Mary Pack Arthritis Program
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MEDICATION INFORMATION FOR PHYSICIANS

Generic Name: METHOTREXATE

Brand Name: RHEUMATREX

Indications

Rheumatoid Arthritis, Persistant Inflammatory Arthritis, Psorasis,Vasculitis and Myositis

Contraindications

Absolute: Pregnancy or nursing mother

Relative:

- Significant liver/kidney dysfunction
- Male & female fertility – avoid conception for 3 months (including at least one menstrual cycle in women) after stopping methotrexate
- Recent or chronic hepatitis
- Recent or chronic cirhosis
- Significant anemia, leukopenia or thrombocytopenia
- Alcohol consumption which exceeds 1 ounce daily

Monitoring Laboratory Tests

Baseline:

- CBC, platelets
- AST, bili, albumin, alkphos
- Creatinine
- ESR
- Hep B, C, and HIV if risk factor present
- Liver biopsy if transaminases elevated or patient has history of high alcohol consumption or hepatitis
- Chest x-ray within last year

Routine: every 4 to 8 weeks

- CBC, platelets

- AST, albumin,
- Creatinine
- ESR
- Liver biopsy if AST elavated in 5 of 9 or 6 of 12 readings over 12 months or a fall in serum albumin

Dosage

Dosing regimens

- should be personalized dependent on benefit desired and the development of side effects.
- Recent trials have used the following protocol:

Initial dose: 7.5 to 15 mg one day/week

Week 4 – 8 : 15 mg – 20 mg one day/week

Maximum dose: generally 25 to 30 mg one day/week s.c. or I.M.

How it is taken

By tablet or injection one day per week.

Tablet:

- Supplied in **2.5 mg** & **10 mg**. tablets
- May be taken without food or with food to avoid G.I. upset.
- May be taken in 1 to 3 doses over a 24 hour period to avoid G.I. upset.
- Splitting the dose in 24 hours may also enhance the bioavailability of oral methotrexate.

Injection

- Supplied in **2 ml vial or 20 ml vial at a concentration 25 mg/ml solution with preservative** for subcutaneous or intramuscular injection
- Generally given subcutaneously versus intramuscular to enhance self-injection learning & adherence on the part of the patient. The bioavailablility of both routes of injection is similar.
- Used to reduce the gastrointestinal side effects of the tablets, or to reduce the elevation of liver enzymes or to enhance the bioavailabity of the the methotrexate.

Managing Side Effects

Gastrointestional: anorexia, nausea, vomiting and diarrhea (10%). Mouthsores /mucositis (6 –10%)

- G.I. symptoms can be reduced by adding 1mg of folic acid per day, to a maximum of 5 mg/day.

- If this is not successful at controlling symptoms, try folinic acid (Leucovorin) 5 mg po once weekly 8 – 12 hours after taking the methotrexate. It is not necessary to continue the folic acid with this regimen. (Note that folinic acid is about $6 per tablet.)
- Treat mucositis with a a local analgesic such as Tantum
- Hold MTX dosage until G.I. /mucositis symptoms have resolved themselves. Restart MTX at 50% of previous dose.

Hepatic (8-38%)
- Elevated liver enzymes are generally dose related.
- *Ensure laboratory tests are performed prior to weekly methotexate dosage, not within the 24 to 48 hour after dosage is taken.*
- **AST > upper normal laboratory limit** ⇒ Reduce MTX by 2.5 mg
- **AST > 2 X the upper normal laboratory limit** ⇒ decrease MTX by 50%
- **AST > 2 X above upper normal labatory limit on 2 consecutive tests** ⇒ Hold MTX
- Repeat blood work every 2 weeks until resolved.
- If over the period of one year, half the AST tests are elevated above normal, or if there is persistant unexplained hypoalbuminemia, there is a risk of liver damage. A liver biopsy may be required to exclude methotrexate liver toxicity.

Hematological (<5%)
- Bone marrow toxicity is usually dose dependent and caused by folate deficiency and can be prevented by folate supplementation.
- Risk factors include renal insufficiency, folic acid deficiency and concommitent use of Bactrim or Septra.
- **WBC between 3,000 to 3,500** ⇒ decrease MTX by 50% of previous dose. Repeat blood work q 2 weeks until resolved
- **WBC < 3,000** ⇒ hold the dose. Repeat blood work in 1 –2 days, then every 2 weeks until resolved.
- In the case of severe bone marrow toxicity, hold methotrexate and administer folinic acid.

Increased Nodularity
- Rheumatoid nodules may increase in up to 10% of patients taking MTX for rheumatoid arthritis.

Pneumonitis (1-5%)

- Generally presents with shortness of breath, dry cough and fever. X-rays show a bilateral interstitial pattern.
- Stop MTX.
- Infection must be ruled out and a bronchoscopy may be necessary.

Reproductive effects

- MTX is highly teratogenic and can cause spontaneous abortions and possible birth defects.
- Women of child bearing years should use a consistent and effective method of birth control.
- *Women and men contemplating conception should not conceive until 3 months after stopping MTX.*

Other

- **Alopecia** (5%)
- **Rash** (1-2%)

Drug interactions

- **Trimethoprim in the sulpha drugs** (Bactrim, Septra) is a folate antagonist and can cause pancytopenia and should be used with caution.
- **Alcohol** consumption can potentiate hepatotoxicity
- **Probenecid** can increase methotrexate levels
- **Salicylates, NSAIDS, or Sulfonamides** may increase methotrexate effect, and conversely, the effect may decrease when the these drugs are stopped.
- **Leflunomide** in combination with methotrexate should be used with caution because of potentially serious liver toxicity.

Considerations

- For discussion of any problems related to Methotrexate therapy, please call the attending rheumatologist or phone the methotrexate clinic at the Vancouver Arthritis Centre at 604-875-4111 local 68864
- Further information is available in the package insert.
- Any unusual reaction should be carefully evaluated and considered a possible MTX reaction. Serious reactions can be avoided by holding the dose of MTX until the symptoms subside, and restarting at 50% of the previous dose of MTX if indicated.

Referral to the clinic	Contact the Methotrexate Clinic at 604-875-4111, local 68864 or fax the following documentation to 604-875-4321. • A completed referral form • Consultation report and copy of last visit notes • Recent laboratory tests

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