Minhas 89-91 30/3/04 10:33 Page 1

OTC statins: the implications for primary prevention in the UK

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The difficulty in delivering a viable primary prevention policy has been evident ever since the publication of the *National Service Framework for Coronary Heart Disease* (NSF-CHD).[1] In this context, the announcement by the Medicines and Healthcare products Regulatory Agency (MHRA) of a consultation exercise[2] on the reclassification of simvastatin 10 mg from POM (prescription only) to P (pharmacist directed) status was unsurprising. As statins represent the single largest item in drug expenditure,[3] the state's incentive to limit drugs expenditure cannot be underestimated, while the attraction for pharmaceutical companies in extending the product life of patent-expired drugs through the over-the-counter (OTC) market is equally considerable. Two applications for OTC status for statins were previously considered and rejected by the Food and Drug Administration (FDA)[4,5] in the United States in July 2000 and, in light of the current UK application, it may be instructive to examine their experience.

In the US, applications for 10 mg doses of pravastatin and lovastatin to be granted OTC status were considered and, as with the current UK application for simvastatin 10 mg, neither dose had been validated in large clinical trials. The applicants maintained that patients often suffered a myocardial infarction (MI) despite having cholesterol levels that were not high enough to warrant treatment. The UK application differs and specifies a slightly higher 'moderate risk' risk population. This is defined as males aged 55 years or over or males between the ages of 45 to 54 years and females over the age of 55 years who have a family history of coronary heart disease (CHD) in a first-degree relative (parent or sibling), are smokers (or have been a smoker in the last 12 months), are overweight or of South Asian ethnicity.[2]

Table 1. Suggested components of a pharmacy protocol for establishing patient suitability for OTC simvastatin[2]

- Estimate the likely level of CHD for the individual based on sex, age, and other risk factors
- Exclude pre-existing conditions that indicate a high CHD risk or a condition best managed under physician supervision (i.e. existing CHD or peripheral vascular disease, known familial high cholesterol, diabetes, hypertension, hypothyroidism, renal impairment, and family history of muscle disorders)
- Check that none of the categories of contraindications or relative contraindications to statin therapy apply
- Check that the individual is not already on prescription cholesterol-lowering therapy or on any prescription medicines, particularly those with recognised potential to interact with simvastatin

US concerns

The FDA judged both applications against multiple criteria. Concerns were expressed about the potential for patients with high cholesterol levels to self-treat without blood testing and in this respect, the UK application does not specify a definite requirement to measure low-density lipoprotein cholesterol (LDL-C) levels either before or after treatment.[2] The FDA accepted the assumption that LDL reduction was a surrogate for CHD risk reduction in the absence of direct trial evidence but questioned the basis upon which patients might request treatment. The UK application for simvastatin 10 mg partially addresses this deficiency by broadly stratifying CHD risk though age, sex and other risk factors and ensuring that a pharmacist protocol (see table 1), patient self-check list and pharmacist training aid appropriate patient selection.

It was also highlighted to the FDA the concern of drug safety experts (one year before cerivastatin was withdrawn) and a lack of evidence that consumers would be able to effectively take such drugs in the OTC setting. Evidence suggests that per-

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Minhas 89-91 30/3/04 10:33 Page 2

sistence with statins is poor and may fall as low as 25% after five years – regardless of whether patients have to pay for treatment.[6] This raises reasonable doubts as to whether clinical benefits will be realised in the OTC setting and contrasts with the view of the MHRA that it is satisfied that simvastatin 10 mg is (*sic*) effective in the proposed population.[7]

Clinical implications

If patients taking OTC statins are able to realise clinical benefits, the implications of a self-selecting population also need to be considered. A further widening of inequalities in CHD mortality between social classes V and I could result – the CHD inequality gap is already wider than it was 20 years ago.[1] Some observers might perceive a partial privatisation of primary prevention while others will seek to defend this on the grounds of health maximisation. One option could be to reduce intervention thresholds for all patients and allow pharmacist prescribing of more efficacious statin doses. The financial implications of treating up to 19.6% of the population might initially render this option unattractive to policy makers at the Department of Health, although it would be preferable in terms of ethics and social equity.

Advertising can be expected to play an increasing role in consumer/patient selection. Advertising is designed to promote benefits, down play risks, engender brand loyalty and sell products. These are not factors typically conducive to making informed choices. A Consumers Association survey found that only 25% of respondents would trust pharmaceutical companies to provide impartial opinion[9] – suggesting consumers also recognise that patient education is not synonymous with advertising.

What would this proposal mean in real life? Excluding patients on the basis of pre-existing hypertension will underestimate the true number of hypertensive patients and may lead to the undertreatment of their CHD risk. Similar emphasis on only excluding patients with pre-existing hypothyroidism may mean that some patients with elevated cholesterol who are hypothyroid will go undetected.

Although a similar scheme for emergency hormonal contraception exists in primary care, within my primary care trust (PCT) population of 300,000 people, only three pharmacies are registered to provide this service. However, more intensive marketing by the pharmaceutical industry may stimulate greater demand amongst both patients and pharmacists. The uptake of OTC statins may also be attenuated, as patients seek to obtain less expensive prescription supplies of statins at lower risk thresholds and this may be an important indirect consequence of the proposal. If the proposal is approved, as seems likely, clinicians will anticipate the adoption of a firm commitment to a CHD intervention threshold of 15% within the future Third Joint British Guidelines on prevention of coronary heart disease in clinical practice. The adoption of a 20% CVD risk threshold for initiating statins in hypertensive patients in recent guidelines from the BHS[10] portends the incorporation of this threshold within the forthcoming consensus guidelines.

Despite the introduction of the NSF-CHD, primary prevention has not been adequately addressed in the UK. There is an absence of published primary prevention audit data, in contrast to the wealth of data on secondary prevention. The omission of any timelines within the NSF-CHD for monitoring progress in primary prevention (in contrast to secondary prevention) is partly responsible. Many patients who experience complications of atheroma, such as MI or sudden death, do not have overt cardiovascular disease[11] but still merit consideration for prevention at risk levels lower than the current 30% threshold. The basic prerequisite of any solution is that it should adequately address the intended problem. In this respect, although the current proposal for OTC statins is designed to minimise the risk of harm it does not necessarily follow that it will deliver significant reductions in CHD mortality.

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