

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr**TYSABRI**™

Natalizumab for injection

Read this carefully before you start taking **Tysabri** and each time you get a Tysabri IV infusion. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Tysabri**.

Keep this leaflet and the Patient Wallet Card. You should read them before starting Tysabri, and before each Tysabri IV infusion.

- It is important that you keep the Card with you during treatment and for three months after the last dose of Tysabri, since side effects may occur even after you have stopped treatment.
- Show your Card and this package leaflet to any doctor involved in your treatment.

Serious Warnings and Precautions

- There have been uncommon cases of a brain infection by JC virus resulting in progressive multifocal leukoencephalopathy (PML) and/or JCV granule cell neuronopathy (JCV GCN) occurring in patients who have been given Tysabri. These infections are associated with an uncontrolled increase of the JC virus in the brain, although reason for this increase in some patients treated with Tysabri is unknown. It usually happens in people with weakened immune systems, but it is difficult to predict who will get these infections. Such infections may lead to severe disability or death; there is no known cure.
- In order to receive Tysabri you must talk to your doctor and understand the benefits and risks of Tysabri and consent to treatment prior to receiving your first treatment. After 24 months of treatment you should again talk to your doctor, understand the benefits and risks of Tysabri treatment and consent to continuation of treatment.
- Tysabri can only be given to patients who are registered in, and meet, all conditions of the Biogen ONE™ Support Program. Biogen ONE™ Support Program is a controlled distribution program for Tysabri or log onto BiogenTherapies.ca.
- You should agree to enrol into the Canadian Biogen ONE™ Support Program, which is a patient registry, by contacting 1-855-MSONE-00 (1-855-676-6300).

What is Tysabri used for?

Tysabri decreases the number of MS attacks and slows down the progression of disabling effects of MS. Therefore, when you receive Tysabri, you might not notice anything happening to your MS, but it may help to prevent your MS from becoming worse.

How does Tysabri work?

Tysabri is a man-made protein. It prevents the active immune cells from reaching the brain. Tysabri is used for decreasing the inflammation in your brain (as seen on magnetic resonance imaging [MRI] scan) and therefore reduces nerve damage caused by multiple sclerosis.

What are the ingredients in Tysabri?

Medicinal ingredients: natalizumab

Non-medicinal ingredients: polysorbate 80, sodium chloride, sodium phosphate, and water for injection

Tysabri comes in the following dosage forms:

Solution for intravenous administration 300mg/15mL

Tysabri comes in the form of a liquid in a vial. The liquid contains 300 mg in a 15 mL dose (20 mg/mL) of natalizumab.- The liquid must be mixed with 0.9% sodium chloride and is administered into a vein over time, which is called infusion.

Do not use Tysabri if:

- You have an allergy or are sensitive to natalizumab or anything else that is in this medicine (see Allergic reaction below).
- You have a serious problem with your immune system (for example, due to a disease such as leukemia or human immunodeficiency virus [HIV], or from using some other medicines that weaken your immune system).
- You have a serious infection, including an uncommon infection of the brain called progressive multifocal leukoencephalopathy (PML) now or in the past.
- You have active cancer.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Tysabri. Talk about any health conditions or problems you may have, including if you:

- **Allergic reaction**
Some patients have had allergic reactions to Tysabri. If you notice any of the following signs of allergy to Tysabri during or shortly after your infusion, tell your healthcare professional (doctor or nurse) immediately:
 - Itchy rash (hives)
 - Swelling of your face, lips or tongue
 - Difficulty breathing
 - Chest pain or discomfort

- **Infections**

There have been uncommon cases of a brain infection by JC virus resulting in progressive multifocal leukoencephalopathy (PML) occurring in patients who have been given Tysabri. PML is a serious condition, which may lead to disability or death. A condition called granule cell neuronopathy (GCN) is also caused by JC virus and has occurred in some patients who have been given Tysabri. The symptoms of JCV GCN are similar to PML.

