

Initial REMS Approval: 10/2011  
Most Recent Modification: 10/2020

**BLA 125104**

**TYSABRI® (natalizumab) Intravenous Injection**

**Monoclonal Antibody**

**Biogen, Inc  
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Cambridge, MA 02142**

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**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

**TYSABRI Outreach: Unified Commitment to Health (TOUCH®) Prescribing  
Program (MS & CD)**

## **I. GOALS:**

### **The goals of the TYSABRI REMS are:**

1. To inform prescribers, infusion center healthcare providers, and patients about the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI including the increased risk of PML with the presence of anti-JCV antibodies, longer treatment duration, and prior immunosuppressant use.
2. To warn against concurrent use with antineoplastic, immunosuppressant, or immunomodulating agents, and in patients who are immunocompromised.
3. To promote early diagnosis of PML and timely discontinuation of TYSABRI in the event of suspected PML.

## **II. REMS ELEMENTS:**

### **A. Medication Guide**

A Medication Guide (MG) for TYSABRI will be dispensed to each patient prior to each TYSABRI infusion in accordance with 21 CFR 208.24.

Please see the appended Medication Guide.

### **B. Elements to Assure Safe Use**

#### **1. Healthcare providers who prescribe TYSABRI are specially certified.**

- A. Biogen will ensure that health care providers who prescribe TYSABRI are specially certified.
- B. To become certified, prescribers will be required to enroll in the TOUCH® Prescribing Program by completing the following requirements:
  - i. Review the TYSABRI REMS prescriber educational materials, including the full Prescribing Information.
  - ii. Complete and sign the Prescriber/Patient Enrollment Form and acknowledge the following:
    - a) I have read and understand the full Prescribing Information for TYSABRI
    - b) I understand that TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing

treatment with TYSABRI, I should consider whether the expected benefit of TYSABRI is sufficient to offset this risk

- c) I am aware that cases of PML have been reported in patients taking TYSABRI who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving TYSABRI monotherapy
- d) I understand that three risk factors identified thus far that increase the risk of PML in TYSABRI-treated patients are:
  - The presence of anti-JCV antibodies.
  - Longer treatment duration, especially beyond 2 years
  - Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)

These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

- e) I understand that MRI findings may be apparent before clinical signs or symptoms. Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML. Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis.
- f) To my knowledge, this patient has no known contraindications to TYSABRI, including PML
- g) I have instructed this patient to promptly report to me any new or worsening symptoms that persist over several days, especially nervous system symptoms
- h) I understand that this patient should be seen and evaluated 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter for as long as this patient receives TYSABRI, and for at least 6 months after TYSABRI has been discontinued
- i) I will determine every 6 months whether this patient should continue on TYSABRI and, if so, authorize treatment for another 6 months
- j) I understand that I am required to submit an “Initial Discontinuation Questionnaire” when TYSABRI is discontinued and a “6-Month Discontinuation Questionnaire” following discontinuation of TYSABRI.

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- k) I should report to Biogen, as soon as possible, cases of PML, hospitalizations due to opportunistic infection, or deaths
- l) I understand that data concerning this patient and me will be entered into the mandatory TOUCH Prescribing Program. Biogen requires my cooperation with periodic data collection. Failure to provide the requested information or otherwise comply with the requirements of the TOUCH Prescribing Program may result in discontinuation of TYSABRI treatment for this patient and termination of my authorization to prescribe TYSABRI
- m) I have received educational materials regarding the benefits and risks of TYSABRI treatment
- n) I have, or another healthcare provider under my direction has, educated this patient on the benefits and risks of treatment with TYSABRI, provided him or her with the Patient Medication Guide and Enrollment Form, instructed him or her to read these materials, and encouraged him or her to ask questions when considering TYSABRI

Acknowledgments specific to Multiple Sclerosis (MS)

- o) I understand that TYSABRI is indicated as monotherapy for relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- p) I understand that this patient has a relapsing form of MS based on clinical and radiological evidence
- q) I understand that TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing treatment with TYSABRI, I should consider whether the expected benefit of TYSABRI is sufficient to offset this risk
- r) I understand that TYSABRI is not ordinarily recommended for patients who are receiving chronic immunosuppressant or immunomodulatory therapy, or who are significantly immunocompromised from any other cause
- s) I understand that an MRI should be performed prior to initiating therapy with TYSABRI in MS patients

Acknowledgments specific to Crohn's Disease (CD)

- t) I understand that TYSABRI is indicated for adult patients with moderately to severely active CD with evidence of inflammation who have had an

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inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF - $\alpha$

- u) I understand that patients receiving TYSABRI should not take concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF- $\alpha$
- v) I understand that this patient has moderately to severely active CD with evidence of inflammation
- w) I have discussed other Crohn's disease treatments with this patient
- x) I understand that TYSABRI should be discontinued if a patient has not experienced a therapeutic benefit by 12 weeks of therapy
- y) I understand that patients receiving steroid therapy at the time of TYSABRI initiation must undergo a steroid tapering regimen once a therapeutic response is achieved. If the patient with Crohn's disease cannot be tapered off of steroids within six months of starting TYSABRI, TYSABRI should be discontinued

C. Biogen will:

- i. Ensure that prescriber enrollment can successfully be completed
- ii. Ensure that prescribers receive the TYSABRI prescribing information and the following materials that are part of the TYSABRI REMS and are appended:
  - TOUCH Prescribing Program Educational Slide Set
  - TOUCH Prescribing Program Enrollment Kits (specific to MS or CD)
    - TOUCH Prescribing Program Overview
    - Medication Guide
    - Prescriber/Patient Enrollment Form (MS or CD)
    - Pre-Infusion Patient Checklist (combined MS and CD)
    - Helpful Information for Evaluation of New Neurologic Symptoms in Patients Receiving TYSABRI (MS)
    - Understanding PML for Gastroenterologists (CD)
  - TOUCH On-Line ([www.TOUCHPROGRAM.com](http://www.TOUCHPROGRAM.com))

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- Change Prescriber Authorization Form
  - Patient Status Report and Reauthorization Questionnaire (specific to MS and CD)
  - Initial Discontinuation Questionnaire (specific to MS or CD)
  - 6-Month Discontinuation Questionnaire (specific to MS or CD)
- iii. Ensure that enrollment forms are complete before activating a prescriber's enrollment in the TOUCH Prescribing Program.
- iv. Ensure that prescribers are notified when they are successfully enrolled in the TOUCH Prescribing Program, and therefore, are certified to prescribe TYSABRI.

**2. TYSABRI will be dispensed only by pharmacies and infusion sites that are specially certified.**

- a. Biogen will ensure that certified pharmacies that dispense TYSABRI are specially certified.
- b. Pharmacies that dispense TYSABRI to infusion sites must enroll in the Tysabri TOUCH Prescribing Program by submitting a completed enrollment form and designating a person with appropriate authority to acknowledge the following:
- i. The pharmacy has received training and educational materials on the TOUCH Prescribing Program.
  - ii. I understand that certified pharmacies may dispense TYSABRI only to authorized infusion sites
  - iii. I understand that, per the requirements of the TOUCH Prescribing Program, this certified pharmacy's compliance may be reviewed by the Food and Drug Administration (FDA) and/or audited by Biogen and/or a third party designated by Biogen.
  - iv. I understand that noncompliance with the requirements of the TOUCH Prescribing Program may result in my pharmacy no longer being enrolled and termination of our participation in the program.

- c. Biogen will:
  - i. Ensure that pharmacies are notified when they are successfully enrolled in the TOUCH Prescribing Program, and therefore, are certified to dispense TYSABRI.
  - ii. Ensure the pharmacies that dispense TYSABRI to authorized infusion sites have been trained on the known risks, potential benefits, and appropriate use of TYSABRI using approved educational materials
- d. The following materials are part of the TYSABRI REMS and are appended:
  - TOUCH Prescribing Program Educational Slide Set
  - TOUCH Prescribing Program Overview
  - Certified Pharmacy Enrollment Form
- e. Biogen will ensure that infusion sites where TYSABRI is dispensed and administered are specially certified.
  - i. Infusion sites that dispense and administer TYSABRI must enroll in the TOUCH Prescribing Program by submitting a completed Infusion Site Enrollment Form and designating a person with appropriate authority to acknowledge the following:
    - a) The infusion site has received training and educational materials on the TOUCH Prescribing Program
    - b) I understand that TYSABRI will be administered only to patients who are currently authorized in the TOUCH Prescribing Program. Patient authorization must be confirmed *prior to each infusion* by:
      - 1) For TOUCH On-Line infusion sites: Patient Authorization Status must be “Authorized” or
      - 2) For paper-based infusion sites: Receipt of current Notice of Patient Authorization and verification that no Notice of Patient Discontinuation is on file
    - c) I understand that each patient will receive a copy of the TYSABRI Patient Medication Guide *prior to each infusion*
    - d) I understand that a TYSABRI Pre-infusion Patient Checklist must be completed *prior to each infusion*. The Pre-infusion Patient Checklist must be

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submitted to Biogen within 1 business day of the patient visit, regardless of whether or not the patient received the infusion, by:

- 1) For paper-based infusion sites: sending a copy of the completed Pre-infusion Patient Checklist to Biogen. A copy must also be placed in the patient's medical record
  - 2) For TOUCH On-Line infusion sites: The infusion nurse can read, complete and submit the Pre-Infusion Patient Checklist directly in TOUCH On-Line
- e) I understand that, per the requirements of the TOUCH Prescribing Program, this infusion site's compliance with the REMS may be reviewed by FDA and/or audited by Biogen and/or a third party designated by Biogen.
- f) I understand that noncompliance with the requirements of the TOUCH Prescribing Program will result in de-enrollment of the infusion site.
- f. Biogen will:
- i. Ensure that infusion sites are notified when they are successfully enrolled in the TYSABRI REMS Program, and therefore, are certified to dispense and administer TYSABRI.
  - ii. Ensure that infusion sites that dispense and administer TYSABRI have been trained on the known risks, potential benefits, and appropriate use of TYSABRI using approved educational materials.
- g. The following materials are a part of the TYSABRI REMS and are appended:
- TOUCH Prescribing Program Educational Slide Set
  - TOUCH Prescribing Program Overview
  - Infusion Site Enrollment Form
  - Pre-Infusion Patient Checklist
  - Medication Guide
- 3. TYSABRI will be dispensed to patients with evidence or other documentation of safe-use conditions.**
- a. Biogen will ensure that certified prescribers enroll all patients into the TOUCH Prescribing Program by completing the Prescriber/Patient Enrollment Form for each new patient.

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- b. A completed and signed Prescriber/Patient Enrollment Form must be submitted to Biogen before the patient may receive an infusion.

The Prescriber/Patient Enrollment Form requires the patient to acknowledge the following:

- i. I understand that TYSABRI increases my chance of getting a rare brain infection that usually leads to death or severe disability
  - a) This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
  - b) There is no known treatment, prevention, or cure for PML
  - c) I should call my doctor right away if I get any new or worsening symptoms that last several days, especially nervous system symptoms, while I am taking TYSABRI, and for at least 6 months after I stop taking TYSABRI. Some of these symptoms include a new or sudden change in my thinking, eyesight, balance, or strength, but I should also report other new or worsening symptoms
  - d) My chance for getting PML increases if I:
    - 1) Have been exposed to John Cunningham Virus (JCV). JCV is a common virus that is harmless in most people but can cause PML in people who have weakened immune systems, such as people taking TYSABRI. Most people who are exposed to JCV do not know it or have any symptoms. This exposure usually happens in childhood. My doctor may do a blood test to check if I have been exposed to JCV before I start receiving TYSABRI or during my treatment
    - 2) Have received TYSABRI for a long time especially longer than 2 years
    - 3) Have received certain medicines that can weaken my immune system before I start receiving TYSABRI

My risk of getting PML is greatest if I have all 3 risk factors listed above. There may be other risk factors for getting PML during TYSABRI treatment that we do not know about yet. My doctor should discuss the risks and benefits of TYSABRI treatment with me before I decide to receive TYSABRI.

ii. Acknowledgments specific to MS

I understand that TYSABRI is a medicine approved to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

- a) TYSABRI increases the risk of PML. I understand that when starting and continuing treatment with TYSABRI, I should talk to my doctor about whether the expected benefit of TYSABRI is enough to outweigh this risk (see important information about PML below)
- b) I have talked to my doctor and understand the benefits and risks of TYSABRI treatment
- c) My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other MS treatments. Even if I use TYSABRI alone to treat my MS, I can still get PML

iii. Acknowledgments specific to CD

I understand that TYSABRI is a medicine approved to treat patients with moderate to severe Crohn's Disease who have not been helped enough by, or cannot tolerate, usual Crohn's disease medicines and medicines called tumor necrosis factor (TNF) inhibitors

- a) I have talked to my doctor and understand the benefits and risks of TYSABRI treatment
  - b) I understand that I should not take certain medicines that weaken the immune system while I am taking TYSABRI
  - c) My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other Crohn's disease treatments. Even if I use TYSABRI alone to treat my Crohn's disease, I can still get PML.
- c. To receive TYSABRI all patients must be enrolled in a special program called the TOUCH Prescribing Program.
- i. The TOUCH Prescribing Program is run by the company that makes TYSABRI. Under this program, the company is required to collect information about my health at regular time periods. I cannot receive TYSABRI if I do not agree to follow the requirements of the TOUCH Prescribing Program

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- ii. The company may use my information to meet the requirements of the TOUCH Prescribing Program, including helping me locate an authorized infusion site
- iii. I must notify the TOUCH Prescribing Program if I switch physicians or infusion sites
- iv. I have received, read, and understand the Patient Medication Guide
- v. I will bring to each TYSABRI infusion a list of all medicines and treatments that I have taken during the last month

The following materials are part of the TYSABRI REMS and are appended:

- Prescriber/Patient Enrollment Forms (specific to MS or CD)
- Medication Guide

Biogen will make these materials available for the enrolled prescribers to provide to their patients.

### **C. Implementation System**

The Implementation system for the TYSABRI REMS includes the following:

- a. Biogen must maintain a secure, validated database of all certified prescribers, certified pharmacies, certified infusion sites, and enrolled patients in the TOUCH Prescribing Program. The TOUCH Prescribing Program is an integrated, computerized, validated database that captures enrollment, patient tracking, and drug distribution data.
- b. Biogen will monitor the distribution of TYSABRI to ensure that the drug is only delivered to certified pharmacies and infused by certified infusion sites.
- c. Biogen will monitor the compliance of certified entities (i.e. pharmacies, infusion sites, and prescribers) as acknowledged in the signed entity specific enrollment form and, if appropriate, institute corrective actions, which could include retraining and de-enrollment
- d. Biogen will maintain TOUCH On-Line, which is an internet-based system that will allow enrolled TOUCH Prescribing Program participants the option of real-time access to view and/or submit required or pertinent patient therapy information collected through the TOUCH Prescribing Program, such as information on the Pre-infusion Patient Checklist, the TYSABRI Patient Status

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Report and Reauthorization Questionnaire, and the TYSABRI Patient Discontinuation Questionnaire.

- e. Biogen will monitor and evaluate the implementation of the elements to assure safe use and take reasonable steps to work to improve implementation of these elements.

**D. Timetable for Submission of Assessments of the REMS**

Biogen will submit REMS Assessments annually from the date of the initial approval of the REMS (October 7, 2011). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Biogen will submit each assessment so that it will be received by the FDA on or before the due date.

