Provisional publication of Never Events reported as occurring between 1 April and 31 August 2019
Report notes 155 serious incidents including 1 methotrexate overdose prescribed and administered, 1 wrong strength potassium given, 1 wrong strength of midazolam administered and 3 oral medications given intravenously.

Monthly data on patient safety incident reports Last updated 18th October 2019
NRLS Monthly Report England October 2018 to September 2019: Data by organisation on incidents reported to the NRLS by each English NHS trust and foundation trust, and regularly reporting social enterprise organisation.
Class 2 **Medicines recall: Zantac all formulations**
GSK recalled all formulations of Zantac as a precautionary measure due to possible contamination with NDMA which has genotoxic and carcinogenic potential. Pharmacy level recall.

Class 2 **Medicines recall: Ranitidine Effervescent Tablets 150mg, Ranitidine Effervescent Tablets 300mg**
Teva recalled as a precautionary measure due to possible contamination with NDMA. Pharmacy level recall.

Class 4: **Emerade 150, 300 and 500 microgram solution for injection in pre-filled syringes**
Some devices have failed to activate. Further information on this and other issues around adrenaline pens (inc. shortage info) is available from MHRA website.
MHRA

Class 2: **Bisacodyl 10mg Suppositories**
Recall of batch BUK901 due to issue with homogeneity

Class 4: **Rifadin (rifampicin) 150mg capsules**
Change to PIL for batch 9G020A not implemented

Class 4: **Xonvea 10mg/10mg gastro-resistant tablets**
PILs of certain batches missing possible side effects from post-marketing experience.

Class 2: **Sayana Press 104mg/0.65mL suspension for injection**
Selected batches recalled – moisture outside sealed area & unreadable expiry on label.

**Company led drug alert (Pfizer): Docetaxel Injection 80mg /8ml**
Batches recalled as routine stability testing identified that levels of 10-oxo-docetaxel (an impurity) may exceed acceptable levels at end of shelf-life.
Drug Safety Updates

1. **Ingenol mebutate gel (Picato®▼)**: Patients should be vigilant for any new skin lesions developing within the treatment area. Increased incidence of benign and malignant skin tumours associated with use.

2. **Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions.** CrCl should be calculated using Cockcroft-Gault formula for patients: taking DOACs, nephrotoxic drugs and renally excreted medicines that have narrow therapeutic indexes. Also in elderly patients (>75) and those at extremes of muscle mass (BMI < 18 or > 40).

3. **MHRA Drug Safety Update: Nivolumab (Opdivo) reports of CMV gastrointestinal infection or reactivation.** Diarrhoea/colitis after initiation of nivolumab should be promptly evaluated to exclude infections/other causes. In severe diarrhoea, nivolumab should stop.

4. **CHMP recommends** restricting co-administration of Evotaz (atazanavir and cobicistat) with dabigatran and lomipramide due to risk of serious and/or life-threatening adverse reactions.
Pharmacovigilance Risk Assessment Committee (PRAC)

Four week limit for use of high-strength estradiol creams
PRAC recommends 4-week limit for using these to minimise risk of side effects. They propose warnings be added to packing and tube size limit to 25g.

New information on known association between SGLT2 inhibitors and diabetic ketoacidosis in surgical patients. PRAC has agreed that product information should be amended to include a recommendation to monitor ketone bodies during surgical procedures.

Ondansetron signal of birth defects following in-utero exposure during the first trimester of pregnancy arising from recent publications
PRAC recommend that it should not be used in 1st trimester. UKTIS & ENTIS suggest use be restricted to 2nd line as only.

PRAC recommends update of product information for:
- Ibrutinib (risk of ischemic central nervous vascular conditions).
- Ibuprofen (risk of acute generalised exanthematous pustulosis).
- Teriflunomide (risk of new/ worsening psoriasis)
**Letter Sept 2019:** PN products for neonates and children < 2 years should be protected from light. Light exposure may lead to increased peroxides and other degradation products causing adverse effects, especially in premature neonates. Affects PN containing amino acid and/or lipids (esp. vitamins and trace elements).

**Letter Sept 2019:** Plunger on some Lucentis® (ranibizumab) 10mg/ml pre-filled syringes too stiff. Check pre-filled syringe plunger can be pushed easily when setting the dose and if there are difficulties, do NOT start to inject dose and use a new syringe. Injection should be stopped if already started and not easy to push.
Cipralex (escitalopram) film-coated tablets (all strengths): SSRIs/SNRIs may cause sexual dysfunction despite discontinuation.

Zanidip (lercanidipine) – all strengths: Contraindicates use in recent myocardial infarction, severe renal impairment and with grapefruit. Associated with cloudy peritoneal effluent*.

Multaq (dronederone) 400mg film-coated tablets: Clinical signs of heart failure and ECG should be monitored regularly when co morbidities present. Dabigatran contraindicated.

Plavix (clopidogrel) tablets: Delayed gastric emptying & absorption with opioids.*

Zocor (simvastatin) film-coated tablets- all strengths: Myopathy and/or rhabdomyolysis with daptomycin.

Eliquis (apixaban) film-coated tablets (all strengths): Reversal agent now available

Victoza (liraglutide) 6 mg/ml solution for injection in pre-filled pens: Delayed gastric emptying listed as uncommon adverse effect.

Oftaquix (levofloxacin) eye drops – all presentations: Advises tendon inflammation and rupture may occur with systemic fluoroquinolones.

