PCSK9 mAb may provide value if LDL-C remains >100 mg/dl despite maximally tolerated statin and ezetimibe therapy in patients at very high or extremely high atherosclerotic cardiovascular disease (ASCVD) risk.

Enhancing the Value of PCSK9 Monoclonal Antibodies (mAb) by Identifying Patients Most Likely to Benefit

Approximate Reduced Cost*
≈ $5,400/YEAR

5-year Number Needed to Treat (NNT):

<table>
<thead>
<tr>
<th>Discount</th>
<th>Price</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-28 (NNT)</td>
<td>= $5,400/Year</td>
<td>$100,000/QALY (Reasonable Value)</td>
</tr>
</tbody>
</table>

Cost per Quality Adjusted Life Year (QALY)

Patients with heterozygous familial hypercholesterolemia (HeFH) or severe hypercholesterolemia (SH)

On Maximally Tolerated Statin & Ezetimibe Therapy

<table>
<thead>
<tr>
<th></th>
<th>High Value &lt;$50,000/QALY</th>
<th>Reasonable Value &lt;$100,000/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year NNT</td>
<td>&lt;14</td>
<td>≥28</td>
</tr>
</tbody>
</table>

Secondary Prevention
HeFH or SH >220 mg/dl with clinical ASCVD (ASCVD risk likely similar when coronary artery calcium >100 Agatston units)
LDL-C ≥100 mg/dl
LDL-C ≥70 mg/dl

Primary Prevention
HeFH or SH >220 mg/dl with risk factor(s)^4
LDL-C ≥190 mg/dl
LDL-C ≥100 mg/dl

Patients with ASCVD on Maximally Tolerated Statin +/- Ezetimibe

<table>
<thead>
<tr>
<th></th>
<th>High Value &lt;$50,000/QALY</th>
<th>Reasonable Value &lt;$100,000/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year NNT</td>
<td>&lt;10</td>
<td>≥21</td>
</tr>
</tbody>
</table>

10-year ASCVD risk
≥40%                      LDL-C ≥130 mg/dl
LDL-C ≥70 mg/dl

30-39%                    LDL-C ≥190 mg/dl
LDL-C ≥100 mg/dl

20-29%                    N/A
LDL-C ≥130 mg/dl

Clinical Trial Data

High Value
< $50,000/QALY

Reasonable Value
< $100,000/QALY

Cost per Quality Adjusted Life Year (QALY)

LDL-C >130 mg/dl

LDL-C >70 mg/dl

LDL-C >100 mg/dl

LDL-C >190 mg/dl

LDL-C >100 mg/dl

LDL-C >130 mg/dl

Extensive or active burden of ASCVD, usually with extremely high risk and poorly controlled cardiometabolic risk factors.

Less extensive ASCVD and extremely high risk cardiometabolic risk factors.

Less extensive ASCVD and poorly controlled cardiometabolic risk factors.

Primary prevention HeFH or SH LDL-C >220 mg/dl and poorly controlled cardiometabolic risk factors.