Simvastatin

Essential medicine status ✓

Section: 12. Cardiovascular medicines > 12.6. Lipid-lowering agents

ATC codes: C10AA01

Indication	Mixed hyperlipidaemia ICD11 code: 5C80.2
INN	Simvastatin
Medicine type	Chemical agent
List type	Core
Additional notes	For use in high-risk patients
Formulations	Oral > Solid: 5 mg ; 10 mg ; 20 mg ; 40 mg
EML status history	First added in 2007 (TRS 946)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	atorvastatin (ATC codes: C10AA05) pravastatin (ATC codes: C10AA03) fluvastatin (ATC codes: C10AA04) lovastatin (ATC codes: C10AA02)
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Simvastatin
DrugBank	Simvastatin

Summary of evidence and Expert Committee recommendations

An application for inclusion of simvastatin 5, 10, 20 and 40-mg tablets was submitted by the NHS Centre for the Evaluation of Effectiveness of Health Care (CeVEAS), Local Health Unit, Modena, Italy and Universities Allied for Essential Medicines (UAEM). The proposal is to list simvastatin with a square box, with pravastatin, fluvastatin, atorvastatin and lovastatin as named alternatives. Expert reviews of the application were prepared by Dr Alar Irs and Professor Hany Abdel-Aleem. Comments in support of the application were received from Dr Shanthi Mendis, Senior Adviser, Cardiovascular Diseases, Chronic Diseases Prevention and Management, WHO. During its meeting in 1997, the Committee added the section on lipid-lowering medicines to the Model List. At that time, no specific medicine was recommended at the global level, although it was recommended that the choice should be made at the national level and the class of medicines, "statins" (beta-hydroxy-beta-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors) was suggested. The following statement has been included in the Model List since that meeting (with minor variations): "The WHO Expert Committee on the Selection and Use of Essential Medicines recognizes the value of lipid-lowering drugs in treating patients with hyperlipidaemia. HMG-CoA reductase inhibitors, often referred to as "statins", are a family of potent and effective lipid-lowering drugs with a good tolerability profile. Several of these drugs have been shown to reduce the incidence of fatal and non-fatal myocardial infarction, stroke and mortality (all causes), as well as the need for coronary by-pass surgery. All remain very costly but may be cost effective for secondary prevention of cardiovascular disease as well as for primary prevention in some very high-risk patients. Since no single drug has been shown to be significantly more effective or less expensive than others in the group, none is included in the Model List; the choice of drug for use in patients at highest risk should be decided at the national level." The Committee noted that the application was of high quality and provided a comprehensive review of the existing evidence regarding the effectiveness and safety of statins used for secondary prevention of cardiovascular disease. The public health need for inclusion of a statin on the Model List was fully substantiated. As noted by the expert reviewers, there is high-quality clinical evidence from many large randomized trials and systematic reviews that establish the benefits of statins, in

conjunction with lifestyle modification, for secondary prevention of cardiovascular disease. For example, the estimates of benefit in the UK National Institute for Clinical Excellence (NICE) systematic review (1) are RR 0.80 (95% CI, 0.71– 0.90) for all-cause mortality and RR 0.75 (95% CI, 0.68–0.83) for cardiovascular mortality. These results are consistent with those of the other studies presented. The Committee noted that statins are generally well tolerated (2). However, some of the rare adverse effects of statins are potentially very serious, including rhabdomyolysis. For the statins included in the application, there is no evidence of a difference in adverse effect profiles although adverse effects appear to be dose-related. The Committee noted that one medicine in the statin class, cerivastatin, had been withdrawn from the market due to unacceptably high rates of adverse reactions. Ideally, regular monitoring of liver function should be available if patients are taking long-term statin treatment, but it is also possible to assess safety on the basis of clinical assessment of muscle symptoms such as pain and fatigue. In general the benefits of statins in preventing cardiovascular deaths outweigh the risk of the rare adverse effects. Generic preparations of simvastatin are available worldwide; the current cost of simvastatin is reasonable and its inclusion on the Model List would potentially contribute to further reductions in prices. The application provided a review of the evidence on cost-effectiveness of long-term statin therapy for secondary prevention. The Committee noted that the cost-effectiveness of statin treatment is closely related to the absolute risk for coronary heart disease. There have been many cost-effectiveness analyses of use of statins in developed countries, but few in developing countries. The study by Murray et al. (3) provided modelled estimates of the average cost per disability-adjusted life year (DALY) of statins for secondary prevention in developing countries and suggested that, using the threshold of gross national income per capita, the products are acceptably cost-effective. Overall the evidence provided in the application supports the public health need, effectiveness, safety and cost-effectiveness of simvastatin as an example statin. The Committee therefore recommended that simvastatin be added to the Model List for risk reduction in high-risk populations with a square box symbol denoting pravastatin, lovastatin, fluvastatin and atorvastatin as possible alternatives, with the choice to be made at the national level. These alternatives were identified on the basis of availability of comparable clinical outcome data. References: 1. Statins for the prevention of coronary events – technology assessment report commissioned to ScHARR by the NICE HTA Programme. London, National Institute for Health and Clinical Excellence, 2005. 2. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density, lipoprotein cholesterol, ischaemic heart disease and stroke: systematic review and meta-analysis. British Medical Journal, 2003, 326:1423–1432. 3. Murray CJL et al. Effectiveness and cost of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. Lancet, 2003, 361:717–725.