



## MULTIPLE SCLEROSIS: SAFETY AND EFFECTIVENESS OF MITOXANTRONE TREATMENT

This fact sheet may help you understand the safety and effectiveness of the drug mitoxantrone in treating multiple sclerosis (MS).

Neurologists from the American Academy of Neurology (AAN) are doctors who identify and treat diseases of the brain and nervous system. The following evidence-based information\* is provided by experts who carefully reviewed all available scientific studies on the safety and effectiveness of mitoxantrone in treating MS.

A 2003 AAN guideline studied the drug's effectiveness and safety in MS. This fact sheet summarizes the AAN's 2010 report, "Evidence Report: The Efficacy and Safety of Mitoxantrone (Novantrone) in the Treatment of Multiple Sclerosis," that updates the guideline.

If you take or plan to take mitoxantrone for MS, it is important to discuss this with your doctor. Mitoxantrone use may lead to serious health problems such as heart failure and acute leukemia. These problems can develop even after you stop taking the drug.

### What is mitoxantrone used for? Does it treat MS effectively?

Mitoxantrone is a cancer drug. It is mainly used to treat certain cancers of the breasts, blood, or lymph nodes. This drug is intended to slow or stop abnormal cell growth. It is also known as mitoxantrone hydrochloride, or MX. Mitoxantrone is given through an IV needle every three months. The maximum lifetime dose is 140 milligrams.

In 2000, the US Food and Drug Administration (FDA) approved mitoxantrone for certain aggressive or severe types of MS. These are aggressive relapsing-remitting (RRMS), secondary-progressive (SPMS), and progressive-relapsing (PRMS). According to the 2003 AAN guideline, good evidence shows mitoxantrone likely has a modest effect in MS treatment. Mitoxantrone likely helps slow the progression of the disease. The drug also likely helps lower the number and frequency of attacks. The 2010 update confirms these findings.

### I have MS, and I am thinking of taking mitoxantrone. What are the health risks of this drug?

Mitoxantrone can lead to serious health problems. These include heart failure and acute leukemia, a type of blood cancer. It is important to understand these risks fully before deciding whether to take this drug. The 2003 guideline reported some evidence of risk. The 2010 update shows these risks to be greater than previously thought.

Mitoxantrone use can lead to heart damage. The damage occurs in the left ventricle or chamber. This pumps blood from the heart to the arteries. The damage can lead to heart

failure. These problems can occur anytime after starting the drug. Heart damage and failure from mitoxantrone use in cancer have been widely reported. A 2002 report looked at heart damage from use of the drug in MS. The report found a low rate of heart failure and slightly higher rate of heart damage. Since then, studies on this topic have reported higher rates of heart damage or failure. The evidence from these studies is weak and sometimes conflicting. However, taken together, this weak evidence gives estimates of risk. The risk is about 12 percent for heart damage and less than one-half percent for heart failure. Another way to understand the risk is the "number needed to harm" (NNH). The NNH is a statistic used to create a picture of the risk. In this case, the NNH is 8 for heart damage. This means for every eight people given mitoxantrone for MS, one will develop heart damage. This heart damage may lead to heart failure.

Another serious risk from mitoxantrone use is acute leukemia. This occurs in some people treated with chemotherapy for cancer. It also can develop in people taking mitoxantrone for MS. The first known case in MS was reported in 1998. Studies have largely reported this risk as low (less than one-quarter percent).

Leukemia can develop while a person is taking mitoxantrone. However, this disease also can develop years after a person stops mitoxantrone treatment. The evidence from these studies is weak and sometimes conflicting. But as a whole, this weak evidence provides estimates of risks. This risk is about less than one percent. The NNH for acute leukemia is roughly 123. This means for every 123 people given mitoxantrone for MS, one will develop acute leukemia.

## The health risks of mitoxantrone seem serious. How do I decide if this drug is right for me?

Deciding whether to take mitoxantrone for MS can be difficult. It is important to discuss this with your doctor. He or she will help you weigh the benefits and risks. In some cases, an MS specialist may be needed.

Some forms of MS are very severe and can progress quickly. In those cases, mitoxantrone may help. But it is important to remember that the evidence shows only a modest effect. What's more, there is not enough evidence to know what is considered a safe dose. Be aware that the health risks of mitoxantrone sometimes can lead to death. Also, understand that mitoxantrone is just one of several drug options to consider. Discuss all your treatment options with your doctor.

In 2005, the FDA issued a "black box" warning for mitoxantrone. The FDA reissued this warning in 2008

because of low compliance. The warning advises heart monitoring for anyone taking mitoxantrone for MS. The doctor is encouraged to monitor the patient before beginning the drug and before each injection. Yearly heart monitoring after stopping the drug is also urged. For more information, visit [www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126445.htm](http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126445.htm). There is not enough evidence to show a benefit of monitoring people for heart problems or acute leukemia. However, regular monitoring might help detect a developing health problem. Doctors may want to check blood cell counts for signs of cancer.

More research is needed on the safety and effectiveness of mitoxantrone use in MS. Such studies should focus on the severity of the risk. They should also examine safety concerns for dose levels and long-term treatment.

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

\*After the experts review all of the published research studies, they describe the strength of the evidence supporting each recommendation:

*Strong* evidence = more than one high-quality scientific study

*Good* evidence = at least one high-quality scientific study or two or more studies of a lesser quality

*Weak* evidence = the studies, while supportive, are weak in design or strength of the findings

*Not enough* evidence = either different studies have come to conflicting results or there are no studies of reasonable quality

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