

SPS/UKMi Observatory

June 2022

Observatory of recent safe medication practice research, reports, and publications

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Recent regulator and statutory body activity



Improvement



NovoRapid PumpCart in the Roche Accu-Chek Inight insulin pump: risk of insulin leakage causing hyperglycaemia and diabetic ketoacidosis (NatPSA/2022/004/MHRA)

Serious reports of harm associated with insulin leakage for the NovoRapid PumpCart prefilled insulin cartridge in the Accu-Chek Insight Insulin pump. In some patients, there were serious consequences arising from inadequate supply of insulin, including diabetic ketoacidosis (DKA).

Recent regulator and statutory body activity



National Patient Safety Alert: Philips Health Systems V60, V60 Plus and V680 ventilators: potential unexpected shutdown leading to complete loss of ventilation (NatPSA/2022/002/MHRA)

Potential unexpected shutdowns of all of their V60 and V60 Plus non-invasive ventilators. All V680 invasive ventilators used in critical care settings are also affected.

Class 2 Medicines Recall: hameln pharma ltd, Water for Injections BP – 100ml vial, EL (22)A/24

Batches recalled additional to the batch recalled on 15 February 2022 (reference EL(22)A/06).

National Patient Safety Alert: NovoRapid PumpCart in the Roche Accu-Chek Insight insulin pump: risk of insulin leakage causing hyperglycaemia and diabetic ketoacidosis (NatPSA/2022/004/MHRA)

Serious reports of harm associated with insulin leakage for the NovoRapid PumpCart prefilled insulin cartridge in the Accu-Chek Insight Insulin pump. In some patients, there were serious consequences arising from inadequate supply of insulin, including diabetic ketoacidosis (DKA).

Class 4 Medicines Defect Information: Orifarm UK Ltd, Loprazolam 1mg Tablets, EL (22)A/25
Error with the PIL packaged within the packs of certain batches. The product name stated in the heading of the PIL has been spelt incorrectly as “lorazolam”, instead of “loprazolam”. All other sections of the PIL are unaffected.

Recent regulator and statutory body activity



Company led medicines recall: Consilient Health UK Ltd, Invita D3 800 IU Soft Capsules, CLMR (22)A/03

Batch recalled due to limited units from the batch being distributed prior to batch release. No indications of any quality or safety concerns.

Class 4 Medicines Defect Information: Esomeprazole 40mg Powder for Solution for Injection/Infusion, EL (22)A/26

Product Code/GTIN (PC) number found on batch 2200855 is incorrect. The GTIN number that should have been allocated for this batch is 5200040321010, however, 05026468771424 was applied in error which scans the batch as Acetylcysteine 200mg/ml injection (2g/10ml ampoules).

Class 4 Medicines Defect Information: OxyContin 20 mg prolonged release tablets, EL (22)A/27

Error relating to the Braille printed on the cartons. The Braille message on the Oxycontin 20mg prolonged release tablets incorrectly states strength as 15mg.

Class 2 Medicines Recall: Bristol Laboratories Limited, Phenobarbital 60 mg Tablets, EL(22)A/28

Batch recalled due to low dissolution test results reported during ongoing stability studies.

Company led medicines recall: PCCA Limited, Ketamine 50mg in 5ml Oral Solution and Ketamine 100mg in 5ml Oral Solution (unlicensed medicines), CLMR (22)A/04

Issue with the appearance of Ketamine 50mg in 5ml Oral Solution and Ketamine 100mg in 5ml Oral Solution – bottles observed to contain crystalline material.

Recent regulator and statutory body activity



Class 4 Medicines Defect Information: Altan Pharma Limited, Phenylephrine 0.08 mg/ml - solution for injection/infusion, EL(22)A/29

Error relating to the product packaging. The incorrect concentration of phenylephrine base is provided on the overwrapping bag label.

Company led medicines recall: A.Vogel Ltd, Linoforce granules 12 years plus (THR 13668/0021), CLMR (22)A/05

Specific batch of Pharmacy only medicine recalled due to a small number of packs that were inadvertently supplied to non-pharmacy retail outlets.

