LOTHIAN PRESCRIBING BULLETIN

NHS Lothian

Supporting prescribing excellence - informing colleagues in primary and secondary care

Issue 119

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Boost your knowledge of oral long term steroid use

Long term high dose steroid therapy is defined as ≥10mg prednisolone or equivalent, for more than 14 days[1&2] increasing the risk of developing a range of complications.

Short term complications include severe hyperglycaemia, an increased risk of GI bleeds and changes in mood and cognition. Longer term complications include osteoporosis, proximal myopathy, suppression of the hypothalamic pituitary axis and cardio-metabolic disorders, such as hypertension and dyslipidaemia.

Steroid-induced severe hyperglycaemia has a high morbidity and mortality, yet there was previously a lack of coherent guidance on screening, treatment and steroid withdrawal advice. New guidance has therefore been developed called the **NHS Lothian Steroid Safety Bundle**.[2] This guideline covers screening, diagnosis and management of complications seen in both primary and secondary care.

The new guidance bundle is available on RefHelp.[1] It gives recommendations in a 'one-stop' document and includes:

INITIATION

Often high dose steroids are started in secondary care. At pre-initiation counselling:

1. Perform an HbA1c and warn patient of symptoms of diabetes
2. Give advice on the 'sick day rules', provide a steroid emergency card and a patient information leaflet[3]
3. Gastroprotection - proton pump inhibitor therapy should not be given routinely but should be considered for people at high risk of gastrointestinal bleeding or dyspepsia
4. Bone protection - bisphosphonates should be considered to prevent vertebral fractures.

SCREENING AND MONITORING FOR STEROID INDUCED DIABETES

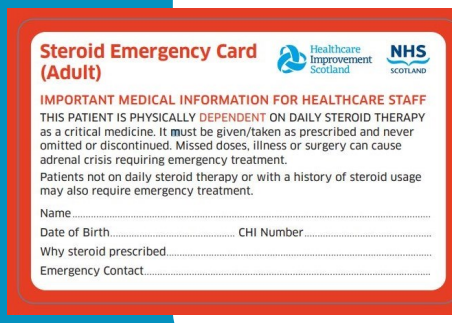
Refer to the safety bundle[2] if the patient is symptomatic of diabetes, or if the HbA1c is ≥42mmol/mol or if blood glucose is >12mmol/l for three continuous days.

WITHDRAWING AND STOPPING STEROIDS

If managing steroid withdrawal, check a morning cortisol level once the steroid weaning dose reaches 4mg in order to stratify risk (as some patients might need referral to endocrine before further reduction). Those at risk of adrenal crisis should be given a steroid emergency card found on RefHelp[1] or on the Healthcare Improvement Scotland[4] website, where additional advice is available on a wider range of steroid use.

The new steroid emergency card does not replace the blue steroid card which should continue to be issued at the point of dispensing from pharmacies.

Thanks to Dr Marcus Lyall, Endocrinology who led the quality improvement initiative.



Steroid Emergency Card (Adult)

Healthcare Improvement Scotland

NHS SCOTLAND

IMPORTANT MEDICAL INFORMATION FOR HEALTHCARE STAFF

THIS PATIENT IS PHYSICALLY DEPENDENT ON DAILY STEROID THERAPY as a critical medicine. It must be given/taken as prescribed and never omitted or discontinued. Missed doses, illness or surgery can cause adrenal crisis requiring emergency treatment.

Patients not on daily steroid therapy or with a history of steroid usage may also require emergency treatment.

Name.....

Date of Birth..... CHI Number.....

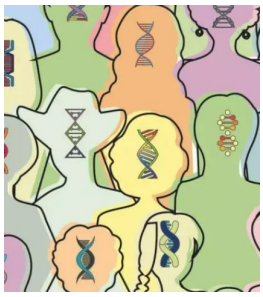
Why steroid prescribed.....

Emergency Contact.....

References

1. RefHelp. apps.nhslothian.scot/refhelp
2. NHS Lothian Steroid Safety Bundle apps.nhslothian.scot/files/sites/2/Lothian-Steroid-Safety-Bundle-approved.pdf
3. NHS Lothian. Long Term Steroid Use. Information for patients. long-term-steroid-use-patient-Information-leaflet.pdf
4. Healthcare Improvement Scotland. Steroid Emergency Card to support early recognition and treatment of adrenal crisis in adults. www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/adtc_resources/steroid_emergency_card.aspx.

Pharmacogenomics: a new era of personalised medicine!



Pharmacogenomics relates to the study of how an individual's genetic makeup can impact on their response to a medication. The PREPARE study was the first large study conducted which focused on the benefits of pharmacogenetic testing for a range of medicines, with results showing that there was a 30% reduction in the occurrence of adverse drug reactions due to its implementation.[1]

Pharmacogenomics enables the delivery of personalised medicine and allows clinicians and patients to make shared decisions on appropriate treatment pathways. Although we still have a long way ahead of us in terms of implementation of personalised medicine, there are a few examples of where this has already begun!

