PCSK9 Inhibitors in the Management of High Cholesterol

Draft Questions for Deliberation: October 27, 2015 Public Meeting

Definitions

For voting questions, we will operationalize that National Lipid Association Statin Intolerance Panel definition of statin intolerance[1].

Statin Intolerance:

1. Inability to tolerate at least 2 statins, with at least one started at the lowest starting daily dose; **and**
2. Statin dose reduction is attempted for symptom and biomarker abnormality resolution, rather than discontinuation of statin therapy altogether; **and**
3. Intolerable symptoms or abnormal biomarker changes are reversible upon statin discontinuation, but reproducible by re-challenge of statins, if clinically appropriate. Statin re-challenge may be appropriate for individuals with **all** of the following:
    a. Symptomatic; **and**
    b. Creatine kinase is less than four times (4) the upper limit of normal per laboratory reference range; **and**
    c. AST/ALT are less than three (3) times the upper limit of normal per laboratory reference range; **and**
4. Symptoms or biomarker abnormalities are not attributable to established predispositions or conditions recognized to increase the risk of statin intolerance, such as:
    - Hypothyroidism;
    - Drug interactions;
    - Concurrent illness;
    - Significant changes in physical activity/exercise;
5. Underlying muscle disease;

[1] An assessment by the Statin Intolerance Panel: 2014 update. Guyton, John R. et al. Journal of Clinical Lipidology , Volume 8 , Issue 3 , S72 - S81

Voting Questions

Comparative Clinical Effectiveness

1. Is there sufficient evidence to distinguish between the overall net health benefits of PCSK9 inhibitors Praluent® and Repatha™, excluding use in homozygous familial hypercholesterolemia for which only Repatha has an indication?

   Sub populations include:

   - Individuals with heterozygous familial hypercholesterolemia (HeFH) who are not at goal (LDL <160mg/dL)
   - Individuals with clinical atherosclerotic cardiovascular disease (CVD) who cannot take statins or who take statins but are not at goal (LDL < 70mg/dL)

For individuals with heterozygous familial hypercholesterolemia (HeFH) who are statin intolerant or who take statins but are not at goal (<160mg/dL)

2. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits?

   If yes,

3. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits more than adding ezetimibe (Zetia®)?

For individuals with clinical atherosclerotic cardiovascular disease (CVD) who are statin intolerant:

4. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits?

   If yes,

5. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits more than adding ezetimibe (Zetia®)?

For individuals with clinical atherosclerotic cardiovascular disease (CVD) who take statins but are not at goal (LDL < 70mg/dL):

6. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits?

   If yes,

7. Is the evidence adequate to demonstrate that adding PCSK9 inhibitors to treatment improves net health benefits more than adding ezetimibe (Zetia®)?

Comparative Value

Care Value

NB: if a majority of the CEPAC vote in a preceding question that the net health benefits of the two PCSK9 drugs can be distinguished, then care value votes will be held separately for each drug

For individuals with heterozygous familial hypercholesterolemia (HeFH) who are statin intolerant or who take statins but are not at goal (LDL <160mg/dL):

8. Given the available evidence, what is the *care value** of ***PCSK9 inhibitors***?
    a. Low b. Intermediate c. High

For individuals with clinical atherosclerotic cardiovascular disease (CVD) who are statin intolerant:

9. Given the available evidence, what is the *care value** of ***PCSK9 inhibitors***?
    b. Low b. Intermediate c. High

For individuals with clinical atherosclerotic cardiovascular disease (CVD) who take statins but are not at goal (LDL < 70mg/dL):

10. Given the available evidence, what is the *care value** of ***PCSK9 inhibitors***?
    c. Low b. Intermediate c. High

For the combined population of patients in these groups

11. Given the available evidence, what is the provisional *care value** of ***PCSK9 inhibitors***?
    d. Low b. Intermediate c. High

Provisional Health System Value

NB: if a majority of the CEPAC vote in a preceding question that the net health benefits of the two PCSK9 drugs can be distinguished, then health system value votes will be held separately for each drug

For individuals with heterozygous familial hypercholesterolemia (HeFH) who are statin intolerant or who take statins but are not at goal (LDL <160mg/dL):

12. Given the available evidence, what is the provisional *health system value** of ***PCSK9 inhibitors***?
    e. Low b. Intermediate c. High

For Individuals with clinical atherosclerotic cardiovascular disease (CVD) who are statin intolerant:

13. Given the available evidence, what is the provisional *health system value** of ***PCSK9 inhibitors***?
    f. Low b. Intermediate c. High

For Individuals with clinical atherosclerotic cardiovascular disease (CVD) who take statins but are not at goal (LDL < 70mg/dL):

14. Given the available evidence, what is the provisional *health system value** of ***PCSK9 inhibitors***?
    g. Low b. Intermediate c. High

For the combined population of patients in these groups

15. Given the available evidence, what is the provisional *health system value** of ***PCSK9 inhibitors***?
    h. Low b. Intermediate c. High