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

Prepared by

Monika Wojtowicz – SPS Medicines Advice Pharmacist

monika.wojtowicz@esneft.nhs.uk

Medicines & Healthcare products Regulatory Agency

Specialist Pharmacy Service

NHS England

Patient Safety Alerts

NHS England

National Patient Safety Alert

Shortage of Pancreatic enzyme replacement therapy (PERT)

24-May-2024

This National Patient Safety Alert supersedes the Medicine Supply Notification (MSN/2024/054) which was issued on 09 May 2024.

There are limited supplies of pancreatic enzyme replacement therapies (PERT): Creon® 10,000 and 25,000, Nutrizym® 22 capsules, Pancrex V® capsules and powder.

Actions required:

- prescribe a maximum of one month's supply of PERT for all patients at a time.
- prioritise available Creon 10,000 capsules for patients unable to take Creon 25,000 capsules only.
- prioritise remaining stock of Nutrizym® 22 capsules for patients unable to tolerate Creon capsules.
- where PERT is prescribed for indications other than cystic fibrosis, consider:
    - prescribing a proton pump inhibitor or H2 receptor antagonist to optimise efficacy
    - if a dose reduction may be suitable for patients based on severity of symptoms
    - where symptoms remain despite a dose of ≥10,000 units lipase/kg/day or 100,000 units lipase with a meal, whether other causes of the symptoms should be investigated
    - prescribing medication to manage symptom control

PSBGI Position Statement: Pancreatic enzyme replacement therapy (PERT) shortage – advice for the management of adults with pancreatic exocrine insufficiency

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Topical steroids: introduction of new labelling and a reminder of the possibility of severe side effects, including Topical Steroid Withdrawal Reactions

Due to regulatory action, topical steroid (TS) products will be labelled with information on their potency to simplify advice for patients. Since last review of TS withdrawal in 2021, MHRA continues to receive reports and concerns from patients regarding such reactions.

Warfarin: be alert to the risk of drug interactions with tramadol

A recent Coroner's report concluded the death of a patient from a bleed on the brain was caused by a generally unknown interaction between warfarin and tramadol. Article reminds healthcare professionals to consider the need for extra monitoring and patient counselling.

Topiramate (Topamax): introduction of new safety measures, including a Pregnancy Prevention Programme

Following a safety review, topiramate is now contraindicated in pregnancy for epilepsy (unless there is no other suitable treatment) and for migraine prophylaxis, and in women of childbearing potential unless the conditions of the Pregnancy Prevention Programme are fulfilled.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Class 2 Medicines Recall: Desitin Pharma UK Ltd, Lamotrigine Desitin 10mg/ml Oral Suspension, EL(24)A/20

All batches being recalled as precautionary measure due to out of specification observation in the appearance of samples during routine stability testing, which is believed to be a homogeneity issue, and a potential for some doses to have too little or too much active ingredient.

Class 3 medicines recall: Neuraxpharm UK Ltd, Atomoxetine 10mg, 18mg, 25mg, 40mg Capsules, EL(24)A/19

The manufacturer is recalling specific batches as a precautionary measure after testing showed variability of the capsule contents beyond permitted levels.

Class 3 Medicines Recall: Teva UK Limited, GoResp Digihaler, EL (24)A/23

For commercial reasons, manufacturers are discontinuing production of the GoResp Digihaler (budesonide and formoterol). Inhalers containing the medicinal product are also being recalled as the App described in the Patient Information Leaflet is no longer available for download.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Class 4 Medicines Defect Information: Manx Healthcare Ltd., Betamethasone Valerate 0.1% Ointment, EL(24)A/18

Manx Healthcare Ltd. has informed MHRA that they have identified a problem with the product packaging of the listed batch. Due to an intermittent equipment fault during secondary packaging, the tamper-evident seal on the outer carton may be missing or deformed on some packs.