Your chance of getting PML increases:

- if you have antibodies against the JC virus, the virus that can cause PML. JC virus is a common virus which infects many people but does not normally cause noticeable illness. It is also very common to have these antibodies against the JC virus. If you do not have antibodies against the JC virus, you are at a lower risk of getting PML. Your doctor may recommend a blood test to see if you have these antibodies before you start Tysabri. If you do not have the antibodies your doctor may repeat the test every 6 months while you are taking Tysabri.
- with a longer period of Tysabri treatment, especially if you have been on treatment for over 24 months.
- if you have received medicines that can weaken or suppress your immune system prior to starting Tysabri (immunosuppressants), for example: azathioprine, cyclophosphamide, methotrexate, mitoxantrone, mycophenolate.

You must carefully consider and discuss with your physician the benefits and risks of Tysabri therapy if you have ALL of the following risk factors: anti-JCV antibody positive, have received more than 2 years of Tysabri therapy, AND have received medicines that can weaken or suppress your immune system (immunosuppressant therapy).

To monitor the risk of PML, your doctor may repeat the test regularly (eg. 6 months) to check if anything has changed if:

- You do not have antibodies to the JC virus in your blood
- OR
- You have been treated for more than 2 years and you have a lower level of JCV antibodies in your blood.

A variety of symptoms of PML can appear and these can get worse over time. This is why it is important that you speak with your partner or caregivers and inform them about your treatment.

The symptoms of PML may be similar to an MS attack, including increasing weakness or clumsiness on one side of the body, trouble with vision, or trouble with thinking. Therefore, if you feel your MS is getting worse, or if you notice any new symptoms, you should speak to your doctor immediately. Symptoms might arise that you might not be aware of yourself and may include changes in mood or behaviour, memory problems,

speech and language difficulties, changes in your balance or walking ability. If any of these symptoms occur, it is important that you, your partner or caregiver inform your doctor as soon as possible. Based on this information your doctor may request further testing to rule out PML.

You and your caregiver should continue to watch for any signs and symptoms of PML for at least 6 months after you stop taking Tysabri. Tell your doctor as soon as possible if you start noticing any symptoms.

It is not known if the chance of getting PML continues to rise, remains the same, or falls after you have been on Tysabri for more than three years.

In most Tysabri treated patients with PML a reaction known as IRIS (Immune Reconstitution Inflammatory Syndrome) has occurred after stopping or removing Tysabri from the blood by a treatment called plasma exchange. IRIS presents as a worsening of your neurological symptoms that may be rapid and require that your doctor treat this condition with other medicines. IRIS can lead to serious complications and may be fatal.

Because Tysabri can weaken your immune system, you may have an increased chance of getting an unusual, serious or opportunistic infection (infection that usually does not cause disease in healthy people), such as herpes encephalitis and meningitis (inflammation of the brain and spinal cord). These infections can sometimes be life-threatening or fatal. Herpes infections of the eye have also occurred. Call your doctor right away if you have changes in vision, redness, or eye pain.

- **Liver or kidney problems**

If you have problems with your kidneys, be sure to tell your doctor. If you experience unusual darkening of the urine, nausea, vomiting, feeling tired or weak and yellowing of the skin and eyes (jaundice), call your doctor right away.

- **Pregnancy**

It is not known if Tysabri can harm your baby if you are pregnant. You should not take Tysabri if you are pregnant. Talk to your doctor if you become pregnant while taking Tysabri.

- **Breastfeeding**

Tysabri has been found in breast milk. You should not breastfeed while taking Tysabri. You should discuss with your doctor whether you should choose to breastfeed or to use Tysabri.

- **Other considerations**

Tysabri is not intended for use in patients under the age of 18. Tysabri has not been well studied in patients over 65 years old.

