Client: HIMS: PQSR 2009

Measure Title: APPROPRIATE MONITORING FOR METHOTREXATE USE

Disease State: Hepatotoxicity, Immunosuppression, Cirrhosis

Indicator Classification: Medication Monitoring

Strength of Recommendation: B

Organizations Providing Recommendation:
- American Academy of Family Physicians
- American College of Rheumatology
- Federal Drug Administration

Clinical Intent: To ensure that all eligible members taking methotrexate receive hematology, renal function and liver function tests at least every 2 months.

Physician Specialties (suggested): Refer to PQSR 2009 Clinical Measures by Specialty.

Background: Disease Burden
- Methotrexate is used for the treatment of rheumatoid arthritis, psoriasis, acute lymphocytic leukemia, cancer, various other immunologic diseases, and other conditions including Crohn’s disease, asthma, and ectopic pregnancy.[1-4]
- Patients treated with methotrexate often develop at least one adverse reaction (usually involving the skin, gastrointestinal tract, or central nervous system). Most of these reactions are not life-threatening.[5-7]
- Up to 30 percent of patients treated for more than five years with methotrexate discontinue the therapy because of unacceptable toxicity.[7]

Reason for Indicated Intervention or Treatment
- 14.5% of patients with psoriatic arthritis experienced hepatic disturbance after using methotrexate treatment for an extended period of time. 7.5% of patients with rheumatoid arthritis also had similar disturbances.[6]
- The incidence of cirrhosis is estimated to be between 0%-2%.[6]
- Most rheumatologists follow the the ACR guideline for follow-up monitoring of methotrexate therapy in rheumatoid arthritis patients. Yet, a recent survey found wide variation in frequency of testing, with 35% ordering blood tests every 4-6 weeks, 38% every 6-8 weeks, and 22% ordering them less than every 2 months.[8]
- 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**

- 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.[9]
- 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.[10]
- 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.[11, 12]
- 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 every 1 to 2 months thereafter.[13]
- The American Academy of Family Physicians recommends that physicians check CBC, AST and serum albumin levels in patients taking methotrexate at baseline, two weeks, and then every eight weeks.[4]
- The Federal Drug Administration in their labeling of methotrexate state “During therapy of rheumatoid arthritis and psoriasis, monitoring of these parameters is recommended: hematology at least monthly, renal function and liver function every 1 to 2 months. More frequent monitoring is usually indicated during antineoplastic therapy. During initial or changing doses, or during periods of increased risk of elevated methotrexate blood levels (e.g. dehydration), more frequent monitoring may be indicated.”[14]

**Source** Health Benchmarks, Inc.

| Denominator Definition | Continuously enrolled members who filled at least a 16 day supply of methotrexate, 4 separate prescriptions for methotrexate, or received 8 injections for methotrexate during the 1 year period beginning 90 days prior to the measurement year. |
### Denominator Exclusion

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<td>Exclusion Definition</td>
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### Numerator

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<tr>
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### Physician Attribution

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<tr>
<td>Description</td>
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### References


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