**MEDICATION GUIDE**  
TYSABRI® (tie-SA-bree)  
(natalizumab)  
injection, for intravenous use

Read this Medication Guide before you start receiving TYSABRI and before you receive each dose. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or your treatment.

**What is the most important information I should know about TYSABRI?**

- **TYSABRI increases your chance (risk) of getting a rare brain infection that usually leads to death or severe disability. This infection is called progressive multifocal leukoencephalopathy (PML). If PML happens, it usually happens in people with weakened immune systems.**
  - There is no known treatment, prevention, or cure for PML.
  - Your chance of getting PML may be higher if you are also being treated with other medicines that can weaken your immune system, including other treatments for Multiple Sclerosis (MS) and Crohn's disease (CD). You should not take certain medicines that weaken your immune system at the same time you are taking TYSABRI. Even if you use TYSABRI alone to treat your MS or CD, you can still get PML.
  - Your risk of getting PML is higher if you:
    - have been infected by the John Cunningham Virus (JCV). JCV is a common virus that is harmless in most people but can cause PML in people who have weakened immune systems, such as people taking TYSABRI. Most people who are infected by JCV do not know it or do not have any symptoms. This infection usually happens in childhood. Before you start receiving TYSABRI or during your treatment, your doctor may do a blood test to check if you have been infected by JCV.
    - have received TYSABRI for a long time, especially longer than 2 years
    - have received certain medicines that can weaken your immune system before you start receiving TYSABRI
- **Your risk of getting PML is greatest if you have all 3 risk factors listed above. There may be other risk factors for getting PML during TYSABRI treatment that we do not know about yet. Your doctor should discuss the risks and benefits of TYSABRI treatment with you before you decide to receive TYSABRI. See “What are the possible side effects of TYSABRI?”**
- **While you receive TYSABRI, and for 6 months after you stop receiving TYSABRI, it is important that you call your doctor right away if you have any new or worsening medical problems that have lasted several days.** These may be new or sudden and include problems with:
  - thinking
  - eyesight
  - strength
  - balance
  - weakness on 1 side of your body
  - using your arms and legs

Tell all your doctors that you are receiving TYSABRI.

- **Because of your risk of getting PML while you receive TYSABRI, TYSABRI is available only through a restricted distribution program called the TOUCH® Prescribing Program.** To receive TYSABRI, you must talk to your doctor and understand the risks and benefits of TYSABRI and agree to follow all of the instructions in the TOUCH® Prescribing Program.
  - **TYSABRI is only:**
    - prescribed by doctors who are enrolled in the TOUCH® Prescribing Program
    - given at an infusion center that is enrolled in the TOUCH® Prescribing Program
    - given to people who are enrolled in the TOUCH® Prescribing Program
  - **Before you receive TYSABRI, your doctor will:**
    - explain the TOUCH® Prescribing Program to you
    - have you sign the TOUCH® Prescriber and Patient Enrollment Form

**What is TYSABRI?**

TYSABRI is a prescription medicine used to treat adults with:

- relapsing forms of Multiple Sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease and active secondary progressive disease. TYSABRI increases the risk of PML. When starting and continuing treatment with TYSABRI, it is important that you discuss with your doctor whether the expected benefit of TYSABRI is enough to outweigh this risk. See “**What is the most important information I should know about TYSABRI?**”
- moderate to severe Crohn's disease (CD). TYSABRI is used:
  - to reduce signs and symptoms of CD
  - in people who have not been helped enough by, or cannot use the usual CD medicines and medicines called tumor necrosis factor (TNF) inhibitors.
- It is not known if TYSABRI is safe and effective in children under 18 years of age.

## Who should not receive TYSABRI?

### Do not receive TYSABRI if you:

- have PML
- are allergic to natalizumab or any of the ingredients in TYSABRI. See the end of this Medication Guide for a complete list of ingredients in TYSABRI.

Talk to your doctor before receiving TYSABRI if you have any of these conditions.

## What should I tell my doctor before receiving each dose of TYSABRI?

### Before you receive TYSABRI, tell your doctor if you:

- have medical conditions that can weaken your immune system, including:
  - HIV infection or AIDS
  - leukemia or lymphoma
  - an organ transplant
  - other medical conditions that can weaken your immune system
- have any new or worsening medical problems that have lasted several days. These may be new or sudden and include problems with:
  - thinking
  - eyesight
  - balance
  - strength
  - weakness on 1 side of your body
  - using your arms and legs
- have had hives, itching or trouble breathing during or after receiving a dose of TYSABRI
- have a fever or infection (including shingles or any unusually long lasting infection)
- are pregnant or plan to become pregnant. It is not known if TYSABRI can harm your unborn baby.
- are breastfeeding or plan to breastfeed. TYSABRI can pass into your breast milk. It is not known if the TYSABRI that passes into your breast milk can harm your baby. Talk to your doctor about the best way to feed your baby while you receive TYSABRI.

**Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins and herbal supplements. Especially tell your doctor if you take medicines that can weaken your immune system. Ask your doctor if you are not sure.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

## How should I receive TYSABRI?

- TYSABRI is given 1 time every 4 weeks through a needle placed in your vein (IV infusion).
- Before each TYSABRI dose you will be asked questions to make sure TYSABRI is still right for you.

## What are the possible side effects of TYSABRI?

### TYSABRI may cause serious side effects, including:

- See **“What is the most important information I should know about TYSABRI?”**

- **Herpes Infections.** TYSABRI may increase your risk of getting an infection of the brain or the covering of your brain and spinal cord (encephalitis or meningitis) caused by herpes viruses that may lead to death. Call your doctor right away if you have sudden fever, severe headache, or if you feel confused after receiving TYSABRI. Herpes infections of the eye, causing blindness in some patients, have also occurred. Call your doctor right away if you have changes in vision, eye redness, or eye pain.

- **Liver damage.** Symptoms of liver damage can include:

- yellowing of the skin and eyes (jaundice)
- nausea
- vomiting
- unusual darkening of the urine
- feeling tired or weak

Call your doctor right away if you have symptoms of liver damage. Your doctor can do blood tests to check for liver damage.

- **Allergic reactions, including serious allergic reactions.** Symptoms of an allergic reaction can include:

- hives
- itching
- trouble breathing
- chest pain
- dizziness
- wheezing
- chills
- rash
- nausea
- flushing of skin
- low blood pressure

Serious allergic reactions usually happen within 2 hours of the start of your infusion, but they can happen at any time after you receive TYSABRI.

Tell your doctor right away if you have any symptom of an allergic reaction, even if it happens after you leave the infusion center. You may need treatment if you are having an allergic reaction.

- **Infections.** TYSABRI may increase your chance of getting an unusual or serious infection because TYSABRI can weaken your immune system. You have a higher risk of getting infections if you also take other medicines that can weaken your immune system.

- **Low platelet counts.** TYSABRI may cause the number of platelets in your blood to be reduced. Call your healthcare provider if you have any of the following symptoms:

- easy bruising
- small scattered red spots on your skin that are red, pink, or purple
- heavier menstrual periods than are normal
- bleeding from your gums or nose that is new or takes longer than usual to stop
- bleeding from a cut that is hard to stop

### The most common side effects of TYSABRI include:

- headache
- feeling tired
- urinary tract infection
- joint pain
- lung infection
- depression
- pain in your arm and legs
- diarrhea
- vaginitis
- rash
- nose and throat infections
- nausea
- stomach area pain

Tell your doctor about any side effect that bothers you or that does not go away.

These are not all the possible side effects of TYSABRI. Ask your doctor for more information.

**Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.**

**General information about the safe and effective use of TYSABRI.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

This Medication Guide summarizes the most important information about TYSABRI. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about TYSABRI that is written for healthcare professionals.

For more information, go to [www.TYSABRI.com](http://www.TYSABRI.com) or call 1-800-456-2255.

**What are the ingredients in TYSABRI?**

Active ingredient: natalizumab

Inactive Ingredients: sodium chloride, sodium phosphate, monobasic, monohydrate; sodium phosphate, dibasic, heptahydrate; polysorbate 80, and water for injection

Manufactured by: Biogen Inc.; Cambridge, MA 02142 USA

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised 06/2020



**Touch**<sup>®</sup> PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health

Please see the Prescribing Information, including **BOXED WARNING**, for more information



**TYSABRI**<sup>®</sup>  
(natalizumab)

# Objectives

- Provide an overview of important safety information
- Provide an overview of the TOUCH Prescribing Program for Multiple Sclerosis (MS) and Crohn's disease (CD)
- Review the process steps to complete TOUCH Prescribing Program components including use of TOUCH On-Line
- Review specific MS TOUCH and/or CD TOUCH Prescribing Program materials
- Review the responsibilities of each participant in the TOUCH Prescribing Program

# Indications and Usage – Multiple Sclerosis

- TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
- TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML).
- When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk.
- See Prescribing Information regarding the risk of PML with TYSABRI.

# Indications and Usage – Crohn's Disease

- TYSABRI® is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF- $\alpha$ .
- TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF- $\alpha$ .

# BOXED WARNING

- TYSABRI® increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability.
- Risk factors for the development of PML include presence of anti-JCV antibodies, duration of therapy, and prior use of immunosuppressants. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.
- Healthcare professionals should monitor patients on TYSABRI® for any new sign or symptom that may be suggestive of PML.
- TYSABRI dosing should be withheld immediately at the first sign or symptom that may be suggestive of PML.

# BOXED WARNING

- For diagnosis, an evaluation that includes a gadolinium-enhanced magnetic resonance imaging (MRI) scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended.
- Because of the risk of PML, TYSABRI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the TOUCH Prescribing Program.

# Contraindications

- TYSABRI is contraindicated in patients who have or have had PML.
- TYSABRI is contraindicated in patients who have had a hypersensitivity reaction to TYSABRI.

# Warnings and Precautions - PML

- Three factors that are known to increase the risk of PML in TYSABRI-treated patients have been identified:
  - The presence of anti-JCV antibodies. Patients who are anti-JCV antibody positive have a higher risk for developing PML.
  - Longer treatment duration, especially beyond 2 years.
  - Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
- These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.
- Retrospective analyses of postmarketing data from various sources, including observational studies and spontaneous reports obtained worldwide, suggest that the risk of developing PML may be associated with relative levels of serum anti-JCV antibody compared to a calibrator as measured by ELISA (often described as an anti-JCV antibody index value).

# Warnings and Precautions – PML

- Infection by the JC virus (JCV) is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- Anti-JCV antibody negative status indicates that antibodies to the JC virus have not been detected.
- Patients who are anti-JCV antibody negative have a lower risk of PML than those who are positive. Patients who are anti-JCV antibody negative are still at risk for the development of PML due to the potential for a new JCV infection, or a false negative test result.

# Warnings and Precautions – PML

- MRI findings may be apparent before clinical signs or symptoms suggestive of PML.
- Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML.
- Consider monitoring patients at high risk for PML more frequently.
- Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis.

# Warnings and Precautions – PML

- The reported rate of seroconversion in patients with MS (changing from anti-JCV antibody negative to positive) is 3 to 8 percent annually. In addition, some patients' serostatus may change intermittently. Therefore, patients with a negative anti-JCV antibody test result should be retested periodically.
- For purposes of risk assessment, a patient with a positive anti-JCV antibody test at any time is considered anti-JCV antibody positive regardless of the results of any prior or subsequent anti-JCV antibody testing. When assessed, anti-JCV antibody status should be determined using an analytically and clinically validated immunoassay.
- After plasma exchange (PLEX), wait at least two weeks to test for anti-JCV antibodies to avoid false negative test results caused by the removal of serum antibodies.
- After infusion of intravenous immunoglobulin (IVIg), wait at least 6 months (5 half-lives) for the IVIg to clear in order to avoid false positive anti-JCV antibody test results

# Warnings and Precautions – Herpes Infections

## Herpes Encephalitis and Meningitis

- TYSABRI increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses.
- Serious, life-threatening, and sometimes fatal cases have been reported in the postmarketing setting in multiple sclerosis patients receiving TYSABRI.
- Monitor patients receiving TYSABRI for signs and symptoms of meningitis and encephalitis. If herpes encephalitis or meningitis occurs, TYSABRI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered.

# Warnings and Precautions – Herpes Infections

## Acute Retinal Necrosis

- A higher risk of Acute Retinal Necrosis (ARN) has been observed in patients being administered TYSABRI.
- Some ARN cases occurred in patients with central nervous system (CNS) herpes infections (e.g., herpes meningitis or encephalitis).
- Serious cases of ARN led to blindness of one or both eyes in some patients.
- Following clinical diagnosis of ARN, consider discontinuation of TYSABRI. The treatment reported in ARN cases included anti-viral therapy and, in some cases, surgery.

# Warnings and Precautions – Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI® in a postmarketing setting.
- Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as 6 days after the first dose; and signs of liver injury have also been reported for the first time after multiple doses.
- In some patients, liver injury recurred upon rechallenge, providing evidence that TYSABRI caused the injury.
- The combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients.
- TYSABRI should be discontinued in patients with jaundice or other evidence of significant liver injury (e.g., laboratory evidence).

# Warnings and Precautions – Hypersensitivity/Antibody Formation

- TYSABRI has been associated with hypersensitivity reactions, including serious systemic reactions (e.g., anaphylaxis), which occurred at an incidence of <1%.
- Patients who receive TYSABRI after an extended period without treatment may be at higher risk of hypersensitivity reactions.
- If a hypersensitivity reaction occurs, discontinue the use of TYSABRI, and initiate appropriate therapy.
- Do not re-treat with TYSABRI.
- Patients who receive TYSABRI for a short exposure (1 to 2 infusions) followed by an extended period without treatment are at higher risk of developing anti-natalizumab antibodies and/or hypersensitivity reactions on re-exposure, compared to patients who received regularly scheduled treatment.

# Warnings and Precautions – Immunosuppression/Infections

- The immune system effects of TYSABRI® may increase the risk for infections.
- Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections, including PML and other opportunistic infections, over the risk observed with use of TYSABRI alone.
- The safety and efficacy of TYSABRI in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established.
- For patients with Crohn's disease who start TYSABRI while on chronic corticosteroids, commence steroid withdrawal as soon as a therapeutic benefit has occurred. If the patient cannot discontinue systemic corticosteroids within 6 months, discontinue TYSABRI.

# Warnings and Precautions – Thrombocytopenia

- Cases of thrombocytopenia, including immune thrombocytopenic purpura (ITP), have been reported with the use of TYSABRI in the postmarketing setting
- Symptoms of thrombocytopenia may include easy bruising, abnormal bleeding, and petechiae
- Delay in the diagnosis and treatment of thrombocytopenia may lead to serious and life-threatening sequelae. If thrombocytopenia is suspected, TYSABRI should be discontinued.

# Adverse Reactions

- The most frequently reported serious adverse reactions in the Study MS1 were infections (3.2% vs 2.6% placebo), acute hypersensitivity reactions (1.1% vs 0.3%), depression (1.0% vs 1.0%), and cholelithiasis (1.0% vs 0.3%).
- The following serious adverse events in the induction Studies CD1 and CD2 were reported more commonly with TYSABRI than placebo and occurred at an incidence of at least 0.3%: intestinal obstruction or stenosis (2% vs. 1% in placebo), acute hypersensitivity reactions (0.5% vs. 0%), abdominal adhesions (0.3% vs. 0%), and cholelithiasis (0.3% vs. 0%).

