



TYSABRI[®]
(natalizumab)

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MS Treatments

MSology Essentials Series

TYSABRI®
(natalizumab)

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Why treat MS?

Multiple sclerosis (MS) is believed to be caused by an abnormal immune response, which results in inflammation and tissue damage in the brain and spinal cord (together called the central nervous system, or CNS). This inflammation is the cause of MS symptoms, such as nerve tingling, muscle weakness, vision problems, balance difficulties and pain. New or worsening MS symptoms that last for more than a day or two are called relapses, and these generally indicate an inflammatory flare-up in the CNS. Relapse symptoms can persist for several days, weeks or months. Some relapses will resolve completely and some will not. As you experience more and more relapses, the body is unable to repair the damage to the brain and spinal cord, which typically leads to physical and mental impairments.

That is why it is so important to treat MS – to reduce inflammation and tissue damage and reduce or delay disability. The medications prescribed are called disease-modifying therapies because they target the underlying MS disease process. They do not heal any tissue damage that has already occurred, but they may prevent further damage that will contribute to disability in the years ahead.

MS medications do not treat specific symptoms, so you will not feel an improvement in the symptoms you are having. The main effects of therapy are to lessen the frequency and severity of relapses and reduce the amount of new inflammation in the brain and spinal cord (seen as lesions on your magnetic resonance imaging [MRI] scan). So treatment can be seen as an investment in your future – lessening the damage that is occurring now to prevent disabilities later on.



How does Tysabri work?

Tysabri is an infusion medication (a slow drip injected into a vein) used to treat relapsing-remitting multiple sclerosis.

In MS, specialized cells of the immune system (called T and B cells) become activated, enter the CNS and cause inflammation and tissue damage. While most MS medications suppress this immune response, Tysabri acts very differently. It blocks immune cells circulating in your blood vessels from entering the CNS so they cannot cause inflammation and tissue damage. This “cools down” the inflammation very rapidly and this effect is maintained with monthly doses of the drug.

Clinical trials have shown that in people with MS, Tysabri reduces the frequency of relapses, decreases the number of inflammatory lesions in the brain and delays the progression of physical disability.

Tysabri is a potent medication. So doctors typically reserve it for people who need it most – individuals with aggressive MS or those who do not have an adequate response to another MS medication.



Tysabri does not suppress your immune system. It protects the brain by blocking immune cells from entering the CNS and causing damage.



How do I take Tysabri?

DOSING

- Tysabri is administered by intravenous infusion at an infusion centre (a clinic or other healthcare facility).
- For the infusion, you will be seated in a chair and a healthcare professional will insert a needle into your vein. The drug is delivered by a slow drip from an IV bag.
- The total amount of time needed for the infusion will be about 2 hours. The infusion itself takes about 1 hour. You will also need to be monitored for 1 hour afterward to ensure that you are not having an allergic reaction.
- During your visit you may need to provide a blood sample (see Tests & Procedures). The full set of procedures will vary depending on the clinic you visit.
- Infusions are generally well tolerated, and most people are able to return to their usual daily activities (e.g. going to work or school) immediately afterward.
- However, for your first few visits you may want to ask someone to drive you to/from the infusion centre in case you feel dizzy or unwell after the infusion.
- One infusion will be needed once a month. In some situations, your doctor may decide that less frequent infusions (e.g. every 6–8 weeks) may be needed.



Your visit to the infusion centre will take 2 hours so remember to bring something to do. Use the time to catch up on your reading, listen to an audiobook or check your social media accounts.



How do I know my treatment is working?

During your course of treatment, your doctor will monitor your response to treatment with a variety of tests and procedures. These typically include neurological examinations to evaluate your nerve and muscle function, and magnetic resonance imaging (MRI) to assess the extent of inflammatory activity in your brain and spinal cord. Periodic blood tests will be required for safety reasons. Other tests and procedures may also be needed during your course of treatment.

Many people will start to feel better soon after their first dose – but it is important to continue having the monthly infusions to maintain the full benefit of the medication.

What if I have a relapse?

A relapse is a new MS symptom you haven't had before, or a worsening of symptoms you've previously experienced. The symptom persists for at least 24 hours. If you become overheated – from exercise, a hot bath, a fever or infection – your MS can worsen for a short period of time, but these symptoms are not a true relapse.