Drug Safety Update

Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk

Decreased vitamin B12 levels, or vitamin B12 deficiency, is now considered to be a common side effect in patients on metformin treatment, especially in those receiving a higher dose or longer treatment duration and in those with existing risk factors. Check vitamin B12 serum levels in patients being treated with metformin who have symptoms suggestive of vitamin B12 deficiency. Periodic monitoring for patients with risk factors for vitamin B12 deficiency should also be considered.

Roche Accu-Chek Insight insulin pump with NovoRapid PumpCart insulin cartridges: alert following cases of insulin leakage

National Patient Safety Alert following serious reports of harm associated with insulin leakage during use of the Accu-Chek Insight Insulin pump with NovoRapid PumpCart prefilled insulin cartridges. Patients should be moved onto alternative insulin pumps where possible.

COVID-19 vaccines and medicines: updates for June 2022

Recent information relating to COVID-19 vaccines and medicines that has been published since the May 2022 issue of Drug Safety Update, up to 17 June 2022.

Recent regulator and statutory body activity



Drug Safety Update

Letters and medicine recalls sent to healthcare professionals in May 2022

Letters:

- Rucaparib (Rubraca)
- Zovirax (aciclovir)
- Zejula ▼ (niraparib)
- Vaxzevria, suspension for injection COVID-19 Vaccine (ChAdOx1-S [recombinant])
- Abraxane (paclitaxel albumin)
- COMIRNATY ▼ 10 micrograms/dose concentrate for dispersion for injection (tozinameran), COVID-19 mRNA Vaccine (nucleoside-modified) for children 5 to 11 years
- Natpar (parathyroid hormone (rDNA))
- Lymphoseek (tilmanocept)

Medicine Recalls and Notifications:

- Mefenamic Acid 500mg film coated tablets
- Zovirax I.V. 500 mg
- Water for Injections BP – 100ml vial
- Loprazolam 1mg Tablets
- Invita D3 800 IU Soft Capsules
- Esomeprazole 40mg Powder for Solution for Injection/Infusion

Medical Device Safety Information:

NovoRapid PumpCart in the Roche Accu-Chek Insight insulin pump



Recent regulator and statutory body activity



CAS alerts

NovoRapid PumpCart in the Roche Accu-Chek Insight insulin pump: risk of insulin leakage causing hyperglycaemia and diabetic ketoacidosis

Serious reports of harm associated with insulin leakage for the NovoRapid PumpCart prefilled insulin cartridge in the Accu-Chek Insight Insulin pump. In some patients, there were serious consequences arising from inadequate supply of insulin, including diabetic ketoacidosis (DKA).

Antivirals or Neutralising Monoclonal Antibodies in the Treatment of Hospital-Onset COVID-19 (CEM/CMO/2022/009)

Independent Advisory Group report on the groups of 'highest' risk patients who are potentially eligible for COVID treatments under this policy.

Antivirals or Neutralising Antibodies for Non-Hospitalised Patients with COVID-19 (CEM/CMO/2022/010)

Independent Advisory Group report on the groups of patients who are potentially eligible for community based COVID treatments under this policy.

Contamination of hygiene products with Pseudomonas aeruginosa

Pseudomonas aeruginosa has been detected in hygiene products manufactured by Vernacare.

Recent regulator and statutory body activity



Quality Matters:

- Legal Defence Against Dispensing Errors—Hospitals
- Risk of Thrombosis when stopping Xagrid® (anagrelide) - abrupt treatment discontinuation should be avoided due to the risk of sudden increase in platelet counts and potentially fatal thrombotic complications, such as cerebral infarction
- Accu-Chek® Insight Device Alert - National Patient Safety Alert on the risk of insulin leakage within the pump causing hyperglycaemia and diabetic ketoacidosis
- DigiFab® - Digoxin Injection Confusion - due to shortages of IV digoxin, nursing staff searching for stock may come across DigiFab® in Emergency Cupboards

Pharmacovigilance Risk Assessment Committee (PRAC)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European PRAC finds no link between mRNA COVID-19 vaccines and absence of menstruation

Insufficient evidence to establish a causal association between the COVID-19 vaccines Comirnaty and Spikevax and cases of amenorrhoea (defined as no bleeding for a period of >90 days).

