Medicines Safety Matters

Newsletter for Primary Care Prescribers & Community Pharmacists

Health and Social Care Board

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Identifying dangerous over-use of paracetamol

What is the risk? It is well known that consuming more than the maximum dose of paracetamol (4g daily) can cause liver injury and potentially lead to death. HSCB Medicines Governance Team used prescription data to search for patients who may be over-using prescribed paracetamol.

How were patients identified? Data contained within the 2D barcode of scanned prescriptions in NI was searched in order to identify patients who may be consuming more than 4g daily. Medicines Management Advisers discussed the patients in each search with GP practices and community pharmacies (if the scripts were dispensed in the same pharmacy). The search was repeated approximately one year later and results are shown in the table below.

Results:

Estimated daily dose of paracetamol	Patients in cycle 1 (yr. end June 2014)	Patients in cycle 2 (yr. end Sept 2015)
>6g	10	2
5-6g	29	25
Total	39	27

None of the patients identified in cycle 1 reappeared in cycle 2 which suggests that they were all reviewed by the GP practice

There was a 30% reduction in the number of patients in cycle 2

Patients in the very high dose group (> 6g) reduced by 80%

The GPs and pharmacists were asked about what measures they put in place to help reduce over use of paracetamol, a summary of their advice is given below.

Advice for prescribers:

- Discuss any significant events with all practice staff
- Tighten repeat and acute prescribing protocols e.g. ensure there are systems in place to highlight over-ordering of paracetamol containing products
- Reception staff should be aware that some patients may be on more than one medication that contains paracetamol and should be vigilant for over-ordering and always inform the prescriber
- In some cases you may wish to keep paracetamol-containing products as an acute prescription
- Bring patients in for face to face review and assess their understanding of paracetamol dosing and potential risks of overdose and optimise pain relief. Some patients may require onward referral to secondary care pain management teams
- Other measures include reducing the quantity of paracetamol available on each script, adding a warning to the patients' records on the clinical system, moving patients to weekly dispensing and discussions with local community pharmacists.

Advice for community pharmacists:

- Increase vigilance for patients presenting early with prescriptions for paracetamol or paracetamol-containing products
- Counsel patients and clarify their understanding around paracetamol dosing and potential risks of overdose
- Speak **directly** to the prescriber about concerns regarding a patient receiving too much paracetamol. Record interventions on the PMR. <u>It is not sufficient to speak to reception staff.</u>

Ticagrelor - Think Twice Daily

Ticagrelor (Brilique®) is an anti-platelet agent that reversibly inhibits the platelet adenosine diphosphate receptors. It is initiated under the supervision of a cardiologist and is used in acute coronary syndromes e.g. post MI in combination with aspirin for up to 12 months.

Ticagrelor is currently the **only** anti-platelet agent that must be taken twice daily. Ticagrelor maintenance dose is 90mg BD.

A number of patients have been reviewed in secondary care who have either been prescribed or are taking their ticagrelor **once daily** instead of **twice daily**.

Anti-platelet agent	Administration
Aspirin	Once daily
Clopidogrel	Once daily
Prasurgel	Once daily
Ticagrelor	Twice daily

- The risk of thrombosis is increased in patients who are taking sub-optimal doses of anti-platelet agents, particularly in patients who have undergone coronary artery stent insertion
- Prescribers and pharmacists are asked to be vigilant in prescribing and clinically checking this specific administration schedule.

Advice for prescribers and community pharmacists:

- Review patients prescribed ticagrelor to ensure that there are clear directions for twice daily administration. Query once daily doses with the prescriber.
- Verbally reinforce the administration directions with patients, especially those who have previous experience of single daily dosing with other anti-platelet agents.

Z drugs on private prescriptions

Patients who are being seen under Health Service arrangements by their own GP should not receive private prescriptions for medications that are otherwise available without charge.

This happened recently when GP practices prescribed schedule 4 controlled drugs to a number of their registered patients on private prescriptions which were then dispensed on an on-going basis.

The private prescriptions were for zopiclone and zolpidem which are available without charge under the Health Service arrangements.

Learning from the investigation to date has identified that:

- Prescribing should have been under Health Service arrangements
- In some cases, prescription of the controlled drugs may have been excessive
- In some cases, the prescriber's signature was illegible and there was no printed prescriber's name on the prescription
- If there is a concern that a prescription may not be wholly appropriate for the patient, the pharmacist must speak directly to the prescriber about this and should only dispense the medication if they are satisfied that it is appropriate to do so.

NICE and the HSCB have previously issued guidance on the prescribing of Z drugs and recommend that hypnotics should be prescribed for short periods of time only, in strict accordance with their licensed indications.