It's important to inform your neurologist or MS nurse if you experience a relapse or any new or worsening symptoms that last more than 24 hours. A relapse can occur soon after starting treatment with Tysabri, especially if your MS was very active before, but this generally means that the medication has not had time to be fully effective.



If you have a relapse after you've been taking Tysabri for several months, it may mean that your body has started to produce antibodies that are neutralizing the effects of the drug. This is uncommon, but your doctor will need to obtain a blood test to ensure that you are still responding to treatment.



Be sure to keep all of your treatment appointments at the infusion centre. Ensure that vacations, business trips and other commitments don't interrupt your treatment. You may experience a relapse or worsening MS if you skip a dose of Tysabri.

What are the possible side effects of this medication?

Infections

There is a low risk of developing a bacterial infection (e.g. bladder infection, respiratory tract infection, pneumonia) or viral infection (e.g. shingles) while taking Tysabri. Contact your doctor or MS clinic nurse immediately if you think you have an infection. You may have to delay your next infusion if you have an active infection.

Hypersensitivity reactions

Some people have an allergic reaction to treatment, which typically occurs within the first two hours of receiving the



infusion. Symptoms may include itchiness or skin rash, dizziness, fever, flushing, low blood pressure, difficulty breathing and chest pain. A healthcare professional will monitor you during your infusion and will treat any symptoms that develop.

PML

Progressive multifocal leukoencephalopathy (PML) is a brain infection caused by the John Cunningham (JC) virus (named after the first person in whom the virus was isolated). Most adults acquire this virus during their lifetime but are unaware of it: there are generally no symptoms and the immune system keeps the virus in check. PML can develop when a person's immune system is compromised by illness or medications and allows the virus to reactivate. If it develops, PML can cause severe disability or death.

There are three known risk factors for developing PML during Tysabri treatment (Table 1):

1. *JC virus infection*. Your doctor will order a blood test either before you start Tysabri or during treatment to determine if your body is harbouring the virus. If the test is negative, the risk of PML is very low (about 1 in 10,000); repeat tests are needed periodically because a negative test can become positive (called seroconversion). If the test is positive (the virus is present), the PML risk is still minimal in the first two years of treatment (less than 1 in 1,000).



2. *Prior use of an immunosuppressant.* Your PML risk is higher if you have ever taken an immunosuppressant drug for any medical condition (often for cancer). Examples of immunosuppressants are Novantrone (mitoxantrone), Imuran (azathioprine), Procytox (cyclophosphamide) and methotrexate. It is not known if taking an MS medication (e.g. Gilenya, Tecfidera, Mavenclad, Ocrevus, Lemtrada) before starting Tysabri increases the risk of PML. It is important to give your neurologist a complete list of all of the medications you have taken.

3. *Taking Tysabri for more than two years.* There is a very low risk of PML in the first year or two of treatment, but the risk will increase thereafter. So after two years of Tysabri, you and your doctor will need to reassess if the benefits of treatment in your particular circumstances outweigh the risk of PML. If you and your doctor decide to continue Tysabri, you will need to provide your consent and agree to have periodic blood tests (every 3-6 months) and MRIs (every 6-12 months) to ensure that you are not developing PML.



All medications can cause a variety of side effects. If you have any new, unusual or worrisome symptoms while taking your medication, report them promptly to your doctor or MS nurse. Your MS nurse can provide helpful advice to minimize treatment-related effects.



Protecting against PML

PML is an uncommon side effect. But if it does develop, it is important to detect it early so it can be treated promptly. The table below summarizes how to distinguish PML symptoms from an MS relapse. Share this information with your family and friends – they may detect changes in your mood or personality that you haven't noticed. You or your family should report any unusual or worrisome symptoms you're having as soon as possible to a healthcare professional.

TABLE 1

	MS relapse*	PML
How does it develop?	<ul style="list-style-type: none">• Over several hours or days• Usually stabilizes• Symptoms often lessen or go away without treatment	<ul style="list-style-type: none">• Over several weeks• Continues to worsen
What are the possible symptoms?	<ul style="list-style-type: none">• Vision (e.g. blurriness, double vision)• Tingling, numbness, nerve pain• Muscle weakness, spasms, stiffness	<ul style="list-style-type: none">• Language impairment (difficulty speaking or understanding speech, difficulty writing or understanding written words)• Changes in mood or behaviour• Partial blindness• Weakness on one side of your body• Seizures
* Does not include a brief worsening of symptoms that can occur because of an active infection (e.g. urinary tract infection) or heat exposure (e.g. hot bath, getting overheated during exercise)		

Adapted from McGuigan and colleagues. *J Neurol Neurosurg Psychiatry* 2016;87:117-125



Tests and procedures

During your course of treatment, your doctor will order a number of tests to ensure that your medication is not causing any unwanted effects. The test procedures vary at different clinics. Your neurologist and MS nurse will schedule which tests you will need and how often they should be done.

