Letter to the Editors

Statins and joint pain

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A 42-year-old man presented to his general practitioner (GP) with a history of several weeks of a painful left knee, which had prevented him doing his usual jogging for 20 min several times each week. There was no history of trauma or other precipitant. Past history revealed a 30-year history of insulin-dependent diabetes, for which he took insulin lispro 5 IU t.d.s. and glargine 20 IU nocte. Four weeks earlier, he had increased simvastatin from 10 to 40 mg daily following the finding of changes at retinal screening. There was no history of previous allergy.

Examination revealed a small effusion of the left knee. This was confirmed on X-ray, which showed no other changes. Bloods for arthropathy screen were normal. Simvastatin was stopped for 2 weeks, following which the symptoms completely resolved. He then started pravastatin 20 mg daily and pain returned, although it resolved completely after reducing the dose to 10 mg daily.

Although the Summaries of Product Characteristics and Patient Information Leaflets for simvastatin, atorvastatin, pravastatin and rosuvastatin all list arthralgia as a possible side-effect, the *British National Formulary* (BNF) is not consistent with this advice since arthralgia is listed as a side effect for atorvastatin and rosuvastatin but not for simvastatin, fluvastatin or pravastatin [1]. BNF does not list arthropathy as a side-effect of any statin. However, the Medicines and Healthcare products Regulatory Agency has reported the following cases of suspected arthralgia/arthropathy as a result of statin use in Table 1.

Some statins are more lipophilic (atorvastatin, fluvastatin, simvastatin), whereas others are more hydrophilic (pravastatin, rosuvastatin) [2]. Table 1 shows that for lipophilic statins there were 294 cases of arthralgia and nine cases of arthropathy, whereas for hydrophilic statins there were cases of 75 arthralgia and one case of arthropathy.

However, although there are relatively high numbers of reports for the more lipophilic simvastatin and atorvastatin, there are very few for fluvastatin. The risk of

arthralgia for one of the more hydrophilic compounds, pravastatin, was detected in clinical trials, indicating that the incidence was relatively common; yet in rosuvastatin post marketing studies, arthralgia has only been detected at a very rare reporting rate of <1/10000. In addition, there are clear limitations to the data above since higher counts for simvastatin and atorvastatin are influenced by higher usage in the UK of these two statins. The duration for which each statin has been available also varies. Therefore based on this data there is not enough evidence to support the theory that arthralgia and arthropathy occur more with the lipophilic statins.

Since arthralgia and arthropathy are not well-recognized side-effects of statins, such symptoms may not be attributed to such medication. Instead, they may be under-reported and attributed to osteoarthritis, which is common in the predominantly older groups of the population taking statins. GPs should be aware that joint pain in this group may be precipitated and exacerbated by statins, and report such reactions. More evidence is required to show that lipophilic statins may be more likely to produce such effects.

Table 1

UK reports of statins and arthralgia/arthropathy between 1 July 1963 and 18 March 2008

Suspected drug	Suspected adverse reaction	n
Atorvastatin	Arthralgia	110
Atorvastatin	Arthropathy	4
Fluvastatin	Arthralgia	8
Fluvastatin	Arthropathy	1
Simvastatin	Arthralgia	176
Simvastatin	Arthropathy	4
Pravastatin	Arthralgia	33
Pravastatin	Arthropathy	1
Rosuvastatin	Arthralgia	42
Rosuvastatin	Arthropathy	0

Medicines and Healthcare products Regulatory Agency [CHH/MHRA, personal communication].

Competing interests

None to declare.

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- 1 British National Formulary. BNF online. Available at: <http://www.bnf.org/bnf> (last accessed: 26 March 2008).
- 2 Schachter M. Chemical, pharmacokinetic and pharmacodynamic properties of statins: an update. *Fundam Clin Pharmacol* 2005; 19: 117–25.

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