Class 4 Medicines Defect Information: Dawa Limited, Paracetamol 500mg, 1000mg Film-Coated Tablets, EL (24)A/21

Dawa Limited has informed the MHRA that the batches listed in alert have been packed with an outdated Patient Information Leaflet (PIL). Section 2 of the PIL does not contain the most up to date information on the use of flucloxacillin as a concomitant medicine

Class 4 Medicines Defect Information: Viatris UK Healthcare Ltd, Oxcarbazepine Mylan 150 mg, 300mg, 600mg Film-Coated Tablets, EL (24)A/22

Viatris UK Healthcare Limited has informed the MHRA that the PIL packaged in the specified batches of Oxcarbazepine 150mg, 300mg & 600mg Film-Coated Tablets do not contain the most up to date safety information. Healthcare professionals should provide a copy of the updated PIL.

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CAR T-cell medicines: PRAC identifies risk of secondary malignancies of T-cell origin

The PRAC has concluded that secondary malignancies of T-cell origin may occur after treatment with CAR T-cell medicines. EU product information and the risk management plans will be updated to include the new information concerning secondary malignancy of T-cell origin.

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

CHMP recommends approval for use of Zegalogue (dasiglucagon) for the treatment of hypoglycaemia

CHMP recommended granting a marketing authorisation for Zegalogue for the treatment of severe hypoglycaemia in adults, adolescents, and children aged 6 years and over with diabetes mellitus.

CHMP supports extension to the existing indication for apixaban (Eliquis) for the treatment and prevention of VTE in children

CHMP has adopted positive opinion on extension to existing indication to include treatment & prevention of recurrent VTE in children, due to addition of new pharmaceutical forms/ strengths (0.15 mg granules in capsules for opening & 0.5, 1.5, & 2 mg coated granules in sachet).

CHMP supports extension to the existing indication for dupilumab (Duxipent) for the treatment of COPD

The CHMP has adopted positive opinion on new indication to include use as add-on maintenance in adults on a combination of inhaled corticosteroid (ICS), long-acting beta 2 agonist (LABA), & long acting muscarinic antagonist (LAMA), or LABA/LAMA if ICS not appropriate.

CHMP supports extension to the existing indication for risankizumab (Skyrizi) for the treatment of ulcerative colitis

The CHMP has adopted a positive opinion on extension of licence to now include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, lost response to, or intolerant to conventional therapy or a biologic therapy.

Direct HCP communication

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

Levemir® InnoLet® 100 units/ml solution for injection in pre-filled pen (insulin detemir), Insulatard® InnoLet® 100 international units/ml suspension for injection in pre-filled pen (insulin isophane human), NovoTwist® 5mm needles (32G), NovoFine® 6mm needles (31G), NovoFine® 8mm needles (30G), NovoFine® Autocover® needle (30G) and NovoFine® Remover: DISCONTINUATION

Sandimmun concentrate for solution for infusion 50mg/ml (ciclosporin): Interim Supply of German Stock to Mitigate Supply Disruption

Wegovy® 0.5 mg, solution for injection in pre-filled pen (semaglutide): Interim supply of Swiss Stock to Mitigate Supply Disruption

Mounjaro® ▼(tirzepatide) 2.5 mg KwikPen® solution for injection in pre-filled pen: Extended Use Beyond Printed Expiry Date, Batches D712074, D720751, D720957

Lanreotide ADVANZ PHARMA 120 mg solution for injection in pre-filled syringe (Lanreotide acetate) Interim Supply of German Stock to Mitigate Supply Disruption

Adoport (tacrolimus) 0.75mg hard capsules Interim Supply of Nordic Stock

Tegretol® 100 mg/5ml Liquid (Carbamazepine): Temporary stock-out and update to posology (reduction of maximum daily dose)

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

Sodiofolin® (folinic acid) 50mg/ml solution for injection/infusion, strengths 100mg and 400mg, PL 11587/0005 – requirement to use a PES or PVDF filter due to observation of particles and potential risk of thrombo-embolic event

SPC changes

New product: Exblifep 2 g/0.5 g (cefepime dihydrochloride monohydrate/enmetazobactam) powder for concentrate for solution for infusion

This 4th generation cephalosporin combined with a penicillanic acid sulfone beta-lactamase inhibitor is licensed for complicated UTIs including pyelonephritis, hospital-acquired pneumonia, and treatment of bacteraemia in association (or potentially linked) with these infections.