# Adverse Reactions (cont'd)

- The most common adverse reactions reported at an incidence of  $\geq 10\%$  were headache (38% vs 33%), fatigue (27% vs 21%), infusion reactions (24% vs 18%), urinary tract infections (21% vs 17%), arthralgia (19% vs 14%), depression (19% vs 16%), lower respiratory tract infection (17% vs 16%), pain in extremity (16% vs 14%), rash (12% vs 9%), gastroenteritis (11% vs 9%), abdominal discomfort (11% vs 10%), vaginitis\* (10% vs 6%), and diarrhea (10% vs 9%).

\*Percentage based on female patients only.

- Other common adverse reactions (incidence  $\geq 10\%$ ) in the CD population were upper respiratory tract infections and nausea.
- Based on animal data, TYSABRI may cause fetal harm. TYSABRI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

# Program Overview

- **What is the TOUCH Prescribing Program?**
- What tools support the TOUCH Prescribing Program?
  - MS TOUCH Educational Materials
  - CD TOUCH Educational Materials
- What is the enrollment process?
- What is the process to infuse TYSABRI®?
- How are patients tracked?
- What is TOUCH On-Line?

# What is the TOUCH Prescribing Program?



A program that makes TYSABRI® available only to prescribers, infusion centers, pharmacies associated with infusion centers, and patients who are enrolled in the program

# What is the TOUCH Prescribing Program designed to do?

- To inform prescribers, infusion center healthcare providers, and patients about the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI® including the increased risk of PML with the presence of anti-JCV antibodies, longer treatment duration, and prior immunosuppressant use
- To warn against concurrent use with antineoplastic, immunosuppressant, or immunomodulating agents and in patients who are immunocompromised
- To promote early diagnosis of PML and timely discontinuation of TYSABRI in the event of suspected PML

# What are the program requirements?

Prescribers

Infusion Sites

Pharmacies

Patients

Must be registered in and meet all the requirements of the TOUCH Prescribing Program to

Prescribe TYSABRI®

Infuse TYSABRI

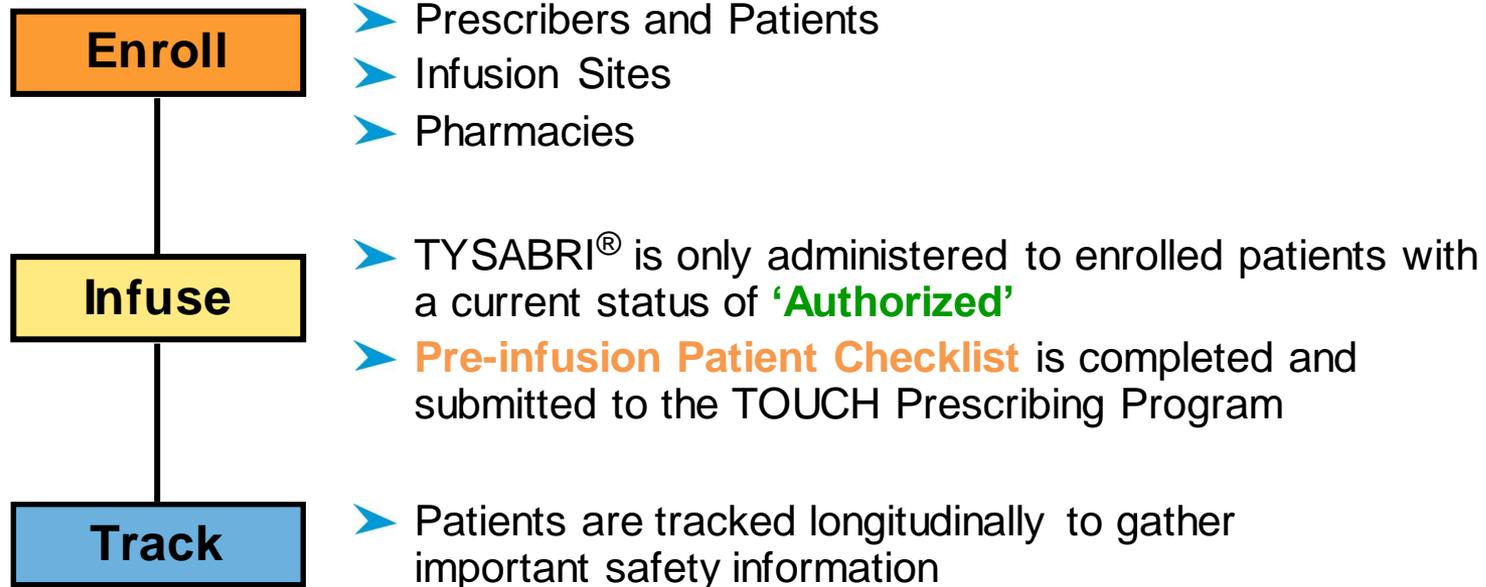
Dispense TYSABRI

Must be enrolled in and meet all the requirements of the TOUCH Prescribing Program to

Receive TYSABRI

# TOUCH Prescribing Program Components

There are 3 main components of the TOUCH Prescribing Program



NOTE: This overview of the TOUCH Prescribing Program components does not include a complete list of the program requirements.

# Program Overview

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# Tools to Support the TOUCH Prescribing Program – MS

## Enrollment Forms

MS Touch Prescriber/Patient Enrollment Form - MS

Prescriber/Patient

MS Touch Infusion Site Enrollment Form

Infusion Site

MS Touch Certified Pharmacy Enrollment Form

Certified Pharmacy



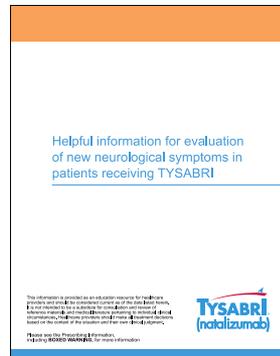
Patient Medication Guide

Notice of Patient Authorization

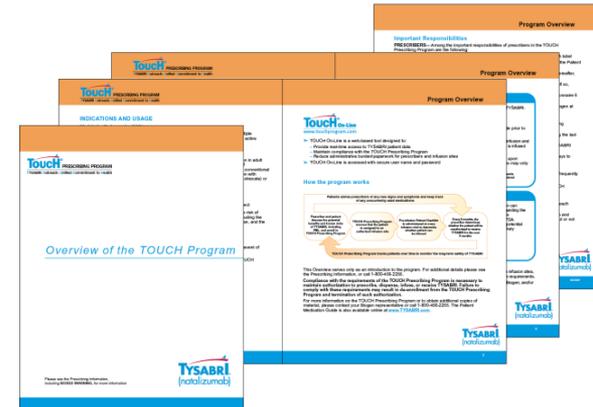
Notice of Patient Authorization

Pre-infusion Patient Checklist

Pre-infusion Patient Checklist



Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI®



TOUCH Prescribing Program Overview

# Tools to Support the TOUCH Prescribing Program – Crohn's Disease

## Enrollment Forms

Prescriber/Patient

Infusion Site

Certified Pharmacy



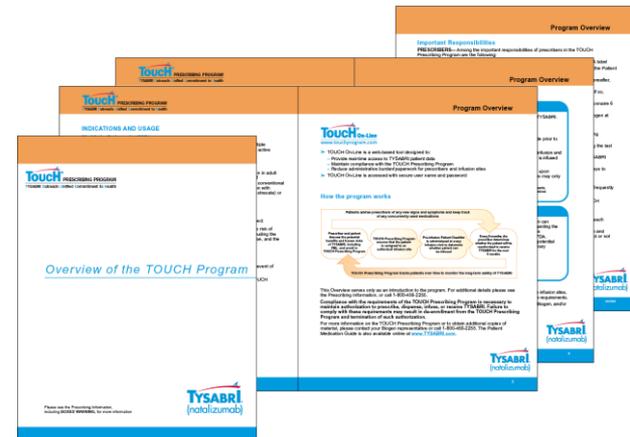
Patient Medication Guide

Notice of Patient Authorization

Pre-infusion Patient Checklist



Understanding PML for Gastroenterologists



TOUCH Prescribing Program Overview

# How Do I Communicate With TOUCH?



**WEB**



**Touch** On-Line  
[www.touchprogram.com](http://www.touchprogram.com)



**PHONE**

**1-800-456-2255**

Monday – Friday



**PAPER**

**Fax: 1-800-840-1278**

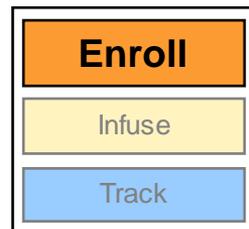
# Satisfying TOUCH Prescribing Program Requirements

- The TOUCH Prescribing Program has been designed to facilitate appropriate use of TYSABRI®
- In order to assess if the Program is meeting its goals, registered sites and enrolled participant's compliance may be reviewed by the FDA, and/or audited by Biogen and/or a third party designated by Biogen
- Compliance with the requirements of the TOUCH Prescribing Program is necessary to maintain authorization to prescribe, dispense, infuse, or receive TYSABRI. Failure to comply with these requirements may result in de-enrollment from the TOUCH Prescribing Program and termination of such authorization

# Program Overview

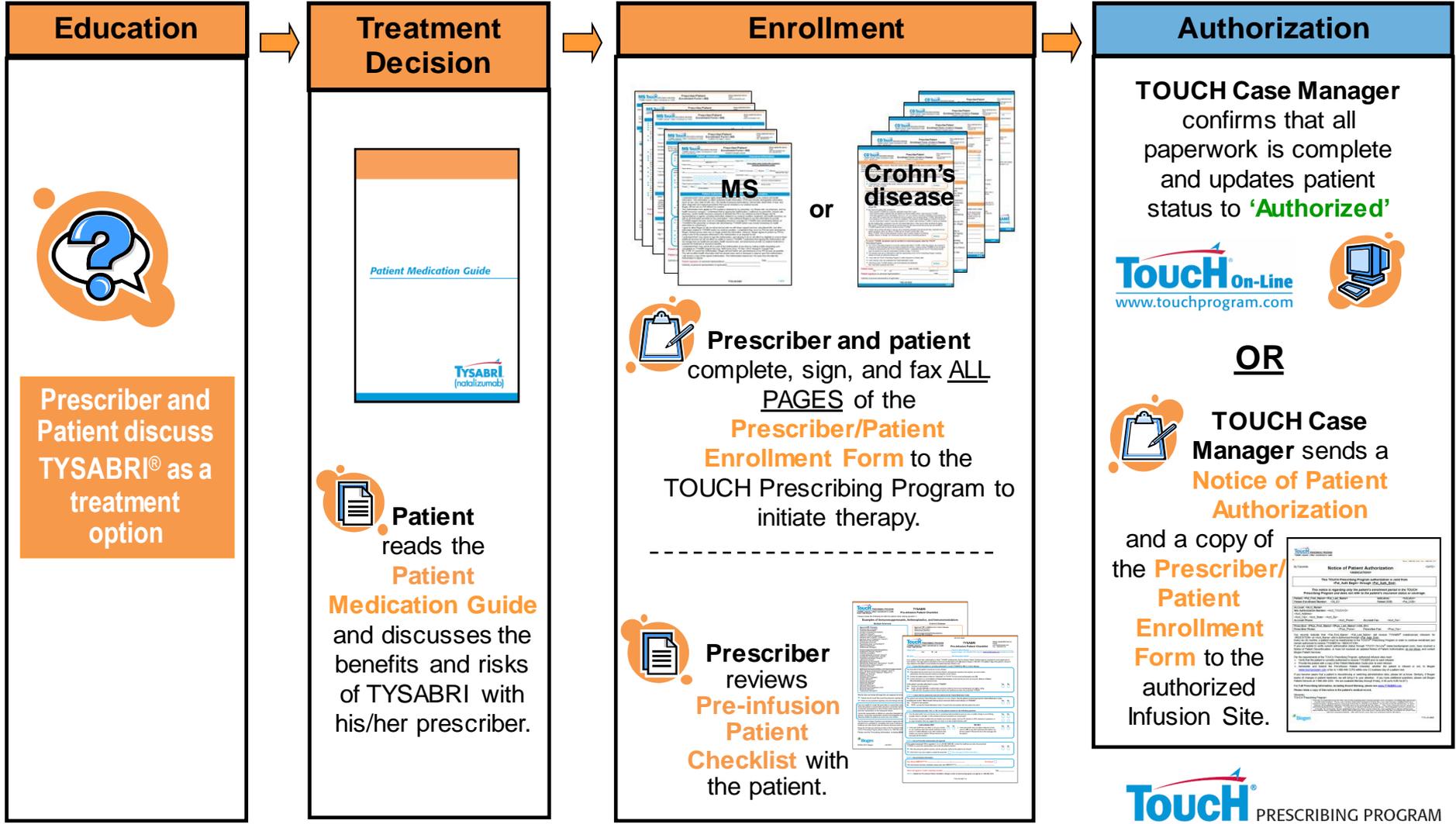
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# Prescriber/Patient Enrollment

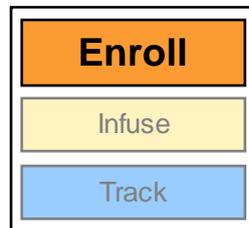


# How do prescribers and patients enroll?

<b>Enroll</b>
Infuse
Track



# Enrollment Tools



# Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI®

## Brochure provided by Biogen Resource for: Neurology specialists

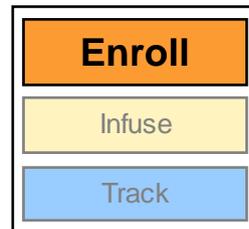
### Key topics include:

- Importance of careful evaluation of any new or recurrent symptoms
- Differentiating between the signs, symptoms, and lesion characteristics typical of MS and PML
- PML diagnostic algorithm incorporating MRI and CSF assessment
- Action steps if PML is suspected
- Guidance on the treatment of relapse and other neurological symptoms

The information provided in this brochure is an educational resource and is not intended to be a substitute for consultation and review of relevant reference materials and medical literature. Treatment decisions should be made based on the context of the situation and clinical judgment.

The image displays four pages from a brochure. The top-left page is titled 'Patient monitoring and management' and discusses the management of patients receiving TYSABRI, including the importance of MRI scans and regular follow-up. The top-right page features a 'Suggested diagnostic algorithm for TYSABRI-treated patients experiencing new neurological symptoms' as a flowchart, starting with 'New neurological symptoms' and leading to 'MRI assessment' and 'CSF assessment'. The bottom-left page is titled 'Evaluation of new neurological symptoms in patients receiving TYSABRI' and includes a table for 'Clinical signs and symptoms typical of MS, relapse, and PML'. The bottom-right page contains 'Table 2. MS lesions characteristic typical of PML and MS' with a table comparing 'Characteristic MS Lesions' and 'PML Lesions'.

