NHS
Suffolk and
North East Essex

Interaction: Phenytoin – Atorvastatin/ simvastatin

Introduction

We are highlighting awareness to a little-known interaction between phenytoin and atorvastatin/simvastatin which can cause a reduction in the lipid lowering effect of the statin. Some statins, particularly atorvastatin and simvastatin are metabolised by cytochrome P450 enzymes. Phenytoin is an inducer of cytochrome P450 enzyme (CYP3A4).

Step 1	**Know the facts** Phenytoin is a cytochrome P450 inducer. Prescribing **phenytoin** with **atorvastatin/simvastatin** can reduce the lipid lowering effect of the statin, potentially leading to higher cholesterol levels and increase risk of cardiovascular events. This interaction is categorised in the BNF as a moderate interaction and the clinical systems warn of co-prescribing. This is not a class effect, rosuvastatin (high intensity statin) and pravastatin (low intensity statin) do not interact with phenytoin.
2	**Patient Identification** Run a search on the practice clinical system to identify current patients on the combination of phenytoin with atorvastatin or simvastatin.

3	**Action Required:**
	• Check patients have a recent non-fasting lipid profile and recommended target (NICE).
	  ○ Primary prevention: a greater than 40% reduction non-HDL cholesterol.
	  ○ Secondary prevention: LDL levels of 2.0 mmol/L or less or non-HDL levels of 2.6 mmol/L or less.
	• Patients who have raised cholesterol levels whilst on the combination should be considered for an alternative high-intensity statin as per NICE lipid modification guidance i.e. rosuvastatin (check for other C/I, interactions, previous intolerance).
	• If switched recheck cholesterol after 2-3 months - refer to SPS for more information on statin monitoring.
	• Check phenytoin interactions with the patients' other medications.

More information on cytochrome P450 interactions

Caution should be exercised when prescribing other drugs with statins. Co-administration of potent or moderate inhibitors of this enzyme (such as 'azole' anti-fungals, calcium channel blockers, macrolide antibiotics (e.g. clarithromycin/erythromycin), HIV protease inhibitors, grapefruit juice) may increase the risk of dose-related side effects including myopathy and/or rhabdomyolysis. Check BNF and/or SPC for full details of all potential drug interactions.

References:

- British National Formulary. BNF (online). Interactions: https://bnf.nice.org.uk/interactions/phenytoin/
- British National Formulary. BNF (online). Treatment summary: dyslipidaemia.
- Medicines.org.uk Summary of product characteristics (SPC): Lipitor
- Medicines.org.uk Summary of product characteristics (SPC): Zocor
- MHRA December 2014. Statins: interactions, and updated advice for atorvastatin.
- SPS November 2024. Statins monitoring.
- NICE guidance NG238 Cardiovascular disease: risk assessment and reduction, including lipid modification

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