Revised SPC: Efexor (venlafaxine) XL prolonged release capsules- all strenghts

The section on other events reported in overdose now includes hypoglycaemia.

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

Immune-mediated myocarditis, which can be fatal, occurred in patients receiving durvalumab. Patients should be monitored for signs and symptoms and managed as recommended in section 4.2 of SPC.

Revised SPC: Provera (medroxyprogesterone acetate) products

Meningiomas reported following long term administration of progestogens, including medroxyprogesterone acetate. Provera should be discontinued if a meningioma is diagnosed. Caution is advised when recommending Provera to patients with a history of meningioma.

Revised SPC: Pirfenidone tablets

Drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, is a potential adverse effect of treatment (frequency unknown). If suggestive signs and symptoms appear, treatment should be discontinued immediately.

SPC changes

Revised SPC: Zinforo (ceftaroline fosamil) 600 mg powder for concentrate for solution for infusion

There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction) with other beta-lactam antibiotics.

Revised SPC: Bimzelx (bimekizumab) 160 mg solution for injection in pre-filled pen

Extension of indication to include treatment of active moderate to severe hidradenitis suppurativa (HS; acne inversa) in adults with an inadequate response to conventional systemic HS therapy.

Revised SPCs: Nilemdo (bempedoic acid) 180mg and Nustendi 180mg/10mg (ezetimibe, bempedoic acid) film-coated tablets

Products are now licensed in adults with established/high risk of atherosclerotic cardiovascular disease, as an adjunct to correction of other risk factors in patients on a maximum tolerated dose of a statin and not adequately controlled with additional ezetimibe.

Revised SPC: Testavan (testosterone) 20mg/g Transdermal gel

The product contains 46.84%w/w ethanol, and it may cause a burning sensation on damaged skin. Because alcohol-based products are flammable, avoid fire, flame or smoking until the gel has dried.

Revised SPC: Vitaros (alprostadil) 3mg/g cream

The product contains 50mg/g (5%w/w) ethanol, and may cause a burning sensation on damaged skin.

Revised SPC: Sivextro (tedizolid phosphate) 200 mg powder for concentrate for solution for infusion

SPC updated with caution & warning following post-marketing experience that co-administration of tedizolid with serotonergic agents can increase risk of serotonin syndrome. These patients should be monitored for cognitive dysfunction, hyperpyrexia, hyperreflexia & incoordination.

Manufacturer Educational RMM

Lecigon (levodopa, carbidopa monohydrate, entacapone) 20mg/ml + 5mg/ml + 20mg/ml intestinal gel

A guide for healthcare professionals includes a recommended follow-up schedule for aftercare consultation for patients on Lecigon with PEG-J insertion. It also includes questions to ask patients and issues to consider during telephone calls and at home visits with patients.

Vanflyta (quizartinib dihydrochloride) 17.7mg and 26.5mg film-coated tablets

A guide for healthcare professionals is provided to read before prescribing and administering this. It focusses on minimising the risk of QTc interval, interactions and monitoring. A patient card is also available - this should be given to any patient receiving Vanflyta treatment.

Drug shortages and discontinuations

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

Shortages:

Shortage of Vecuronium bromide 10mg powder for solution for injection vials

Shortage of Imiquimod (Aldara) 5% cream

Shortage of Quetiapine 150mg, 200mg and 300mg tablets

Shortage of Erythromycin 250mg gastro-resistant tablets

Shortage of Aliskiren (Rasilez) tablets

Shortage of Humalog (insulin lispro) 100units/ml solution for injection 10ml vials

Shortage of Flixotide (fluticasone) 125micrograms/dose and 250micrograms/dose Evohaler

Discontinuations:

Discontinuation of Nortriptyline oral solution sugar-free

Discontinuation of Somatropin (NutropinAq) 10mg/2ml solution for injection cartridges and Somatropin (Humatrope) 6mg, 12mg and 24mg powder and solvent for solution for injection cartridges

Discontinuation of Interferon beta-1b 300microgram powder and solvent for solution for injection vials

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

Specialist Pharmacy Service

Specialist Pharmacy Service

Treating lice during breastfeeding

Wet combing, dimeticone, malathion or permethrin can be used during breastfeeding; choice will depend on the indication. Other treatments can be considered.

