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Joan Claybrook, President

May 18, 2004

Lester Crawford, DVM, Acting Commissioner  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20854

Dear Dr. Crawford,

As you are aware, on March 4<sup>th</sup> of this year, we petitioned the FDA to ban the recently-marketed cholesterol-lowering drug rosuvastatin (Crestor/AstraZeneca) because of seven post-marketing cases of life-threatening rhabdomyolysis and nine cases of renal failure or renal insufficiency, both of which problems had also been identified during the pre-approval clinical trials. Of these post-approval cases, one case of rhabdomyolysis occurred in the United States, where the drug had only been on the market for little over five months, as did two cases of kidney toxicity. The other cases of rhabdomyolysis and drug-induced kidney disease occurred in the UK or Canada, where the drug had been on the market for a longer time.

We have now obtained new information from the FDA about many additional post-marketing cases of rhabdomyolysis and kidney toxicity in reports updated to April 13<sup>th</sup>. In the relatively short interval since our first petition, 11 additional cases of rhabdomyolysis in patients using rosuvastatin, including at least 10 in the United States, have been reported to the FDA, as have three additional cases of renal failure or renal insufficiency in the United States, all in people using 10 milligrams.

Of the 10 new U.S. cases of rhabdomyolysis, seven of them were at the very low dose of 10 milligrams and three were at the next higher dose of 20 milligrams. Five of the eight U.S. patients whose ages are known were under the age of 50 and nine of the 10 U.S. patients had to be hospitalized because of the severity of the rhabdomyolysis.

Despite the fact that the majority of U.S. cases of rhabdomyolysis were in people using the 10 milligram dose, AstraZeneca has just sent a warning out to physicians that patients should start at that dose, blaming the four cases of rhabdomyolysis they report on higher doses but failing to mention

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the seven patients who suffered from rhabdomyolysis at the 10 milligram dose.

According to an alert posted on May 17<sup>th</sup> on the British government's web site <http://www.druginfozone.nhs.uk/home/default.aspx>

“AstraZeneca have written [on May 14<sup>th</sup>] to healthcare professionals to warn prescribers to initiate Crestor (rosuvastatin) at a dose of 10mg. This follows reports of 4 cases of rhabdomyolysis and 1 case of myoglobinuria/renal impairment secondary to myositis, in patients initiated on rosuvastatin at doses greater than 10 mg.

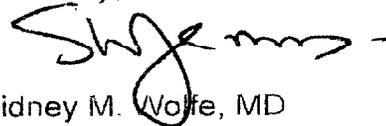
The manufacturer recommends that those patients who have already been started on doses greater than 10 mg should be reviewed at their next appointment, and appropriate down-titration of dose should be considered.

Patients should be asked to report muscle pain, weakness or cramps immediately, and if symptoms are severe or if the CPK is greater than 5 times the upper limit of normal, treatment should be stopped.  
(Ref. Dear Healthcare Professional issued 14 May 2004.)”

Rosuvastatin is a doomed drug. It should never have been approved, given the clear evidence of renal toxicity and the seven cases of rhabdomyolysis prior to approval. None of the other statins, including the ultimately doomed cerivastatin (Baycol) had any cases of rhabdomyolysis prior to approval and the primary renal toxicity (separate from the secondary renal damage done as a consequence of rhabdomyolysis) is unique to rosuvastatin. When the first months of marketing predictably brought additional cases of renal failure and rhabdomyolysis, the FDA should have responded by removing the drug from the market as we had urged in our March 4<sup>th</sup> petition.

AstraZeneca is obviously desperate to save this drug which they have so counted on to cut a swath in the \$10+ billion dollar statin market that they are spending what has been estimated to be \$1 billion on its promotion. We renew our effort to get the FDA to ban this uniquely dangerous drug before it does any further damage.

Sincerely,



Sidney M. Wolfe, MD

Director, Public Citizen's Health  
Research Group