# Enrollment Tools



# Understanding PML

## Flashcard provided by Biogen

Resource for: Gastroenterologists, Internists, or other non-Neurology specialists

Key topics include:

- Characteristics of PML
- Guidance on recognizing PML in context of Crohn's disease
- Action steps if PML is suspected

**Action Steps if PML is Suspected**

- TYSABRI dosing should be suspended immediately in all cases in which PML is suspected<sup>1</sup>
- Immediate referral to a neurologist for assessment, potentially including<sup>2</sup>
  - A brain MRI to determine if lesions that could be due to PML are present
  - Cereospinal fluid evaluation for the presence of JCVDNA
- Potential cases of PML should be reported immediately to Biogen at 1-800-456-2255, or to the FDA's MedWatch reporting system at 1-800-FDA-1088, or via the MedWatch Web site at [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

**Indication**

TYSABRI is indicated for inducing and maintaining remission in adult patients with moderately to severely active Crohn's disease who are unable to tolerate, or have had an inadequate response to, or are unable to tolerate, conventional CD therapies and immunosuppressants (e.g., 6-mercaptopurine, azathioprine, or methotrexate) or concomitant inhibitors of TNF.

**Important Safety Information**

**WARNING: Progressive Multifocal Leukoencephalopathy (PML)**

TYSABRI (natalizumab) increases the risk of PML, a rare but potentially fatal brain infection. PML is usually fatal. Prior use of immunosuppressants should be considered in the context of assessing the risk of PML.

Healthcare professionals should monitor for symptoms of PML. For diagnosis, an MRI of the brain and, when indicated, cerebrospinal fluid analysis should be performed. Because of the risk of PML, TYSABRI is contraindicated in patients with PML. See the Important Safety Information (ISI) for TYSABRI (natalizumab) for more information.

**Important Safety Information Continues**

**Understanding PML for Gastroenterologists**

The following information should be considered when undertaking the assessment and management of progressive multifocal leukoencephalopathy (PML) in adult patients treated with TYSABRI for moderately to severely active Crohn's disease (CD). During clinical trials for TYSABRI, 3 cases of PML were identified (2 in multiple sclerosis and 1 in Crohn's disease). Both multiple sclerosis patients were receiving concomitant immunomodulatory therapy and the Crohn's disease patient had been treated in the past with immunosuppressive therapy. In the postmarketing setting, additional cases of PML have been reported in multiple sclerosis and Crohn's disease patients who were receiving no concomitant immunomodulatory therapy.<sup>1</sup>

**About PML**

PML is a demyelinating disease that attacks the central nervous system.<sup>2</sup> It is an opportunistic infection caused by the JC virus that typically occurs in patients who are immunocompromised.<sup>3</sup> The virus removes myelin that surrounds the nerves, and without this protection the nerves cannot transmit signals.<sup>2</sup> There are no known interventions that can reliably prevent PML, or adequately treat PML, if it occurs.<sup>2</sup>

**How to Recognize PML**

Typical symptoms associated with PML are diverse, progress over days to weeks, and include<sup>4,5</sup>:

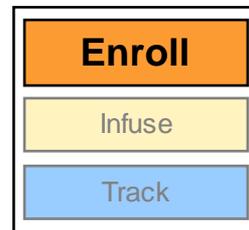
- Progressive weakness on one side of the body or clumsiness of limbs
- Disturbance of vision
- Changes in thinking, memory, and orientation, leading to confusion and personality changes
- Seizures

The progression of deficits usually leads to death or severe disability over weeks or months.<sup>6</sup> Since these symptoms are very different from those of Crohn's disease, the appearance of any symptoms of PML, including those listed above, should be investigated immediately.<sup>7</sup> In Crohn's disease patients, a baseline brain MRI may also be helpful to distinguish pre-existent lesions from newly developed lesions, but brain lesions at baseline that could cause diagnostic difficulty while on TYSABRI therapy are uncommon.<sup>8</sup>

**TYSABRI (natalizumab)**

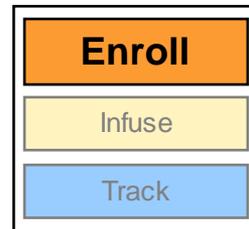
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# Infusion Site Enrollment





# Certified Pharmacy Enrollment

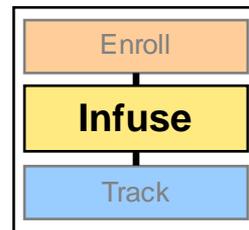




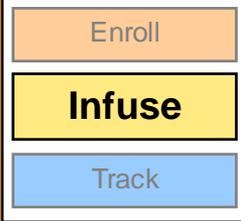
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# Infusion Overview



# What process must be completed in order to infuse TYSABRI®?



TYSABRI should NOT be prepared until the **Pre-infusion Patient Checklist** has been successfully completed

## Prior to EVERY infusion of TYSABRI:

Patient arrives for TYSABRI infusion

- 1 **Confirm** that the patient is currently **'Authorized'** to receive TYSABRI on TOUCH On-Line\*
- 2 **Provide** the patient with the **Patient Medication Guide**
- 3 **Complete** the **Pre-infusion Patient Checklist** on TOUCH On-Line\*
- 4 If the patient answered **YES** to question 1, 2 or 3, in Step 3 of the Pre-infusion Patient Checklist, **DO NOT INFUSE**. Contact the healthcare provider who prescribed TYSABRI and review the patient's answers. Confirm authorization for infusion.

## Infusion

ONLY upon successful completion of the **Pre-infusion Patient Checklist**:

- Start an IV line
- Mix TYSABRI



**Infuse** TYSABRI over 1 hour and observe patient for 1 hour post-infusion



**Submit** completed **Pre-infusion Patient Checklist** via TOUCH On-Line\* within 1 business day



\*Paper process: Check patient record for current **Notice of Patient Authorization** and fax completed **Pre-infusion Patient Checklist** to 1-800-840-1278.

# Checking Patient Authorization Status

- Enroll
- Infuse
- Track

Only patients with a status **'Authorized'** can receive TYSABRI®

➤ Check patient status as **'Authorized'** on TOUCH On-Line



Paper process: **Notice of Patient Authorization** is faxed to both Prescriber and Infusion Site; a copy must be placed in the patient record

**Touch** PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health

Phone: 1 800 456 2255 | Fax: 1 800 840 1278

---

By Facsimile 9/19/2016

**Notice of Patient Authorization**  
<INDICATION>

This TOUCH Prescribing Program authorization is valid from  
1/01/2016 through 6/30/2016.

*This notice is regarding only the patient's enrollment period in the TOUCH Prescribing Program and does not refer to the patient's insurance status or coverage.*

Patient: Jennifer Patient		Indication: <Indication>	
Patient Enrollment Number: PTXXXXXXX		Patient DOB: 1/1/1978	

Account: Test Infusion Site			
Site Authorization Number: ST123456			
123 Infusion Site Lane			
Durham, NC 27709			
Account Phone: 555-555-1234	Account Fax: 555-555-1236		

Prescriber: John Prescriber (MDXXXXXXX)			
Prescriber Phone: 555-555-7896	Prescriber Fax: 555-555-7894		

Today's Infusions							
(show the next 3 days)							
Patient Enrollment #	Last Name	First Name	Date of Birth	Status	Last Infusion Date	Next Infusion Date	Pre-Infusion Patient Checklist Status
[REDACTED]	PATIENT	JENNIFER	01/01/1978	Authorized	10/12/2007	09/28/2007	<a href="#">Start</a>

1 patient found.



# Pre-infusion Patient Checklist



➤ All Infusion Sites must complete, sign, and submit the **Pre-infusion Patient Checklist** at every infusion visit

➤ Submit form within 1 business day of patient's visit via TOUCH On-Line



Paper process: Fax page one to 1-800-840-1278 and place original in the patient's record

**Patient Actions**

This patient is currently Authorized to receive TYSABRI.

Yes  No Has the patient received and read the [Patient Medication Guide](#), including the section "What should I tell my doctor and nurse before each infusion of TYSABRI?"

---

Yes  No 1. Over the past month, have you had any new or worsening medical problems (such as a new or sudden change in your thinking, eyesight, balance, strength, or other problems) that have persisted over several days?

Yes  No 2. Do you have a medical condition that can weaken your immune system, such as HIV infection or AIDS, leukemia or lymphoma, or an organ transplant, that may suggest that your body is not able to fight infections well?

Yes  No 3. In the past month, have you taken medicines to treat cancer or MS or any other medicines that weaken your immune system? ([Click here to review the list with the patient.](#))

---

Yes  No Was TYSABRI infused?

09/28/2007 Date infused  
(mm/dd/yyyy)

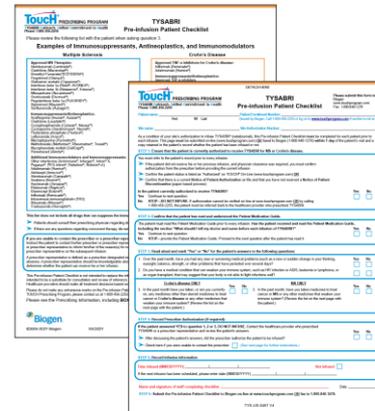
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10/30/2007 Date of next infusion appointment  
(mm/dd/yyyy)

**Verify and Sign the Pre-Infusion Patient Checklist**

TOUCH On-Line username

Password

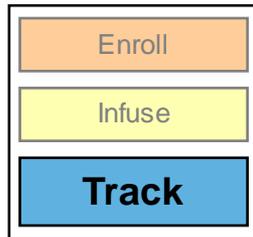


**NOTE:** Pre-infusion Patient Checklist **must** be completed and submitted whether or not the patient is infused.

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# Tracking Overview



# Tracking Overview

Enroll

Infuse

Track

MS

## Infusion Site

### Pre-infusion Patient Checklist



## Prescriber

### Patient Status Report and Reauthorization Questionnaire



## Prescriber

### Initial and 6-Month Discontinuation Questionnaire

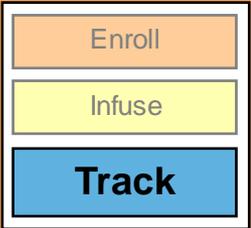


Crohn's disease



**NOTE: Missing or incomplete TOUCH Prescribing Program forms will prompt continued follow-up by a TOUCH Compliance Manager.**

# Prescriber Must Reauthorize the Use of TYSABRI® Every 6 Months



## TYSABRI Patient Status Report and Reauthorization Questionnaire

➤ Prescriber will receive a **Patient Status Report and Reauthorization Questionnaire** every 6 months

➤ Completion of this form is **required** as it determines whether the prescriber authorizes the patient to receive TYSABRI for the next 6 months

**CD Touch** PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health  
Phone: 1-800-456-2255

**TYSABRI Patient Status Report and Reauthorization Questionnaire—Crohn's Disease**

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-943-1278

Re: <Patient Name>  
Patient Enrollment Number: <Patient TOUCH ID>  
Patient date of birth: <DOB>  
Authorization expiration date: <MMDDYYYY>

Dear <MD Name>:  
Our records indicate that <Patient name>'s authorization to receive TYSABRI will expire on <MMDDYYYY> and he/she will no longer be able to receive TYSABRI. Please submit the completed form to Biogen via TOUCH On-Line (www.touchprogram.com) OR fax (1-800-943-1278) on <expiration date> and place a copy in the patient's record.

**MS Touch** PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health  
Phone: 1-800-456-2255

**TYSABRI Patient Status Report and Reauthorization Questionnaire—MS**

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-943-1278

Re: <Patient Name>  
Patient Enrollment Number: <Patient TOUCH ID>  
Patient date of birth: <DOB>  
Authorization expiration date: <MMDDYYYY>

Dear <MD Name>:  
Our records indicate that <Patient name>'s authorization to receive TYSABRI will expire on <MMDDYYYY> and he/she will no longer be able to receive TYSABRI. Please submit the completed form to Biogen via TOUCH On-Line (www.touchprogram.com) OR fax (1-800-943-1278) on <expiration date> and place a copy in the patient's record.

**TOUCH Certified Prescriber or (if applicable) Print TOUCH Cert**

Please Note: A TOUCH certified prescriber is responsible for each patient under his/her care. This cert with HCPA and applicable privacy rules. Please see full Prescribing Info.

**Biogen**

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**TYSABRI** (natalizumab)



OR



# If a patient discontinues TYSABRI®, important health information is collected and tracked over time

Enroll

Infuse

Track

**CD Touch** PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health  
Phone: 1-800-456-2255

**TYSABRI Initial Discontinuation Questionnaire-Crohn's Disease**

Please submit this form to: Biogen, www.touchprogram.com, Fax: 1-800-840-1278

Re: <Patient Name>  
Patient Enrollment Number: <Patient TOUCH ID>

**MS Touch** PRESCRIBING PROGRAM  
TYSABRI Outreach: Unified Commitment to Health  
Phone: 1-800-456-2255

**TYSABRI Initial Discontinuation Questionnaire-MS**

Please submit this form to: Biogen, www.touchprogram.com, Fax: 1-800-840-1278

Prescriber name: \_\_\_\_\_  
Prescriber address: \_\_\_\_\_  
Patient: \_\_\_\_\_  
Patient date of birth (MM/DD/YYYY): \_\_\_\_\_

**A** Is the patient still under <MD name>'s care?  
 Yes  No/ don't know  
If No, please provide name and phone number for new prescriber, if available: \_\_\_\_\_

**B** Is the patient alive?  
 Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have not reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)  
 Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized  
 Yes  No or  Under investigation

**E** MALIGNANCY  
 Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?  
 Yes  Not performed  
If performed, since <last authorization> date, test result:  
 Positive  Negative  Pending  
If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_ Date: \_\_\_\_\_

TOUCH Certify Prescriber or Delegate Name: \_\_\_\_\_  
(If applicable) Print TOUCH Certify Prescriber or Delegate Name: \_\_\_\_\_

Please Note: A TOUCH certifier or delegate may complete and submit this form on behalf of the certifier. Prescriber of record. The certifier, TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under their care. This questionnaire will be used in conjunction with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HMPA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including BOXED WARNING, for more information

Biogen TYSABRI (natalizumab)

02006-202Y Biogen XX/02Y TYS-US-0478 V4

The prescriber will be sent **Discontinuation Questionnaires**, which must be completed and submitted to the TOUCH Prescribing Program via TOUCH On-Line

Paper process: Upon notification of patient discontinuation, the **Discontinuation Questionnaire** will be faxed to the prescriber

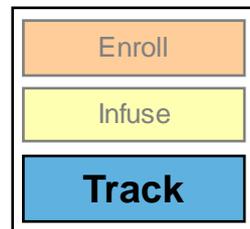
- Fax completed form to 1-800-840-1278 and place original in the patient's file



**\*NOTE: Discontinuation Questionnaires are ONLY sent upon notification of discontinuation and again six months following discontinuation of TYSABRI**



# Tracking Tools



# Tracking Overview – MS

The TOUCH Prescribing Program will track all patients over time, so that Biogen can inform the FDA, prescribers, and patients in a timely manner of information regarding the safety of TYSABRI®.

## Pre-infusion Patient Checklist (Every 28 days)

This form is used to track patient safety before each TYSABRI infusion. It includes sections for:
 

- Examples of Immunosuppressants, Antineoplastic, and Immunomodulators:** Lists various medications like Azathioprine, Cyclophosphamide, and Rituximab.
- Additional immunosuppressants and immunomodulators:** A section for other relevant drugs.
- Medical History:** Questions about current and past conditions, including infections, malignancies, and organ transplants.
- Current Medications:** A list of all medications the patient is taking, including over-the-counter drugs and supplements.
- Other Health Information:** Questions about pregnancy, breastfeeding, and recent blood work.

