

Wyoming Drug Utilization Review



Edited by
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Statin Comparison

Kate L. Ramirez, Pharm.D.

The statins can be divided into subclasses that include the naturally or fungi derived 1st generation statins and the synthetically or heptanoic acid 2nd generation statins. The 1st generation statins include lovastatin, pravastatin and simvastatin and the 2nd generation includes atorvastatin, fluvastatin and rosuvastatin which contains a sulfur moiety.¹ They can further be divided into the lipophilic group containing simvastatin, lovastatin and atorvastatin while the hydrophilic group contains fluvastatin, pravastatin and rosuvastatin. All statins are excreted through urine and feces. Patients with renal impairment require reduced doses of all statins excluding atorvastatin and fluvastatin. Statins utilize the cytochrome P 450 system, with some affecting the system more than others. Lovastatin, simvastatin and atorvastatin utilize the 3A4 system, fluvastatin and rosuvastatin utilize 2C9 and pravastatin does

not use the CYP450 system. Food interactions are just as important as drug-drug interactions. Grapefruit juice has been shown to increase levels of lovastatin, simvastatin and atorvastatin. Pravastatin, atorvastatin and fluvastatin, on the contrary, can have decreased effects when taken with food. Side effects, especially myopathy, are main concerns with statins.

Table 1 shows specific product information adapted from Pharmacist's Letter, Current Perspectives on Statins³, a trial by Brown et al⁴, and a trial by Davidson et al.⁵ Table 2 on page 2 shows equivalent doses of several statins based on the CURVES trial, which demonstrated comparative doses of statins (excluding rosuvastatin) and determined dose equivalents. The information in Table 2 is adapted from Brown et al⁴.

Table 1: Product Information

Statin	Dose	LDL	TC	TG	HDL
Atorvastatin	10 mg	-39	-29	-19	+6
	20 mg	-43	-33	-26	+9
	40 mg	-50	-37	-29	+6
	80 mg	-60	-45	-37	+5
Fluvastatin	20 mg	-22			
	40 mg	-24			
	80 mg	-36			
Lovastatin	20 mg	-25	-18.4	-12.7	+6
Pravastatin	10 mg	-22	-16	-15	+7
	20 mg	-32	-24	-11	+2
	40 mg	-34	-25	-24	+12
Simvastatin	5 mg	-24	-17	-10	+7
	10 mg	-33	-24	-10	+9
	20 mg	-33	-25	-19	+11
	40 mg	-40	-28	-19	+12
Rosuvastatin	10 mg	-45.8	-32.9	-19.8	+7.7
	20 mg	-52.4	-37.6	-23.7	+9.5
	40 mg	-55	-40.2	-26.1	+9.6

(LDL= low-density lipoprotein, TC= total cholesterol, TG= triglycerides, HDL= high-density lipoprotein)

ACE Inhibitor Conversion Dose

Kate L. Ramirez, Pharm.D.

The table below allows easy conversion from non-preferred ACEI to a preferred ACEI. This table does not represent exact equivalent doses of ACEI. Doses are based on mid-dosing ranges of the drugs. Direct comparison trials are needed to determine exact dosing except where noted. The table is adapted from references 2 and 3 except where noted.

References:

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2. Stoysich AS and Massoomi F. Automatic Interchange of the ACE inhibitors: Decision-making Process and Initial Results. *Formulary* 2002;37:41-4.
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		Preferred Drugs			
		Captopril 12.5mg tid	Trandolapril (Mavik®) 2 mg	Benazepril (Lotensin®) 20 mg	Lisinopril 20 mg
Non-Preferred Drugs	Moexipril (Univasc®)	7.5 mg	7.5 mg	7.5 mg	7.5 mg
	Fosinopril (Monopril®)	10 mg	10 mg	10 mg	15 mg ¹
	Enalapril (Vasotec®)	10 mg	5 mg	5 mg	5 mg
	Quinapril (Accupril®)	10 mg	10 mg	10 mg	10 mg
	Ramipril (Altace®)	2.5 mg	2.5 mg	2.5 mg	2.5 mg
	Perindopril (Aceon®)	4 mg	4 mg	4 mg	4 mg

Continued from page 1 (Statin Comparison)

