**Measure Title**

LIVER FUNCTION TESTS (LFT) AND COMPLETE BLOOD COUNTS (CBC) FOR PATIENTS INITIATED ON CARBAMAZEPINE OR VALPROIC ACID

<table>
<thead>
<tr>
<th>Disease State</th>
<th>Indicator Classification</th>
<th>Strength of Recommendation</th>
<th>Specialties</th>
<th>Clinical Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver function</td>
<td>Medication</td>
<td>B</td>
<td>Family Practice, Gerontology, Internal Medicine,</td>
<td>• Carbamazepine and valproic acid are commonly used to treat seizure and mood disorders[1, 2].</td>
</tr>
<tr>
<td></td>
<td>Monitoring</td>
<td></td>
<td>Neurological Surgery, Neurology, Pediatrics, Psychiatry</td>
<td>• 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]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reason for Indicated Intervention or Treatment</th>
<th>Evidence supporting Intervention or Treatment</th>
</tr>
</thead>
</table>
| • Carbamazepine use can lead to hematological toxicity, such as rare aplastic anemia, persistent leukopenia, and isolated thrombocytopenia [6-15]. | • **Carbamazepine**
  o A review of 13 cases of fatal aplastic anemia developing in patients taking carbamazepine showed that the medication was the probable cause in only 3 patients [17].
  o Clinical trials have shown that approximately 10% of patients taking carbamazepine develop transient leukopenia, usually during the first month of treatment. This resolves despite continuation of the medication [7, 11, 13].
  o Case reports and clinical trials show that up to 8% of patients taking carbamazepine develop persistent leukopenia. This is usually evident during the first few weeks of therapy, and responds to discontinuation of the medication [9, 10, 14].
  o A case report on four patients developing thrombocytopenia while taking carbamazepine found that all cases appeared 14 to 16 days after the medication was initiated, and all resolved within 7 days after discontinuation. [15] |
| • Valproic acid use has been associated with multiple hematologic abnormalities, including thrombocytopenia [8, 12, 16]. | **Valproic acid**
  o 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.
  o 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 FDA black box warning for Carbamazepine indicates that patients taking this medication have a risk that is 5-8 times greater than the general population for developing aplastic anemia and agranulocytosis. Therefore, they recommend:
  - performing complete pretreatment blood counts (including platelets and possibly reticulocytes and serum ion) and periodic monitoring through therapy.[22]
- 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.

**Denominator**

Continuously enrolled members, who had at least a one prescription for either carbamazepine or valproic acid during the one year period beginning two months prior to the measurement year.

**Denominator Exclusion**

Members who received a prescription for either Carbamazepine or Valproic Acid in the 1-365 days prior to the index prescription.

**Numerator**

Members who have had appropriate monitoring lab work done 0-60 days prior to the index prescription. NB: Appropriate monitoring for CARBAMAZEPINE and VALPROIC ACID differ from each other as defined below.

**Interpretation of Score**

High score implies better performance

**Physician Attribution**

Score all physicians who saw the member 0-60 days prior to the index prescription date.

**External Files Required for Analysis**

Source: HBI, Master NDC

Updated: Annually

**References**