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PATIENT **E** DUCATION

SOME THOUGHTS TO OUR PATIENTS ABOUT . . .

METHOTREXATE

What is your diagnosis? You have been diagnosed with rheumatoid arthritis (RA) or another disease for which your physician has prescribed **methotrexate**. RA is a disease that can damage joints as well as organs in your body. RA can cause severe deformity and disability.

You must decide if you want to take methotrexate. You and your physician will discuss your diagnosis and why methotrexate is being prescribed. You need to inform your physician if you have had kidney or liver problems, infections or may have been exposed to hepatitis or HIV/AIDs. You must weigh the risks and benefits of methotrexate therapy.

What is methotrexate? It is a medicine developed to treat cancer. It was found to be effective in treating RA. It was then approved by the FDA for the treatment of adults with "severe, active, recalcitrant" RA. It is sometimes called a "DMARD" or disease modifying drug because it can slow progression of RA.

Rheumatologists use methotrexate "off label" – for uses not approved by the FDA – such as for treatment of less than severe RA and other diseases. Using methotrexate for less severe (but active) RA may prevent the disease from becoming severe. Also, using methotrexate sometimes allows the physician to reduce use of other medications, such as prednisone.

Patients usually take a nonsteroidal anti-inflammatory (NSAID) as initial therapy for RA. Other drugs, like Plaquenil® (hydroxychloroquine) may also be prescribed. Patients with very active RA are sometimes put immediately on methotrexate by rheumatologists without first trying an NSAID.

How soon will it work? It usually shows some benefit in 3 to 6 weeks. It doesn't work for all patients, but it works for many.

How do you take it? Methotrexate comes in 2.5 mg tablets. Tablets are taken **weekly** rather than daily. This is different than most medications. The starting dose is usually 7.5 mg per week – that is, 3 tablets taken on one day (the same day) every week.

The importance of this **weekly** schedule cannot be overstated. The **weekly** dose is usually taken all at one time. The dose can be split up and taken within a 24-hour period – for example, a portion at 8 am Tuesday morning, some on Tuesday night and the rest 8 am Wednesday morning. For people who have stomach problems from the tablets, methotrexate is also available by a **weekly** injection.

Taking methotrexate incorrectly can result in serious side effects. If doses are taken too often, notify your physician **at once**. If an accidental overdose occurs, an antidote is necessary and must be given as early as possible.

Are there side effects? Methotrexate can cause side effects, which occasionally can be serious and, sometimes, fatal. Side effects can occur at **any time** during your treatment. Most side effects can be detected **before** they become serious and, for that reason, your physician will keep you under close supervision. Methotrexate can negatively affect organs in the body, including the liver, kidney and bone marrow (where essential blood cells and platelets are made).

You will have frequent visits and lab tests (to check your kidney, liver and blood). For the safest treatment of your disease, it is important that you carry out your physician's instructions faithfully and report any side effects or symptoms that you develop.

The most common side effects of methotrexate are: Loss of appetite, nausea, vomiting, diarrhea, or sores or ulcers in the mouth. Other side effects include: Headaches, dizziness, mood changes, skin rashes, increased sun sensitivity or unexplained weight loss. Effects of methotrexate on your blood cells or platelets can cause increased risk of infection, bleeding, fatigue and anemia.

If these or other problems trouble you, or should you develop any signs of infection, bruising, fatigue or unusual bleeding, notify your doctor **immediately** (and before you take any more methotrexate). These side effects are usually temporary, but frequently require dosing changes. Your physician may recommend that you take folic acid, which may reduce some side effects associated with methotrexate.

Methotrexate may lower your body's resistance. Do not get vaccinated (immunized) without asking your doctor. You may get the disease you are trying to prevent.

Other medications you are taking may result in an increase in side effects or a decrease in the effectiveness of methotrexate. Tell your physician **all** of the medications you are taking, whether they are prescription or nonprescription medicines. This is **especially** true of aspirin, aspirin-like drugs, or other "arthritis drugs" (including NSAIDs) and antibiotics. Antibiotics like *Bactrim*, *Septra* and *Cotrim* must not be taken with methotrexate because your bone marrow may stop functioning.

