SPS Medication Safety Update
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Observatory of recent safe medication practice research, reports, and publications

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Patient Safety Alerts

CAS alert - Supply of Licensed and Unlicensed Epidural Infusion Bags

- There are supply issues impacting Fresenius Kabi (FK) unlicensed epidural bags containing bupivacaine only and levobupivacaine with fentanyl. These are also impacting Sintetica's licensed epidural bags containing bupivacaine only and bupivacaine with fentanyl.
- Review products in use and current stock holding, to establish the impact of the supply shortage.

Recent regulator and statutory body activity

MHRA

New Product: Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose concentrate for dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified)

- A new, age-appropriate presentation of the bivalent vaccine, which is for use in children aged 5 to 11 years. Minor, consequential updates have been made to the product information for the other Comirnaty bivalent vaccines (for use in adults and adolescents).

MHRA grants Conditional Marketing Authorization for Kinpeygo® (budesonide 4mg modified release capsules) for the treatment of primary immunoglobulin A (IgA) nephropathy

- Kinpeygo is a hybrid medicine of Entocort but has a different formulation. It is approved for the treatment of primary IgA nephropathy in adults at risk of rapid disease progression with a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/gram.
- **MHRA approves upadacitinib for the treatment of moderately to severely active Crohn's disease**
- Approval of the Janus kinase inhibitor for the treatment of patients who have lost response, had an inadequate response, or were intolerant to either a biological agent or conventional therapy, was based on results from the U-EXCEED, U-EXCEL and U-ENDURE Phase III studies.

Recent regulator and statutory body activity

MHRA

Drug Safety Update

Topical testosterone (Testogel): risk of harm to children following accidental exposure

- Premature puberty and genital enlargement have been reported in children who were in close physical contact with an adult using topical testosterone and who were repeatedly accidentally exposed to this medicine. Patients should be counselled on measures to reduce these risks e.g advise patients to wash their hands after application of topical testosterone, cover the application site with clothing once the product has dried, and wash the application site before physical contact with another adult or child.

Xaqua (metolazone) 5mg tablets: exercise caution when switching patients between metolazone preparations

- Caution is advised if switching people between different metolazone preparations as rate and extent of absorption are formulation dependent, and can impact bioavailability of product. Licensed formulation (Xaqua) should be used in preference to unlicensed imports in new patients.

Pharmacovigilance Risk Assessment Committee (PRAC)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European PRAC starts safety review of pseudoephedrine-containing medicines

- This review by the EMA's safety committee was initiated following concerns about the risk of posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome, cases of which have been reported in pharmacovigilance databases and medical literature.

European Medicines Agency accepts Marketing Authorization Application for AVT04, biosimilar to Stelara® (ustekinumab)

- Company had announced that a confirmatory clinical, safety and efficacy study for AVT04 had met its primary endpoint, demonstrating therapeutic equivalence with the Stelara reference product in patients with moderate to severe chronic plaque-type psoriasis.

EMA update on shortages of antibiotics in the EU

- EU regulators have met with main parties involved in supply chain of amoxicillin to provide regulatory support so as to increase production capacity. At present, ongoing shortage is not considered to be a major event & mitigating measures are improving short term supply situation

SPC changes or Manufacturer RMM

Revised SPC: Calcium Folinate 10 mg/ml Injection

- SPC updated to include statements regarding insufficient data with respect to reproductive toxicity and fertility, and section 5.3 now includes information on embryo-foetal toxicity studies in rats and rabbits.

Revised SPC: Voltarol (diclofenac sodium) – all presentations

- Updated warnings incl risk of oligohydramnios from 20th week of pregnancy therefore use in 1st/2nd trimester is cautioned. Use in 3rd trimester is contraindicated due to cardiopulmonary toxicity, renal dysfunction, prolongation of bleeding, & inhibition of uterine contractions.

Revised SPC: Rapifen (alfentanil)

- SPC updated with information on the risk of developing opioid use disorder, and to note the concomitant use of opioids and gabapentinoids increases the risk of opioid overdose, respiratory depression and death.

