managing glucocorticoid withdrawal.

Workforce and patient safety: temporary staff - integration into healthcare providers

- Report found widespread discrimination against temporary staff in the NHS, due to their work status and sometimes due to their ethnicity, which has a negative impact on their wellbeing and creates a culture of fear that stops them speaking up about patient safety.

NHS England decision support tools

- Support tools designed to support shared decision making between patients and clinicians. Variety of subjects e.g. angina, AF, chronic pain, epilepsy, mental health…

# Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0484: Prevention of future deaths report

Date of report: 09/09/2024

Patient had in error been prescribed a medicine at double the stipulated maximum dose.

Matters of concern:

- Drug prescribed for 6 months at double max stipulated dose.
- Pharmacist dispensed dose and nurse administered without querying it. MDT meetings didn't check dose or identify drug interactions.
- No effective resilience in the hospital's systems to safeguard against drugs being prescribed or administered in error.

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# Primary research- Medication Safety

NIHR commentaries: How to choose the right antidepressant or antipsychotic

- Commentaries provided on information collated by researchers on ADRs of antidepressant and antipsychotics to develop a tool that provides visual display of potential treatments, highlighting ADRs of most concern to patients. This could be used to inform shared decision-making.

Errors associated with co-names of medicines: The nomenclature of combination medicinal products

- A search of the literature describing errors associated with prescribing the 26 combination formulations available in the UK has led the authors to call for a standard nomenclature for these products that includes the international non-proprietary name and dose of each component.