Don't Become Dehydrated. Dehydration (excess loss of body fluid), can also increase the risk of methotrexate toxicity. Abdominal upset, especially when accompanied by significant vomiting, diarrhea, or decreased fluid intake, can lead to dehydration. So can the flu. Excessive thirst may be a symptom of dehydration. Notify your physician immediately if these symptoms develop.

Name: _____ Date: _____

Avoid alcohol. Alcoholic beverages (including beer and wine) may increase some of the side effects, including the chance of liver damage. Alcohol use should be severely restricted and preferably avoided altogether.

NO Pregnancy. Methotrexate is known to cause **birth defects** and may cause **miscarriage** or stillbirth, especially in the first three months of pregnancy. Pregnant women **must not** take methotrexate and women of childbearing age **must not** become pregnant during or shortly after taking methotrexate. Adequate birth control (contraceptive) measures are essential. Both men and women should avoid conception during and for several months after stopping methotrexate. Nursing women **must not** take methotrexate because it gets in their breast milk. Methotrexate may lower sperm count in men.

Uncommon side effects of methotrexate include:

- Development of scarring (fibrosis) in the liver. If liver blood tests are consistently abnormal, removal of a small specimen of liver tissue with a needle (liver biopsy) is sometimes necessary to determine if liver damage is present
- A lung reaction similar to pneumonia. The symptoms are usually fever, cough (often dry and hacking) and shortness of breath (which can be quite severe). If you develop such symptoms, notify your physician at once. Smokers should not take methotrexate. Your doctor may order a chest x-ray before you take methotrexate.
- Allergic (anaphylactic) reactions
- Cancers called lymphomas.

Other Treatment Options include:

- Prednisone and Medrol® are corticosteroids used to treat RA and other diseases. Because of their many side effects, methotrexate is used so they can be reduced or stopped.
- Leflunomide (Arava®) is another DMARD that is used to treat RA. While it has some similar side effects, it has not been shown to have the pulmonary toxicity of methotrexate.
- Plaquenil® and Azulfidine® are two other drugs used to treat RA. They are not as potent as methotrexate and are sometimes used in combination with methotrexate, though such combinations have not been approved by the FDA.
- New biologic drugs, Enbrel® (injections) and Remicade® (infusions), have been shown to be effective in preventing RA joint damage. Remicade® must be taken with a drug like methotrexate to maintain its efficacy.

Questions. If you have any questions, write them down and ask your physician at your next visit.

The occurrence of a symptom does not always mean you are having a methotrexate side effect. Your physician may ask you to see a primary physician to first check on other causes.

This handout does not list every possible use, precaution, side effect, symptom or drug interaction relating to methotrexate. Your bottle of medicine often has a package insert that goes into great detail about the medicine and potential side effects. This information is also available in the Physician's Desk Reference (the PDR). Many patients read this information. You may do the same.

SUMMARY

Be compliant:

- Follow your doctor's instructions **faithfully**.
- Keep the visits with your doctor.
- Obtain the tests ordered by your doctor.

Take your methotrexate correctly:

- Take your methotrexate **weekly**, not daily.
- Take your methotrexate on the same day each week.
- If you miss a dose, do not take the missed dose, and do not double the next dose. Just continue your regular dosing schedule and call your physician.
- Notify your doctor at once if an accidental overdose is suspected.

Notify your doctor **at once** (and **before** you take another dose of methotrexate) if :

- You develop fever, cough, or shortness of breath.
- You get the flu or an infection
- Any side effects or symptoms occur
- You get dehydrated

Follow these "**DO NOT** rules" to reduce the risk of problems:

- Do not change any medications or start any new medications without first checking with your physician
- Do not take the antibiotics *Bactrim*, *Flagyl*, *Septra* or *Cotrim* (trimethoprim/sulfamethoxazole) or other sulfa-containing when you take methotrexate.
- Do not get any vaccination (immunization) without first asking your doctor.
- Do not drink alcoholic beverages.
- Do not take methotrexate if you are pregnant or nursing.
- Do not get pregnant (or get anyone pregnant) while you take and for a time after taking methotrexate.

This medication is **only for you**:

- It must not be given to or taken by other people.
- Keep this medicine out of the reach of children and anyone else who may not understand that it can be dangerous to them.