SPS Medication Safety Update
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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

Action category: Action

Title: Shortage of Human Albumin 4.5% and 5% dose vials

Broadcast content: There will be limited stock of Human Albumin from July 2024 until at least December 2024. Resolution date for a resumption of full market coverage is still to be confirmed.
The supply disruption is caused by a combination of increased global demand for Human Albumin resulting in one supplier being unable to bring in sufficient stock and a sustained overall increase in demand for the product.
Volumes of Human Albumin 20% remain available but cannot support an uplift to meet the additional demand from the 4.5% and 5% preparations.
Human Albumin is licensed for restoration and maintenance of circulating blood volume where volume deficiency has been demonstrated, and use of a colloid is appropriate. However, in practice it is used extensively for:
•Plasma expansion after paracentesis
•Plasma exchange in neuroinflammatory crises
•Treatment of hepatorenal failure in association with terlipressin
Remaining volumes of Human Albumin should be prioritised for patients that clinical leads have indicated are critical.
This National Patient Safety Alert provides further background, clinical information and actions for providers.

Additional information: This alert is not relevant to Primary Care.

Alert reference: NatPSA/2024/009/DHSC

Action underway deadline: 01-Aug-2024

Action complete deadline: 07-Aug-2024

Medicines & Healthcare products Regulatory Agency

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NHS England

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

Yellow Card Biobank: call to contribute to study of genetic links to side effects

This collaboration between MHRA & Genomics England aims to improve understanding of how patient's genetic makeup may increase risk of experiencing harmful ADR. A Yellow card report should be submitted if patient has experienced one of ADRS included in pilot phase of study.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

[Class 2 Medicines Recall: Strides Pharma UK Limited, Loperamide Hydrochloride Capsules 2mg, EL(24)A/38]

- Strides Pharma UK Ltd is recalling the above batch as a precautionary measure due to an out of specification result for microbial contamination, reported during retesting. Only the batch specified in the table in the notice, a prescribed loperamide product, is known to be affected.

[Class 3 Medicines Recall: Accord-UK Ltd, Trandolapril 0.5mg, 2mg, 4mg Capsules, EL(24)A/35]

- Accord-UK Ltd is recalling specified batches after retesting showed out of specification results. The listed batches in the notice are being recalled as a precautionary measure after testing showed variability of the Trandolapril content beyond permitted levels. Note: the problem is limited to the batches listed in this notification.

[Class 3 Medicines Recall: Glenmark Pharmaceuticals Europe Ltd, Atomoxetine 10mg, 18mg, 25mg, 10mg, 40mg, 60mg, 80mg & 100mg Hard Capsules, EL(24)A/33]

- Glenmark Pharmaceuticals Europe Ltd is recalling some batches after retesting showed out of specification results. The batches specified in the notice are being recalled as a precautionary measure after testing showed variability of the capsule contents beyond permitted levels.

[Class 3 Medicines Recall: Glenmark Pharmaceuticals Europe Ltd, Fingolimod 0.5 mg Hard Capsules, EL(24)A/39]

- Glenmark Pharmaceuticals Europe Ltd is recalling specified batches after retesting showed out of specification results. The tabled batches in the notice are being recalled as a precautionary measure after testing showed variability of the capsule contents beyond permitted levels.

Recent regulator and statutory body activity

Medicines & Healthcare products Regulatory Agency

[Class 4 Medicines Defect Information: Fresenius Kabi Limited, Hartmann's Solution for Injection BP as Steriflex No. 11 or freeflex, EL(24)A/31]

- Fresenius Kabi Limited has informed the MHRA of a labelling error on the packaging of Hartmann's solution for Injection BP as Steriflex No.11 or freeflex. The calcium content in the active ingredient section of the infusion bag label is incorrectly stated as '12 mmol/500 mL'; this should state '1 mmol/500 mL'. The calcium content is stated correctly on the outer carton, and the infusion bags contain the correct amount of calcium (1 mmol/500 mL).

[Class 4 Medicines Defect Information: Aspen Pharma Trading Limited, Co-trimoxazole 80mg/400mg per 5ml adult suspension, EL (24)A/32]

- Aspen Pharma Trading Limited has informed the MHRA that an error has been found in the Patient Information Leaflet. The error is in the section, 'What co-trimoxazole looks like and contents of the pack'. The PIL states '4001mg sulfamethoxazole' instead of '400 mg sulfamethoxazole'. The other sections of the PIL and product information state the correct strength.

