

## PUBLIC ADVISORY

### Health Canada Endorsed Important Safety Information on CRESTOR® (rosuvastatin)



March 8, 2005

**Subject: Important safety information for CRESTOR® (rosuvastatin)**

AstraZeneca Canada Inc., in consultation with Health Canada, would like to inform patients of important safety information for CRESTOR® (rosuvastatin) tablets.

CRESTOR® is a cholesterol-lowering drug in the “statin” family. Statins are a specific type of medication used to lower cholesterol.

In Canada, and internationally, CRESTOR® has been associated with rare reports of a serious condition called rhabdomyolysis. Rhabdomyolysis is a condition that results in muscle breakdown and release of muscle cell contents into the bloodstream. In severe cases, rhabdomyolysis can lead to kidney failure and be life-threatening. Some patients may have pre-existing medical conditions which might cause them to have a greater risk of developing muscle related problems, including rhabdomyolysis, if they are using “statin” medications.

Because the number of reports of rhabdomyolysis is increased at the highest recommended daily dose of CRESTOR®, 40 mg daily, this dose must not be used in patients who have pre-existing medical conditions or other factors which put them at increased risk for rhabdomyolysis. These factors include:

- Personal or family history of muscle problems
- Past history of significant muscle pain or muscle weakness while using a “statin” drug
- Taking other cholesterol-lowering medication such as fibrates (gemfibrozil, fenofibrate) or niacin
- Serious liver problems
- Serious kidney problems
- An underactive thyroid gland
- Alcohol abuse
- **Asian ethnicity**

**Asian** patients (having either Filipino, Chinese, Japanese, Korean, Vietnamese or Asian-Indian origin) may be at greater risk of developing muscle related adverse events, including rhabdomyolysis, with CRESTOR® (rosuvastatin) because in a recent US study, rosuvastatin drug levels in the blood were found to be approximately 2 times higher in Asians when compared to Caucasians.

To ensure the safe and effective use of CRESTOR<sup>®</sup>, patients should be using the lowest dose that will meet their treatment goal. A new lower 5 mg starting dose is recommended for:

- **Asian** patients
- Patients with serious kidney problems

The 5 mg starting dose may also be considered for patients who might have other risk factors for muscle problems or require less aggressive cholesterol lowering therapy.

In addition, Health Canada has asked all brand-name manufacturers of statin drugs, including CRESTOR<sup>®</sup> to update the Canadian Product Monographs for each medication, including the **Information to the Patient** leaflets, to help patients recognize if they have pre-disposing factors for muscle problems and to advise them to discuss these factors with their physician before starting CRESTOR<sup>®</sup> or any statin. This information will also help patients recognize symptoms of potentially serious muscle related problems and know when to seek prompt medical attention.

The Information to the Patient leaflet advises that before taking a statin, patients should tell their doctor or pharmacist if they:

- have thyroid problems
- regularly drink three or more alcoholic drinks daily
- are taking other cholesterol lowering medication such as fibrates (gemfibrozil, fenofibrate) or niacin
- are taking other medications, including prescription, non-prescription and natural health products as drug interactions are possible
- have a family history of muscular disorders
- had any past problems with the muscles (pain, tenderness), after using an HMG-CoA reductase inhibitor (statin)
- have kidney or liver problems
- have diabetes
- have undergone surgery or other tissue injury
- do excessive physical exercise

As side effects such as myalgia (muscle pain), myopathy (muscle disease with aching or weakness) and rhabdomyolysis can be serious, patients are advised to contact their physician promptly if they experience any of the following while on statin therapy:

- muscle pain that they cannot explain
- muscle tenderness or muscle weakness
- generalized weakness, especially if they do not feel well (i.e. fever or fatigue)
- brownish or discoloured urine

This information, accompanied by a revised copy of the updated Canadian Product Monograph for CRESTOR<sup>®</sup>, has been provided to Canadian health care professionals in a letter issued by AstraZeneca Canada Inc. A copy of this letter is available on the website of the Therapeutic Products Directorate of Health Canada, at the following address:

[http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index\\_advisories\\_professionals\\_e.html](http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_advisories_professionals_e.html)

Past advisories of safety information about CRESTOR<sup>®</sup> can be found at:

[http://www.hc-sc.gc.ca/english/protection/warnings/2004/2004\\_34.htm](http://www.hc-sc.gc.ca/english/protection/warnings/2004/2004_34.htm)

If you have questions about your CRESTOR<sup>®</sup> (rosuvastatin) prescription, you should contact your doctor.

Health Canada will continue to monitor the safety profile of statins, including CRESTOR<sup>®</sup> (rosuvastatin), and will examine new safety information as it emerges. If you have had a serious or unexpected adverse reaction while taking CRESTOR<sup>®</sup> you should notify your doctor or AstraZeneca Canada Inc. and/or Health Canada as follows:

AstraZeneca Canada Inc.  
1004 Middlegate Road  
Mississauga, ON, L4Y 1M4  
Tel: 1-800 433-0733  
Fax: 1-800-267-5743  
www.astrazeneca.ca

**Any suspected adverse reaction can also be reported to:**

Canadian Adverse Drug Reaction Monitoring Program (CADRMP)  
Marketed Health Products Directorate  
HEALTH CANADA  
Address Locator: 0701C  
OTTAWA, Ontario, K1A 0K9  
Tel: (613) 957-0337 or Fax: (613) 957-0335

To report an Adverse Reaction (AR), consumers and health professionals may call toll free:  
Tel: (866) 234-2345  
Fax: (866) 678-6789  
cadrmp@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialities*.

For further information call AstraZeneca Medical Information at 1-800-668-6000 (English) and/or 1-800-461-3787 (French). For media inquiries, please contact Liana Del Medico at (905) 804-5819.

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