Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors
Nebraska Health Network: Criteria for Use

GENERAL INFORMATION

- The effect of PCSK9 inhibitors on cardiovascular morbidity and mortality has NOT been established. Use should be limited to patients at exceptionally high risk for cardiovascular events where no alternative treatment option is available.
- Prescribing of PCSK9 inhibitors should be limited to cardiologists and endocrinologists.
- Annual cost for currently marketed PCSK9 inhibitors ranges between $14,100 and $14,600.

EXCLUSION CRITERIA

(If answer is yes to any item below, patient should NOT receive PCSK9 inhibitor)

☐ Age <18 years
☐ Pregnant or breastfeeding
☐ History of severe hypersensitivity to selected PCSK9 inhibitor

CAUTION

(If answer is yes to any item below, risk/benefit of therapy should be considered)

☐ Severe hepatic impairment or renal dysfunction (CrCl <30ml/min)
  - Populations not studied in clinical trials

CRITERIA FOR USE: ALL CRITERIA MUST BE MET

("See attachment A for diagnosis criteria and definitions")

☐ Homozygous Familial Hypercholesterolemia confirmed* OR
☐ Heterozygous Familial Hypercholesterolemia confirmed* OR
☐ Hyperlipidemia in patient with established atherosclerotic cardiovascular disease (ASCVD) (ex. previous MI; stable or unstable angina; stroke/TIA; peripheral artery disease)

AND

☐ Patient is receiving high intensity statin*, or statin therapy at maximum tolerated dose OR
☐ Patient is statin intolerant* OR
☐ Patient has contraindication to statin that does not exist for PCSK9 inhibitor (ex. active liver disease, unexplained persistent elevation in serum aminotransferase)

AND

☐ Patient is receiving ezetimibe in addition to statin therapy (for patients tolerant to statins)

AND

☐ Failure to achieve greater than 50% reduction in LDL-C (if baseline value known) OR
☐ LDL-C >100mg/dL if no documented CVD or LDL-C >70mg/dL if documented CVD after demonstrated adherence (medication possession ratio >80%) for at least 3 months of optimized lipid lowering therapy and lifestyle modifications

DISCONTINUATION CRITERIA

☐ Discontinue if little or no improvement in lipid parameters (e.g. LDL, non-HDL) is noted after 1-2 months of therapy

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be reviewed as new information becomes available. The purpose of this document is to assist providers in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. Prescribing in alignment with the recommendations in this document DOES NOT guarantee coverage by insurers.
### Attachment A: Diagnosis Criteria and Definitions

#### Diagnostic Criteria for Homozygous Familial Hypercholesterolemia (HoFH)\(^1,2\)
- Presence of two mutant alleles at the LDL-receptor; apoB; PCSK9, or LDL receptor accessory protein 1 (LDLRAP1) genes **OR**
- Untreated LDL >500mg/dL (on treatment LDL >300mg/dL) **AND**
  - Cutaneous or tendon xanthomas before age 10 **OR**
  - Elevated LDL-C in both parents suggestive of HeFH

#### Diagnostic Criteria for Heterozygous Familial Hypercholesterolemia (HeFH)\(^3\)
- Presence of mutation in LDL-receptor; apoB; PCSK9, or LDLRAP1 genes **OR**
- Score greater than 8 based on WHO Criteria (Table 1)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family History</td>
<td></td>
</tr>
<tr>
<td>1° relative known to have premature CAD and/or 1° relative with LDL-C &gt;95th percentile</td>
<td>1</td>
</tr>
<tr>
<td>1° relative with tendon xanthomata and/or children &lt;18 with LDL-C &gt;95th percentile</td>
<td>2</td>
</tr>
<tr>
<td>Clinical History</td>
<td></td>
</tr>
<tr>
<td>Patient with premature CAD (male &lt;55 years, female &lt;60 years)</td>
<td>2</td>
</tr>
<tr>
<td>Patient with premature cerebral/peripheral vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Physical Examinations</td>
<td></td>
</tr>
<tr>
<td>Tendon xanthomata</td>
<td>6</td>
</tr>
<tr>
<td>Arcus cornealis below age of 45 years</td>
<td>4</td>
</tr>
<tr>
<td>LDL-C</td>
<td></td>
</tr>
<tr>
<td>&gt;330 mg/dL</td>
<td>8</td>
</tr>
<tr>
<td>250-329 mg/dL</td>
<td>5</td>
</tr>
<tr>
<td>190-249 mg/dL</td>
<td>3</td>
</tr>
<tr>
<td>155-189 mg/dL</td>
<td>1</td>
</tr>
<tr>
<td>Definite FH</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Probably FH</td>
<td>6-8</td>
</tr>
<tr>
<td>Possible FH</td>
<td>3-5</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>&lt;3</td>
</tr>
</tbody>
</table>


#### Statin Intolerance\(^5\)
- The inability to tolerate ≥ 2 statins: one at the lowest starting daily dose AND another statin at any daily dose, due to either objectionable symptoms (real or perceived) or abnormal lab determinations, which are temporally related to statin treatment and reversible upon statin discontinuation, but reproducible by re-challenge with other known determinants being excluded (such as hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity or exercise, and underlying muscle disease).

#### High Intensity Statin\(^4\)
- Atorvastatin (Lipitor) ≥ 40mg
- Rosuvastatin (Crestor) ≥ 20mg