

## Drug Information Response Center Questions

### Highlights of the new cholesterol guideline March 17, 2014

The American College of Cardiology (ACC) and American Heart Association (AHA), in conjunction with the National Heart, Lung, and Blood Institute (NHLBI), issued a guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk in adults, published in November 2013.<sup>1</sup> In their recommendations, the ACC/AHA identify 4 groups of patients most likely to benefit from statin therapy. The groups include individuals with 1) clinical ASCVD; 2) primary elevation of low density lipoprotein-cholesterol (LDL-C)  $\geq 190$  mg/dL; 3) diabetes and LDL-C 70-189 mg/dL, aged 40-75 years; and 4) LDL-C 70-189 mg/dL in addition to an estimated 10-year ASCVD risk  $\geq 7.5\%$ . Clinical ASCVD is defined according to the inclusion criteria of the reviewed randomized controlled trials (RCTs). These criteria were acute coronary syndrome (ACS), or history of myocardial infarction (MI), stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral arterial disease of atherosclerotic origin. Instead of using the 10-year coronary heart disease (CHD) risk equivalents described in previous guidelines, the new guideline recommends the new Pooled Cohort Risk Assessment for an estimated 10-year ASCVD risk that predicts the risk of both CHD and stroke.<sup>2</sup>

In the ASCVD statin benefit groups, high-intensity statin therapy is generally preferred unless contraindicated or intolerable.<sup>1</sup> See Table 1 for definitions of high-, moderate-, and low-intensity statin treatment. High-intensity statin therapy lowers LDL-C by approximately by 50% or greater, whereas moderate-intensity statin therapy lowers LDL-C by about 30% to 50%. If high-intensity statin therapy is not feasible, moderate-intensity statin therapy is recommended. For individuals  $>75$  years of age with clinical ASCVD, there is no clear evidence supporting aggressive statin regimen over moderate-intensity statin therapy. Therefore, moderate-intensity statin therapy may be appropriate in this population. In general, therapy should be individualized, based on the potential benefits, adverse effects, drug interactions, and patient preference.

**Table 1: Definitions of statin intensity.<sup>1</sup>**

	<b>Average LDL-C lowering</b>	<b>Statin dosing*</b>
<b>High-intensity</b>	≥ 50%	Atorvastatin 40-80 mg Rosuvastatin 20- 40 mg
<b>Moderate-intensity</b>	30% - < 50%	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg <i>Fluvastatin XL 80 mg</i> Fluvastatin 40 mg BID <i>Pitavastatin 2-4 mg</i>
<b>Low-intensity</b>	< 30%	<i>Simvastatin 10 mg</i> Pravastatin 10-20 mg Lovastatin 20 mg <i>Fluvastatin 20-40 mg</i> <i>Pitavastatin 1 mg</i>

Dosing is daily, unless otherwise noted. LDL= low density lipoprotein-cholesterol; BID=twice daily.

\*All dosing recommendations were evaluated in RCTs; dosing recommendations italicized were not evaluated in RCTs, but are FDA approved for LDL-C lowering.

Finally, the new guidelines encourage prescribers to utilize the ASCVD risk score and to consider additional factors such as LDL ≥160 mg/dL, family history, genetic hyperlipidemia, and high-sensitivity C-reactive protein ≥2 mg/L in order to determine the intensity of statin therapy in those individuals who do not belong to any of the statin benefit groups.<sup>1</sup>

Unlike the Adult Treatment Panel (ATP III), the ACC/AHA make no recommendations regarding specific LDL-C or non-HDL-C targets since data from RCTs have not demonstrated improved ASCVD outcomes related to these specific targets.<sup>1-2</sup> In the Atherosclerosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) trial, adding extended-release niacin to intensive statin therapy to provide additional non-HDL-C lowering did not improve cardiovascular outcomes.<sup>3</sup> Similarly, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial also demonstrated that adding fenofibrate to a statin only increased the risk of myositis and did not improve cardiovascular outcomes.<sup>4</sup> Based on these data, targeting specific LDL-C and non-HDL-C goals does not appear to improve cardiovascular outcomes and may result in the overuse of non-statin drugs and increase the risk for adverse events.<sup>1</sup>

As stated earlier, controversy surrounds the release of the new ACC/AHA dyslipidemia guidelines.<sup>5</sup> Several leading cardiologists have raised concerns over both the new risk assessment tool and the change from monitoring LDL-C. For the new risk assessment tool, cardiologists believe it overestimates the risk of MI or stroke. There is also disagreement about only using evidence from RCTs, which differs from how previous guidelines were developed; since neither genetic nor population data were considered in drafting the new guidelines. Other objections include the fact that no public comment period was provided and many experts believe international collaboration is needed. It is important to note that the National Lipid Association is

not endorsing the new guidelines and the U.S. Preventative Services Task Force is in the process of devising its own dyslipidemia guidelines (to be released in 2 years). Also, the *British Medical Journal* recently reported that 8 of the 15 panelists have ties to pharmaceutical companies, potentially raising conflict of interest concerns.<sup>6</sup>

In light of the controversy and potential limitations of the new guidelines, how should clinicians interpret and utilize the new guidelines? Until more definitive guidance is provided by cardiology experts, clinicians should continue to use their professional judgment and consider patient specific factors when evaluating treatment and monitoring of dyslipidemia. At the time of this writing, the New York State Department of Health is also evaluating the information relative to the new guidelines and its implications on clinical practice.

### References:

1. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. Nov 7 2013.
2. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. Dec 17 2002;106(25):3143-3421.
3. Boden WE, Probstfield JL, Anderson T, et al. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy. *N Engl J Med*. Dec 15 2011;365(24):2255-2267.
4. Ginsberg HN, Elam MB, Lovato LC, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. *N Engl J Med*. Apr 29 2010;362(17):1563-1574.
5. Kolata G. Bumps in the road to new cholesterol guidelines. *The New York Times*. November 25, 2013.
6. Lenzer J. Majority of panelists on controversial new cholesterol guideline have current or recent ties to drug manufacturers. *BMJ*. 2013;347:f6989.