European PRAC recommends monitoring of vision disorders in paediatric patients treated with crizotinib (Xalkori)

Reports of vision disorders in paediatric patients treated for non-small cell lung cancer and anaplastic large cell lymphoma. Healthcare professionals are advised to conduct baseline ophthalmologic examinations and monitor for vision disorders and ocular toxicity.

Committee for Medicinal Products for Human Use (CHMP)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European CHMP negative opinion on trastuzumab biosimilars (Hervelous and Tuznue)

Concerns about differences in the manufacturing process used during clinical testing and commercial production and insufficient evidence to show that the commercially produced medicine will be biosimilar to the reference medicine.

European CHMP positive opinion for Cevenfacta (Eptacog beta-activated)

Blood coagulation factor for the prevention and treatment of bleeding episodes in adults or adolescents with congenital haemophilia undergoing surgery or invasive procedures.

European CHMP positive opinion for generic sitagliptin/metformin hydrochloride (Accord)

Bioequivalent generic of Janumet approved for the same licensed indications for adult patients with type 2 diabetes mellitus.

European CHMP positive opinion for Kinpeygo (budesonide 4mg modified release capsules)

Hybrid medicine of Entocort but has a different formulation and is indicated for the treatment of primary immunoglobulin A nephropathy in adults at risk of rapid disease progression with a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/gram.

European CHMP positive opinion for Xenpozyme (olipudase alfa)

Enzyme replacement therapy for the treatment of non-Central Nervous System manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B ASMD, historically referred to as Niemann-Pick disease.

Committee for Medicinal Products for Human Use (CHMP)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European CHMP recommends license extension of Cosentyx (secukinumab)

License extension for juvenile idiopathic arthritis (JIA), enthesitis-related arthritis & JIA, alone or in combination with methotrexate, in patients ≥ 6 years whose disease has responded inadequately to, or cannot tolerate, conventional therapy.

European CHMP recommends license extension of Keytruda (pembrolizumab)

License extension for the treatment of adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma or Stage IIB/IIC melanoma that has undergone complete resection.

European CHMP recommends license extension of Nexpovio (Selinexor)

License extension for use in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

European CHMP recommends license extension of Rinvoq (upadacitinib)

License extension for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent.

Direct HCP communication

SPC changes according to BNF chapter

1. Gastro-intestinal system

- Imodium (loperamide) – all formulations
- Duphalac (lactulose) 3.335 g/5 ml Oral Solution
- Pancrex V (pancreatin) 340 mg hard capsules – store in refrigerator

2. Cardiovascular system

- Labetalol 5 mg/ml solution for injection/ infusion
- Rosuvastatin film-coated tablets – all strengths
- Jardiance (empagliflozin) film-coated tablets
- Plavix (clopidogrel) film-coated tablets
- Amiodarone Hydrochloride 50 mg/ml Concentrate for Solution for Injection/Infusion (Hameln) – reports of crystallisation

3. Respiratory system

4. Nervous system

- Zamadol (tramadol) 50 mg Capsules
- BOTOX (botulinum toxin type 1) – all presentations
- PecFent (fentanyl citrate) 400 micrograms/spray nasal spray, solution
- Vimpat (lacosamide) preparations
- Reminyl (galantamine hydrobromide) XL prolonged release capsules (all strengths) and solution
- Tylox (codeine, paracetamol) 30 mg / 500 mg hard capsules
- Cipralex (escitalopram) 5 mg film-coated tablets
- Myloxifin (oxycodone hydrochloride, naloxone hydrochloride dehydrate) prolonged-release tablets – all strengths