[Class 4 Medicines Defect Information: Sandoz Limited, Omeprazole products, EL(24)A/34]

- Sandoz Ltd. has informed the MHRA that there is missing safety information in the Patient Information Leaflet (PIL) and Summary of Product Characteristics (SmPCs) of the specific products listed in this notification. The product information does not include a warning/precaution for severe cutaneous adverse reactions (SCAR) in section 4.4, and adverse events of drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP) in section 4.8 of the SmPC.

[Class 4 Medicines Notification, Star Pharmaceuticals Limited, Diflucan Oral Suspension 40mg/ml, EL(24)A36]

- Star Pharmaceuticals Limited has informed the MHRA that an error has been identified in the Patient Information Leaflet (PIL) for two batches of Diflucan Oral Suspension 40mg/ml. Section 6 of the PIL states "50mg of fluconazole per 5ml" instead of "200mg of fluconazole per 5ml". The other sections of the PIL and product information state the correct strength of 200mg of fluconazole per 5ml

[Class 4 Medicines Defect Information: Dawa Limited, Trazodone Hydrochloride 50mg, 100mg Capsules & 50mg/5ml Oral Solution, EL (24)A/37]

- Dawa Limited has informed the MHRA of an error with the Patient Information Leaflets (PILs) that have been packed in the listed batches of Trazodone Hydrochloride 50mg and 100mg Capsules and Trazodone Hydrochloride 50mg/5ml Oral Solution. The PIL does not contain the latest safety information relating to serotonergic products (trazodone) and the interaction with buprenorphine.

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Advises risk about using the medicine Mysimba

- Following a routine review of the safety of the weight loss medicine Mysimba (naltrexone/bupropion), EMA recommends strengthening existing advice to minimise the risks from interactions between Mysimba and opioid-containing medicines (including painkillers such as morphine and codeine, other opioids used during surgery, and certain medicines for cough, cold or diarrhoea).

Direct HCP communication

Abecma ▼, Breyanzi ▼, Carvykti ▼, Kymriah ▼, Tecartus ▼ and Yescarta ▼ (CD19- or BCMA-directed CAR T-cell therapies): risk of secondary malignancy of T-cell origin

- Secondary malignancies of T-cell origin, including chimeric antigen receptor (CAR)-positive malignancies, have been reported within weeks and up to several years following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy. Patients should be monitored life-long for secondary malignancies.

Privigen (human normal immunoglobulin (IVIg)) 10% 50 mL: flakes reported in some batches of finished product.

- During internal stability testing of Privigen® 10% 50 mL, it was discovered that certain batches exhibited flakes predominantly composed of IgG protein. As a precaution, vials from this batch should not be administered to patients

SPC changes or Manufacturer RMM

Revised SPC: Ethambutol 400 mg Tablets

Drug reaction with eosinophilia and systemic symptoms (DRESS) has been added as an adverse effect reported post-marketing in association with ethambutol treatment (frequency not known).

Revised SPC: Xaluprine (mercaptopurine) 20 mg/ml oral suspension

The PRAC considers a causal relationship between mercaptopurine and stomatitis, cheilitis, mucosal inflammation, pellagra, cholestasis of pregnancy and decreased coagulation factors is at least a reasonable possibility. The product information has been amended accordingly.

Revised SPC: Zyvox (linezolid) – all formulations and strengths

SPC updated to include rare adverse effect of rhabdomyolysis with advice to use with caution in patients with pre-disposing factors for rhabdomyolysis. If signs or symptoms are observed, linezolid should be discontinued.

Revised SPC: Imuran (azathioprine) 25mg and 50mg Tablets

SPC updated to include information about cholestasis in pregnancy with azathioprine, advising that if it occurs, a case by case assessment is necessary on its risk-benefit profile to determine if potential withdrawal or dose reduction, is required.

SPC changes or Manufacturer RMM

Revised SPC: APO-go (apomorphine) PFS Solution for Injection or Infusion- all products

SPC now warns concomitant use of apomorphine with ondansetron may lead to severe hypotension and loss of consciousness and is therefore contraindicated. Such effects might also occur with other 5-HT3 antagonists.

Revised SPC: Padcev (enfortumab vedotin) powder for concentrate for solution for infusion

The SPC has been updated to include serious infections such as sepsis as a commonly encountered adverse effect and diabetic ketoacidosis as one of unknown incidence. It is advised that patients should be carefully monitored for emergence of possible serious infections.