## TYSABRI Patient Status Report and Reauthorization Questionnaire (Every 6 months)

This questionnaire is administered every six months to assess patient safety and determine if TYSABRI treatment should continue. Key sections include:
 

- Demographics:** Patient name, address, and contact information.
- Current Status:** Whether the patient is still under TYSABRI care and if they have had any reauthorizations.
- Medical History:** Questions about new or ongoing conditions, including infections, malignancies, and organ transplants.
- Medication Review:** A detailed list of all current medications, including immunosuppressants and immunomodulators.
- Health Changes:** Questions about changes in thinking, behavior, or physical health.
- Reauthorization Decision:** A section for the prescriber to indicate if treatment should continue, with a justification.

## Initial and 6-Month Discontinuation Questionnaire\*

These forms are used when a patient's TYSABRI treatment is discontinued. They include:
 

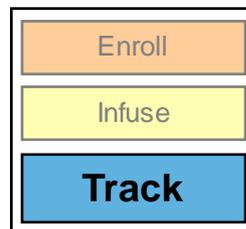
- TYSABRI 6-Month Discontinuation Questionnaire-MS:** A form to be completed 6 months after the last infusion, tracking any subsequent health events.
- TYSABRI Initial Discontinuation Questionnaire-MS:** A form to be completed at the time of discontinuation, providing details about the patient's history and the reasons for stopping treatment.



**\*NOTE: Discontinuation Questionnaires are ONLY sent upon notification of discontinuation and again six months following discontinuation of TYSABRI**



# Tracking Tools





# Program Overview

- What is the TOUCH Prescribing Program?
- What tools support the TOUCH Prescribing Program?
  - MS TOUCH Educational Materials
  - CD TOUCH Educational Materials
- What is the enrollment process?
- What is the process to infuse TYSABRI®?
- How are patients tracked?
- **What is TOUCH On-Line?**
- How is TYSABRI acquired?

# TOUCH On-Line Overview

- TOUCH On-Line is a Web-based tool designed to:
  - Provide real-time access to TYSABRI® patient data
  - Maintain compliance with the TOUCH Prescribing Program
  - Streamline communication to/from Prescribers and Infusion Sites
- TOUCH On-Line is available only to enrolled TOUCH participants
- TOUCH On-Line is accessed with secure user name and password

A screenshot of the TOUCH On-Line login interface. At the top, a blue header bar contains the text "Please Login to TOUCH On-Line". Below this, there are two input fields: "TOUCH On-Line Username" and "Password". A blue link "Forgot your password?" is positioned below the password field. A blue "Login" button is centered below the input fields. At the bottom of the login area, there is a section titled "Having trouble logging in?" with the text: "Check with your Site Administrator or call us at 1-800-456-2255 Monday through Friday, 8:30 am to 8:00 pm EST."

# Summary Review

- The TOUCH Prescribing Program makes TYSABRI® available only to prescribers, infusion sites, pharmacies associated with infusion sites, and patients who are enrolled in the program
- There are 3 main components of the program: Enroll – Infuse – Track
- TYSABRI must be administered only to patients who are enrolled in and meet all the conditions of the TOUCH Prescribing Program
- Indication-specific training and educational materials are required for a site to become authorized on MS TOUCH, CD TOUCH or both
- TOUCH On-Line is a web-based tool available only to authorized infusion sites and prescribers enrolled in TOUCH
- Only authorized infusion sites and their associated certified pharmacies may acquire TYSABRI



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07/2020

TYS-US-0482 V5

The logo for TYSABRI (natalizumab) features the word "TYSABRI" in a large, bold, blue, sans-serif font. A red swoosh with a blue arrowhead at its end curves over the top of the letters. Below "TYSABRI" is the text "(natalizumab)" in a smaller, blue, sans-serif font.

**TYSABRI**<sup>®</sup>  
(natalizumab)

# *Overview of the TOUCH Program*

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Please see the Prescribing Information,  
including **BOXED WARNING**, for more information

**TYSABRI**<sup>®</sup>  
(natalizumab)

## INDICATIONS AND USAGE

### Multiple Sclerosis (MS)

- TYSABRI is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults

### Crohn's Disease (CD)

- TYSABRI is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF- $\alpha$ . TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine or methotrexate) or inhibitors of TNF- $\alpha$

### Why the program was developed

Biogen is committed to patient safety. The TOUCH<sup>®</sup> Prescribing Program was designed:

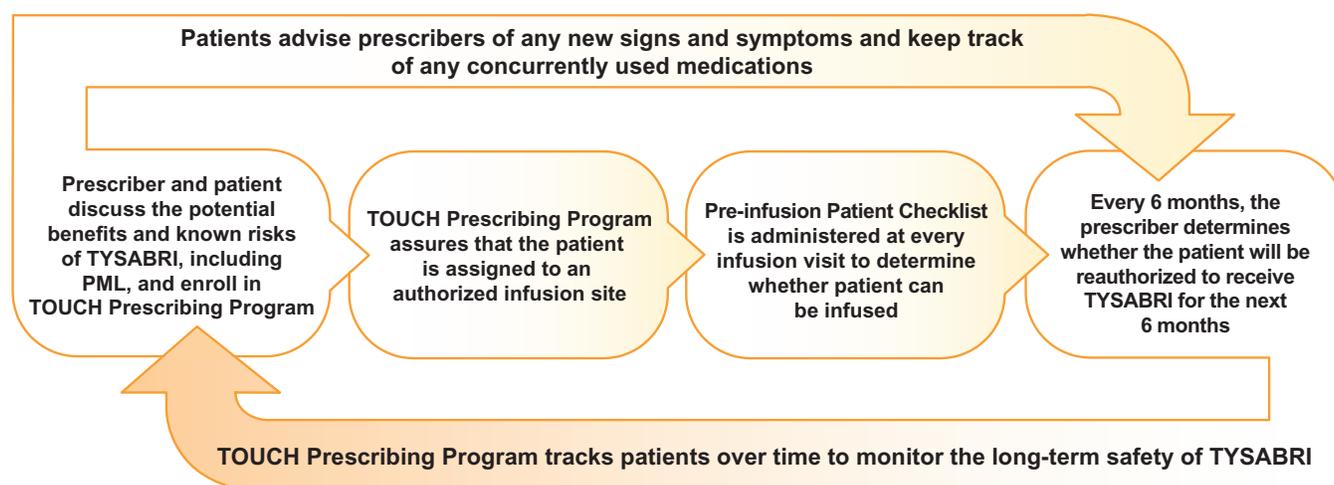
- To inform prescribers, infusion center healthcare providers, and patients about the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI including the increased risk of PML with the presence of anti-JCV antibodies, longer treatment duration, and prior immunosuppressant use
- To warn against concurrent use with antineoplastic, immunosuppressant, or immunomodulating agents and in patients who are immunocompromised
- To promote early diagnosis of PML and timely discontinuation of TYSABRI in the event of suspected PML

Prescribers, infusion sites, certified pharmacies and patients must all enroll in the TOUCH Prescribing Program in order to prescribe, infuse, dispense, or receive TYSABRI. All completed Enrollment Forms must be faxed to Biogen at 1-800-840-1278.



- TOUCH On-Line is a web-based tool designed to:
  - Provide real-time access to TYSABRI patient data
  - Maintain compliance with the TOUCH Prescribing Program
  - Reduce administrative burden/paperwork for prescribers and infusion sites
- TOUCH On-Line is accessed with secure user name and password

## How the program works



This Overview serves only as an introduction to the program. For additional details please see the Prescribing Information, or call 1-800-456-2255.

**Compliance with the requirements of the TOUCH Prescribing Program is necessary to maintain authorization to prescribe, dispense, infuse, or receive TYSABRI. Failure to comply with these requirements may result in de-enrollment from the TOUCH Prescribing Program and termination of such authorization.**

For more information on the TOUCH Prescribing Program or to obtain additional copies of material, please contact your Biogen representative or call 1-800-456-2255. The Patient Medication Guide is also available online at [www.TYSABRI.com](http://www.TYSABRI.com).



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## Enrollment

All participants must enroll in the TOUCH Prescribing Program by completing an Enrollment Form.

### **Prescribers and Patients**

Prior to enrollment, prescribers must receive and review the Prescribing Information and educational materials relating to the TOUCH Prescribing Program. Before completing and signing a Prescriber/Patient Enrollment Form, prescribers and patients are required to:

- Understand and discuss the benefits and risks of treatment with TYSABRI, including PML and other opportunistic infections
- Understand and acknowledge their respective program responsibilities as outlined in the Enrollment Kit

Patients should be fully counseled by either the enrolled prescriber or a healthcare provider under that prescriber's direction before an initial prescription is written. A copy of the completed Prescriber/Patient Enrollment Form should be retained in the patient's medical record. Upon receipt of a properly completed Enrollment Form:

- A Patient Enrollment Number will be assigned
- A Biogen Case Manager will be assigned to assure that the patient is assigned to an authorized infusion site

### **Infusion Sites and Certified Pharmacies\***

Before completing and signing their respective Enrollment Forms, infusion sites and certified pharmacies must receive training from a Biogen representative.

\*A certified pharmacy is a pharmacy that is part of a hospital, group practice, or infusion site, and is affiliated with one or more infusion sites. Retail pharmacies, wholesalers, and specialty distributors are excluded from holding inventory and dispensing TYSABRI.

2

## Infusion

Only infusion sites authorized by the TOUCH Prescribing Program can infuse TYSABRI. They are required to:

- Confirm that the patient is currently authorized to receive TYSABRI
- Provide the patient with a copy of the TYSABRI Patient Medication Guide prior to each infusion
- Administer the Pre-Infusion Patient Checklist to every patient prior to each infusion and submit it to Biogen within 1 business day, regardless of whether the patient is infused or not

Authorized infusion sites must use the Authorization Number that is provided upon enrollment to order and receive shipments of TYSABRI.\* Certified pharmacies may only dispense TYSABRI to authorized infusion sites.

\*The TOUCH Prescribing Program utilizes a closed distribution system that restricts all product shipments. This system includes a single distributor, specialty pharmacies under contract with Biogen and authorized certified pharmacies.

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## Tracking

The TOUCH Prescribing Program will track all patients over time so that Biogen can inform the FDA, prescribers, and patients in a timely manner of information regarding the safety of TYSABRI. Prescribers are required to report any case of PML, serious opportunistic infection, or death in TYSABRI-treated patients to Biogen or the FDA. Furthermore, prescribers are also required to cooperate in the investigation of potential adverse events including providing relevant information upon request. The primary tracking tools include:

- Pre-infusion Patient Checklist
- Patient Status Report and Reauthorization Questionnaire
- Initial and 6-month Discontinuation Questionnaires

Missing or incomplete forms will prompt TOUCH Case Managers to follow up with infusion sites, patients, and/or prescribers to obtain such information in compliance with program requirements. Prescribers, infusion sites, and certified pharmacies may be audited by the FDA, Biogen, and/or a third party authorized by Biogen.

# Program Overview

## Important Responsibilities

**PRESCRIBERS**— Among the important responsibilities of prescribers in the TOUCH Prescribing Program are the following:

- Acknowledge that TYSABRI should only be prescribed in accordance with the FDA label
- Educate the patient on the benefits and risks of treatment with TYSABRI by using the Patient Medication Guide
- Evaluate the patient 3 and 6 months after the first infusion, and every 6 months thereafter, and for 6 months after TYSABRI has been discontinued
- Determine every 6 months whether the patient should continue on treatment, and if so, reauthorize treatment
- Submit to Biogen the TYSABRI Patient Status Report and Reauthorization Questionnaire 6 months after initiating treatment and every 6 months thereafter
- Report serious opportunistic infections and atypical infections with TYSABRI to Biogen at 1-800-456-2255 and to the Food and Drug Administration's MedWatch program at 1-800-FDA-1088

**PATIENTS**—Among the important responsibilities of patients in the TOUCH Prescribing Program are the following:

- Bring to each infusion a list of all medicines and treatments they have taken during the last month
- Read the Patient Medication Guide before starting TYSABRI and before each TYSABRI infusion
- Promptly report any continuously worsening symptoms that persist over several days to their prescriber
- Inform all of their physicians that they are receiving TYSABRI
- Plan to see their prescriber 3 and 6 months after the first infusion, and at least as frequently as every 6 months thereafter

**INFUSION SITES**—Among the important responsibilities of infusion sites in the TOUCH Prescribing Program are the following:

- Confirm that the patient is currently authorized to receive TYSABRI
- Provide the patient with a copy of the TYSABRI Patient Medication Guide *prior to each infusion*
- Administer the Pre-infusion Patient Checklist to every patient prior to each infusion and submit to Biogen within 1 business day, regardless of whether the patient is infused or not

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# Prescriber/Patient Enrollment Form-MS

Completion of all pages required.

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

## Patient Information

Date of birth: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 (MM/DD/YYYY)

Patient name: \_\_\_\_\_  
 First MI Last

Street address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

Work telephone    -    -

Home telephone    -    -

Patient may be contacted at  Home  Work Best time: \_\_\_\_\_

Female  Male

E-mail address \_\_\_\_\_

## Insurance Information

**Please attach copies of both sides of patient's insurance and pharmacy card(s).**

Check if no insurance  Medicare  Medicaid \_\_\_\_\_  
 Medicaid Plan Type

Policyholder's name: \_\_\_\_\_  
 First MI Last

Primary insurance \_\_\_\_\_ Insurance company telephone \_\_\_\_\_

Policy number \_\_\_\_\_ Group number \_\_\_\_\_

Pharmacy benefit manager \_\_\_\_\_

## Patient Authorization to Use/Disclose Health Information

I understand that I have certain rights related to the collection, use, and disclosure of my medical and health information. This information is called "protected health information" (PHI) and includes demographic information (such as sex, race, date of birth, etc.), the results of physical examinations, clinical tests, blood tests, X-rays, and other diagnostic and medical procedures that may be included in my medical records. Biogen will not use my PHI without my consent.

This Authorization form applies to PHI created or obtained by my prescriber, my infusion site, my pharmacy, and my health insurance company. I understand that by signing this Authorization, I authorize my prescriber, infusion site, pharmacy, and/or health insurance company to disclose the PHI in my medical records to Biogen and its representatives or agents, including information related to my medical condition, treatment, and health insurance, as well as all information provided on any prescription. I also authorize Biogen to use this information to provide TYSABRI support services, such as investigating insurance coverage for TYSABRI and coordinating delivery of TYSABRI to the prescriber or infusion site administering TYSABRI (which may include forwarding my health information to a pharmacy).

I agree to allow Biogen to ask me about and provide me with these support services, educational kits, and other information related to TYSABRI and/or my medical condition. I understand that, once my PHI has been disclosed to Biogen, federal privacy laws may no longer protect the information. However, Biogen agrees to protect my PHI by using it only for the purposes authorized in this Authorization or as required by law.

I understand that I may refuse to sign this Authorization, and refusing to do so will affect my eligibility to receive these additional services but will not affect my ability to receive TYSABRI. I understand that signing this Authorization will not change how my healthcare providers, health insurance plan, and pharmacies provide my medical treatment or payment for treatment or insurance benefits.

I understand that I may cancel all or a part of this Authorization at any time by mailing a letter requesting such cancellation to TYSABRI Support Services, 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709. If I cancel this Authorization, Biogen will end further use and disclosure of my PHI as soon as possible. This will not affect health information that has already been used or disclosed in reliance upon this Authorization.

I will receive a copy of this signed Authorization. This Authorization expires ten (10) years from the date this Authorization is signed.