SPC changes according to BNF chapter

5. Infection

- Vosevi (sofosbuvir, velpatasvir and voxilaprevir) tablets
- Piperacillin/Tazobactam Powder for Solution for Infusion
- Doravirine products (Pifeltro 100 mg film-coated tablets, Delstrigo 100mg/300mg/245mg film-coated tablets)
- Epclusa (sofosbuvir and velpatasvir) tablets
- Xevudy (sotrovimab) 500 mg concentrate for solution for infusion
- Vaborem 1g/1g (meropenem, and vaborbactam) infusion
- Erythromycin 1g Powder for Solution for Infusion

6. Endocrine system

- Glucophage SR (metformin) prolonged release tablets – all strengths – use in pregnancy and in periconceptual phase
- Estradot (estradiol) transdermal patches- all strengths
- Progynova (estradiol valerate) 1 and 2 mg tablets
- Jardiance (empagliflozin) film-coated tablets

7. Genito-urinary system

SPC changes according to BNF chapter

8. Immune system and malignant disease

- Mayzent (siponimod) film-coated tablets
- Keytruda (pembrolizumab) concentrate for solution for infusion – 2 updates
- Azacitidine injection
- Glivec (imatinib) tablets
- Obinutuzumab (Gazyvaro) concentrate for solution for infusion
- Tacrolimus (all formulations)
- Trisenox (arsenic trioxide) 2mg/ml Concentration for Solution for Infusion
- Rubraca (rucaparib camsylate) film-coated tablets – all strengths
- Nulojix (belatacept) 250 mg powder for concentrate for solution for infusion
- Tyverb (lapatinib) 250 mg film-coated tablets
- Certican (everolimus) Tablets
- Tysabri (natalizumab) 150 and 300 mg solution for injection in pre-filled syringe

9. Blood and nutrition

- Galafold (migalastat hydrochloride) 123 mg hard capsules

10. Musculoskeletal system

- Infliximab (Zessly) powder for concentrate for solution for infusion
- Cosentyx (secukinumab) preparations
- Rinvoq (upadacitinib) prolonged-release tablets- all strengths

11. Eye

- Xalatan (latanoprost) 50 micrograms/ml eye drops solution
- Xalacom (latanoprost, timolol maleate) eye drops, solution

12. Ear, nose and oropharynx

SPC changes according to BNF chapter

13. Skin

- Tacrolimus (all formulations)
- Podophyllotoxin (Condylina) 5 mg/ml Cutaneous Solution
- Diprosone (betamethasone dipropionate) & Diprosalic (betamethasone dipropionate/salicylic acid) – all presentations – withdrawal syndrome
- Elocon (mometasone furoate) – all presentations – withdrawal syndrome

14. Vaccines

- Comirnaty 10 micrograms/dose concentrate for dispersion for injection Children 5 to 11 years COVID-19 mRNA Vaccine (nucleoside modified)
- Nimenrix (meningococcal groups A, C, W-135 and Y conjugate vaccine) powder and solvent for solution for injection in pre-filled syringe
- Shingrix powder and suspension for suspension for injection, Herpes zoster vaccine (recombinant, adjuvanted)
- Spikevax (formerly COVID-19 Vaccine Moderna)
- Product information update for Spikevax COVID-19 vaccine

15. Anaesthesia

16. Emergency treatment of poisoning

Drug shortages and discontinuations

Shortages:

Fluoxetine 20mg dispersible tablets sugar free

Estradiol (Oestrogel® Pump-Pack 750microgram per actuation) 0.06% gel

Estriol (Ovestin® 1mg) 0.1% cream

Estradiol (Sandrena®) 500microgram and 1mg gel sachets

Estradiol (Lenzetto®) 1.53mg/dose transdermal spray

Methylphenidate (Xaggitin® XL) 18mg, 27mg, 36mg and 54mg prolonged-release tablets

