

PART III: CONSUMER INFORMATION

PrTYSABRI®
natalizumab (pronounced tie-SA-bree)

This leaflet is part III of a three-part "Product Monograph" published when TYSABRI was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about TYSABRI. Contact your doctor or pharmacist if you have any questions about the drug.

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

ABOUT TYSABRI

What is TYSABRI and what is it used for?

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.

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.

Who should not take TYSABRI?

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).
- 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).
- A serious infection, including an uncommon infection of the brain called progressive multifocal leukoencephalopathy (PML) now or in the past.
- If you have active cancer.

What is in TYSABRI?

The active ingredient is called natalizumab. TYSABRI contains other ingredients including sodium chloride, sodium phosphate and Polysorbate 80 and water for injection. Before you get TYSABRI, 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.

What dosage form does TYSABRI come in?

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. TYSABRI will be prepared and given to you by a healthcare professional.

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 BIOGENcareforMS.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).

• **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).

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.

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.

PROPER USE OF THIS MEDICATION

TYSABRI can only be prescribed by a doctor 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 doctor 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 have taken too much TYSABRI, contact your 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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, TYSABRI can have side effects. If you have any worrying side effects including any that are not included here, contact your doctor or pharmacist. Show your Wallet Card and this package leaflet to any doctor involved in your treatment.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom/Effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor
		Only if severe	In all cases	
Common	Urinary (bladder) infection		✓	
	Sore throat and runny or blocked up nose	✓		
	Shivering		✓	
	Itchy rash (hives)		✓	
	Headache	✓		
	Dizziness	✓		
	Feeling sick (nausea)	✓		
	Being sick (vomiting)	✓		
	Joint pain	✓		
	Fever		✓	
Tiredness	✓			
Uncommon	Severe allergy (hypersensitivity)			✓
	Progressive multifocal leukoencephalopathy (PML), a rare brain infection. Typical symptoms include: - progressive weakness on one side of the body - clumsiness of			✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom/Effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor
		Only if severe	In all cases	
	limbs - disturbance of vision - changes in thinking, memory and orientation - confusion - personality changes			
Rare	Unusual infections			✓
	Liver symptoms		✓	
	Severe anemia (decrease in red blood cells). Symptoms include pale skin, feeling breathless, lack of energy		✓	

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 will monitor you for 1 hour.

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

This is not a complete list of side effects. For any unexpected effects while taking TYSABRI, contact your doctor or pharmacist.

HOW TO STORE TYSABRI

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 vial label and carton.

Diluted solution: After your healthcare professional has prepared TYSABRI for injection, 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.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect](#);
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 0701E
Ottawa, ON
K1A 0K9

Postage paid labels and the Patient Side Effect Reporting Form are available at [MedEffect](#).

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.

MORE INFORMATION

This document plus the full Product Monograph, prepared for health professionals can be obtained by contacting Biogen Canada Inc. at: Biogen ONE® (1-855-676-6300). This leaflet was prepared by Biogen Canada Inc. Last revised: January 2017 © Biogen 2006-2016. All rights reserved.