Test/procedure*	Reason	How often
Blood test	<ul style="list-style-type: none"> To evaluate liver function To see if you have been exposed to the JC virus To determine if your body is producing antibodies that are neutralizing the medication 	<ul style="list-style-type: none"> Before starting Tysabri Before starting Tysabri and during treatment During treatment if you have a relapse or new lesions on your MRI
Magnetic resonance imaging (MRI) scan	<ul style="list-style-type: none"> To ensure you do not have PML To evaluate your response to treatment 	<ul style="list-style-type: none"> Before starting Tysabri and periodically thereafter Periodically
Pregnancy test	To ensure that you are not pregnant	Before starting Tysabri or if pregnancy is suspected
STRATIFY JCV assay (blood test)	To check the level of antibodies to the JC virus	Every 3–6 months (depending on prior test results)
Spinal tap (lumbar puncture)	To ensure you do not have PML	<ul style="list-style-type: none"> If PML is suspected If you are stopping Tysabri and starting another disease-modifying therapy for MS

* The frequency of tests will vary depending on your MS clinic. Your neurologist or MS nurse will tell you more about the specific tests and when you'll need them during treatment. Please ensure that you DO all of the necessary tests at the recommended times.



Pregnancy

For the health of you and your baby, it is best that your MS is stable for at least a year before you become pregnant. If you have very active MS (frequent or severe relapses), your doctor may advise you to start treatment now with Tysabri. Once your MS is well-controlled, you can consider stopping treatment as you start trying to get pregnant.



It is best if your MS is stable for a year before trying to get pregnant.

If you become pregnant during treatment, you and your neurologist will need to discuss how to interrupt your treatment. If you have had very active MS, there's a risk that your MS may worsen if you stop Tysabri too abruptly. In these special circumstances, it may be best to continue on treatment for the first few months of your pregnancy. You can then resume therapy once the baby is born.

Tysabri should generally not be taken while breastfeeding. Since there is a higher risk of relapses in the first 3-6 months after childbirth, you will need to decide whether it is best to breastfeed (and for how long) or to resume treatment right away. Your neurologist and MS nurse can advise you on the best course of action according to your unique circumstances and personal preferences.



Other medications

All medications have the potential to interact with other drugs you are taking. This includes other prescription medications, as well as non-prescription drugs and alternative/complementary therapies. There are no known drug interactions with Tysabri. For safety reasons, you should not take Tysabri with other disease-modifying therapies used to treat MS, or immune-suppressing drugs commonly used to treat cancer.

Talk to a healthcare professional before taking any new medication. Your doctor, MS nurse or pharmacist can advise you about any interactions that may occur.

There are no known interactions between Tysabri and food so you can eat just before or after your infusion.

Other medical conditions

Always ensure that your doctor is aware of any other medical conditions you may have. This includes high blood pressure, liver or kidney problems, diabetes, infections, or other illnesses.



Resources in your community

Your neurologist or MS nurse can provide you with information on the Biogen ONE™ program, which offers information and support for people taking Tysabri. A program member will also send you reminders about your next visit to the infusion centre.

The healthcare professionals at your local infusion centre will ask you about any unusual symptoms or problems you've been having and will monitor your safety during and after the infusions.



The MS Essentials series provides the latest information on multiple sclerosis medications, research, and lifestyle issues such as health, nutrition and exercise. All of the booklets are developed by Lind Publishing, publishers of MSology, to help people affected by MS remain active and informed. MS Essentials is provided free of charge. The full series of publications is available for download on <http://www.MSology.com>.

The information reflects use of the medication in Canada; use may vary in other countries. MSology does not approve, endorse or recommend any specific product or therapy. Contact your healthcare providers before you start treatment, alter the dose, interrupt or discontinue your therapy. For full information about a specific medication, consult the prescribing information or package insert provided by the manufacturer for your country.



This booklet is produced by:

Lind Publishing Inc.
Montreal, Quebec, Canada

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