What is Methotrexate?

Methotrexate (MTX) is a trade name for amethopterin, a substance that neutralizes folic acid to inhibit DNA synthesis.
**What is it used for?**

MTX is a cancer chemotherapy agent, and is used for the treatment of severe psoriasis and rheumatoid arthritis.

**Human Health Effects:**

MTX kills dividing cells. It is not metabolized in the body to an appreciable degree. When metabolism does occur, the metabolites can also be toxic. Because MTX interferes with vital biological processes, it is listed in EPA Class 3 for general toxicity: may cause irreversible effects which can be life threatening.

**Acute Health Effects:**

The effects of acute exposure are well documented because of its use as a chemotherapy agent. The body readily absorbs MTX by ingestion and injection. MTX produces many of acute effects typical of drugs which kill rapidly growing cells, including nausea, stomatitis, vomiting, diarrhea, gastrointestinal bleeding, elevation of serum levels of liver enzymes, and skin rash and skin redness. It has potentially irreversible effects on the lungs and kidneys. Other effects include the suppression of bone marrow, and life-threatening neutropenia (a decrease in the number of white blood cells.)

**Chronic Health Effects:**

All of the acute effects mentioned above can also occur with repeated exposures. In addition, neurological changes, including behavioral abnormalities, abnormal reflexes, abnormal sensory motor signs, motor dysfunction, paralysis, palsies, and seizures may occur after two or three weekly doses. MTX used with other agents, such as radiation, can increase the side effects. Persons with pre-existing liver, kidney, or bone marrow disease may have increased affects when exposed to MTX.

**Reproductive Effects:**

MTX causes multiple skeletal birth defects when taken in the first trimester of pregnancy. The most characteristic MTX malformation syndrome is a “clover-leaf” skull with large head, swept-back hair, low-set ears, prominent eyeballs, and wide nasal bridge. Other frequently reported malformations are limb defects and absent ossification centers, and central nervous center (CNS) abnormalities, such as anencephaly, hydrocephaly, and meningomyelocele. Even low doses of MTX, less than usual chemotherapy levels, can induce human malformations. Nurses and technicians who administer chemotherapy may be unknowingly exposed to doses of MTX that may damage their unborn children. Although normal pregnancies and children have occurred when mothers have been exposed to MTX after the first trimester of pregnancy, insufficient numbers of studies have been conducted to accurately assess the risk to the unborn of MTX exposure after the first trimester. Because small amounts of MTX can be transferred to breast milk, the Academy of Pediatrics Committee on Drugs does not recommend breast feeding while taking MTX.

Since MTX may induce severe reduction of sperm and damage DNA, it is advisable for men of reproductive age not to attempt to father children while receiving MTX and for a...
period of at least 3 months after termination of exposure to allow sufficient time for healthy sperm to develop.

MTX is listed as EPA Class A+ for reproductive hazard: that is, the no-effect dose is not known. MTX is categorized by the manufacturer and the US Food and Drug Administration (USFDA) to be Pregnancy Category X, “Studies in animals or humans have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk clearly outweighs any possible benefit.” MTX is also categorized in a reference guide to natal and neonatal risks as a USDA Pregnancy Category D, “Positive evidence of human fetal risk exists, but benefits in certain situations (e.g., life threatening situations or serious diseases for which safer drugs cannot be used or are ineffective) may make use of the drug acceptable despite the risks.”

Carcinogenic Effects:

MTX has been reported to increase the risk of leukemias and lymphomas, and skin cancer in humans. Liver tumors were also reported in a child who received MTX for 6 years.

Genetic Effects:

MTX inhibits DNA synthesis and has caused genetic damage in a variety of short-term genetic assays.

Fact Sheet by:
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