



## What Makes CRESTOR® (rosuvastatin calcium) Different?

### **CRESTOR** effectively lowers LDL-C (bad) cholesterol and raises HDL-C (good) cholesterol<sup>1,2</sup>

- Across the dose range, CRESTOR has been shown to provide a 45-63% reduction in LDL-C and a 8-14% increase in HDL-C, versus a 7% LDL-C reduction and 3% HDL-C increase with placebo.<sup>1</sup>
- CRESTOR is contraindicated in patients with a known hypersensitivity to any component of this product, in patients with active liver disease, and in women who are pregnant, nursing or could become pregnant.

### **CRESTOR is also the only branded statin indicated to slow the progression of atherosclerosis** in adult patients with elevated cholesterol at any stage of the disease

- CRESTOR is a once-daily prescription statin medication indicated for use as an adjunct to diet in the treatment of primary hyperlipidemia, mixed dyslipidemia and hypertriglyceridemia, available in a 5-, 10-, 20-, and 40-mg dose. In November 2007, the FDA approved CRESTOR to slow the progression of **atherosclerosis** in patients with elevated cholesterol as part of a treatment strategy to lower total-C and LDL-C, based largely on the results of a pivotal study called **METEOR** (**M**asuring **E**ffects on intima media **T**hickness: an **E**valuation **O**f **R**osuvastatin).
- METEOR measured the effects of CRESTOR on plaque-build up in the carotid arteries using b-mode ultrasonography to measure carotid intima-media thickness (CIMT). Results demonstrated a slowing of progression of atherosclerosis in people taking CRESTOR 40 mg with subclinical atherosclerosis, elevated LDL cholesterol, and low cardiovascular risk.
  - CRESTOR 40 mg should only be used for those patients not achieving their LDL-C goal with 20 mg. Patients initiating CRESTOR therapy or switching from another statin should begin treatment with CRESTOR at the appropriate starting dose.



### **CRESTOR has been shown to reduce LDL-C and raise HDL-C in a trial comparing its efficacy with that of atorvastatin, simvastatin, and pravastatin**

- The **STELLAR** (Statin Therapies for Elevated Lipid Levels compared Across doses to Rosuvastatin) study was a six-week, randomized, open-label study comparing the efficacy of specific doses and the dose range of CRESTOR with specific doses and the dose ranges of atorvastatin, pravastatin and simvastatin in patients with primary hypercholesterolemia.
- In STELLAR, 2,431 patients with hypercholesterolemia (LDL-C  $\geq$ 160 mg/dL and  $<$ 250 mg/dL; triglycerides  $<$ 400 mg/dL) were randomized to one of 15 open-label treatment arms for six weeks. Results showed:

STELLAR RESULTS		
Treatment	LDL-C Reduction	HDL-C Increase
<b>CRESTOR 10-40 mg</b>	<b>46-55%</b>	<b>7.7-9.6%</b>
atorvastatin 10-80 mg	37-51%	2.1-5.7%
simvastatin 10-80 mg	28-46%	5.2-6.8%
pravastatin 10-40 mg	20-30%	3.2-5.6%

P<.002 CRESTOR 10 mg vs. atorvastatin 10 mg; simvastatin 10 mg, 20 mg, 40 mg; pravastatin 10 mg, 20 mg, 40 mg  
 P<.002 CRESTOR 20 mg vs. atorvastatin 20 mg, 40 mg; simvastatin 20 mg, 40 mg, 80 mg; pravastatin 20 mg, 40 mg.  
 P <.002 CRESTOR 40 mg vs. atorvastatin 40 mg; simvastatin 40 mg, 80 mg; pravastatin 40 mg.

**CRESTOR is not metabolized by cytochrome P450 3A4 to a clinically significant extent. The significance of these data in a clinical setting has not been shown.**

**CRESTOR is a hydrophilic (water soluble) statin, rather than lipophilic (fat soluble). The significance of these data in a clinical setting has not been shown.**

<sup>1</sup> Prescribing Information for CRESTOR. AstraZeneca Pharmaceuticals LP, Wilmington, DE.

<sup>2</sup> Jones PH, Davidson MH, Stein EA, et al, for 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;92:152-160.