Atorvastatin (Lipitor®) 10mg chewable tablets

Paracetamol 120mg suppositories

Hydrocortisone 2.5mg Muco-Adhesive Buccal Tablets

Remifentanyl – all strengths and presentations

Triamcinolone hexacetonide 20mg/1ml suspension for injection ampoules

Vimovo 500mg/20mg modified-release tablets – now resolved

Contrast media agents - Omnipaque™ and Visipaque™

Vincristine Sulphate 1mg/1ml and 2mg/2ml solution for injection vials

Discontinuations:

Colestipol (Colestid®) orange and plain 5g granules sachets

Mitomycin 2mg powder for solution for injection (Kyowa)

Oxybutynin (Lyrinel XL) 5mg and 10mg prolonged release tablets

Specialist Pharmacy Services



SPS Spotlight monthly digest - May

Updates on existing materials and activities from across SPS, and signpost to upcoming events and activities. Includes resources to support healthcare professionals working in all areas of the health system.

Using smallpox vaccine for monkeypox exposure

Guidance for giving smallpox vaccine pre or post exposure during a monkeypox incident including current available stock, licence status, legal mechanism, handling and clinical information

How to develop a Patient Group Direction

Guide to help organisations, potential authors and signatories of PGDs consider, plan and follow necessary processes involved in the development and authorisation of PGDs.

Use of individually named medicines in HM Prisons

Guidance for the use of individually named patient supplies versus stock medication for residential custodial settings.

Parkinson's disease medicines formulations for adults with swallowing difficulties

Covers the interaction between Parkinson's disease medicines and food, licensed medicines in suitable formulations, licensed medicines used in an unlicensed manner and Special-order medicines.

Specialist Pharmacy Services



Using chloramphenicol in breastfeeding

Topical chloramphenicol can be used in women who are breastfeeding with caution and monitoring, but systemic chloramphenicol is not recommended, as discussed in this resource. The advice applies to full term and healthy infants.

Using Proton Pump Inhibitors (PPIs) alongside warfarin – clinical considerations

Considers the management and clinical impact on anticoagulation when prescribing PPI's alongside warfarin. It outlines the evidence and mechanism for the interaction, choosing a suitable PPI, monitoring when initiating and stopping a PPI and counselling points.

Using haem arginate (human hemin) in acute porphyria attacks

Use of haem arginate should always be discussed with the National Acute Porphyria Service. It covers dosage, method of administration, cautions and monitoring as well as describing the mechanism of action in detail.

Compatibility of nebuliser solution combinations

Mixing nebuliser solutions is often done but rarely licenced. It covers compatibility of these solutions that have been studied along with a handy compatibility tool.

SPS Spotlight Monthly Digest June 2022

Set of slides provide updates on existing materials and activities from across SPS, and signpost to upcoming events and activities, including resources to support healthcare professionals working in all areas of the health system.

National guidance, publications and resources

DHSC: Further action taken to improve supply of HRT

SSPs to allow pharmacists to safely offer substitute high-demand products – Oestrogel, Ovestin cream, Lenzetto transdermal spray and Sandrena gel sachets – with appropriate alternatives, such as transdermal patches, which are in good supply.

UKHSA: Investigation into acute hepatitis of unknown aetiology in children in England:

Technical briefing 3

There are 197 paediatric cases of acute non-A-E hepatitis with serum transaminases > 500 IU/l, of which 11 have received a liver transplant. The leading hypotheses remain those which involve adenovirus; however, the role of SARS-CoV-2 is still being considered.

BNF/BNFC Newsletter May 2022

One new drug monograph (pegcetacoplan) and updated guidance on glaucoma and ocular hypertension added to BNF; updated indications and dosing for remdesevir in the BNF and BNFC; MHRA advice on amiodarone, cladribine and metformin hydrochloride.

Off label use of chloral hydrate to sedate neonates and children in critical care – NPPG position statement

Information and clarity around the off-label use of chloral hydrate in management of neonates & children when used to provide sedation in critical care, information on the indications for use, advice on how to use it & when to wean doses.