**Patient signature** (or personal representative): \_\_\_\_\_ Date: \_\_\_\_\_

Authority of personal representative (if applicable): \_\_\_\_\_

**Patient Acknowledgment**

Biogen considers patient safety a priority. Read each section below and **initial in the space provided** if you understand the information. **Do not sign this form if there is anything you do not understand about all the information you have received. Ask your doctor about anything you do not understand before you initial and sign this form.**

**I understand that TYSABRI is a medicine approved to treat relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.**

- I have talked to my doctor and understand the benefits and risks of TYSABRI treatment
- TYSABRI increases the risk of PML. I understand that when starting and continuing treatment with TYSABRI, I should talk to my doctor about whether the expected benefit of TYSABRI is enough to outweigh the risk (see important safety information about PML below)

**Initials:** \_\_\_\_\_

**I understand that TYSABRI increases my chance of getting a rare brain infection that usually leads to death or severe disability.**

- This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
- There is no known treatment, prevention, or cure for PML
- My chance for getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other MS treatments. Even if I use TYSABRI alone to treat my MS, I can still get PML
- My chance for getting PML increases if I:
  - Have been exposed to John Cunningham Virus (JCV). JCV is a common virus that is harmless in most people but can cause PML in people who have weakened immune systems, such as people taking TYSABRI. Most people who are exposed to JCV do not know it or have any symptoms. This exposure usually happens in childhood. My doctor may do a blood test to check if I have been exposed to JCV before I start receiving TYSABRI or during my treatment
  - Have received TYSABRI for a long time, especially longer than 2 years
  - Have received certain medicines that can weaken my immune system before I start receiving TYSABRI

My risk of getting PML is greatest if I have all 3 risk factors listed above. There may be other risk factors for getting PML during TYSABRI treatment that we do not know about yet. My doctor should discuss the risks and benefits of TYSABRI treatment with me before I decide to receive TYSABRI

- I should call my doctor right away if I get any new or worsening symptoms that last several days, especially nervous system symptoms, while I am taking TYSABRI, and for at least 6 months after I stop taking TYSABRI. Some of these symptoms include a new or sudden change in my thinking, eyesight, balance, or strength, but I should also report other new or worsening symptoms

**Initials:** \_\_\_\_\_

**To receive TYSABRI, all patients must be enrolled in a restricted program called the TOUCH® Prescribing Program.**

- The TOUCH Prescribing Program is run by the company that makes TYSABRI. Under this program, the company is required to collect information about my health at regular time periods. **I cannot receive TYSABRI if I do not agree** to follow the requirements of the TOUCH Prescribing Program. I understand that the TOUCH Prescribing Program does not require me to sign the Authorization included on page 1 of this form
- The company may use my information to meet the requirements of the TOUCH Prescribing Program, including helping me locate an authorized infusion site
- I must notify the TOUCH Prescribing Program if I switch physicians or infusion sites
- I have received, read, and understand the Patient Medication Guide
- I will bring to each TYSABRI infusion a list of all medicines and treatments that I have taken during the past month

**Initials:** \_\_\_\_\_

**Patient name:** \_\_\_\_\_ **Date of birth:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

**Patient signature** (or personal representative): \_\_\_\_\_ **Date:** \_\_\_\_\_

**Authority of personal representative** (if applicable): \_\_\_\_\_

**Patient History**

Patient name: \_\_\_\_\_ DOB: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

Date of first MS symptoms: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(MM/DD/YYYY)

Please indicate the patient's **MOST RECENT** therapy for MS (if patient was most recently on combination therapy, check all that apply). None

- |                                       |   |                                       |                                       |  |                                     |                                    |
|---------------------------------------|---|---------------------------------------|---------------------------------------|--|-------------------------------------|------------------------------------|
| Aubagio® <input type="checkbox"/>     | AVONEX® <input type="checkbox"/>          | Betaseron® <input type="checkbox"/>   | Copaxone® <input type="checkbox"/>    | Extavia® <input type="checkbox"/>      | Gilenya® <input type="checkbox"/>   | Lemtrada® <input type="checkbox"/> |
| Mavenclad® <input type="checkbox"/>   | Mayzent® <input type="checkbox"/>         | Ocrevus® <input type="checkbox"/>     | PLEGRIDY® <input type="checkbox"/>    | Rebif® <input type="checkbox"/>        | TECFIDERA® <input type="checkbox"/> | TYSABRI® <input type="checkbox"/>  |
| Azathioprine <input type="checkbox"/> | Cyclophosphamide <input type="checkbox"/> | Methotrexate <input type="checkbox"/> | Mitoxantrone <input type="checkbox"/> | Mycophenolate <input type="checkbox"/> | Other <input type="checkbox"/>      |                                    |

Please indicate the start and stop dates of most recent therapy: Start date  /  /  Stop date  /  /   
M M Y Y Y Y M M Y Y Y Y

Has the patient ever received TYSABRI before? Yes  No

Has the patient **EVER** been prescribed an immunosuppressant or an antineoplastic therapy for any condition? Yes  No

If yes, please check all of the following that apply:

- Azathioprine  Cyclophosphamide  Methotrexate  Mitoxantrone  Mycophenolate  Other

Has the patient **EVER** been tested for the presence of anti-JCV antibodies? Yes  No  Unknown

If yes, has the patient **EVER** tested **POSITIVE** for the presence of anti-JCV antibodies? Yes  No  Pending

If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_ . \_\_\_\_\_

**Prescription for TYSABRI**

**Dose: TYSABRI® (natalizumab) 300 mg Dispense: 1 vial Refills: 12 Directions: IV infusion per Prescribing Information every 4 weeks**

I authorize Biogen as my designated agent and on behalf of my patient to (1) use the information on this form to enroll the above-named patient in the TOUCH Prescribing Program, (2) furnish any information on this form to the insurer of the above-named patient, (3) forward the information on this form to the prescriber or infusion site administering TYSABRI, if applicable, (4) forward the above prescription by fax or by another mode of delivery to a pharmacy, if applicable, and (5) coordinate delivery of TYSABRI on behalf of the above-named patient.

**Prescriber signature** (stamps not acceptable): \_\_\_\_\_ Date: \_\_\_\_\_

**Prescriber**

Prescriber name: \_\_\_\_\_  
First MI Last

Office contact \_\_\_\_\_

Street address \_\_\_\_\_

Tax ID # \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

DEA # \_\_\_\_\_

Telephone  -  -

NPI/UPIN/provider ID # with patient's insurer(s) \_\_\_\_\_

Fax  -  -

**Continued on next page**

## Prescriber Acknowledgment

- I have read and understand the Prescribing Information for TYSABRI
- I understand that TYSABRI is indicated as monotherapy for relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- I understand that this patient has a relapsing form of MS based on clinical and radiological evidence
- I understand that TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing treatment with TYSABRI, I should consider whether the expected benefit of TYSABRI is sufficient to offset the risk
- I am aware that cases of PML have been reported in patients taking TYSABRI who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving TYSABRI monotherapy
- I understand that three risk factors identified thus far that increase the risk of PML in TYSABRI-treated patients are:
  - The presence of anti-JCV antibodies
  - Longer treatment duration, especially beyond 2 years
  - Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
- These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI
- I understand that TYSABRI is not ordinarily recommended for patients who are receiving chronic immunosuppressant or immunomodulatory therapy, or who are significantly immunocompromised from any other cause
- To my knowledge, this patient has no known contraindications to TYSABRI treatment, including PML
- I understand that an MRI should be performed prior to initiating therapy with TYSABRI in MS patients
- I understand that MRI findings may be apparent before clinical signs or symptoms. Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML. Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis
- I have instructed this patient to promptly report to me any continuously worsening symptoms that persist over several days, especially nervous system symptoms
- I understand that this patient should be seen and evaluated 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter, and for at least 6 months after TYSABRI has been discontinued
- I will determine every 6 months whether this patient should continue on TYSABRI and if so, authorize treatment for another 6 months. I understand that I am required to submit an "Initial Discontinuation Questionnaire" when TYSABRI is discontinued and a "6-Month Discontinuation Questionnaire" following discontinuation of TYSABRI
- I should report, as soon as possible, cases of PML, hospitalizations due to opportunistic infection, or deaths to Biogen
- I understand that data concerning this patient and me will be entered into the mandatory TOUCH Prescribing Program. Biogen requires my cooperation with periodic data collection. Failure to provide the requested information or otherwise comply with the requirements of the TOUCH Prescribing Program may result in discontinuation of TYSABRI treatment for this patient and termination of my authorization to prescribe TYSABRI
- I have received educational materials regarding the benefits and risks of TYSABRI treatment
- I have, or another healthcare provider under my direction has, educated this patient on the benefits and risks of treatment with TYSABRI, provided him or her with the Patient Medication Guide and Enrollment Form, instructed him or her to read these materials, and encouraged him or her to ask questions when considering TYSABRI

**Patient name:** \_\_\_\_\_ **Date of birth:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

**Prescriber signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

# Prescriber/Patient Enrollment Form—MS

Completion of all pages required.

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-840-1278

## Patient Information

Date of birth: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ Patient name: \_\_\_\_\_  
(MM/DD/YYYY) First MI Last

In addition, I allow the sharing of my health information to the person or people I name below. Biogen may contact the people named below to discuss my enrollment in the TOUCH Program.

Designated Individual (print name): \_\_\_\_\_ Relationship: \_\_\_\_\_

## Infusion Site Information\*

**1 Prescriber will administer TYSABRI** and request the following services (check only one):

- No services required **OR**  Forward this prescription to a specialty pharmacy provider to investigate pharmacy coverage and coordinate delivery to prescriber's office **OR**  Please conduct insurance research and procurement options for TYSABRI

**OR**

**2 Prescriber will refer TYSABRI treatment to another site** (check only one):

- I require assistance in locating an infusion site **OR**  I am referring the patient to the following infusion site or healthcare provider:

\_\_\_\_\_  
Name of infusion site

\_\_\_\_\_  
Office contact

\_\_\_\_\_  
Name of healthcare provider (First, Last)

Telephone    -    -

\_\_\_\_\_  
Street address or site Authorization Number

Fax    -    -

\_\_\_\_\_  
City State ZIP

\*Note: TYSABRI can only be infused at authorized infusion sites. Biogen will contact you if the infusion site you have indicated is not authorized to infuse TYSABRI.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

**Patient Information**

**Insurance Information**

Date of birth: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 (MM/DD/YYYY)

Patient name: \_\_\_\_\_  
 First MI Last

Street address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

Work Telephone    -    -

Home Telephone    -    -

Patient may be contacted at Home  Work  Best time: \_\_\_\_\_

Female  Male

E-mail address \_\_\_\_\_

**Please attach copies of both sides of patient’s insurance and pharmacy card(s).**

Check if no insurance  Medicare  Medicaid \_\_\_\_\_  
 Medicaid Plan Type

Policyholder’s name: \_\_\_\_\_  
 First MI Last

Primary insurance \_\_\_\_\_ Insurance company telephone \_\_\_\_\_

Policy number \_\_\_\_\_ Group number \_\_\_\_\_

Pharmacy benefit manager \_\_\_\_\_

**Patient Authorization to Use/Disclose Health Information**

I understand that I have certain rights related to the collection, use, and disclosure of my medical and health information. This information is called “protected health information” (PHI) and includes demographic information (such as sex, race, date of birth, etc.), the results of physical examinations, clinical tests, blood tests, X-rays, and other diagnostic and medical procedures that may be included in my medical records. Biogen will not use my PHI without my consent.

This Authorization form applies to PHI created or obtained by my prescriber, my infusion site, my pharmacy, and my health insurance company. I understand that by signing this Authorization, I authorize my prescriber, infusion site, pharmacy, and/or health insurance company to disclose the PHI in my medical records to Biogen and its representatives or agents, including information related to my medical condition, treatment, and health insurance, as well as all information provided on any prescription. I also authorize Biogen to use this information to provide TYSABRI support services, such as investigating insurance coverage for TYSABRI and coordinating delivery of TYSABRI to the prescriber or infusion site administering TYSABRI (which may include forwarding my health information to a pharmacy).

I agree to allow Biogen to ask me about and provide me with these support services, educational kits, and other information related to TYSABRI and/or my medical condition. I understand that, once my PHI has been disclosed to Biogen, federal privacy laws may no longer protect the information. However, Biogen agrees to protect my PHI by using it only for the purposes authorized in this Authorization or as required by law.

I understand that I may refuse to sign this Authorization, and refusing to do so will affect my eligibility to receive these additional services but will not affect my ability to receive TYSABRI. I understand that signing this Authorization will not change how my healthcare providers, health insurance plan, and pharmacies provide my medical treatment or payment for treatment or insurance benefits.

I understand that I may cancel all or a part of this Authorization at any time by mailing a letter requesting such cancellation to TYSABRI Support Services, 5000 Davis Drive, PO Box 13919, Research Triangle Park, NC 27709. If I cancel this Authorization, Biogen will end further use and disclosure of my PHI as soon as possible. This will not affect health information that has already been used or disclosed in reliance upon this Authorization.

I will receive a copy of this signed Authorization. This Authorization expires ten (10) years from the date this Authorization is signed.

**Patient signature** (or personal representative): \_\_\_\_\_ Date: \_\_\_\_\_

**Authority of personal representative** (if applicable): \_\_\_\_\_

**Patient Acknowledgment**

Biogen considers patient safety a priority. Read each section below and **initial in the space** provided if you understand the information.

**Do not sign this form if there is anything you do not understand about all the information you have received. Ask your doctor about anything you do not understand before you initial and sign this form.**

**I understand that TYSABRI is a medicine approved to treat patients with moderate to severe Crohn’s disease who have not been helped enough by, or cannot tolerate, usual Crohn’s disease medicines and medicines called tumor necrosis factor (TNF) inhibitors.**

- I have talked to my doctor and understand the benefits and risks of TYSABRI treatment
- I understand that I should not take certain medicines that weaken the immune system while I am taking TYSABRI

**Initials:** \_\_\_\_\_

**I understand that TYSABRI increases my chance of getting a rare brain infection that usually leads to death or severe disability.**

- This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
- There is no known treatment, prevention, or cure for PML
- My chance of getting PML may be higher if I am also being treated with other medicines that can weaken my immune system, including other Crohn’s disease treatments. Even if I use TYSABRI alone to treat my CD, I can still get PML
- My chance of getting PML increases if I:
  - Have been exposed to John Cunningham Virus (JCV). JCV is a common virus that is harmless in most people but can cause PML in people who have weakened immune systems, such as people taking TYSABRI. Most people who are exposed to JCV do not know it or have any symptoms. This exposure usually happens in childhood. My doctor may do a blood test to check if I have been exposed to JCV before I start receiving TYSABRI or during my treatment
  - Have received TYSABRI for a long time, especially longer than 2 years
  - Have received certain medicines that can weaken the immune system before I start receiving TYSABRI

My risk of getting PML is greatest if I have all 3 risk factors listed above. There may be other risk factors for getting PML during TYSABRI treatment that we do not know about yet. My doctor should discuss the risks and benefits of TYSABRI treatment with me before I decide to receive TYSABRI

- I should call my doctor right away if I get any new or worsening symptoms that last several days, especially nervous system symptoms, while I am taking TYSABRI and for at least 6 months after I stop taking TYSABRI. Some of these symptoms include a new or sudden change in my thinking, eyesight, balance, or strength, but I should also report other new or worsening symptoms

**Initials:** \_\_\_\_\_

**To receive TYSABRI, all patients must be enrolled in a restricted program called the TOUCH® Prescribing Program.**

- The TOUCH Prescribing Program is run by the company that makes TYSABRI. Under this program, the company is required to collect information about my health at regular time periods. **I cannot receive TYSABRI if I do not agree** to follow the requirements of the TOUCH Prescribing Program. I understand that the TOUCH Prescribing Program does not require me to sign the Authorization included on page 1 of this form
- The company may use my information to meet the requirements of the TOUCH Prescribing Program, including helping me locate an authorized infusion site
- I must notify the TOUCH Prescribing Program if I switch physicians or infusion sites
- I have received, read, and understand the Patient Medication Guide
- I will bring to each TYSABRI infusion a list of all medicines and treatments that I have taken during the last month

**Initials:** \_\_\_\_\_

**Patient name:** \_\_\_\_\_ **Date of birth:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

**Patient signature** (or personal representative): \_\_\_\_\_ **Date:** \_\_\_\_\_

**Authority of personal representative** (if applicable): \_\_\_\_\_

# Prescriber/Patient Enrollment Form—Crohn's Disease

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

Completion of all pages required.

