PRACTICE GUIDANCE: OTC SIMVASTATIN

Coronary heart disease is the most common cause of premature death in the UK. Following its reclassification from prescription-only to pharmacy status, simvastatin 10mg is now available for sale from pharmacies for individuals at moderate risk of CHD. This guidance outlines important points to consider when counterprescribing

Royal Pharmaceutical Society of Great Britain

There is a correlation between an individual's serum cholesterol level, (specifically low density lipoprotein [LDL] cholesterol) and the risk of developing CHD. Current evidence suggests that for adults in western societies it may be beneficial to reduce serum cholesterol level whatever their baseline level is. Serum cholesterol alone, however, is a poor predictor of CHD risk because of the number of other risk factors that contribute to an individual's overall risk profile. The National Service Framework for CHD has prioritised those individuals at greatest risk of CHD and a number of interventions, including lipid-lowering treatment, will be provided by the NHS to all patients who have had an event as well as all those at 30 per cent or greater 10-year CHD event risk (with an aim to reduce this to 15 per cent when resources permit). The target population for pharmacy self-care is those at "moderate" risk of CHD (approximately a 1 in 10 to 1 in 7 [10 to 15 per cent] chance of developing CHD in the next 10 years). It is possible to determine moderate risk through an individual's self-reported risk factors.

WHO IS ELIGIBLE FOR OTC SIMVASTATIN?

Simvastatin 10mg is suitable for individuals at moderate risk of coronary heart disease. The following individuals are likely to be at moderate risk:

- Men aged 55–70 with or without risk factors
- Men aged 45–54, with one or more listed risk factors
- Post-menopausal women aged 55–70, with one or more listed risk factors
  (see below: "Who to refer to GP")

Risk factors for assessing moderate CHD risk

- SMOKER — currently or within the last five years
- FAMILY HISTORY OF EARLY HEART DISEASE — father or brother had a heart attack or angina before age 55; mother or sister had a heart attack or angina before age 65
- OVERWEIGHT/OBESE — Waist measurement greater than 40in (102cm) in men or 35in (88cm) in women, and/or body mass index more than 25kg/m^2
- South Asian family origin (eg, India, Pakistan, Bangladesh, Sri Lanka)

If none of the three categories applies, the individual may be at a lower risk of CHD and OTC simvastatin is not indicated. Consider counselling where appropriate on lifestyle modifications that will reduce the future risk of CHD — eg, smoking cessation, regular exercise, eating a healthy diet, weight reduction and diabetic control.

WHO TO REFER TO GP

- Men aged 55 or over with a family history of early heart disease plus at least one other risk factor (see above: "Risk factors for assessing moderate CHD risk")
- People diagnosed with: diabetes, angina, a previous heart attack or stroke, peripheral vascular disease, familial hypercholesterolaemia/hyperlipidaemia, hypertension, liver disease or history of abnormal liver function tests, hypothyroidism, renal impairment, family history of muscle disorders (eg, muscular dystrophies)
- People who have their cholesterol levels measured and the test results indicate a need for referral (fasting LDL-cholesterol level of 5.5mmol/l or greater)
- Individuals who have their blood pressure measured within the pharmacy and the results indicate a need for referral within the context of existing Society practice guidance.
- People who:
  - Currently experience unexplained heart/chest pain brought on by exercise or exertion
  - Drink on average more than recommended levels of alcohol: ie, more than four units alcohol/day (men), or three units alcohol/day (women). (1 unit = $^1/_2$ pint of beer, 1 small glass of wine or 1 single measure of spirits)
  - Drink grapefruit juice in large amounts (more than one litre daily).
- People who have taken simvastatin or other cholesterol-lowering medication and report symptoms of:
  - Myopathy/rhabdomyolysis (unexplained generalised muscle pain, tenderness or weakness not associated with flu, exercise, strain or injury)
  - Liver dysfunction (yellowing of the skin and whites of eyes; itching)
  - Allergic reaction or new skin complaints

