**Client**

HMSA: PQSR 2007

**Measure Title**

LIVER FUNCTION TESTS (LFT) FOR PATIENTS INITIATED ON VALPROIC ACID

**Disease State**

Liver function

**Indicator Classification**

Medication Monitoring

**Strength of Recommendation**

C

**Clinical Intent**

To ensure that eligible members newly initiated on valproic acid receive a heptotoxicity monitoring test within a clinically appropriate timeframe.

**Physician Specialties (suggested)**

Refer to PQSR 2007 Specialty Matrix

**Clinical Rationale**

- Valproic acid is commonly used to treat seizure and mood disorders\[1, 2\].
- Epilepsy and seizures affect 2.7 million Americans of all ages, at an estimated annual cost of $12.5 billion in direct and indirect costs. Approximately 200,000 new cases of seizures and epilepsy occur each year. \[3, 4\]
- The World Health Organization monitors adverse drug reactions. In a recent systematic investigation of adverse drug reactions leading to liver injury and fatalities (88.3% of cases in the United States), valproate was the third most common drug associated with such fatalities. \[5\]

**Reason for Indicated Intervention or Treatment**

- Valproic acid use has been associated with multiple hematologic abnormalities, including thrombocytopenia \[8, 12, 16\].

**Evidence supporting Intervention or Treatment**

- **Valproic acid**
  - Several retrospective studies of patients taking valproic acid have shown that fatal hepatotoxicity is a side effect of the medication \[18-21\]. From 1987 to 1993, 29 patients on valproic acid developed fatal hepatotoxicity \[18\], and in a study of adverse drug reactions in the UK, anticonvulsants, and more specifically sodium valproate was associated with the greatest number of fatalities and more specifically, hepatotoxicity.
  - Cases of life-threatening pancreatitis have been reported in both children and adults receiving valproate. Some of the cases have been described as hemorrhagic with a rapid progression from initial symptoms to death.
  - There is no evidence that early, presymptomatic detection of hematologic side effects with laboratory testing alters patient outcomes in patients taking carbamazepine or valproic acid.

**Clinical Recommendations**

- The National Headache Foundation guidelines recommend routine monitoring of both CBC and liver function tests for patients taking Valproic Acid, however the frequency of monitoring is not stated.
- The FDA black box warning for Valproic Acid indicates that patients taking this medication have an increased risk for developing hepatotoxicity and pancreatitis. Therefore they recommend:
  - performing pretreatment liver function tests and frequent monitoring through therapy, particularly within the first 6 months.
  - informing patients of the warning signs for pancreatitis.\[23\]
Source
Health Benchmarks, Inc.
Adapted for HMSA, Removed DENEX criteria: Members who received a prescription for Valproic Acid in the 1-365 days prior to the index prescription.
DEN Logic: [A] or [B] or [C]

Denominator
Continuously enrolled members, who had at least a 180 day supply of valproic acid during the one year period beginning 60 days prior to the measurement year.

Denominator Exclusion
None

Numerator
Members who have had appropriate monitoring lab work completed 1-60 days after the index prescription.

Relevant Billing Codes:
CPT-4 code: 80076, 80053, 84450, 84460

Interpretation of Score
High score implies better performance

Physician Attribution
Score physician who prescribed the index date prescription.

External Files Required for Analysis
Denominator Filename: neuromed_medlist1_2007.xls
Source: HBI, Master NDC
Updated: Annually

References
**Indicator Classification** (Adapted from Health Plan Employer Data Information Set (HEDIS®) technical specifications)

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</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

**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)