## Patient History

Patient name: \_\_\_\_\_ DOB: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

Date of first Crohn's disease symptoms: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(MM/DD/YYYY)

Please indicate the patient's Crohn's disease therapy(ies) within the past one year AND whether the therapy is ongoing or stopped. **Ongoing therapies, except corticosteroids, must be stopped before starting TYSABRI.** (If patient was on multiple therapies, check all that apply.)

Medication	Ongoing	OR	Stopped	Medication	Ongoing	OR	Stopped
<input type="checkbox"/> None				Methotrexate	<input type="checkbox"/>		<input type="checkbox"/>
Remicade®	<input type="checkbox"/>		<input type="checkbox"/>	Systemic steroids	<input type="checkbox"/>		<input type="checkbox"/>
Humira®	<input type="checkbox"/>		<input type="checkbox"/>	Entyvio®	<input type="checkbox"/>		<input type="checkbox"/>
Azathioprine or Mercaptopurine or Thioguanine	<input type="checkbox"/>		<input type="checkbox"/>	Other immunomodulatory therapy or immunosuppressant therapy (not including aminosaliclates)	<input type="checkbox"/>		<input type="checkbox"/>
Cimzia®	<input type="checkbox"/>		<input type="checkbox"/>				

Has the patient had a surgery for Crohn's disease within the previous year? Yes  No

Has the patient ever received TYSABRI before? Yes  No

Has the patient **EVER** been prescribed an immunosuppressant or an antineoplastic therapy for any condition? Yes  No

If yes, please check all that apply:

Remicade  Humira  Azathioprine or Mercaptopurine or Thioguanine  Cimzia  Methotrexate   
 Systemic steroids  Vedolizumab (Entyvio)  Other

Has the patient **EVER** been tested for the presence of anti-JCV antibodies? Yes  No  Unknown

If yes, has the patient **EVER** tested **POSITIVE** for the presence of anti-JCV antibodies? Yes  No  Pending

If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_

## Prescription for TYSABRI

**Dose: TYSABRI® (natalizumab) 300mg Dispense: 1 vial Refills: 12 Directions: IV infusion per Prescribing Information every 4 weeks**

I authorize Biogen as my delegated agent and on behalf of my patient to (1) use the information on this form to enroll the above-named patient in the TOUCH Prescribing Program, (2) furnish any information on this form to the insurer of the above-named patient, (3) forward the information on this form to the prescriber or infusion site administering TYSABRI, if applicable, (4) forward the above prescription by fax or by another mode of delivery to a pharmacy, if applicable, and (5) coordinate delivery of TYSABRI on behalf of the above-named patient.

**Prescriber signature** (stamps not acceptable): \_\_\_\_\_ Date: \_\_\_\_\_

## Prescriber

Prescriber name: \_\_\_\_\_  
First MI Last

Office contact \_\_\_\_\_

Street address \_\_\_\_\_

Tax ID # \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

DEA # \_\_\_\_\_

Telephone    -    -

NPI/UPIN/provider ID # with patient's insurer(s) \_\_\_\_\_

Fax    -    -

**Prescriber Acknowledgment**

- I have read and understand the Prescribing Information for TYSABRI
- I understand that TYSABRI is indicated for adult patients with moderately to severely active Crohn’s disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional Crohn’s disease therapies and inhibitors of TNF-α
- I understand that patients receiving TYSABRI should not take concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α
- I understand that this patient has moderately to severely active Crohn’s disease with evidence of inflammation
- I understand that TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. When initiating and continuing treatment with TYSABRI, I should consider whether the expected benefit of TYSABRI is sufficient to offset this risk
- I am aware that cases of PML have been reported in patients taking TYSABRI who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving TYSABRI monotherapy
- I understand that the three risk factors identified thus far that increase the risk of PML in TYSABRI-treated patients are:
  - The presence of anti-JCV antibodies
  - Longer treatment duration, especially beyond 2 years
  - Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil)
 These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI
- I understand that MRI findings may be apparent before clinical signs or symptoms. Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML. Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis
- I have discussed other Crohn’s disease treatments with this patient
- To my knowledge, this patient has no known contraindications to TYSABRI treatment, including PML
- I have instructed this patient to promptly report to me any continuously worsening symptoms that persist over several days, especially nervous system symptoms
- I understand that this patient should be seen and evaluated 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter, and for at least 6 months after TYSABRI has been discontinued
- I understand that TYSABRI should be discontinued if the patient has not experienced a therapeutic benefit by 12 weeks of therapy
- I will determine every 6 months whether this patient should continue on TYSABRI and if so, authorize treatment for another 6 months. I understand that I am required to submit an “Initial Discontinuation Questionnaire” when TYSABRI is discontinued and a “6-Month Discontinuation Questionnaire” following discontinuation of TYSABRI
- I understand that patients receiving steroid therapy at the time of TYSABRI initiation must undergo a steroid-tapering regimen once a therapeutic response is achieved. If the patient with Crohn’s disease cannot be tapered off steroids within 6 months of starting TYSABRI, TYSABRI should be discontinued
- I should report, as soon as possible, cases of PML, hospitalizations due to opportunistic infection, and any death to Biogen
- I understand that data concerning this patient and me will be entered into the mandatory TOUCH Prescribing Program. Biogen requires my cooperation with periodic data collection. Failure to provide the requested information or otherwise comply with the requirements of the TOUCH Prescribing Program may result in discontinuation of TYSABRI treatment for this patient and termination of my authorization to prescribe TYSABRI
- I have received educational materials regarding the benefits and risks of TYSABRI treatment
- I have, or another healthcare provider under my direction has, educated this patient on the benefits and risks of treatment with TYSABRI, provided him or her with the Patient Medication Guide and Enrollment Form, instructed him or her to read these materials, and encouraged him or her to ask questions when considering TYSABRI

**Patient name:** \_\_\_\_\_ **Date of birth:** \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
First MI Last (MM/DD/YYYY)

**Prescriber signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

# Prescriber/Patient Enrollment Form—Crohn's Disease

Completion of all pages required.

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-840-1278

## Patient Information

Date of birth: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ Patient name: \_\_\_\_\_  
(MM/DD/YYYY) First MI Last

In addition, I allow the sharing of my health information to the person or people I name below. Biogen may contact the people named below to discuss my enrollment in the TOUCH Program.

Designated Individual (print name): \_\_\_\_\_ Relationship: \_\_\_\_\_

## Infusion Site Information\*

**1 Prescriber will administer TYSABRI** and request the following services (check only one):

- No services required **OR**  Forward this prescription to a specialty pharmacy provider to investigate pharmacy coverage and coordinate delivery to prescriber's office **OR**  Please conduct insurance research and procurement options for TYSABRI

**OR**

**2 Prescriber will refer TYSABRI treatment to another site** (check only one):

- I require assistance in locating an infusion site **OR**  I am referring the patient to the following infusion site or healthcare provider

\_\_\_\_\_  
Name of infusion site or healthcare provider (first, last)

\_\_\_\_\_  
Office contact

\_\_\_\_\_  
Street address or Site Authorization Number

Telephone    -    -

\_\_\_\_\_  
City State ZIP

Fax    -    -

\*Note: TYSABRI can only be infused at authorized infusion sites. Biogen will contact you if the infusion site you have indicated is not authorized to infuse TYSABRI.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

**TYSABRI**  
**Pre-infusion Patient Checklist**

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

Patient name: \_\_\_\_\_ Patient Enrollment Number: \_\_\_\_\_  
 First MI Last (Issued by Biogen. Call 1-800-456-2255 or log on to [www.touchprogram.com](http://www.touchprogram.com) if number is not on file.)

Site name: \_\_\_\_\_ Site Authorization Number: \_\_\_\_\_

As a condition of your site's authorization to infuse TYSABRI<sup>®</sup> (natalizumab), this Pre-infusion Patient Checklist **must** be completed for each patient prior to each infusion. This page **must** be submitted on-line ([www.touchprogram.com](http://www.touchprogram.com)) **OR** faxed to Biogen (1-800-840-1278) **within 1 day** of the patient's visit and a copy retained in the patient's record whether the patient has been infused or not.

**STEP 1: Ensure that the patient is currently authorized to receive TYSABRI for MS or Crohn's disease.**

You must refer to the patient's record prior to every infusion.

- If the patient did not receive his or her previous infusion, and physician clearance was required, you must confirm authorization from the prescriber before providing the current infusion
- Confirm the patient status is listed as "Authorized" on TOUCH<sup>®</sup> On-Line ([www.touchprogram.com](http://www.touchprogram.com)) **OR**
- Confirm that there is a current **Notice of Patient Authorization** on file and that you have not received a **Notice of Patient Discontinuation** (paper-based process)

**Is the patient currently authorized to receive TYSABRI?**

Yes  No

**Yes** Continue to next question.

**No STOP—DO NOT INFUSE.** If authorization cannot be verified on-line at [www.touchprogram.com](http://www.touchprogram.com) **OR** by calling 1-800-456-2255, the patient must be referred back to the healthcare provider who prescribed TYSABRI.

**STEP 2: Confirm that the patient has read and understood the Patient Medication Guide.**

The patient must read the Patient Medication Guide prior to every infusion. **Has the patient received and read the Patient Medication Guide, including the section "What should I tell my doctor and nurse before each infusion of TYSABRI?"**

Yes  No

**Yes** Continue to next question.

**No STOP**—provide the Patient Medication Guide. Proceed to the next question after the patient has read it.

**STEP 3: Read aloud and mark "Yes" or "No" for the patient's answers to the following questions:**

- |   |                              |                             |
|---|------------------------------|-----------------------------|
| 1. Over the past month, have you had any new or worsening medical problems (such as a new or sudden change in your thinking, eyesight, balance, strength, or other problems) that have persisted over several days?       | Yes <input type="checkbox"/> | No <input type="checkbox"/> |
| 2. Do you have a medical condition that can weaken your immune system, such as HIV infection or AIDS, leukemia or lymphoma, or an organ transplant, that may suggest that your body is not able to fight infections well? | Yes <input type="checkbox"/> | No <input type="checkbox"/> |

**Crohn's disease ONLY**

3. In the past month have you taken, or are you currently on, any medicines other than steroid medicines to treat cancer or **Crohn's disease** or any other medicines that weaken your immune system? (Review the list on the next page with the patient.)
- Yes  No

**MS ONLY**

3. In the past month, have you taken medicines to treat cancer or **MS** or any other medicines that weaken your immune system? (Review the list on the next page with the patient.)
- Yes  No

**STEP 4: Record Prescriber Authorization (if required):**

**If the patient answered YES to question 1, 2 or 3, DO NOT INFUSE.** Contact the healthcare provider who prescribed TYSABRI or a prescriber representative and review the patient's answers.

Yes  No

- After discussing the patient's answers, did the prescriber authorize the patient to be infused?
- Check here if you were unable to contact the prescriber.  (See next page for further instructions.)

**STEP 5: Record infusion information**

Date infused (MM/DD/YYYY): \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ Not infused

If the next infusion has been scheduled, please enter date (MM/DD/YYYY): \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_

Name and signature of staff completing checklist: \_\_\_\_\_ Date \_\_\_\_\_

**STEP 6: Submit the Pre-infusion Patient Checklist to Biogen on-line at [www.touchprogram.com](http://www.touchprogram.com) **OR** fax to 1-800-840-1278.**

## TYSABRI Pre-infusion Patient Checklist

Please review the following list with the patient when asking question 3.

### Examples of Immunosuppressants, Antineoplastics, and Immunomodulators

#### Multiple Sclerosis

##### Approved MS Therapies:

Alemtuzumab (Lemtrada®)  
Cladribine (Mavenclad®)  
Dimethyl Fumerate (TECFIDERA®)  
Fingolimod (Gilenya®)  
Glatiramer acetate (Copaxone®)  
Interferon beta-1a (Rebif®, AVONEX®)  
Interferon beta-1b (Betaseron®, Extavia®)  
Mitoxantrone (Novantrone®)  
Ocrelizumab (Ocrevus®)  
Peginterferon beta-1a (PLEGRIDY®)  
Siponimod (Mayzent®)  
Teriflunomide (Aubagio®)

##### Immunosuppressants/Antineoplastics:

Azathioprine (Imuran®, Azasan®)  
Cladribine (Leustatin®)  
Cyclophosphamide (Cytoxan®, Neosar®)  
Cyclosporine (Sandimmune®, Neoral®)  
Fludarabine phosphate (Fludara®)  
Leflunomide (Arava®)  
Mercaptopurine (Purinethol®)  
Methotrexate (Methotrex®, Rheumatrex®, Trexall®)  
Mycophenolate mofetil (CellCept®)  
Pemetrexed (Alimta®)

##### Additional Immunomodulators and Immunosuppressants:

Other interferons (Actimmune®, Infergen®, Intron® A,  
Pegasys®, PEG-Intron®, Rebetrone®, Roferon®-A)  
Adalimumab (Humira®)  
Alefacept (Amevive®)  
Alemtuzumab (Campath®)  
Anakinra (Kineret®)  
Daclizumab (Zenapax®)  
Efalizumab (Raptiva®)  
Etanercept (Enbrel®)  
Infliximab (Remicade®)  
Intravenous immunoglobulin (IVIG)  
Rituximab (Rituxan®)  
Trastuzumab (Herceptin®)

#### Crohn's Disease

##### Approved TNF- $\alpha$ inhibitors for Crohn's disease:

Infliximab (Remicade®)  
Adalimumab (Humira®)

##### Immunosuppressants/Antineoplastics:

Approved TNF- $\alpha$  inhibitors  
Azathioprine (Imuran®, Azasan®)  
Chlorambucil (Leukeran®)  
Cladribine (Leustatin®)  
Cyclophosphamide (Cytoxan®, Neosar®)  
Cyclosporine (Sandimmune®, Neoral®)  
Fludarabine phosphate (Fludara®)  
Leflunomide (Arava®)  
Mercaptopurine (Purinethol®)  
Methotrexate (Methotrex®, Rheumatrex®, Trexall®)  
Mycophenolate mofetil (CellCept®)  
Pemetrexed (Alimta®)  
Thioguanine (Tabloid®)

##### Additional Immunomodulators and Immunosuppressants:

Interferon beta-1a (Rebif®, AVONEX®)  
Interferon beta-1b (Betaseron®)  
Alefacept (Amevive®)  
Abatacept (Orencia®)  
Anakinra (Kineret®)  
Daclizumab (Zenapax®)  
Efalizumab (Raptiva®)  
Etanercept (Enbrel®)  
Glatiramer acetate (Copaxone®)  
Intravenous immunoglobulin (IVIG)  
Mitoxantrone (Novantrone®)  
Other interferons (Actimmune®, Infergen®, Intron® A,  
Pegasys®, PEG-Intron®, Rebetrone®, Roferon®-A)  
Rituximab (Rituxan®)  
Trastuzumab (Herceptin®)  
Vedolizumab (Entyvio®)

**This list does not include all drugs that can suppress the immune system.**

- Patients should consult their prescribing physician regarding drugs that may be taken concurrently with TYSABRI
- If there are any questions regarding concurrent therapy, **do not infuse** at this time and consult the healthcare provider who prescribed TYSABRI

#### If you are unable to contact the prescriber or a prescriber representative:

Instruct the patient to contact his/her prescriber or prescriber representative and to reschedule as soon as possible. Continue efforts to reach the prescriber or prescriber representative to inform him/her of the reason(s) for not infusing this patient. You will need to confirm authorization from the prescriber or prescriber representative on the subsequent infusion.