Further information issued to GPs and pharmacies is available here:
http://primarycare.hscni.net/3817.htm
http://www.medicinesgovernance.hscni.net/primary-care/controlled-drugs/correspondence/

Amlodipine + simvastatin = review statin dose

A number of patients have been identified who are still taking amlodipine and simvastatin 40mg.

Concurrent use of amlodipine and simvastatin causes a significant increase in blood levels of simvastatin such that, in practice, the effect is double that compared to uninhibited simvastatin. Therefore, in patients on amlodipine 10mg plus simvastatin 20mg, the effect is similar to receiving simvastatin 40mg alone. The same applies for higher doses of simvastatin where the risk of adverse effects is much greater. Simvastatin 80mg is no longer recommended due to the increased risk of myopathy.

In 2012, the MHRA issued advice regarding the increased risk of myopathy associated with prescribing simvastatin 80mg or lower doses of simvastatin in conjunction with other interacting medicines. Following this advice, the licensed doses in the medicine SPCs were updated.

- No clinically significant interaction between amlodipine and atorvastatin has been reported.
- Atorvastatin is the statin of choice in the Northern Ireland Formulary http://niformulary.hscni.net

Commonly prescribed interacting medicines*	Prescribing recommendations
Potent CYP3A4 inhibitors e.g. Erythromycin Clarithromycin	Contraindicated with simvastatin
Fusidic acid	Not recommended with simvastatin
Verapamil Amiodarone Amlodipine Diltiazem	Do not exceed 20 mg simvastatin daily
Other fibrates (except fenofibrate)	Do not exceed 10 mg simvastatin daily

Advice for prescribers and community pharmacists:

- Amlodipine, diltiazem & verapamil are frequently prescribed in patients who are also taking statins. Prescribers and pharmacists should be aware that the dose of simvastatin should not exceed 20mg.
- Identify patients taking these calcium channel blockers with simvastatin 40mg & at their next routine review, either:
  - Switch to atorvastatin 10-20mg or
  - Reduce simvastatin to 20mg

* Full list of interacting medicines see http://www.medicines.org.uk/emc/medicine/1201

Prescribing mix-ups

Drug prescribed	Drug intended
Mebeverine 50mg/5ml suspension x 300ml Take one 5ml dose now then repeat dose if necessary after two weeks	**Mebendazole 100mg/5ml suspension x 300ml** Take one 5ml dose now then repeat dose if necessary after two weeks

Prescription was for a child. The parent had taken the prescription to a number of pharmacies who had been unable to supply the product immediately as it was a 'special'. The unusual dose was eventually queried by a pre-reg pharmacist & the GP was contacted.

Drug prescribed	Drug intended
Mercaptamine 25mg capsules	**Mercaptopurine 50mg tablets**

Both are used under the supervision of specialists; *mercaptopurine* is used in Crohn's disease, ulcerative colitis and leukaemia and *mercaptamine* for nephropathic cystinosis. A reminder about this potentially serious mix up is noted in the BNF.

It's all about the base!

There have been some reports of confusion around the supply of dexamethasone injection. Care must be taken to ensure that the correct dose of dexamethasone is prescribed, dispensed and administered.

Key points to prevent dexamethasone errors

Prescribe dexamethasone as base

- Doses of dexamethasone should be prescribed as dexamethasone base
- All prescriptions written as 'dexamethasone' are assumed to be dexamethasone base
- This will mean the dose of dexamethasone on the prescription will mirror that on the product packaging and will be in line with the current BNF.

Two strengths of injection are available

- Dexamethasone injection is available as 3.8mg/ml and 3.3mg/ml. (See Table 1).
- Where appropriate prescribe doses in increments of 3.3mg or 3.8mg
- When a dose is not prescribed in increments of 3.3mg or 3.8mg, the volume required will require use of part ampoules or vials. (See Table 2).

Table 1. Comparison of available dexamethasone products

Manufacturer	Aspen	Hameln	Hospira
Dexamethasone Base in each ml of product	3.8mg/mL	3.3mg/mL	3.3mg/mL
Presentation	1ml	1ml & 2ml	1ml & 2ml

The Aspen product requires storage at 2-8^{0}c whereas the other products are stored at standard room temperature.

Table 2. Equivalent dose volumes

Dose of dexamethasone base prescribed	Volume of Aspen dexamethasone 3.8mg/ml injection	Volume of Hameln or Hospira dexamethasone 3.3mg/ml injection
1mg	0.26mL	0.3mL
2mg	0.53mL	0.6mL
3mg	0.79mL	0.9mL
4mg	1.05mL	1.2mL
6mg	1.58mL	1.8mL
8mg	2.1mL	2.4mL

Note: The **Hameln** 3.3mg/mL product contains ***propylene glycol*** which should be used with caution in patients with hepatic and renal failure, children and pregnancy.