Revised SPC: Olumiant (baricitinib) Film-Coated Tablets – all strengths

The SPC has been updated to state that there have been reports of hypoglycaemia occurring in patients with diabetes when JAK inhibitor treatment (including baricitinib) is started. It is noted that dose adjustment of anti-diabetic medicines may be necessary should this occur.

Revised SPC: Decapeptyl SR (triptorelin acetate) 3mg powder and solvent for suspension for injection

SPC updated to note convulsions have been reported with GnRH analogues, including triptorelin, particularly in women. Some of these patients had risk factors for seizures (e.g. history of epilepsy, intracranial tumours, co-medication with drugs known to present seizure risk).

Drug shortages and discontinuations

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

Shortage of Human Albumin 4.5/5% vials

- A National Patient Safety Alert was issued on 30 July 2024

Shortage of Gastrografin gastroenteral solution

- Anticipated resupply date 8th November 2024
- Omnipaque/Visipaque are able to support demand

Shortage of Alteplase 10/20/50mg powder and solvent for solutions for injection and infusion vials

- Anticipated resupply date 6th September 2024
- Streptokinase/Urokinase can support an uplift in demand

Drug shortages and discontinuations

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

Shortage of Desmopressin (DDAVP) 4mcg/ml solution for injection ampoules

- Anticipated resupply date 20th September 2024
- Specialist importers can source unlicensed ampoules

Discontinuation of Acetazolamide (Diamox SR) 250mg MR Capsules

- Shortage amended to discontinuation – Capsules have been unavailable since 10 Feb 2023
- Immediate release 250mg tablets remain available

Specialist Pharmacy Service

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Treating acute hypokalemia in adults

- Untreated hypokalaemia can lead to life threatening arrhythmias. SPS guide on the safe management of potassium for acute hypokalaemia.

Assessing suitability of medicines in a ketogenic diet

- SPS advises on how to establish the carbohydrate content of a medicine and assess its suitability for a person on a medical ketogenic diet

Assessing injectables for enteral administration

- Clinical decisions on the use of injectable formulations for enteral administration should be guided by safety and practicality.

Managing reactions to dental local anaesthetic injections

- Reactions to dental local anaesthetics (LA) are usually psychogenic. SPS describes symptoms and management of allergy, adverse effects and psychogenic reactions.

License and supporting evidence for ustekunimab bisoimilars

- SPS advises on the indications, formulations, and evidence of licensed ustekinumab biosimilars

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NHS England

National guidance, publications and resources

National Measles Guidelines Update [July 2024] – new section on –neonates born to measles infected mothers

British Medical Journal

WHO and African CDC declare mpox a public health emergency

- The World Health Organization has declared mpox a public health emergency of international concern (PHEIC) for the second time, warning that the viral disease could spread quickly to new countries.
- The number of infections is 160% higher than in 2023, and the virus has spread to six new countries in 10 days, Jean Kaseya, director general of the African CDC told a press conference on 8 August.
- The monkeypox virus comes from the same family as the smallpox virus and is believed to circulate in small mammals, such as monkeys and squirrels.1 In humans the infection commonly causes a skin rash or pus filled lesions, and sometimes flu-like symptoms

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

Ref: 2024-0457: Prevention of future death report

Date of report: 16/08/2024

It was concluded that the death was drug related and that the actions of the Pharmacy contributed more than minimally in supplying additional methadone on multiple occasions, not in accordance with the prescription for such.

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

The Pharmacist in this case gave evidence that he believed that he had discretion to provide CNS depressing drugs in advance, and not in accordance with the prescription for supervised provision of X drug on specific days and maintained this was a “standard practice” when the Pharmacy was open for half a day on Saturdays.

He interpreted the wording on the prescription namely “please dispense instalments due on a Pharmacy closed days on a prior suitable date” to include Saturdays when the Pharmacy was open for half a day, despite the prescriptions stipulating the specific days that the drug was to be provided, including specification of the dose each Saturday.

This led to a situation where the deceased was in possession of multiple doses of a controlled drug, on a regular basis in the period leading up to his death, which was not in accordance with the prescription, which had been carefully considered to attempt to manage the obvious risks of such. The Pharmacy had been specifically chosen by the deceased’s drug treatment provider because it was able to provide supervised administration on a 6 day per week basis and because in their assessment this was required to attempt to manage the risks inherent in the deceased having access to multiple doses.

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