

Medicines

Optimisation news headlines

April - May 2019

DOACs and interactions

DOACs are now prescribed more widely and as a consequence are being requested for patients who are taking a wide range of other medications. Just like warfarin, they are subject to a number of significant interactions with other agents. However as INR does not need to be monitored with DOACs these interactions can sometimes be overlooked, with severe consequences. A recent serious incident when a patient suffered a pulmonary embolism whilst on a combination of a DOAC and anticonvulsant medication has high-lighted the issue.

Most interactions occur due to the metabolic pathways that are common to DOACs and many other agents. All four DOACs are substrates for the P-glycoprotein (P-gp) transport system. Their action will therefore be enhanced by inhibitors of P-gp and reduced by inducers of P-gp. Apixaban and rivaroxaban are metabolised by cytochrome P450 enzyme CYP3A4 as is a small proportion of edoxaban (less than 10%). The effect of these DOACs will therefore be raised or lowered by other drugs that are inhibitors or inducers of CYP3A4. Drugs that are strong inhibitors or inducers of these pathways will have a significant effect on the bioavailability DOAC.

Please see the appendix for a table of documented interactions, but be aware that this list is not exhaustive and any possible interaction should be considered when initiating a DOAC, especially bearing in mind the commonly encountered biochemical pathways mentioned above.

Phenytoin Infatabs shortage

Pfizer has notified clinicians that there will be a shortage of Phenytoin 50mg Infatabs until November 2019. To mitigate the shortage Pfizer have received agreement to import Dilantin 50mg infatabs from Canada. The active ingredient in Epanutin 50 mg Infatabs and Dilantin 50 mg Infatabs is the same, however in the absence of bioequivalence data, there may be clinically relevant differences between the two products. Any switches to different presentations must be managed under medical supervision and monitoring of phenytoin serum levels to ensure the correct dosage is being given. Full information has been sent to practices and can also be found [here](#).

Monitoring, Administration and Prescribing service (MAPs)

[The \(MAPs\) summary sheet](#) has been updated to include monitoring recommendations for mycophenolate mofetil as specified in the rheumatology shared care guideline.



Schools, nurseries and OTC medicines

There have been a number of queries about schools and nurseries refusing to administer over the counter (OTC) medications without a prescription.

Wessex LMC has issued a statement on this topic:

“The Clinical and Prescribing Subcommittee wishes to remind GPs that the MHRA licenses medicines and classifies them when appropriate as OTC (P or GSL). This is to enable access to those medicines without recourse to a GP. It is appropriate for OTC medicines to be given by parents, as they consider necessary, in the home or nursery environment. It is a misuse of GP time to take up an appointment just to acquire a prescription for a medicine, wholly to satisfy the needs of a nursery/school. The Clinical and Prescribing Subcommittee wrote to the Department of Children, Schools and Families seeking an amendment to this paragraph in the Statutory Framework and we have now heard from that Department. They will amend their guidance to stay consistent with current national standards for day care and childminding, whereby non-prescription medication can be administered where there is parents' prior written consent. Should any practice find that this continues to be a problem in their area we have produced a [template letter](#) which can be downloaded and sent to the Nursery/School.”

Advice about this topic for parents is also available on the [Healthier Together website](#).

Kliniderm superabsorbent dressing

There has been an update to the Wound Formulary. After a review and evaluation of the super absorbent dressings, the wound formulary group has made the decision to remove Vliwasorb Pro dressings from the wound formulary, and replace with Kliniderm Superabsorbent dressing. Vliwasorb Pro has an extra border so 12.5cm x 12.5cm is equivalent to 10cm x 10cm Kliniderm.

Kliniderm superabsorbent	Vliwasorb Pro
10cm x 10cm 49p	12.5cm x 12.5cm 90p
10cm x 15cm 69p	
10cm x 20cm 85p	12.5cm x 22.5cm £1.06
20cm x 20cm 99p	22cm x 22cm £1.90
20cm x 30cm £1.49	22cm x 32cm £2.39
20cm x 40cm £1.99	

It is estimated that a saving of up to £80,000 per year will be made within the West Hampshire CCG area by effecting this change.

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Significant interactions with DOACs

	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Enhanced effect of DOAC and increased risk of bleeding				
Ketoconazole	Contraindicated	Contraindicated	Caution - reduce dose to 30mg a day	Not recommended
Itraconazole				
Voriconazole				
Posaconazole		Caution		
Fluconazole				Avoid in patients at high risk of a bleed

Protease inhibitors e.g. Ritonavir	Contraindicated	Combination not recommended	Effect not known	Combination not recommended
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Tacrolimus		Not recommended		
Ciclosporin		Contraindicated	Caution - reduce dose to 30mg a day (except amiodarone)	Avoid combination
Dronedarone				Avoid in patients at high risk of a bleed
Amiodarone	Generally increase plasma level of apixaban but a dose change is not recommended	Caution - reduce dose to 110mg twice a day with verapamil		No dose reduction recommended
Erythromycin				
Clarithromycin				
Verapamil				

Reduced effect of DOAC with risk of clot formation				
Rifampicin	Caution	Contraindicated	Caution	Avoid combination
Phenytoin				
Carbamazepine				
St John's Wort				
Phenobarbitone				

Combination increases risk of bleeding	
Aspirin	Caution. Apixaban not recommended when other concomitant agents are associated with a serious risk of bleeding. Edoxaban not recommended if aspirin dose is greater than 100mg a day. NB: The 2.5mg strength of rivaroxaban is licensed for concomitant use with antiplatelet agents
Clopidogrel	
Other antiplatelets and thrombolytics	

NSAIDs	Caution Chronic use of NSAIDs not recommended with Edoxaban
SSRIs	
SNRIs	

Heparin (UFH and LMWH)	Contraindicated except to maintain catheter patency or when transferring between anticoagulants NB:
Other oral anticoagulants	

Information taken from the [Summary of Product Characteristics](#) (SPC) for Eliquis, Pradaxa, Lixiana and Xarelto, May 2019. Where boxes have been left blank, the effect of combination treatment is not stated in the SPC.