Using and prescribing thiamine in alcohol dependence

Intramuscular (IM) Pabrinex has been discontinued and IV Pabrinex is affected by a long-term supply issue. Intravenous or intramuscular thiamine is an alternative to Pabrinex that can be used in people at high risk of Wernicke's encephalopathy (no UK licensed product available).

Auditing Patient Group Directions

SPS have updated the PGD Audit Tool which was developed to support organisations in auditing aspects of PGD use and development. This page hosts a short video which summarises when to undertake and review the results of audits, and an explanation of the SPS audit tool template.

Purchasing for safety

Webpage reviews the principles of purchasing for safety when making purchasing decisions to help support the safe clinical use of medicines and minimise inadvertent harm. Highlights factors that can present an inherent risk (e.g. poor labelling and packaging).

Specialist Pharmacy Service

Specialist Pharmacy Service

Anticoagulant suggestions for adults with swallowing difficulties

This updated page provides information on oral anticoagulant formulations that are suitable for adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

Antiplatelet suggestions for adults with swallowing difficulties

This updated page provides information on antiplatelet formulations that are suitable for use in adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

PPI suggestions for adults with swallowing difficulties

This updated page provides information on proton pump inhibitor (PPI) formulations that are suitable for use in adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

ACEI suggestions for adults with swallowing difficulties

This updated page provides information on angiotensin converting enzyme inhibitor (ACEI) formulations that are suitable for adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

ARB suggestions for adults with swallowing difficulties

This updated page provides information on angiotensin II receptor antagonist formulations that are suitable for adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

SSRI suggestions for adults with swallowing difficulties

This updated page provides information on selective serotonin reuptake inhibitor (SSRI) formulations that are suitable for adults with swallowing difficulties. The choice of medicine formulation should be made on an individual basis, taking account of patient factors.

Quality Matters

Tresiba® FlexTouch 100u/ml shortage and errors

May 2024

Reminder - If a switch to the higher strength Tresiba® FlexTouch 200 u/ml pen is undertaken, healthcare professionals must not adjust the dose of insulin. Pharmacists must ensure that patients are made aware that Tresiba® FlexTouch pen delivery devices dial up in unit increments rather than volume, therefore **no dose change is necessary**, despite using the double strength pen.

NPSA - Potential for inappropriate dosing of insulin when switching insulin degludec (Tresiba) products

National guidance, publications and resources

Pharmacy: Third Report of Session 2023–24

Report finds current funding and contractual framework for community pharmacy is not fit for purpose and a complete overhaul is therefore needed, with a focus on reducing complexity and ensuring mechanisms to fund both dispensing and clinical service delivery.

Are prescribing restrictions for pregabalin working?

Despite reclassification as Class C CD in 2019, NHS data show increase in prescribing since then, specifically for pregabalin.Article looks at what is driving rise in prescribing, who are gabapentinoids prescribed for, co-prescription with opioids rising & what can pharmacists do

Pregabalin prescribing increases by almost 25% since restrictions imposed

The number of patients prescribed pregabalin in England each year has risen by 23% since April 2019, when prescribing restrictions were imposed as part of its reclassification as a Class C controlled drug, increasing from 669,632 during 2018/2019 to 823,231 in 2023/2024.

DTB select: Prescribing changes following fluoroquinolone safety warning

Summary & context provided on study that found regulatory actions on reducing fluoroquinolone use were not linked to significant impact on prescribing in primary care across 6 countries. This aligns with other studies showing limited prescribing impact following safety notices.