In 2020, the MHRA[2] advised oncology centres to conduct **dihydropyrimidine dehydrogenase (DPYD)** testing for any patients commencing on **fluorouracil** and its prodrugs **capecitabine** and **tegafur**. The DPYD gene encodes an enzyme involved in the metabolism of the named drugs and resulting deficiencies (full or partial) can lead to serious or fatal outcomes for the patient.

The Edinburgh Cancer Centre in NHS Lothian began implementing the advice in December 2020 after the completion of a pilot programme. Currently all patients undergoing treatment with fluorouracil or capecitabine are routinely tested upfront for four common variants of DPYD, which can then support prescribing decisions. Detailed guidance has been approved by the NHS Lothian Cancer Therapeutics Advisory Committee on suggested actions once results are known. Although dose reduction advice is given where this is applicable, there is potential for gradual escalation of doses to be made relative to any toxicity assessment for each patient. In some cases, advice may be to avoid prescribing altogether thereby protecting patients from severe harm.[3]

Another example of personalised medicine in oncology is testing for programmed death ligand 1 (PD-L1) to assess appropriateness of treatment with **pembrolizumab** for certain cancers, as per guidance in the product license.[4] The outcomes can help inform whether the patient is likely to respond to treatment thereby ensuring optimal outcomes for patients and appropriate use of NHS resources.

Lastly, genetic testing also exists for assessment of genetic variants in cytochrome P450 isoenzymes including CYP2C19 which is involved in the conversion of **clopidogrel** to its active form. NICE recommend starting patients on clopidogrel post-stroke. An estimated 32% of people in the UK have at least one of the highlighted CYP2C19 gene variants, which are more commonly found in people with an Asian family background but can be found in people of any ethnicity.[5] A strategic network has been launched by NICE to assess whether routine genotype testing for patients post-stroke should be recommended.[6-7]

References

1. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. Feb 2023. www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01841-4/fulltext
2. MHRA Drug Safety Update October 2020. 5-fluorouracil (intravenous), capecitabine, tegafur: DPD testing recommended before initiation to identify patients at increased risk of severe and fatal toxicity
3. The Pharmaceutical Journal. May 2022. Cancer pharmacogenomics testing: are we hitting the mark?
4. EMC. Summary of Product Characteristics (SmPC) KEYTRUDA 25 mg/mL concentrate for solution for infusion
5. The BMJ. May 2023. Stroke: Take test for genetic variant to ensure clopidogrel works for prevention, says NICE
6. The Pharmaceutical Journal. May 2023. NICE to recommend genetic testing before prescribing clopidogrel
7. NICE. May 2023. Clopidogrel genotype testing after ischaemic stroke or transient ischaemic attack.

With thanks to Sheeba Zahir, Cancer Care Pharmacist and Bruce Watson, Lead Clinical Pharmacist, Medicine of the Elderly & Stroke, for advice on clopidogrel genetic testing.

Drug Safety Updates 2023 and key messages

Pholcodine-containing cough and cold medicines: withdrawal from UK market as a precautionary measure because there is evidence that using pholcodine-containing medicines leads to an increased risk of the very rare event of an allergic reaction (anaphylaxis) in patients who receive general anaesthesia involving neuromuscular blocking agents (NMBAs) during surgery.

KEY MESSAGES

- ask patients scheduled to undergo general anaesthesia involving NMBAs whether they have used pholcodine-containing medicines, particularly in the past 12 months, and maintain awareness about the potential for perianaesthetic anaphylaxis related to NMBAs
- healthcare professionals are advised not to sell or dispense pholcodine-containing medicines
- pharmacies should follow the MHRA Class 2 Medicines Recall Notice to quarantine stock of pholcodine-containing medicines and return it to the manufacturer.

Nitrofurantoin: reminder of the risks of pulmonary and hepatic adverse drug reactions

- advise patients and caregivers to be vigilant for new or worsening respiratory symptoms while taking nitrofurantoin and promptly investigate any symptoms that may indicate a pulmonary adverse reaction - reactions may occur with short- or long-term use of nitrofurantoin, and increased vigilance for acute pulmonary reactions is required in the first week of treatment
- patients receiving long-term therapy, for example for recurrent urinary tract infections, should be closely monitored for new or worsening respiratory symptoms, especially if elderly
- immediately discontinue nitrofurantoin if new or worsening symptoms of pulmonary damage occur
- be vigilant for symptoms and signs of liver dysfunction in patients taking nitrofurantoin for any duration, but particularly with long-term use, and monitor patients periodically for signs of hepatitis and for changes in biochemical tests that would indicate hepatitis or liver injury
- use caution when prescribing nitrofurantoin in patients with pulmonary disease or hepatic dysfunction, which may mask the signs and symptoms of adverse reactions
- advise patients to carefully read the advice in the Patient Information Leaflet about symptoms of possible pulmonary and hepatic reactions and to seek medical advice if they experience these symptoms.

