NATIONAL LIPID ASSOCIATION

2017 RECOMMENDATIONS OF THE NLA Expert Panel on Treatment with PCSK9 Inhibitors

An Expert Panel convened by the National Lipid Association (NLA) was charged with updating the recommendations on the use of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor therapy that were provided by the 2015 NLA Recommendations for the Patient-Centered Management of Dyslipidemia: Part 2.

Atherosclerotic Cardiovascular Disease (ASCVD)

1. PCSK9 inhibitor therapy should be considered for ASCVD risk reduction in patients with **stable ASCVD,** particularly in those with additional ASCVD risk factors, on maximally-tolerated statin therapy ± ezetimibe, with on-treatment LDL-C ≥70 mg/dL or non-HDL-C ≥100 mg/dL. Strength: A, Quality: High.
2. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in patients with **progressive ASCVD** on maximally-tolerated statin therapy ± ezetimibe, and on-treatment LDL-C ≥70 mg/dL or non-HDL-C ≥100 mg/dL. Strength: B, Quality: Moderate.

Very High Risk/Statin Intolerance

4. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in selected very high-risk patients who meet the definition of statin intolerance (as previously defined by the NLA Statin Expert Panel)** and who require substantial additional atherogenic cholesterol lowering, despite the use of other lipid lowering therapies. Strength: C, Quality: Low.

LDL-C ≥ 190 mg/dL

(including polygenic hypercholesterolemia, HeFH, and the HoFH phenotype)

3a. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in **patients age 40-79 years** with pre-treatment LDL-C ≥ 190 mg/dL, **no uncontrolled ASCVD risk factors** or other key additional high risk markers*, and on-treatment LDL-C ≥ 100 mg/dL or non-HDL-C ≥ 130 mg/dL on maximally-tolerated statin therapy ± ezetimibe. Strength: B, Quality: Moderate.

3b. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in **patients age 40-79 years** with pre-treatment LDL-C ≥ 190 mg/dL and the presence of **uncontrolled ASCVD risk factors,** key additional high risk markers*, or genetic confirmation of FH, and on-treatment LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL on maximally-tolerated statin ± ezetimibe. Strength: B, Quality: Moderate.

3c. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in **patients age 18-39 years** with pre-treatment LDL-C ≥ 190 mg/dL and the presence of either **uncontrolled ASCVD risk factors,** key additional high risk markers*, or genetic confirmation of FH, and on-treatment LDL-C ≥ 100 mg/dL or non-HDL-C ≥ 130 mg/dL on maximally-tolerated statin ± ezetimibe. Strength: E, Quality: Low.

3d. PCSK9 inhibitor therapy may be considered to further reduce LDL-C in patients with **homozygous FH,** either of unknown genotype, or those known to be LDL receptor defective, on maximally-tolerated statin therapy ± ezetimibe with LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL. Strength: B, Quality: Moderate.

*Including history of uncontrolled high blood pressure, diabetes, current cigarette smoking or family history of premature ASCVD; or additional high risk markers (coronary calcium ≥ 300 Agatston units [or ≥ 75th percentile for the patient's age, gender and ethnicity]; Lp(a) ≥ 50 mg/dL using an isoform insensitive assay, hs-CRP ≥ 2 mg/L or CKD including albumin/creatinine ratio ≥ 30 mg/g)

**Such as those who had previous ASCVD events in the presence of additional risk factors.

Note: All patients considered for PCSK9 therapy should have updated screening for secondary causes of hypercholesterolemia, particularly hypothyroidism, nephrotic syndrome, obstsructive liver disease, and drug therapy.