Minocycline Fact Sheet

What is minocycline?
Minocycline belongs to a class of second generation tetracycline oral antibiotics. It is used to treat bacterial infections including acne; pneumonia and other respiratory tract infections; and infections of the skin, genital, and urinary systems. It is sometimes used to treat mild rheumatoid arthritis.

Minocycline has an established and relatively safe clinical track record since its introduction in 1971 as an acne medication. It comes in capsule form in a variety of formulations to control its bioavailability and release into the body.

In addition to its antibiotic effects, minocycline appears to dampen detrimental immune responses. Laboratory studies also suggest that minocycline protects neurons from injury in models of neurological diseases. The combined anti-inflammatory and neuroprotective effects have incited MS researchers to investigate this drug as a potential therapeutic for people living with MS.

How does minocycline work?
Minocycline’s antibacterial effects are exerted through the molecule’s ability to pass through the membrane of vulnerable strains of pathogenic (disease-causing) bacteria. Once inside, minocycline binds to a specific coding region in the bacterium’s genetic machinery and prevents protein synthesis, thus effectively killing the pathogen.

Unrelated to its antibacterial activity, minocycline also boasts anti-inflammatory properties that make it an indication for certain chronic inflammatory conditions like rheumatoid arthritis and, importantly, render it a potential candidate for the treatment of MS. Although its anti-inflammatory mode of action is not fully understood, minocycline is believed to prevent the migration of disease-causing white blood cells called T-cells into the central nervous system, and also suppresses certain compounds that disrupt the blood-brain barrier in animals with an MS-like disease. Finally, minocycline suppresses the activity of various pro-inflammatory cells and molecules, including microglia and certain cytokines and chemokines.

In addition to its anti-inflammatory properties, minocycline has recently drawn considerable research attention for its ability to promote neuroprotection in models of neurological diseases, which makes it a promising candidate for the treatment of several neurodegenerative disorders, including MS. Minocycline has been shown to exert its neuroprotective effects primarily through at least three mechanisms. The first is the inhibition of a process of cell death called apoptosis, which affects myelin-producing cells in MS that normally mediate myelin repair. Secondly, minocycline has antioxidant activity that reduces cellular damage caused by oxidative stress that can cause damage to nerve fibres. Lastly, minocycline protects against excitotoxicity, which can lead to cell death and inflammation. It is not clear whether minocycline acts through one or a combination of these neuroprotective or
inflammatory mechanisms to potentially alleviate the MS disease process.

What research has been done on minocycline and MS?

Early studies were conducted in animals with an MS-like disease to provide preliminary evidence of its potential as an MS therapeutic and to examine its mechanisms of action. Pioneering research conducted by Drs. V. Wee Yong and Luanne Metz and team and funded by the MS Society of Canada demonstrated that minocycline targeted an enzyme that is involved in stimulating inflammatory cell infiltration into the brain and inflammation. When minocycline was given to mice with both mild and severe forms of MS-like disease, symptom severity was significantly reduced and course of the disease was delayed.

Several clinical studies have since been conducted that have tested the efficacy and safety of minocycline in persons living with MS. Two pilot studies, also conducted by Drs. Metz and Wee Yong, have shown promising results. The studies demonstrated that minocycline was safe and well tolerated by people living with MS. The first study of 10 people with relapsing-remitting MS revealed preliminary evidence of reduced inflammatory activity on MRI scans, compared to the baseline period pre-treatment; the benefit held for up to three years.

A larger phase II, multi-centre, double-blind, placebo-controlled trial led by Dr. Metz and team compared the efficacy of minocycline administered in combination with glatiramer acetate (Copaxone) to glatiramer acetate and placebo in 44 participants with relapsing-remitting MS. The combination of minocycline and glatiramer acetate reduced the total number of T1 gadolinium-enhanced lesions on brain MRI by 63% and the total number of new and enlarging T2 lesions by 65% over 9 months. The results, although not statistically significant, were encouraging enough to warrant further study.

Most recently, Dr. Metz has been leading an MS Scientific Research Foundation-funded, phase III clinical trial to determine if minocycline, taken orally at a dose of 100mg twice daily, is better than placebo at reducing the proportion of participants with clinically-isolated syndrome (CIS) who convert to MS over 6-months. The study was a double-blind, randomized, placebo-controlled clinical trial carried out in 142 participants after they experienced their first demyelinating event. More details about the study design are available at clinicaltrials.gov/. The study was carried at MS clinics in Vancouver, Burnaby, Calgary, Edmonton, Winnipeg, London, Toronto, Ottawa, Montreal, Greenfield Park, Quebec City, and Halifax. Unpublished results presented at the 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) demonstrated that minocycline reduced conversion to MS. The MS Society and the medical community are awaiting the published results to understand the details which are needed to guide recommendations about the use of minocycline.
Glossary

- **Apoptosis**: A process of programmed cell death; although this is a naturally-occurring and beneficial process in the body, abnormal levels of apoptosis can lead to tissue injury.
- **Blood-Brain Barrier**: A barrier formed by a continuous layer of tightly connected endothelial cells; prevents most large molecules and cells found in the blood from entering the brain tissue.
- **Chemokines**: A protein beacon that attracts white blood cells bearing a receptor for the chemokine.
- **Cytokines**: A small messenger molecule that influences the actions of immune system cells. There are many different cytokines, each acting only on cells that have receptors for that cytokine.
- **Excitotoxicity**: The process by which nerve cells are damaged or destroyed by excessive stimulation by certain brain chemicals, or neurotransmitters.
- **Neuroprotection**: The preservation of the structural and functional integrity of nerve cells.
- **Oxidative Stress**: An imbalance between the levels of free radicals – highly reactive molecules resulting from energy production – in cells and the body’s ability to counteract them with antioxidants, resulting in damaging effects.

References