Febuxostat: updated advice for the treatment of patients with a history of major cardiovascular disease

- in patients with pre-existing major cardiovascular diseases, febuxostat therapy should be used cautiously, particularly in those with evidence of high urate crystal and tophi burden or those initiating urate-lowering therapy
- following initiation of febuxostat, prescribers should titrate the febuxostat dose to minimise gout flares and inflammation
- note that clinical guidelines for gout (see, eg, NICE guideline 219 – Gout: diagnosis and management) recommend that allopurinol should be offered as first line treatment for people with gout who have major cardiovascular disease. Allopurinol is first line for prophylaxis of gout on the East Region Formulary.

Adrenaline auto-injectors (AAIs): new guidance and resources for safe use

- use the materials to inform patients and caregivers what to do if they suspect anaphylaxis and how to use adrenaline auto-injectors (AAIs). Downloadable videos and infographic available on MHRA website or via this link
- to ensure patients always have a backup, prescribe two AAIs
- take this opportunity to refresh your own knowledge and share with your colleagues the safe use of AAIs and the signs of anaphylaxis using the mnemonic A, B, C for Airway, Breathing and Circulation.

Non-steroidal anti-inflammatory drugs (NSAIDs): potential risks following prolonged use after 20 weeks of pregnancy

- we remind healthcare professionals that systemic (oral and injectable) NSAIDs are contraindicated during the last trimester (after 28 weeks) of pregnancy due to the risk of premature closure of the ductus arteriosus and renal dysfunction in the foetus and due to prolongation of maternal bleeding time and inhibition of uterine contractions during labour
- avoid prescribing systemic NSAIDs from week 20 of pregnancy unless clinically required and prescribe the lowest dose for the shortest time in these circumstances – see drug safety update for 2022 study details and antenatal monitoring advice
- please advise patients who are pregnant to avoid use of NSAIDs available without prescription from week 20 of pregnancy onwards unless advised by their healthcare professional
- continue to follow clinical guidelines about taking and recording current and recent medicines, including over-the-counter medicines, at each antenatal appointment (for example, see NICE guideline on antenatal care [NG201]).

SUMMARY OF DRUG SAFETY UPDATES FOR SPECIALIST SERVICES - FOR MORE INFORMATION FOLLOW THE LINKS OR ACCESS WWW.GOV.UK/DRUG-SAFETY-UPDATE:

- Terlipressin: new recommendations to reduce risks of respiratory failure and septic shock in patients with type 1 hepatorenal syndrome
- Janus kinase (JAK) inhibitors: new measures to reduce risks of major cardiovascular events, malignancy, venous thromboembolism, serious infections and increased mortality
- Isotretinoin (Roaccutane): new safety measures to be introduced in the coming months, including additional oversight on initiation of treatment for patients under 18 years
- Glucose solutions: recommendations to minimise the risks associated with the accidental use of glucose solutions instead of saline solutions in arterial lines
- Direct-acting oral anticoagulants (DOACs): paediatric formulations; reminder of dose adjustments in patients with renal impairment
- Calcium chloride, calcium gluconate: potential risk of underdosing with calcium gluconate in severe hyperkalaemia.

Report suspected adverse drug reactions associated with all of the above-mentioned medicines on a Yellow Card yellowcard.mhra.gov.uk.

The palliativedrugs.com Bulletin Board has moved

In May 2023 we made you aware that the palliativedrugs.com website was closing and would be replaced with the Palliative Care Formulary (PCF) Syringe Driver Database and a discussion board. Both resources are now **live** and accessed as follows:

PCF SYRINGE DRIVER DATABASE accessed through **Medicines Complete** > **Drug Compatibility Checker** (for syringe driver enquiries click **Syringe**) www.medicinescomplete.com/#/compatibility.
TOP TIP: click '**See detailed results**' for additional information on dose in the syringe, final volume and diluent.

PCF DISCUSSION BOARD you will need to register for your complimentary account and confirm you are a health professional to use the PCF Discussion Board www.pharmaceuticalpress.com/palliative-care-forum/?utm_source=referral&utm_medium=ema&utm_campaign=rebrand_lch_forum_june23.

The **Scottish Palliative Care (SPC) Guidelines** are the national guidelines used by all Scottish Health Boards: www.palliativecareguidelines.scot.nhs.uk.

The **PCF** is a trusted resource that can be used to complement the national guidance.