MAIN POINTS TO CONSIDER WHEN RECOMMENDING OTC SIMVASTATIN

- Simvastatin 10mg is intended to reduce the risk of a first major coronary event (non-fatal myocardial infarction and CHD deaths) in adults who are likely to be at moderate risk of CHD.
- Simvastatin 10mg may lower LDL-cholesterol by about 27 per cent in practice, and is considered likely to produce beneficial effects. However, no specific clinical trials have been conducted with simvastatin 10mg in individuals at moderate risk.
- OTC simvastatin is given as a single 10mg dose in the evening and should be taken regularly on a long-term basis. Individuals need to understand that benefits will not be obtained from intermittent courses of treatment.
- People aged over 70 years should not take simvastatin except on medical advice.
- Simvastatin should be taken as part of a programme of actions designed to reduce the risk of CHD and provides an opportunity for pharmacy staff to discuss other life style interventions: smoking cessation, regular exercise, eating a healthy diet, weight reduction and diabetic control.
- Pharmacists should be involved in all initial sales of simvastatin but may delegate subsequent sales where appropriate to medicines counter assistants (MCAs).
- MCAs involved in simvastatin sales should be given training in when to refer to a pharmacist.
- Cholesterol tests are not required before starting simvastatin, but it is considered good practice to offer cholesterol monitoring where appropriate.
- Although measuring blood pressure is not necessary before starting simvastatin, it is good practice to offer a blood pressure test if this service is available.
- Liver function tests are not required before starting simvastatin.
- It is considered good practice to record (after seeking the individual's permission), if possible, the sale of simvastatin in the patient medication record.
- Pharmacists need to liaise with their local GPs or primary care organisation (PCO) on how information from customers purchasing simvastatin should be fed back and on any local policies on management of CHD risk and prescribing simvastatin.
- Pharmacists should encourage individuals to inform their GP that they are taking simvastatin and provide the GP with the results of any diagnostic tests or contact the GP with the individual's consent.
- Individuals on simvastatin therapy should be monitored (at least annually wherever possible) for adverse effects, interactions, changes in risk factors and compliance issues. Further cholesterol tests may also be offered as this may help and encourage compliance.
- Pharmacists should advise on the warning signs of rare adverse effects but emphasise that these are rare: myopathy/rhabdomyolysis (unexplained generalised muscle pain, tenderness or weakness not associated with 'flu, exercise or recent strain or injury), liver dysfunction (yellowing of the skin and whites of eyes; itching), any unexplained allergic symptoms or new skin complaints. See summary of product characteristics (SPC) for complete list.
- Pharmacists should exclude potentially serious drug interactions before commencing treatment (see BNF/SPC for complete list).
- Pharmacists should advise customers to avoid drinking grapefruit juice.

OTC INDICATION AND DOSAGE?

Simvastatin 10mg is indicated to reduce the risk of a first major coronary event (non-fatal myocardial infarction and CHD deaths) in people who are likely to be at moderate risk — a 1 in 10 to 1 in 7 (10–15 per cent) chance of developing CHD in the next 10 years. Simvastatin is given as a single 10mg in the evening and should be taken regularly on a long-term basis.

HOW SIMVASTATIN WORKS

Simvastatin competitively inhibits 3-hydroxy-2-methylglutaryl coenzyme A (HMG CoA) reductase, an enzyme involved in cholesterol synthesis, especially in the liver. Simvastatin reduces levels of low density lipoprotein (LDL) cholesterol and increases levels of high density lipoprotein (HDL) cholesterol. Reductions in LDL-cholesterol correlate closely with reduction in CHD risk.

CHOLESTEROL TESTING AND BLOOD PRESSURE MONITORING

CHOLESTEROL TESTING: It is not essential to know someone's cholesterol status to identify them as being at moderate risk (see over, "Risk factors for assessing moderate CHD risk"). Cholesterol testing is not a prerequisite to selling simvastatin; however, it is good practice to offer a cholesterol test or ascertain a recent cholesterol level when making an initial sale — both to to screen for people with high cholesterol (an initial fasting LDL-cholesterol level of 5.5 mmol/l or greater who might require GP treatment) and to establish a baseline level against which to measure progress.

It is good practice to offer an annual cholesterol test to monitor progress. This may help determine whether the medicine is being taken properly and encourage the individual to continue taking simvastatin.

See also Society practice guidance on cholesterol testing (www.rpsgb.org.uk/pdfs/choltestguid.pdf)

BLOOD PRESSURE MONITORING: Although it is not necessary to measure an individual's blood pressure prior to commencing simvastatin, it is good practice to offer a blood pressure test if this service is available. This is primarily to screen for hypertension that may alter an individual's risk factors and warrant medical treatment.

See also Society practice guidance on blood pressure monitoring (www.rpsgb.org.uk/pdfs/bpmonitguid.pdf)

WHO SHOULD SELL SIMVASTATIN?

INITIAL SALES: The pharmacist should be involved in all initial sales of simvastatin. Initial sales should not be delegated to medicines counter assistants (MCAs), although MCAs may be used to elicit some of the information from the individual. However, the pharmacist should be involved in the counselling of the individual and authorise the sale.

SUBSEQUENT SALES: It is a matter for professional judgement whether the pharmacist needs to be personally involved in subsequent sales or whether these may be delegated to appropriately trained MCAs.

Regular customers should be offered an annual review wherever possible, covering issues such as changes to risk factors, adverse effects, interactions and compliance. Any MCAs involved in subsequent sales should check that there have been no changes to an individual's risk factors, adverse effects, etc, that might warrant referral to the pharmacist.

A questionnaire may be useful to elicit information from the customer and define the suitability of the individual for treatment with simvastatin.