National guidance, publications and resources

UKHSA: Monkeypox vaccination during a monkeypox incident

Information on pre-exposure vaccination for occupational exposure; post-exposure vaccination; vaccine prescribing and administration; consent/record forms; Imvanex® patient information leaflet and monkeypox contact tracing classification and vaccination matrix.

Asthma quality improvement toolkit published

This toolkit is designed to help UK general practices improve asthma outcomes whilst also reducing carbon emissions. It contains step-by-step quality improvement projects and is accompanied by various project resources.

NIHR alert: A short course of antibiotics is effective for treating pneumonia in children

A UK hospital study (n=814) found a 3-day course of amoxicillin was as effective as a 7-day course for treating children with community-acquired pneumonia.

The Innovative Medicines Fund Principles

£340 million has been made available through the new Innovative Medicines Fund which will provide more rapid access to innovative treatments, with similar terms to the Cancer Drugs Fund. This document sets out NHS England's guidance and policy approach.

Vaccine update: issue 330, June 2022, COVID-19 spring special edition

COVID-19 vaccination update covers Autumn COVID-19 boosters, changes to COVID-19 Green Book chapter 14a, guide to COVID-19 vaccinations received overseas, COVID-19 vaccinator assessment tool and outcomes of a vaccine uptake programme.

National guidance, publications and resources

More healthcare professionals given powers to certify fit notes

Regulations laid on 10 June 2022 to allow nurses, occupational therapists, **pharmacists**, and physiotherapists to certify fit notes digitally will come into effect on 1 July 2022 and will be delivered in general practice and hospital settings.

Joint position statement by the British Menopause Society, Royal College of Obstetricians and Gynaecologists and Society for Endocrinology on best practice recommendations for the care of women experiencing the menopause

This position statement recommends an individualised approach in assessing women going through the menopause, with particular reference to lifestyle advice, diet modification as well as discussing the role of interventions including HRT.

NIHR Alert: People with polymyalgia rheumatica need a falls assessment and regular treatment reviews

Expert commentary is provided on the PMR Cohort study, which found participants took steroids for longer than anticipated, and few were using recommended calcium and vitamin D supplements, or bisphosphonates, to protect bone.

MHRA approves expanded use of empagliflozin to include patients with heart failure and preserved ejection fraction

The SGLT2 inhibitor empagliflozin, previously approved for the treatment of symptomatic chronic heart failure only in patients with reduced ejection fraction, has now also been approved for those with preserved ejection fraction, based on results from the EMPEROR-~~P~~reserved study.

National guidance, publications and resources

UKHSA: Monkeypox outbreak: vaccination strategy

JCVI and UKHSA guidance recommends targeted pre-exposure vaccination (with smallpox vaccine) as soon as feasible to MSM at highest risk using markers of high-risk behaviour similar to those used to assess eligibility for HIV PrEP but applied regardless of HIV status.

BNF/BNFC Newsletter June 2022

BNF - Colecalciferol and Ergocalciferol [maximum daily dose added for treatment of vitamin D deficiency]; Esketamine (Spravato®): new requirement to register patients onto Spravato® Register and Alert system; Pregabalin (Lyrica®): findings of safety study on risks during pregnancy [MHRA/CHM advice]; Isavuconazole [addition of dose equivalence and conversion statement]

BNF/BNFC - New monograph: Givlaari® [givosiran] for acute hepatic porphyria (initiated under specialist supervision); Ear: updated guidance for the management of acute otitis media; Human papillomavirus vaccine, Immunisation schedule and Influenza vaccine: updated guidance; Erythromycin [amended age range for otitis media and sore throat in children]; Human papillomavirus vaccines [update to indications and dosing].

BNFC - New monograph: Rinvoq® [upadacitinib] for atopic eczema (specialist use only); Paediatric Steroid Treatment Card; Pain, chronic: new guidance for management in children; Dexamethasone [update to dosing for COVID-19 requiring supplemental oxygen]

Material Regulation 28 – to prevent future deaths

Nil reported this month