Medicines (gonadotrophin-releasing hormone analogues) (emergency prohibition) (England, Wales and Scotland) order 2024

The government has introduced regulations to restrict prescribing & supply of ‘puberty blockers’, to children & young people under 18 in England, Wales & Scotland. The emergency ban will last from 3 June to 3 Sept 2024. This follows the Cass Review into gender identity services.

National guidance, publications and resources

Government introduces 'emergency ban' on overseas prescriptions for puberty blockers

The new arrangements, lasting from 3 June 24 to 3 September 24, which apply to gonadotropin-releasing hormone analogues and include UK private prescriptions, follow the Cass Review recommendation that inappropriate overseas prescribing of hormone supplies should be prevented.

Open letter to political parties ahead of the General Election: a manifesto for community pharmacy

Joint manifesto outlines 6-point plan to commit to a long-term funding solution, support & enhance the workforce, review the medicines supply chain, rollout an enhanced Pharmacy First service, empower community pharmacists, and make pharmacies centres for public health.

Joint statement on Whooping Cough from RCPCH, RCOG, RCM and RCGP

Statement notes whooping cough vaccine uptake levels have steadily fallen in pregnant women, babies and young children, and that this may be responsible for the current unusually high number of cases. It contains advice for the public and links to updated guidance from the UKHSA.

Provisional Never Events 2024/25 data: 1 April 2024 – 30 April 2024

When data for this report were extracted on 27 May 2024, 20 serious incidents were designated by their reporters as Never Events, including 3 cases of overdose of insulin due to use of wrong syringe.

Harm to a child caused by the off-label use of prochlorperazine maleate tablets due to the discontinuation of licensed prochlorperazine mesilate liquid in the UK

Article describes a case report, where a patient established on liquid prochlorperazine mesilate who was switched to crushed prochlorperazine maleate tablets experienced uncontrolled vomiting and multiple healthcare attendances.

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0293 – End stage renal failure due to Tazocin (31 May 2024)

- Patient had previously been prescribed Tazocin twice and was found to have an allergy to the drug which has caused tubulo interstitial nephritis. On each occasion she suffered an acute kidney injury which was successfully treated with steroids.
- The information relating to her allergy to Tazocin was not recorded in the hospital records, although it was available, and accessible through her SCR held by her GP and clinic letters, which were not accessed.

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

- Ref: 2024-0312 - Morphine and Zopiclone toxicity (4 June 2024)
- Patient with PMHx of depression, suicide attempts, being sectioned, chronic alcohol misuse and an opioid dependence. The GP stopped prescribing Zopiclone in 2017 when patient admitted supplementing this with online purchases. Patient was being weaned off Morphine by the GP.
- Admitted to hospital with opioid overdose where he had abrupt cessation of morphine use. Following discharge, hospital letter was not actioned and patient was able to access one weeks' worth of Morphine, prescribed and prescription post-dated prior to his hospital stay.
- Patient had been purchasing Zopiclone online prior to his death. Exact dose and quantity not stated but mentioned as being a large dose and much larger quantity than would ordinarily be prescribed.
- Online company did not contact the GP practice about Zopiclone or check patient's medical history, nor did they inform the GP practice of the purchase.

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

- Ref: 2024-0313 – Digoxin and Clarithromycin interaction (5 June 2024)
- Patient with AF on digoxin. Admitted to hospital with chest infection and prescribed Clarithromycin. Interaction recognised by hospital pharmacist, risk of digoxin toxicity stated in medical notes and alternative drug or monitoring advised.
- No alternative drug was prescribed and no monitoring took place until a week later where results showed elevated digoxin level. Digoxin was withheld.
- Patient displayed no recognised symptoms of digoxin toxicity during her stay in hospital. Patient suffered cardiac arrest after stopping digoxin.
- The clinicians had not seen the entry in medical records due to the way the entries are displayed and the number of entries recorded.

Medicines & Healthcare products Regulatory Agency
Specialist Pharmacy Service
NHS England