SALES TO THIRD PARTIES: It is good practice to make all initial sales directly to the client. Sales to third parties may be considered for subsequent sales provided that the pharmacist or MCA can establish that the individual's risk factors, adverse effects, etc, have not changed.

CONTACT WITH LOCAL GPs/PCOs

Pharmacists or their representatives (eg, local pharmaceutical committees) need to liaise with their local GPs or primary care organisation to:

- Ascertain any local policies on management of CHD risk and on prescribing simvastatin — ie, the local NHS threshold for treatment in the area and how the 15–30 per cent 10-year CHD event risk group are managed.
- Establish local communications — eg, how GPs wish to be informed of purchases of simvastatin or test results should the individual consent to sharing information with their GP.
- Agree local policy for referrals.

Pharmacists should consider documenting this information for possible future reference.

RECORD KEEPING

It is good practice to keep a record, if possible, of the sale of simvastatin in the patient medication record. The individual's permission should be sought before a record is made. The record will be important in case the individual is prescribed an interacting medicine in the future or is subsequently prescribed a statin by their GP. It is also good practice to record if cholesterol/blood pressure tests are offered (with results).

BENEFITS OF OTC SIMVASTATIN

Based on evidence from clinical trials with a number of statins at various dosages, simvastatin 10mg is considered likely to confer benefits in terms of reducing CHD events. Simvastatin 10mg may lower LDL-cholesterol by about 27 per cent in practice. However, no specific clinical trials have been conducted with simvastatin 10mg in individuals at moderate risk of CHD.

CONTRA-INDICATIONS

Hypersensitivity to simvastatin or any excipients; history of muscular toxicity with a statin or fibrate; individuals already taking prescription cholesterol lowering drugs; concomitant administration of potent CYP3A4 inhibitors (eg, itraconazole, ketoconazole, HIV protease inhibitors, nefazodone, erythromycin, clarithromycin and telithromycin); active liver disease or unexplained persistent elevations of serum transaminases; pregnancy and breast feeding; women of childbearing potential.

CAUTIONS

Simvastatin 10mg is not intended for those who are known to have: existing CHD, diabetes, history of stroke or peripheral vascular disease or familial hypercholesterolaemia. Individuals with these conditions are at higher risk of cardiovascular disease and should be managed under the supervision of a doctor. Individuals who have been diagnosed as having hypertension are also at increased risk of cardiovascular disease. Therefore, these individuals should consult their doctor before undertaking treatment with OTC simvastatin.

Simvastatin should also be used with caution in those with a history of liver disease or with a high alcohol intake (use should be avoided in active liver disease). See SPC and/or "Who to refer to GP" (overleaf) for more information.

ADVERSE EFFECTS

The reclassification of simvastatin 10mg tablets to pharmacy status poses no safety concerns additional to those in the SPC. Simvastatin is generally well tolerated; side effects have been usually mild and transient.

Simvastatin may cause abdominal pain, constipation, flatulence, asthenia (weakness or loss of strength) and headache (see SPC for full details).

Muscle effects (myopathy/rhabdomyolysis), liver dysfunction and an apparent hypersensitivity syndrome have been reported rarely with simvastatin. If symptoms of these more serious reactions occur (see overleaf), advise customers to discontinue simvastatin therapy immediately and seek medical advice. Any unexplained allergic symptoms or new skin complaints should also be reported to the pharmacist and/or GP. Pharmacists are reminded to send a yellow card report to the Medicines and Healthcare products Regulatory Agency if a serious adverse drug reaction is suspected.

DRUG INTERACTIONS

Risk of myopathy is increased with concomitant administration of: gemfibrozil and other fibrates; lipid-lowering doses (more than 1g/day) of niacin (nicotinic acid); ciclosporin; the azole antifungals itraconazole and ketoconazole; HIV protease inhibitors; the antidepressant nefazodone and the macrolide antibiotics erythromycin, clarithromycin and telithromycin. To be on the safe side, any individual on simvastatin who is given any macrolide should be warned to be alert for any signs of myopathy. Simvastatin may modestly potentiate the effect of coumarin anticoagulants and prothrombin time should be determined before starting simvastatin and during early therapy. Pharmacists should advise customers to avoid drinking grapefruit juice. See SPC for full details.

OVERALL ASSESSMENT

Simvastatin 10mg is likely to produce beneficial effects in people at moderate risk of CHD. However, no specific clinical trials have been conducted with simvastatin 10mg in this particular population. Community pharmacists are ideally placed to help assess an individual's risk of developing CHD and to discuss the benefits of healthy lifestyle interventions.

This guidance on best practice when recommending OTC simvastatin has been prepared by the Practice Division of the Royal Pharmaceutical Society of Great Britain.

Royal Pharmaceutical Society of Great Britain

1 Lambeth High Street
London SE1 7JN

July 2004