- Talk to your doctor if you are taking or have recently taken any other medications, including over-the-counter medicines or herbal (natural healthcare) products.
- Tysabri can have an effect on the results of some laboratory tests showing an increase in the number of some blood cells.
- Talk to your doctor if you have easy bruising, unusual or prolonged bleeding from cuts, pinpoint or round spots that appear on your skin, abnormally heavy menstrual periods, or bleeding from the nose or gums that is new.
- Before you get TYSABRI IV, it is mixed with 0.9% sodium chloride. After mixing, each dose of TYSABRI contains 406 mg of sodium. This should be taken into consideration if you are on a controlled sodium diet.
- **Driving and using machines**
Tysabri is not expected to have an effect on your ability to drive or to operate machines. However, if you experience dizziness while taking Tysabri, avoid driving or operating machines until it has resolved.

Tell your doctor about all of the medicines you take now or have taken in the last while, including those that are prescribed for you as well as those that you buy over-the-counter. It is not known if Tysabri interacts with food or herbal (natural healthcare) products.

You may not be able to take Tysabri with some medicines that affect your immune system.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with TYSABRI:

Interactions with food and other drugs have not been established.

How to take Tysabri IV:

Tysabri can only be prescribed by a healthcare professional who is trained in treating neurological conditions. Tysabri will be prepared and given to you by a healthcare professional.

Usual dose:

The usual adult dose is 300 mg given by intravenous infusion once every 4 weeks.

Overdose:

If you receive more Tysabri than your healthcare professional prescribed, you should be monitored closely for any harmful signs or symptoms and given treatment for these right away, should they appear.

If you think you, or a person you are caring for, have taken too much Tysabri, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss your usual dose of Tysabri, contact your doctor to schedule your appointment as soon as possible. You should then continue to receive your dose of Tysabri every 4 weeks.

What are possible side effects from using Tysabri?

These are not all the possible side effects you may have when taking Tysabri. If you experience any side effects not listed here, tell your healthcare professional. Show your Wallet Card and this package leaflet to any doctor involved in your treatment.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Dizziness	✓		
Feeling sick (nausea)	✓		
Headache	✓		
Joint pain	✓		
Sore throat and runny or blocked up nose	✓		
Tiredness	✓		
Urinary (bladder) infection		✓	
COMMON			
Being sick (vomiting)	✓		
Fever		✓	
Itchy rash (hives)		✓	
Shivering		✓	
UNCOMMON			
Progressive multifocal leukoencephalopathy (PML), a rare brain infection. Typical symptoms include:			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<ul style="list-style-type: none"> - progressive weakness on one side of the body - clumsiness of limbs - disturbance of vision - changes in thinking, memory and orientation - confusion - personality changes 			
Reduction in blood platelets and easy bruising (purpura)		✓	
Severe allergy (hypersensitivity)			✓
RARE			
Liver symptoms		✓	
Severe anemia (decrease in red blood cells). Symptoms include pale skin, feeling breathless, lack of energy.		✓	
Unusual infections			✓

If any of these occur during or shortly after the infusion, tell your doctor or nurse immediately.

Some patients have had allergic reactions during or shortly after receiving Tysabri. Your doctor or nurse will stop your Tysabri infusion if he or she sees any signs or symptoms of an allergic reaction.

After you have received Tysabri, a doctor or nurse may monitor you for 1 hour.

Speak to your doctor as soon as possible if you think you have an infection.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Unopened vial: Store in a refrigerator at 2°C to 8°C. Do not freeze. Keep the vial in the outer carton to protect it from light. Do not shake. Do not use after the expiry date found on the label and carton.

Diluted solution: After your healthcare professional has prepared Tysabri for infusion, the diluted solution must either be used immediately or should be stored in a refrigerator (2°C to 8°C). Infusion of the diluted product should be started as soon as possible and completed within 8 hours of dilution.

Keep out of reach and sight of children.

If you want more information about Tysabri:

- Talk to your healthcare professional

Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website:

(<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.biogen.ca/products/TYSABRI_PM_EN; or by calling Biogen Canada Inc. at: Biogen ONE™ (1-855-676-6300).

This leaflet was prepared by Biogen Canada Inc.

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