- **Revised SPC: Asacol (mesalazine) preparations**

- Drug reaction with eosinophilia and systemic symptoms (DRESS) has been added as a potential adverse effect (frequency unknown). It should be discontinued at first appearance of signs/symptoms of severe skin reactions, eg. rash, mucosal lesions, or other signs of hypersensitivity.

SPC changes or Manufacturer RMM

Revised SPC: Alunbrig (brigatinib) film-coated tablets- all strengths

- SPC updated to advise that the median time to onset for amylase elevations has been amended to 16 days and a new photosensitivity and photodermatosis section has been added.

Revised SPC: Seroxat (paroxetine)- all presentations

Sections on QT Prolongation (QTP) & implicated drugs have been added. Caution advised in patients with a (family) history of QTP, concomitant use of anti-arrhythmics/other drugs prolonging QT interval, relevant pre-existing cardiac disease, & hypokalaemia/hypomagnesemia

Revised SPC: Salofalk (mesalazine) – all preparations

- Updated warnings include: red-brown urine discolouration after contact with sodium hypochlorite bleach, and recommendation to discontinue treatment in event of deterioration of renal function, serious blood dyscrasias, cardiac hypersensitivity and DRESS adverse reactions.

Revised SPC: Revlimid (lenalidomide) Hard Capsules

- SPC updated with new renal dosing information for patients with follicular lymphoma and a warning highlighting that male patients should not donate semen or sperm during, and for at least 7 days after the end of treatment.

SPC changes or Manufacturer RMM

Revised SPC: Imodium (loperamide) products

- SPC now warns that upon cessation, cases of drug withdrawal syndrome have been observed in individuals abusing, misusing, or intentionally overdosing with excessively large doses of loperamide.

Risk minimisation materials: Amfexa (dexamfetamine sulfate) tablets

- A number of resources have been published including information for patient and carers, pharmacists and physicians and an introduction which facilitates awareness and adoption of recommendations for the use of dexamfetamine sulfate.

Risk minimisation materials: Nexviadyme (avalglucosidase alfa) 100 mg powder for concentrate for solution for infusion

- Materials for healthcare professionals include a guide on home infusion and a guide to immunological testing which will help in the management of infusion-associated reactions and hypersensitivity reactions, and loss of treatment response due to antidrug antibodies.

Risk minimisation materials: Amfexa (dexamfetamine sulfate) tablets

- A number of resources including checklists for prescribing; monitoring growth, psychiatric and cardiovascular status; and discontinuing treatment and growth charts intended to assess the growth of school age boys and girls have been published.

Drug shortages & Discontinuations

- **Recent medicine shortages and discontinuations are available via: the SPS Medicines Supply Tool (registration required to access)**
- **This is not a comprehensive list.**

New Shortages:

- Aprotinin 10,000 KIU/ml Injection BP, Paracetamol 120mg suppositories, Lamotrigine (generic) 5mg dispersible tablets sugar free
- Medroxyprogesterone (Provera®) 2.5mg tablets , Promethazine hydrochloride (Phenergan® elixir) 5mg/5ml oral solution sugar free and Midazolam 2mg/2ml solution for injection ampoules

Updates on existing shortages:

- Methylphenidate prolonged-release tablets , Tenecteplase (Metalyse) 10,000 units powder and solvent for solution for injection and Estradot ® 50mcg and 100mcg patches.

Discontinuations:

- Instanyl (fentanyl) nasal sprays (50/100/200 micrograms), Fluoxetine 10mg tablets, Insuman Comb 25 cartridges and pre-filled Solostar pens and Insuman Basal cartridges and pre-filled Solostar pens

Specialist Pharmacy Services

Specialist Pharmacy Service

Antidepressant switching - Establishing whether a person needs to switch their antidepressant

- Guidance provides advice on how to choose an antidepressant based on its adverse effect profile, interactions, previous response, patient's individual characteristics and how to identify complex switches which should be undertaken under the advice of a mental health specialist (part of a series of guidance).

