Client: HEALTH BENCHMARKS, INC. STANDARD ALGORITHM

Measure Title: HEPATIC ENZYME MONITORING BEFORE INITIATING STATIN THERAPY

Disease State: Hyperlipidemia

Indicator Classification: Medication Monitoring

Strength of Recommendation: B

Organizations Providing Recommendation:
- American College of Cardiology
- American Heart Association
- National Heart, Lung, and Blood Institute
- US Food and Drug Administration

Clinical Intent: To ensure that eligible members newly initiated on statin therapy receive baseline liver function tests.

Background: Disease Burden
- In clinical trials and phase IV studies of Lovastatin, increases in alanine aminotransferase enzyme (ALT) levels of greater than 3 times the upper limit of normal (ULN) were observed in 1% to 3% of patients.[1, 2]
- In a clinical trial examining 16,495 patients using atorvastatin, elevated hepatic transaminases were found in 0.4% of the study population.[3]
- A more comprehensive systematic review of all current statins found elevated transaminases greater than 3 times the upper limit of normal in 1.5% of high intensity statin users and 0.4% of low intensity statin users. Medications included in this study were: fluvastatin, simvastatin, rosuvastatin, lovastatin, atorvastatin, cerivastatin, and pravastatin.[4]
- There are 232 reports of hepatitis associated with lovastatin, translating into a reporting rate of 9.7 cases/million patient-treatment years.[1]
- There are 22 reported cases of acute liver failure associated with lovastatin. This translates into a reporting rate of 1/1.14 million patient-treatment-years, approximately equal to the rate of idiopathic acute liver failure.[1]

Reason for Indicated Intervention or Treatment
- The United States Food and Drug Administration recommendations indicate that liver function tests for statins should be performed for patients initiating statins and who take them regularly.[5]

Evidence Supporting Intervention or Treatment
- In randomized controlled trials and comparative studies of statin therapy, elevated hepatic transaminases occur in 0.5% to 2.0% of cases and are dose dependent.[6, 7]
- In a randomized controlled trial of lovastatin therapy, the 2 year incidence of serum transaminase elevation was 0.1% for 20 mg/day and...
1.9% for 80 mg/day.[8]

- A large retrospective review of 385,000 HMO patients found that the majority of patients (65%) with alanine aminotransferase levels greater than 10 times the upper limit of normal experienced severe enzyme elevation within the first month after statin initiation, which was due to dosage and/or additions of medications that might interact with statins.[9]

**Clinical Recommendations**

- The American College of Cardiology/American Heart Association/National Heart, Lung, and Blood Institute Clinical Advisory Panel on the Use and Safety of Statin states: “Current labeling for all statins requires baseline measurements of liver function, including alanine transferase and aspartate transferase, although this is not agreed on by many liver experts and will likely undergo review in the future.”[10] A 2004 update to these guidelines does not alter the recommendation.[11]

- The 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) also recommends that physicians take baseline measurements of liver function tests (i.e., alanine transferase (ALT) or aspartate transferase (AST) levels) before initiating statin therapy.[12] The 2004 update of this report does not alter the recommendation.[13]

- On the product label for lovastatin, the US Food and Drug administration recommends monitoring for potential hepatotoxicity before beginning statin treatment, at 6 and 12 weeks after initiation of treatment, after a dosage increase, and periodically (i.e. semiannually) thereafter.[14]

**Source**

Health Benchmarks, Inc.

**Denominator**

**Denominator Definition**
Continuously enrolled members who filled at least 1 prescription for a statin during the first 358 days of the measurement year.

**Drug List**
Fluvastatin, Atorvastatin, Simvastatin, Pravastatin, Lovastatin, Rosuvastatin

**Denominator Exclusion**

**Denominator Exclusion Definition**
Members who filled a prescription for a statin during the 1-365 days prior to the index date.