## CRESTOR is accessible

- AstraZeneca has been successful in working with managed care organizations and through Medicare Part D formularies to ensure CRESTOR is offered as an important treatment option for patients
  - CRESTOR is reimbursed for 91.5% of member lives for commercial plans<sup>3</sup>
  - 90.3% of Medicare Part D plans reimburse CRESTOR,<sup>\*\*4</sup> and 38 out of 51 state Medicaid formularies have CRESTOR on their preferred drug lists<sup>5</sup>
  - Preferred access for CRESTOR increased from 54.8% in Jan. 2008 to 67% in Feb. 2009<sup>\*\*\*6</sup>
  - CRESTOR is available for no more than \$25 per month for eligible<sup>+</sup> patients with commercial prescription drug coverage

<sup>3</sup>Defined as Tier 1 through Tier 7 on Commercial, Commercial (BCBS), Commercial (Medicaid), Employer, Municipal Plan, PBM, and Union by Fingertip Formulary as of 3/1/09. Data include covered lives whose prescriptions may be subject to step-therapy requirements.

<sup>\*\*</sup>Defined as Tier 1 through Tier 7 on Medicare MA, Medicare PDP, and Medicare SN by Fingertip Formulary as of 3/1/09. Data include covered lives whose prescriptions may be subject to step-therapy requirements.

<sup>\*\*\*</sup> Defined as Tier 1 & Tier 2 on Commercial (BCBS), Commercial (Medicaid), Employer, Medicare MA, Medicare PDP, Medicare SN, Municipal Plan, PBM, State Medicaid, and Union formularies by Fingertip Formulary as of 3/5/09. Data include covered lives whose prescriptions may be subject to step-therapy requirements.

<sup>+</sup> Other restrictions may apply.

## CRESTOR has received regulatory approval in over 90 countries<sup>7</sup>

- Worldwide, over 13 million patients have been treated with CRESTOR and more than 140 million prescriptions have been written<sup>7</sup>

## CRESTOR has an established safety profile

- CRESTOR has a well established safety profile in line with other leading statins, which is supported by extensive large-scale clinical trials, postmarketing experience, and several real-world pharmacoepidemiology studies<sup>1,8,9,10,11,12,13</sup>

## CRESTOR growth in 2008 and 2009

- CRESTOR is the only branded statin to grow share in 2008<sup>\*14,15</sup> and CRESTOR has continued to grow in 2009<sup>\*\*16</sup>

<sup>\*</sup>Based on TRx share growth, relative to other branded statins in the market, during the time period December 2007 to December 2008. The analysis only includes statins and statin combination products (excluding Caduet®) that were approved as of January 1, 2008. Data Source: IMS NPA Monthly Data.

<sup>\*\*</sup>Based on TRx share growth, relative to other branded statins in the market, during the time period January to February 2009. The analysis only includes statins and statin combination products (excluding Caduet®). Data Source: IMS NPA Monthly Data.

## About CRESTOR

CRESTOR is indicated as adjunct to diet to reduce elevated total-C, LDL-C, ApoB, nonHDL-C, and triglycerides and to increase HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia, and to slow the progression of atherosclerosis in adult patients as part of a treatment strategy to lower Total-C and LDL-C to target levels. CRESTOR is not approved to reduce cardiovascular morbidity and mortality. For patients with hyperlipidemia and mixed dyslipidemia, the usual recommended starting dose of CRESTOR is 10 mg. The 40-mg dose of CRESTOR is reserved only for those patients who have not achieved their LDL-C goal utilizing the 20-mg dose of CRESTOR once daily. When initiating statin therapy or switching from another statin therapy, the appropriate CRESTOR starting dose should first be utilized, and only then titrated according to the patient's individualized goal of therapy.

For more information about CRESTOR, including full Prescribing Information, visit [www.crestor.com](http://www.crestor.com)

## Important Safety Information

<sup>3</sup> Fingertip Formulary. Data accessed: Percentage of covered lives - Commercial Plans. Accessed March 1, 2009.

<sup>4</sup> Fingertip Formulary. Data accessed: Percentage of covered lives - Medicare Part D. Accessed March 1, 2009.

<sup>5</sup> Fingertip Formulary. Data accessed: State Medicaid Plans. Accessed March 1, 2009.

<sup>6</sup> Fingertip Formulary. Data accessed: Percentage of covered lives - Preferred access data trend from Jan. 2008 to Feb. 2009. Accessed March 16, 2009.