Table 2: Equivalent Doses

Atorvastatin	Simvastatin	Lovastatin	Pravastatin	Fluvastatin
-----	10 mg	20 mg	20 mg	40 mg
10 mg	20 mg	40 mg	40 mg	80 mg
20 mg	40 mg	80 mg	-----	-----
40 mg	80 mg	-----	-----	-----
80 mg	-----	-----	-----	-----

References

1. Chong PH. Lack of Therapeutic Interchangeability of HMG-CoA Reductase Inhibitors. *Ann Pharmacother* 2002;36:1907-17.
2. Dunham D and Patel TC. Statin Comparison. *The Pharmacist's Letter* 1998;14(1):140110.
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5. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM, Miller E, Cain VA, Bassetto JW: The STELLAR Study Group. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR* Trial). *Am J Cardiol* 2003;92(2):152-60.

COX-2 Inhibitors Plus PPIs

Hanni B. Jensen, Pharm.D.

The adverse gastrointestinal (GI) side effects of nonsteroidal anti-inflammatory drugs (NSAIDs) are well known. Cyclooxygenase 1 inhibition seems to be the cause of GI toxicity. Consequently selective cyclooxygenase 2 (COX-2) inhibitors were developed in hopes of creating a safer medication. These medications have been shown to cause limited GI injury, and may be an alternative to traditional NSAIDs in patients at risk of bleeding.¹

Some practitioners prescribe a COX-2 inhibitor to be used concomitantly with a proton pump inhibitor (PPI). Unfortunately no studies have been performed to determine if combination of these two classes of medications is a reasonable therapeutic option.^{2,3} The benefits of PPIs are rarely seen when an already low risk of GI events is present, as is the case with the use of COX-2 inhibitors. Proton pump inhibitors are more effective in high risk individuals.³

The cost-effectiveness of this combination of medications is also unknown. Studies that have been performed to determine the cost-effectiveness of preventing an upper GI event compared use of a COX-2 inhibitor to use of a traditional NSAID plus a PPI.⁴ With the advent

of generic omeprazole the cost-effectiveness of the latter strategy should improve even further. Both of these studies would probably be more cost-effective than the combination of a COX-2 inhibitor and a PPI, simply as a result of the increased cost of COX-2 inhibitors.

In conclusion, until studies have been performed on the simultaneous use of COX-2 inhibitors and PPIs, the combination should probably be avoided. No evidence exists to document increased efficacy in preventing upper GI events, to make the additional costs associated with treatment worthwhile.

References

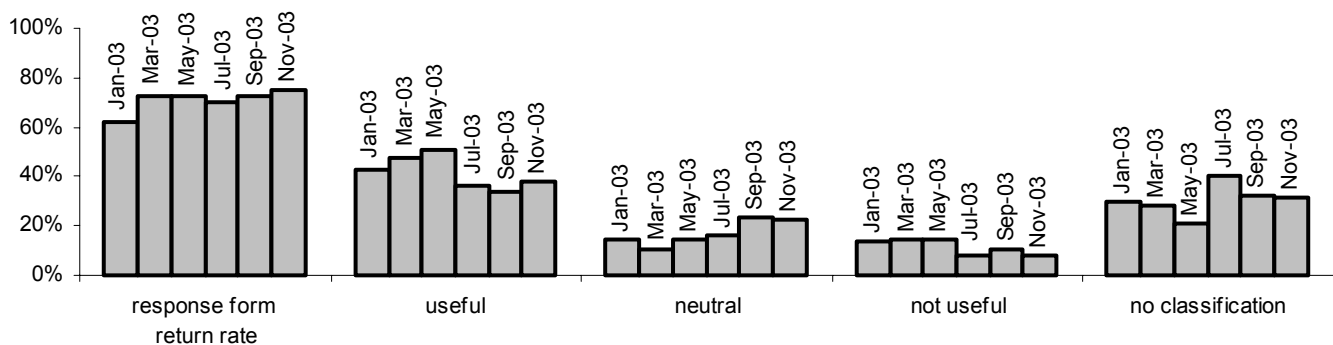
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Prescriber Response Forms

(2003)

Each prescriber who receives an education alert letter is asked to complete and return a response form. In the response form, we ask the prescriber to classify the information in the alert letter as *useful*, *neutral*, or *not useful*.

The graph below shows the following information: the return rate for prescriber response forms for 2003, the percentage of returned provider response forms that fall into each of the 3 classifications (*useful*, *neutral*, and *not useful*), and the percentage of *no classification*, which is assigned if the provider fails to classify the information in the alert letter.



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