**Drug List**
Fluvastatin, Atorvastatin, Simvastatin, Pravastatin, Lovastatin, Rosuvastatin

**Numerator**
Numerator Definition Members who received at least 1 liver function test 60 days prior through 7 days after index date.

Numerator Claims Criteria CPT-4 code(s): 80050, 80053, 80076 84450, 84460

Physician Attribution

If client data contains prescribing provider:
Score only the physician (in the selected specialties) who prescribed the member the statin on the index date.

If client data does not contain prescribing provider:
Score all physicians (in the selected specialties) who saw the member 0-60 days prior to the index date.

References


1 Indicator Classification (Adapted from HEDIS® technical specifications)

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Measures applicable to patients receiving diagnostic workups for a symptom or condition that delineate appropriate laboratory or radiological testing to be performed (e.g., evaluation of thyroid nodule; pregnancy test in patients with vaginal bleeding or abdominal pain).</td>
</tr>
<tr>
<td>Effectiveness of Care</td>
<td></td>
</tr>
<tr>
<td>Prevention</td>
<td>Measures applicable to asymptomatic individuals that are designed to prevent the onset of the targeted condition (e.g., immunizations).</td>
</tr>
<tr>
<td>Screening</td>
<td>Measures applicable to asymptomatic patients who have risk factors or pre-clinical disease, but in whom the condition has not become clinically apparent (e.g., pap smears; screening for elevated blood pressure).</td>
</tr>
<tr>
<td>Disease Management</td>
<td>Measures applicable to individuals diagnosed with a condition that are part of the treatment or management of the condition (e.g., cholesterol reduction in patients with diabetes; radiation therapy following breast conserving surgery; appropriate follow-up after acute event).</td>
</tr>
<tr>
<td>Medication Monitoring</td>
<td>Measures applicable to patients taking medications with narrow therapeutic windows and / or potential preventable significant side effects or adverse reactions (e.g., thyroid stimulating hormone (TSH) testing after levothyroxine dose change; hepatic enzyme monitoring for patients using antimycotic pharmacotherapy).</td>
</tr>
<tr>
<td>Medication Adherence</td>
<td>Measures applicable to patients taking medications for chronic conditions that are designed to assess patient adherence to medication (e.g., adherence to lipid lowering medication).</td>
</tr>
<tr>
<td>Utilization</td>
<td>Measures applicable to patients receiving treatment for a symptom or condition that advocate appropriate utilization of laboratory and pharmaceutical resources (e.g., conservative use of imaging for low back pain; inappropriate use of antibiotics for viral upper respiratory infection).</td>
</tr>
</tbody>
</table>
2 Strength of Recommendation

Strength of Recommendation Based on a Body of Evidence

Is this a key recommendation for clinicians regarding diagnosis or treatment that merits a label?  
Yes → Is the recommendation based on patient-oriented evidence (i.e., an improvement in morbidity, mortality, symptoms, quality of life, or cost?)  
Yes → Is the recommendation based on opinion, bench research, a consensus guideline, usual practice, clinical experience, or a case-series study?  
Yes → Is the recommendation based on one of the following?  
- Cochrane Review with a clear recommendation  
- USPSTF Grade A recommendation  
- Clinical Evidence rating of Beneficial  
- Consistent findings from at least two good-quality randomized controlled trials or a systematic review/meta-analysis of same  
- Validated clinical decision rule in a relevant population  
- Consistent findings from at least two good-quality diagnostic cohort studies or systematic review/meta-analysis of same  
No → Strength of Recommendation = C  
No → Strength of Recommendation not needed

No → Strength of Recommendation = B

FIGURE 2. Algorithm for determining the strength of a recommendation based on a body of evidence (applies to clinical recommendations regarding diagnosis, treatment, prevention, or screening). While this algorithm provides a general guideline, authors and editors may adjust the strength of recommendation based on the benefits, harms, and costs of the intervention being recommended. (USPSTF = U.S. Preventive Services Task Force)