<sup>7</sup> AstraZeneca Pharmaceuticals LP. Rosuvastatin Clinical Information. Postmarketing experience- patients treated. Last updated March 31, 2008. Available at <http://www.rosuvastatininformation.com/518986/518988/517586?itemId=3098955&nav=yes>. Accessed on January 8, 2009.

<sup>8</sup> Shepherd J, Vidt DG, Miller E, et al. Safety of rosuvastatin: update on 16,876 rosuvastatin-treated patients in a multinational clinical trial program. *Cardiology*. 2007;107:433-443.

<sup>9</sup> AstraZeneca Pharmaceuticals LP. Rosuvastatin Clinical Information - Postmarketing Experience, Safety Information: Spontaneous Adverse Event Reporting Information. Available at: <http://www.rosuvastatininformation.com>. Accessed March 18, 2009.

<sup>10</sup> McAfee AT, Ming EE, Seeger JD, et al. The comparative safety of rosuvastatin: a retrospective matched cohort study in over 48,000 initiators of statin therapy. *Pharmacoepidemiol Drug Saf*. 2006;15:444-453.

<sup>11</sup> Goettsch WG, Heintjes EM, Kastelein JJP, et al. Results from a rosuvastatin historical cohort study in more than 45,000 Dutch statin users, a PHARMO study. *Pharmacoepidemiol Drug Saf*. 2006;15:435-443.

<sup>12</sup> Garcia-Rodriguez LA, Gonzalez-Perez A, Stang MR, et al. The safety of rosuvastatin in comparison with other statins in over 25,000 statin users in the Saskatchewan Health Databases. *Pharmacoepidemiol Drug Saf*. 2008;17:953-961.

<sup>13</sup> Garcia-Rodriguez LA, Gonzalez EM, Wallander M, et al. The safety of rosuvastatin in comparison with other statins in over 100,000 statin users in UK primary care. *Pharmacoepidemiol Drug Saf*. 2008;17:943-952.

<sup>14</sup> IMS NPA Monthly Data. January 2009.

<sup>15</sup> IMS Health NPA + 7 Weekly Data. January 2009.

<sup>16</sup> IMS NPA Monthly Data. February 2009.

CRESTOR is contraindicated in patients with a known hypersensitivity to any component of this product and in patients with active liver disease, which may include unexplained persistent elevations of hepatic transaminase levels, in women who are or may become pregnant, and in nursing mothers. Cases of myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with drugs in this class, including CRESTOR. These risks can occur at any dose level but are increased at the highest dose (40 mg). The risk of myopathy during treatment with CRESTOR may be increased with concurrent administration of some other lipid-lowering therapies (fibrates or niacin), gemfibrozil, cyclosporine, or lopinavir/ritonavir. Combination therapy with rosuvastatin and gemfibrozil should be avoided. CRESTOR should be prescribed with caution in patients with predisposing factors for myopathy, such as renal impairment, advanced age, and inadequately treated hypothyroidism. Patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. It is recommended that liver enzyme tests be performed before and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter. A large US pharmacokinetics study demonstrated an approximate 2-fold elevation in median exposure in Asian subjects compared to a Caucasian control group. This increase should be considered when making decisions about dosing with CRESTOR in Asian patients. The most frequent adverse reactions thought to be related to CRESTOR were headache (3.7%), myalgia (3.1%), abdominal pain (2.6%), asthenia (2.5%), and nausea (2.2%).<sup>1,17</sup> The most common adverse reactions(%) in the METEOR trial for CRESTOR vs placebo, respectively, were myalgia (12.7 vs 12.1), arthralgia (10.1 vs 7.1), headache (6.4 vs 5.3), dizziness (4.0 vs 2.8), increased CPK (2.6 vs 0.7), abdominal pain (2.4 vs 1.8), ALT >3x ULN (2.2 vs. 0.7)

Please see accompanying full Prescribing Information.

#### **About AstraZeneca**

AstraZeneca is engaged in the research, development, manufacturing and marketing of meaningful prescription medicines and in the supply of healthcare services. AstraZeneca is one of the world's leading pharmaceutical companies with global healthcare sales of \$ 31.6 billion and is a leader in gastrointestinal, cardiovascular, neuroscience, respiratory, oncology and infectious disease medicines. In the United States, AstraZeneca is a \$13.5 billion dollar healthcare business.

For more information about AstraZeneca in the US or our AZ&Me™ Prescription Savings programs, please visit: [www.astrazeneca-us.com](http://www.astrazeneca-us.com).

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