Client: HMSA: PQSR 2007

Measure Title: APPROPRIATE MONITORING FOR METHOTREXATE USE

Disease State: Hepatotoxicity, Immunosuppression, Cirrhosis

Indicator Classification: Medication Monitoring

Strength of Recommendation: C

Clinical Intent: To ensure that all eligible members taking Methotrexate medication receive the appropriate monitoring tests within a clinically appropriate frequency.

Physician Specialties: Refer to PQSR 2007 Specialty Matrix

Clinical Rationale: Disease Burden
- Methotrexate is used for the treatment of rheumatoid arthritis, psoriasis, acute lymphocytic leukemia, various other immunologic diseases, and other conditions including Crohn’s disease, asthma, and ectopic pregnancy.[1-3]
- 60 to 93 percent of patients treated with methotrexate eventually develop at least one adverse reaction (usually involving the skin, gastrointestinal tract, or central nervous system). Most of these reactions are not life-threatening.[4]
- Up to 30 percent of patients treated for more than five years with methotrexate discontinue the therapy because of unacceptable toxicity.[4]
- The incidence of life-threatening side effects resulting from methotrexate use is approximately 1.7%.[5]

Reason for Indicated Intervention or Treatment
- Methotrexate use can lead to hepatic damage, cirrhosis, and myelosuppression.[5-10]
- Regular monitoring of complete blood counts and liver function tests can help detect these side effects at an early stage, so that methotrexate dose adjustments can be made accordingly.

Evidence supporting Intervention or Treatment
- Clinical studies in which liver biopsies were obtained from psoriatic patients on continued methotrexate treatment showed the development of methotrexate-induced hepatotoxicity and liver cirrhosis.[6-8, 10]
- A prospective study of 94 patients receiving long-term weekly methotrexate treatments who underwent 354 liver biopsies revealed a significant correlation between increasing serum aspartate aminotransferase (AST) levels and progression of hepatic histologic damage.[11]
- Another prospective study following 27 patients for over 8 years showed that when the methotrexate dose is adjusted for AST and albumin abnormalities, patients have little hepatic architecture deterioration.[2]
- A 13 year retrospective cohort study of 673 patients taking methotrexate found that 102 patients (15.2%) developed potentially serious side effects and had to discontinue the medication. This included 25 patients...
with neutropenia, 9 with thrombocytopenia, 2 with pancytopenia, and 37 with liver function abnormalities.[5]

- An 11 year prospective cohort study of 481 patients on methotrexate followed for 2,323 person-years of methotrexate exposure found abnormal laboratory test results in 22 patients (4.6%), the majority of whom (17/22, 77%) had elevated AST levels.[12]
- Some studies have suggested that methotrexate may not be directly responsible for hepatic complications, which may instead result from rheumatoid arthritis and/or other drugs.[13, 14]
- There are no studies examining the desired frequency of complete blood count and liver function testing.

**Clinical Recommendations**

- The American College of Rheumatology recommends checking complete blood counts (CBC) and liver function tests monthly for the first six months of treatment and 1 to 2 months thereafter.[15]
- The American Academy of Family Physicians recommends that physicians check baseline, two week, and then every eight week CBC, AST and serum albumin levels in patients taking methotrexate.[16]

**Source**
Health Benchmarks, Inc.

**Denominator**
Continuously enrolled members who received at least 180 days supply of Methotrexate during the one year period beginning 120 days prior to the measurement year.

**Denominator Exclusion**
N/A

**Numerator**
Members who received at least one complete blood count and liver function test 1-120 days after the index prescription date.

**Relevant Billing Codes:**
CPT-4 code(s): 80050, 85025, 85027, 80053, 80076, 84450, 84460

**Interpretation of Score**
High score implies better performance

**Physician Attribution**
Score physician (in the selected specialties) who prescribed the index date prescription.

**References**


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

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></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><strong>Effectiveness of Care</strong></td>
<td></td>
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<tr>
<td><strong>Prevention</strong></td>
<td>Measures applicable to asymptomatic individuals that are designed to prevent the onset of the targeted condition (e.g. immunizations).</td>
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<tr>
<td><strong>Screening</strong></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>
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<tr>
<td><strong>Disease Management</strong></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>
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<tr>
<td><strong>Medication Monitoring</strong></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 antifungal pharmacotherapy)</td>
</tr>
<tr>
<td><strong>Medication Adherence</strong></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><strong>Utilization</strong></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>
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</table>
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)