PRIMARY CARE PRESCRIBER

The monthly prescribing bulletin for GPs, pharmacists, trainees, AHPs & community nurses.

Dec 2018

NHS Tayside

Primary Care Services & Medicines Advisory Group

What would you like for Christmas?

Merry Christmas: you've got Atrial fibrillation!

The Apple Watch ECG App went live earlier this month.

The studies done to establish benefits from anticoagulation have been conducted on patients found to have AF during an acute presentation or those with symptoms.

We still do not know what benefit/harm there might (or might not) be from anticoagulation of people who are otherwise healthy and found by screening. There is a ***study*** ongoing to establish if we should screen over 65s for AF—we await the results.

With low prevalence in a healthy population, there will a high number of false positives—rates of GP attendance are likely to increase.

UK National Screening Council does not recommend screening for AF due to a "paucity of evidence".

With the risk of harms from anticoagulation, we must be cautious in conveying possible benefits in risk reduction drugs (anticoagulation) as we simply don't know if the same benefit will be realised.

The ***NICE PDA*** helps explain, but take this with a pinch of cinnamon! Thank goodness whole-body CT scans are more expensive to give at Christmas!

Target Drug

In this festive season, it is worth (in the New Year) considering the treatment duration for allopurinol.

We know the dose should be titrated to maximum 900mg daily to maintain the urate at <300 µmol/l.

Although helpful, there is no mention in ***local guidance*** and lack of clear deprescribing advice in ***national guidelines*** .

Alternative

Helpfully, colleagues in Tasmania have created this useful deprescribing ***algorithm*** which takes quite a sensible approach to aid prescribers. As I hinted at above, personally I'd wait until the New Year before incorporating this into practice, but having tried this out, it seems useful to consider for patients who have not been reviewed recently. ***RDD*** recommends maximum 300mg daily in CrCl 20-50ml/min. (you can get the login from your pharmacist)

Drug Supply Update

FemSeven® is no longer being manufactured by Teva UK and is instead being made by Theramex. There may be a lull in supply as this transfers over. In the interim the choice is to switch to Evorel® Sequi/Conti or alternatively to use an Estradiol only patch 50mcg/day(Evorel®) plus Provera® (5-10 mg day 15-28 or 2.5- 5 mg OD) or Utrogestan® (200 mg nocte day 15-28 or 100 mg OD). ***Provera®*** gives better bleeding control, but utrogestan [non-formulary/not SMC approved] is probably safer with regards to breast ca, CVD and VTE risks.

Formulary HRT prescribing advice is summarised ***here***.

BNF Updates

The ***BNF*** now explicitly suggests 7 days of additional contraception prior to initial IUS fitting.

Formulary Updates

No formulary updates of note this month.

How good is the drug?

A 64 year old woman has a calculated CV risk of 20% on ASSIGN score. After discussion, the person starts atorvastatin 20mg. What is the absolute risk reduction of CV events over the next 10 years? *See page 3 for result.*

Costs to note

In this section we'll highlight some surprises, price drops, price increases and drugs coming off patent. Worth a search to see how many you might have on repeat...!

Festive treats! omeprazole 20mg 28 caps £0.91 versus lansoprazole 30mg £1.11

Peptac® 500mls £1.95 versus Gaviscon® Advance £5.12

SGLT2 Inhibitors and the heart

In 2015, NEJM published a now famous ***study*** on empagliflozin. Boehringer Ingelheim and Eli Lilly supported the design, data collection, analysis, interpretation and writing of the paper. All participants had established cardiovascular disease.

Participants received placebo, 10mg or 25mg dose. After 3 years there was no difference between groups for the primary outcomes (death from CV causes, non-fatal MI and non-fatal stroke). Of course, this wasn't a great result, so the study combined all intervention groups into pooled data which did show benefit (NNT of 62 over 3 years to prevent 1 event).

The Lancet then published a ***review*** of 100,000 people on SGLT2 inhibitors. 1 year follow up, 25% had CVD and over 90% of people in the study were on dapagliflozin. There was no change in nonfatal MI/CVA rate, but there was a reduction in CV events/admissions in those with established CV disease. Use in Tayside is high and ***SIGN*** and ***EASD-ADA*** endorse prescribing, but our ***CV event rates*** are no better than Boards using it much less over the past 3 years (but that's not a trial!) All should also be on metformin if they have previous CV disease & HBA1c >53 to consider starting

DTB ***highlights*** this is observational data and does not demonstrate causation. AstraZeneca have now done an ***RCT***. They combined CV death with hospitalisation for heart failure, but there was no difference in CV death rates when considered alone. There may be population-level benefit in established CV disease but we need to affirm causation.