Acitretin (Neotigason) 10mg Capsules: Treatment should be discontinued in case of uncontrolled hypertriglyceridemia / symptoms of pancreatitis.
Drug shortages and discontinuations

- **Supply disruption - Fluoxetine 10mg, 30mg and 40mg capsules** not be available until Dec 19. Consider alternative preparations/ strengths as per Serious Shortage Protocol.

- **Supply delay - Quadrivalent non-adjuvanted flu vaccine for at risk-groups aged 16 to 65 from Sanofi** Some supplies delayed by 1-2 weeks. Check stock before booking patients.

- **Supply disruptions for HRT and new restrictions on parallel exports** Apply to all variations of HRT products (e.g. Evorel & Indivina) and are expected to reduce impact.

- **Temporary supply disruption - Nardil (phenelzine sulfate) 15mg tablets** Resupply expected March 2020. Supplies available from specialist importers (unlicensed). Consider referral for review by specialist mental health teams if unlicensed products unsuitable.

- **Discontinuation Loestrin 20 and 30 tablets** Contact Galen Pharma for alternatives.

- **Temporary supply disruption - Isoniazid tablets 50mg** until Dec 19. Use half x 100mg (unscored and uncoated) tablets from Morningside as alternative (unlicensed).

- **Supply disruption - Moclobemide 150mg tablets** out of stock until further notice. 300mg tablets available from Mylan and scored but not licensed for splitting.

- **Supply disruption – Glibenclamide 2.5mg and 5mg tablets** – SPS memo published

- Full list of shortages available via SPS
Using Standardised Strengths of Unlicensed Liquid Medicines in Children: joint statement from NPPG and RCPCH
Chloral hydrate strength now 500mg/5mL (from 1g/5mL) as smaller doses more common.

Safe prescribing of high-risk drugs – NICE Shared learning database
New templates prompt monitoring for a range of high risk drugs (based on NICE guidelines).

Alert – reuse of GTIN codes
Caution on reuse of globally registered bar codes on different products or different strengths.

NEW: National Ambulance Patient Group Directions
Two National PGDs (flumazenil and tranexamic acid) developed for ambulance services.

Judiciary.uk publication – case of Deborah Chapman
Patient with underlying COPD died as a consequence of illicit drug use and strong opiate (oxycodone) with pregabalin for pain whilst awaiting hip replacement. Consider depressive effect on respiratory system of opioids, act on signs of opioid dependence and record information about illicit drug use to enable informed assessment of risks.

UKMi Q&A - Glucosamine – what are its drug interactions?
Considers the limited information available on potential drug interactions with conventional medicines including warfarin which interacts.
This month’s papers - overview

1. **NIHR Signal: Better strategies are needed to reduce preventable patient harm in healthcare**, October 2019. doi: 10.3310/signal-000825

2. **How rephrasing terminology can avoid medicines errors** Rx Clinical Pharmacy Magazine, September 2019


7. Moral distress in intensive care unit personnel is not consistently associated with adverse medication events and other adverse events Journal of Critical Care, Oct 2019; 53: 258-263


Medication-related harm in older adults following hospital discharge: development and validation of a prediction tool


- **Background**: Older adults at higher risk of MRH due to multimorbidity & polypharmacy etc. Transition of care post hospital discharge is high risk period and 17-51% experience MRH within 30 days of discharge costing the NHS ~£400m.

- **Study details**: Multicentre, prospective cohort study in 1280 older adults (≥65 years) discharged from five UK teaching hospitals between 2013 and 2015.
- **Aim**: To develop and validate a tool to predict risk of medication-related harm (MRH) requiring healthcare use post discharge.
- **Participants followed up for 8 weeks in community by senior pharmacists to identify MRH* (ADRs, harm from non-adherence/medication error).

- **PRIME tool* developed & internally validated** using 3 data sources - healthcare use information: hospital readmissions & telephone interview.

- Binary **primary outcome measure** = MRH and healthcare utilisation
Medication-related harm in older adults following hospital discharge: development and validation of a prediction tool (open access)


Results

• MRH requiring healthcare use within 8 weeks of discharge = 107 per 1000

• Modelling resulted in PRIME tool which found EIGHT variables measured at hospital discharge predictive of MRH following hospital discharge (gives risk score as %):

\[
\text{Model equation for risk score} = -2.384 + 0.85 \times (0.025 \times \text{age-81}) - 0.398 \times \text{gender} + 0.515 \times \text{antiplatelet drug} - 0.042 \times \text{sodium-137} + 0.591 \times \text{antidiabetic drug} + 0.477 \times \text{past ADR} + 0.056 \times \text{number of medicines} + 0.397 \times \text{living alone}
\]

Gender (female = 0), On antiplatelet drug at discharge (= 1), On antidiabetic drug at discharge (= 1), Past adverse drug reaction (= 1), Living alone (= 1)

Use of MCA’s, weak hand grip strength, renal impairment, Charlson comorbidity index were not associated with MRH following discharge using PRIME model
Medication-related harm in older adults following hospital discharge: development and validation of a prediction tool (open access)

Strengths
• Developed using multicentre, prospective data. C Statistic of 0.69 & decision curve suggested potential value.
• Candidate predictors derived with senior clinical and patient input.
• Possible/ probable cases eliminated reducing uncertainly & adequate power

Limitations
• N= 147 lost to follow up as not contactable.
• Pharmacists in study not blinded.
• Needs evaluation in other settings.
• Excluded pts who were terminally ill, lacked capacity, had intentional overdose and transferred to other acute settings or possible/ probable MRH.

Implications
• Could flag up high risk pts for intervention post discharge, possibly by PCN pharmacists?