Drug Safety Update for October 2012 (PDF) contains drug safety information advising clinicians that there is risk of dose-related hepatotoxicity and liver failure with agomelatine (Valdoxan). It is already recommended that liver tests are performed before starting treatment and frequently after initiation. This recommendation has now been extended to include testing periodically after a dose increase. Treatment should be stopped if there are symptoms or signs of potential liver injury or if serum transaminases levels exceed three times the upper limit of normal. In Cornwall, the recommendation from the Cornwall Area Prescribing Committee Technical Working Group is that any initiation of prescribing by clinicians in CPFT would require that CPFT also continue the ongoing prescribing ie not ask GPs to pick up the prescribing but still communicate to the GP that their patient is now on this drug.

The hot topic section contains a summary of the evidence that supports the recent advice to restrict the daily dose of simvastatin when used in conjunction with amlodipine or diltiazem. The stop press section contains information from a recent safety review that provides further evidence that diclofenac carries a higher cardiovascular risk than other non-selective NSAIDs and similar to selective COX-2 inhibitors.

CAPC TECHNICAL WORKING GROUP

The Newly Licensed Drugs SubCommittee, (now renamed CAPC Technical Working Group), met in Nov’12 to consider the following drugs, the recommendations of which were approved at the Nov’12 meeting of the overarching Cornwall Area Prescribing Committee:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Flutiform</td>
<td>Flutiform MDI is a combination of fluticasone propionate and formoterol fumarate indicated for regular treatment of asthma when a combination inhaler is appropriate. It is less expensive than Seretide across the equivalent dose ranges and may be an option for patients requiring low or high strength steroid. Fostair (beclometasone/formoterol) remains the combination MDI of choice for adults requiring medium strength steroid (generally those at Step 3 of the British guidelines on the management of asthma). Reviewing patients on combination inhalers to see if they can be stepped down to a lower steroid dose is a key part of managing their treatment.</td>
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In addition, argatroban and fondaparinux were accepted for hospital prescribing.

NICE GUIDANCE

The Crohn's Disease clinical guideline discusses the management of Crohn's disease in adults, children and young people. The guideline covers the induction and maintenance of remission, surgery and maintaining remission after surgery. Additionally, the guideline discusses the impact of Crohn's disease on pregnancy and fertility as well as considering monitoring for osteopenia and assessing fracture risk.

The Psoriasis clinical guideline discusses the assessment and management of psoriasis in adults, young people and children. The guideline covers topical and systemic therapies and phototherapy. Attention is also drawn to ‘difficult-to-treat sites’ that include the face, flexures, genitalia, scalp, palms and soles. Psoriasis at these sites may result in functional impairment and be more difficult to treat.

METFORMIN IN POLYCYSTIC OVARY SYNDROME (PCOS)

At the recent Cornwall Area Prescribing Committee meeting it was noted that metformin is used off-label in PCOS on the basis that it will reduce the effects of high serum insulin and androgen concentrations in patients. A large metaanalysis1 concluded that metformin improved the odds of ovulation when compared with placebo (odds ratio [OR] 2.94 95% confidence interval (CI) 1.43-6.02, number needed to treat (NNT) =4.0). More recently, a Cochrane review2 concluded that although clomifene is more effective at improving ovulation rates than metformin, adding metformin to clomifene therapy significantly improves ovulation rates, particularly in clomifene-resistant patients. Furthermore, draft NICE guidelines on fertility read: “Offer
women with WHO Group II anovulatory infertility one of the following treatments, taking into account potential adverse effects, ease and mode of use, and monitoring needed: Metformin or clomifene citrate or a combination of the above.”

Hence the CAPC agreed that an acceptable management pathway is for the specialist to diagnose and initiate metformin treatment, and for the GP to maintain prescribing, overseen by the specialist.


**SICK CHILD RESOURCE**

This ‘spotting the sick child’ resource (commissioned by the Department of Health) is now available on line free. It has excellent video clips of sick children allowing you to ‘spot the sick child’, thereby targeting urgent resources at them. It is really good for junior health professionals who may not recognise some of the signs, as many are fortunately infrequent. Even senior experienced staff may also benefit.

https://www.spottingthesickchild.com/

**ANTIPSYCHOTICS LEARNING MODULE**

This self-directed learning package from the MHRA outlines the key risks of this widely prescribed class of medicines. For each adverse effect, the learning module outlines: the main features of the adverse effect; factors that increase the risk; how the risk can be reduced; and specific treatment for the adverse effect.

http://www.mhra.gov.uk/NewsCentre/CON189176

**ANTIBIOTIC PRESCRIBING – USEFUL RESOURCES**

The RCGP has launched a toolkit containing new guidance for GPs and their patients on the appropriate prescription of antibiotics. The guidance provides a simple, effective, and cost-effective approach to the treatment of common infections to minimise the emergence of bacterial resistance in the community. It is launched as part of a TARGET toolkit (Treat Antibiotics Responsibly, Guidance and Education Tool) and has been produced in partnership with the Health Protection Agency and the Antimicrobial Stewardship in Primary Care Group. As well as antibiotics management guidance, the TARGET toolkit also comprises:

- Clinical resources - including posters and links to useful web pages
- Patient resources - including information leaflets and a self-management form
- Audit report template for throat infection

http://www.rcgp.org.uk/TARGETantibiotics

**FROM THE DRUG & THERAPEUTICS BULLETIN (SEPT’12 ISSUE)**

An analysis by the US-based Institute for Safe Medication Practices, of all adverse events recorded by the Food and Drug Administration in 2011, shows that the anticoagulants dabigatran and warfarin were the leading reported causes of serious, disabling or fatal adverse events. The FDA received a total of 179,855 reports of adverse drug events or injuries associated with prescription drug therapy in the USA in 2011.

Dabigatran accounted for 3,781 serious adverse events overall (both manufacturer and direct reports), including 542 deaths, 2,367 cases of haemorrhage, 291 cases of acute renal failure and 644 cases of stroke. It was also suspected in 15 cases of liver failure. Warfarin accounted for 1,106 cases overall including 72 deaths.

The report also lists the five drugs most commonly cited in litigation in the USA in 2011: Metoclopramide, Drospirenone/ethinyl estradiol, Rosiglitazone, Varenicline, Isotretinoin

The DTB Comment notes that the reporting rates for adverse reactions differ significantly between older and newer drugs. Nevertheless, these figures provide a useful reminder of the need for careful monitoring of the use of drugs that are associated with a high risk of serious adverse effects.


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