Remember SGLT2 inhibitors ***double the rate of lower limb amputation and DKA***—the benefits are not universal and the harms noteworthy though rare.

Avoid a dry kidney this Christmas

Since the advent of eGFR, we have increasingly depended upon it to assist in drug dosing. Most commonly we encounter dose changes in those age over 65, in particular for those over 85.

In this UK ***study***, the ***calculated renal function*** was not good enough for the drug prescribed in 4–40% of people aged ≥65 years and 24–80% of people aged ≥85 years—this despite >90% of patients having recent renal function available.

In this older population, ***Cockcroft-Gault (Creatinine Clearance*** mls/min (CrCl)) underestimates renal function by 10%, whereas the eGFR overestimates by as much as 69%.

The study looked at drugs to be avoided: alendonic acid (CrCl <35); metformin (CrCl <30; drugs needing a reduced dose: simvastatin CrCl <30 should be 10mg); Gabapentin/pregabalin CrCl dependant dose; Ineffective at low CrCl: thiazides CrCl <30; nitrofurantoin <45; or only used with caution: NSAIDs CrCl <30; ACE/ARB CrCl <30.

Something of interest from the Journals…

In the never ending line of publications to find broader uses for DOACs, we come across another indication where they should not be used. This time post acute myocardial infarction: rivaroxaban will increase harm with no benefit and the study was prematurely stopped. ***Prescrire*** summarises 2 studies involved.

Rather coincidently for the article above, SPS has published ***guidance*** which considers when calculating ***Creatinine Clearance*** for DOAC dose if we should use actual body weight or ideal body weight as this is what was used in the studies. We shouldn't use eGFR in these patients for the reasons outlined above.

Lastly, this ***study*** helps remind us how little we know about managing cellulitis! It also reminds us to treat concurrent dry skin/athletes foot and suggests consideration for ***prophylactic antibiotics*** in recurrent infections with low dose penicillin 250mg BD (or 500mg BD if BMI>33) for up to 2 years—that said the evidence is limited!

How good is this drug?

A 64 year old woman has a calculated CV risk of 20% on ASSIGN score. After discussion, the person starts atorvastatin 20mg. What is the absolute risk reduction of CV events over the next 10 years?

A statin can reduce the calculated cardiovascular risk providing you get a 40% reduction in non-HDL cholesterol (and you need to take at least 20mg atorvastatin (or equivalent) to achieve this).

Given the overall risk of 20% in this person, to give a statin you will reduce the absolute risk in this case by 7%. NICE again helps with a ***PDA***, but in reality most of time it will make no difference in what happens to the person. It is a population drug as the individual is unlikely to ever benefit and depends upon lots of people taking it to achieve a population improvement.

That said, this does not apply to those age >75 who will ***not benefit*** from statins in primary prevention unless they have diabetes.

As previously cited, many thanks to Julian Treadwell of the Nuffield Department of Primary Care Health Sciences, Oxford for focussing on this type of issue and we look forward to an open resource to help us all better articulate and understand the intended benefits of medications.

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Useful prescribing websites

Renal Drug Database (authoritative CKD drug dosing) Username/password via your practice pharmacist

Safe for lactation (type the medicine name in the top search box)

Anticholinergic Drug Burden (a useful calculator to add up cumulative anticholinergic burden)

UKTIS (advice on prescribing drugs in pregnancy) [Hit **continue** at the warning.]

BUMPS (patient leaflets for each drug in the website above)

HIV drug Interaction Checker

Hepatitis Drug Interaction Checker

Syringe Driver Compatibility (Register for free and hit **SDSD** (4th tab at the top))

Knowledge Network has links to Enteral feeding guide (can it be crushed via PEG?!) & Drugs safe in lactation book in the **Medicines Information Resources** section. Use an Athens login.

TOXBASE Username/password given on registration. You can register the practice.

Tayside Pharmacy Publications (Previous Tayside Prescribers, PCP and ADTC Supplements)

The NNT.com The NNT for medications. It doesn't quantify the gain, but the NNT to get a benefit (which it itself might be small). The NNT also assumes an 'ideal' patient and again not bespoke to all.

Tayside Medicines Information Centre TAY-UHB.medinfo@nhs.net or 01382 632351 will always help with prescribing issues covered on the websites above