Using contraception with enzyme-inducing medicines

- Guidance on using contraception with enzyme inducing medicines

Using tricyclic antidepressants during breastfeeding

- This webpage resource recommends using imipramine and nortriptyline as TCAs of choice for all indications during breastfeeding owing to their lower sedating effects, thereby reducing risk of infant sedation. Recommendations apply to full term and healthy infants only.

Using insulins during breastfeeding

- Guidance on continuing or initiating insulins in breastfeeding mothers. Recommendations apply to full term and healthy infants only.

Specialist Pharmacy Service MHRA NHS England

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Mental health medicines: useful resources to support answering questions

- This webpage discusses the resources available to help primary care healthcare professionals find information on psychotropic and other medicines used in psychiatry.

HRT Overview

- HRT availability varies currently, SPS have produced a page which lists available and affected HRT products, with links to individual posts for affected products where necessary

List of new product launches

- **Update:** List of new products and formulations that have launched, and had licence changes approved in 2022.

National guidance, publications and resources

Patient Safety Commissioner: 100 days report

- The report outlines how Dr Hughes (first patient safety commissioner for England) has heard from patients, families and healthcare professionals on what needs to change to improve the safety of medicines and medical devices. She calls for a cultural change throughout the health system.
- The priorities highlighted include sodium valproate, with planned actions including:
- working with health leaders to ensure that all relevant patients are on a Pregnancy Prevention Plan (PPP) and given the necessary information
- collaboration with partners to ensure annual reviews are carried out by specialist prescribers
- working with partners across healthcare to eliminate dispensing of sodium valproate in unlabelled white boxes

Source: The Patient's Association

Healthcare Safety Investigation Branch (HSIB) National Report - Access to critical patient information at the bedside

- This investigation aims to improve patient safety by supporting staff to access critical information about patients, at their bedsides, in emergency situations.
- One recommendation is for the RCN to develop guidance for ward-based nursing handovers with consideration of the following: how handovers are organised, their content, the environment in which they take place and the technology needed to support them.

National guidance, publications and resources

NPPG Position Statement – alternative to oral rehydration solutions to Dioralyte®

- Published in response to Medicines Supply Notification (MSN/2022/082) for shortage of Dioralyte® . Supports HCPs in making decisions on prescribing most suitable available alternatives and outlines product compositions. As well as advantages and disadvantages associated with them.

Government advisers warn of ‘negative impact’ of two-clinician sign-off on valproate patients

- Potential negative impacts on the proposed two-clinician sign off have been noted at the Valproate Safety Implementation Group, e.g. difficulties for appropriate patients accessing treatment, and the pressures on the workforce to deliver it. Some charities have voiced concerns

Source: Pharmaceutical Journal

Prevention of Future Death Reports (Regulation 28)

Courts and Tribunals Judiciary

- No medication related deaths located this month.

Specialist Pharmacy Service MHRA NHS England

Primary research- Medication Safety

- **Preventable harm because of outpatient medication errors among children with leukemia and lymphoma: A multisite longitudinal assessment**

Source: American Cancer Society Journals

- **Near-Miss Events Detected Using the Emergency Department Trigger Tool**

Source: Journal of Patient safety

- **Professionals' Perception of a Strategy to Avoid Interruptions During Medication Handling**

Source: Journal of Clinical Nursing

- **Shape Matters: A Neglected Feature of Medication Safety : Why Regulating the Shape of Medication Containers Can Improve Medication Safety**

Source: Journal of Medical Systems

Primary research- Medication Safety

- **Standardized neonatal continuous infusion concentrations: A quality improvement initiative.**

Source: American Society of Health-System Pharmacists

- **The accuracy of the Global Trigger Tool is higher for the identification of adverse events of greater harm: a diagnostic test study.**

Source: International Journal for Quality in Health Care

- **Take action now to prevent medication errors: lessons from a fatal error involving an automated dispensing cabinet**

Source: British Journal of Anaesthesia