A prescriber representative is defined as a prescriber-designated individual who can make decisions regarding patients under his or her care in their absence. A prescriber representative should be knowledgeable about the Prescribing Information, including Boxed Warning, and should be able to determine whether the patient can receive his or her infusion.

This Pre-infusion Patient Checklist is not intended to replace the infusion site's general infusion protocol(s). Nor is this Pre-infusion Patient Checklist intended to be a substitute for consultation and review of reference materials and medical literature pertaining to individual clinical circumstances. Healthcare providers should make all treatment decisions based on the context of the situation and their clinical judgment.

Please do not make any extraneous marks on the Pre-infusion Patient Checklist. If there is information that you would like to share with Biogen and the TOUCH Prescribing Program, please contact us at 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

# Helpful information for evaluation of new neurological symptoms in patients receiving TYSABRI

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This information is provided as an education resource for healthcare providers and should be considered current as of the date listed herein. It is not intended to be a substitute for consultation and review of reference materials and medical literature pertaining to individual clinical circumstances. Healthcare providers should make all treatment decisions based on the context of the situation and their own clinical judgment.

Please see the Prescribing Information,  
including **BOXED WARNING**, for more information

The logo for TYSABRI (natalizumab) features the brand name "TYSABRI" in a bold, blue, sans-serif font. A red swoosh with a blue arrowhead at its end curves over the top of the letters. Below "TYSABRI" is the generic name "(natalizumab)" in a smaller, blue, sans-serif font. A registered trademark symbol (®) is located to the right of the generic name.

**TYSABRI**<sup>®</sup>  
(natalizumab)

# Background information

## JCV infections: Progressive multifocal leukoencephalopathy (PML) and JC virus granule cell neuronopathy (JCV GCN)

### 1. PML

PML is a demyelinating disease that attacks the central nervous system (CNS). It is caused by a polyomavirus called the JC virus (JCV), which is common and widespread in humans. JCV usually remains latent, typically causing PML only in the setting of immunodeficiency.

The clinical picture of PML or other neurological conditions can be difficult to distinguish from multiple sclerosis (MS), especially early in the disease course. Therefore, this information is intended to offer an overview of some of the key issues regarding the definitive diagnosis of PML, especially as they relate to treatment with TYSABRI. These include:

- Patient monitoring and management
  - Obtaining a pretreatment MRI
  - Performing regular follow-ups
  - Treatment of relapses or other neurological symptoms
- Evaluation of new neurological symptoms in patients receiving TYSABRI
  - Distinguishing PML from MS
  - Suggested diagnostic algorithm
  - Action steps if PML is suspected, including MRI assessment, JCV testing, and plasma exchange (PLEX)
  - Immune Reconstitution Inflammatory Syndrome (IRIS)

### 2. JCV GCN

JC virus infection of granule cell neurons in the cerebellum (i.e., JCV GCN) has been reported in patients treated with TYSABRI. JCV GCN can occur with or without concomitant PML. JCV GCN can cause cerebellar dysfunction (e.g., ataxia, incoordination, apraxia, visual disorders), and neuroimaging can show cerebellar atrophy. For diagnosis of JCV GCN, an evaluation that includes a gadolinium-enhanced MRI scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA, is recommended. JCV GCN should be managed similarly to PML.

Adapted from Kappos L et al. *Lancet Neurol.* 2007;6(5):431-441.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

# Patient monitoring and management

## Management of patients receiving TYSABRI

### Pretreatment MRI

Obtaining a pretreatment brain MRI scan is recommended. It may assist in determining whether MRI lesions noted at the time of new neurological signs or symptoms were preexistent. This may assist in the differential diagnosis between PML and MS activity.

### Regular follow-ups

All patients treated with TYSABRI should have regular clinical follow-ups to allow for early detection of changes in neurological status. To that end, Biogen, in conjunction with the Food and Drug Administration (FDA), developed a risk management plan for the United States called the TOUCH® Prescribing Program. As part of the TOUCH Prescribing Program:

- Physicians evaluate the patient 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter, and for at least 6 months after discontinuing TYSABRI
- Physicians submit the TYSABRI Patient Status Report and Reauthorization Questionnaire to Biogen 6 months after initiating treatment and every 6 months thereafter, ensuring additional monitoring and reporting by Biogen
- Infusion sites administer the Pre-Infusion Patient Checklist and report to the prescriber any changes in the patient's status prior to infusing
  - Infusion sites will not infuse TYSABRI if the patient reports a change in symptoms, unless the prescriber authorizes the infusion

### Patient history

Knowing the history and pattern of prior and ongoing MS signs and symptoms can help in the management of patients treated with TYSABRI.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# Evaluation of new neurological symptoms in patients receiving TYSABRI

- If new neurological symptoms develop, withhold TYSABRI dosing and evaluate the patient

## Distinguishing PML from MS

The following information should be considered when undertaking the assessment and management of new or worsening neurological symptoms in MS patients treated with TYSABRI. There are no pathognomonic signs or symptoms that distinguish an MS relapse from PML, but there are certain clinical features that may help differentiate between the 2 conditions (see Table 1).

**Table 1. Clinical signs and symptoms typical of MS relapse and PML**

	MS relapse	PML
<b>ONSET</b>	<b>Acute</b>	<b>Subacute</b>
<b>EVOLUTION</b>	<ul style="list-style-type: none"> <li>➤ Over hours to days</li> <li>➤ Normally stabilize</li> <li>➤ Resolve spontaneously or with treatment</li> </ul>	<ul style="list-style-type: none"> <li>➤ Days to weeks</li> <li>➤ Progressive</li> </ul>
<b>CLINICAL PRESENTATION</b>	<ul style="list-style-type: none"> <li>➤ Diplopia</li> <li>➤ Paresthesia</li> <li>➤ Paraparesis</li> <li>➤ Optic neuritis</li> <li>➤ Myelopathy</li> </ul>	<ul style="list-style-type: none"> <li>➤ Cortical symptoms/signs</li> <li>➤ Behavioral and neuropsychological alteration</li> <li>➤ Retrochiasmal visual deficits</li> <li>➤ Seizures</li> <li>➤ Hemiparesis</li> </ul>

Not intended to be inclusive of all clinical signs and symptoms indicative of MS and PML.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

## Treatment of MS relapse

- Relapses should be managed according to usual clinical practice

### If treating with corticosteroids:

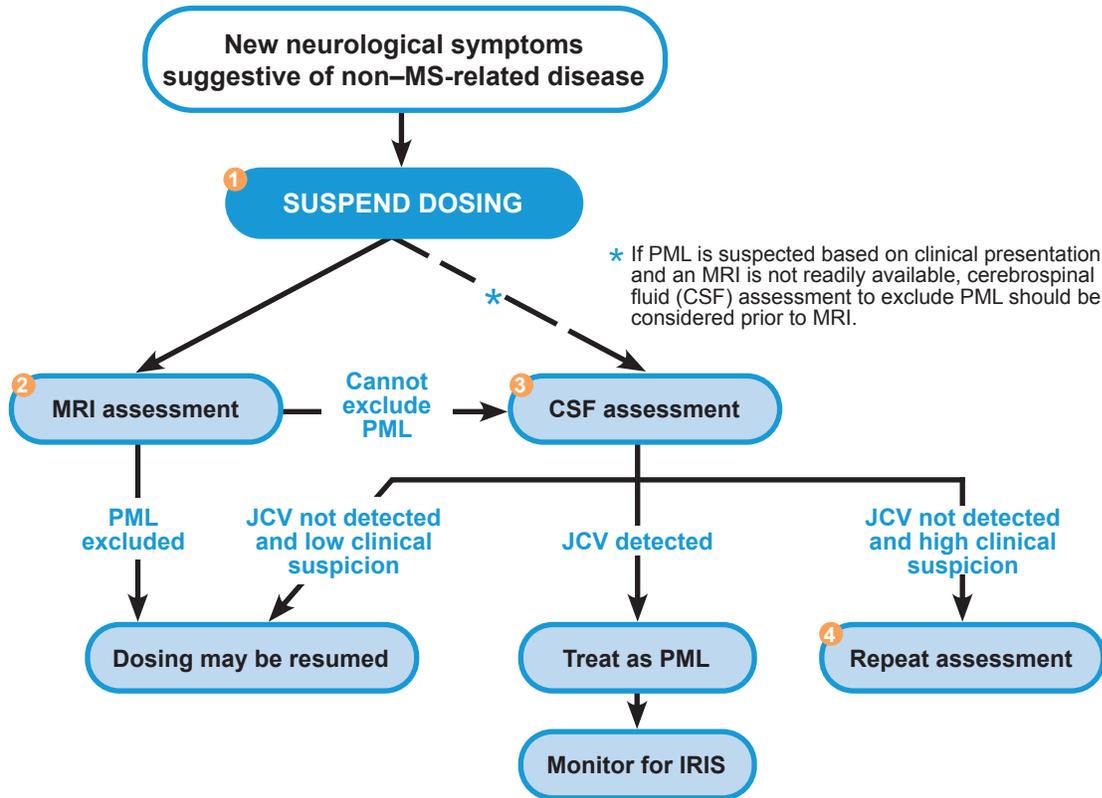
- A single short course of corticosteroids can be considered for cases in which PML is unlikely on clinical grounds
  - Progression of symptoms, despite treatment with corticosteroids, should trigger further investigation
- In addition to PML and MS, other medical and CNS conditions including other infections should be considered when evaluating a patient with new neurological symptoms

**New or recurrent neurological symptoms should prompt careful evaluation.**

Please see the Prescribing Information, including **BOXED WARNING**, for more information

  
**TYSABRI**<sup>®</sup>  
(natalizumab)

**Suggested diagnostic algorithm for TYSABRI-treated patients experiencing new neurological symptoms suggestive of non-MS-related disease**



**Note:** TYSABRI dosing should only be restarted when the diagnosis of PML is excluded, if necessary, by repeating clinical, MRI, and CSF assessment if clinical suspicion of PML remains.

CSF assessment for presence of JCV DNA should be performed using a highly sensitive quantitative real-time PCR assay with a limit of quantification (LOQ) of at least 50 copies/mL.

For more information, please call Biogen Medical Information at 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

## Action steps if PML is suspected

### 1 SUSPEND DOSING

TYSABRI dosing should be suspended **immediately** in all cases in which PML is suspected.

### 2 MRI assessment

If the clinical presentation is suggestive of PML, further investigation should include brain MRI evaluation as soon as possible.

### 3 CSF assessment

If MRI evaluation reveals lesions suspicious for PML (see [Table 2 on page 9](#)), a lumbar puncture with evaluation of CSF for the detection of JCV DNA should be undertaken with a highly sensitive quantitative real-time PCR assay.

### 4 Repeat testing

If clinical suspicion of PML remains despite a negative evaluation, then MRI and CSF assessments should be repeated to exclude a diagnosis of PML.

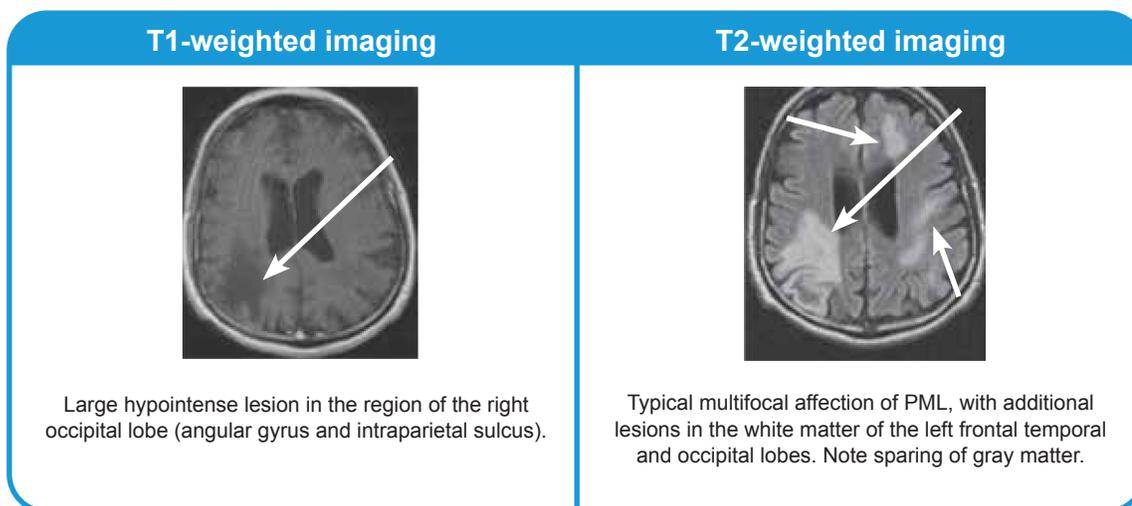
**A definitive diagnosis of PML is made by evaluating clinical and MRI findings plus the identification of JCV in the CNS.**

- There is no prevention, FDA-approved treatment, or cure for PML. Rapid recognition of PML and early discontinuation of TYSABRI are key interventions
- PLEX (see [page 10](#)) may be considered as a means to accelerate the clearance of TYSABRI
- Healthcare providers should promptly report serious adverse events to Biogen at [1-800-456-2255](tel:1-800-456-2255) — Biogen can provide additional resources, including suggested next steps

## MRI assessment

- Although there are no pathognomonic findings that differentiate PML from MS, a brain MRI scan that includes fluid-attenuated inversion recovery (FLAIR) and T1- and T2-weighted sequences, with and without gadolinium (Gd), should be performed to assess patients with neurological changes suggestive of PML (see [Table 1 on page 4](#))
- Comparison with a baseline scan may assist with interpretation of the findings on the new MRI. See [Figure 1](#) and [Table 2](#) for differences in lesion characteristics that may help differentiate between PML and MS

**Figure 1. MRI presentation features of PML**



Adapted from Weber T. *Neurol Clin.* 2008;26(3):833-854. Used with permission.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

**Table 2. MRI lesion characteristics typical of PML and MS**

Characteristic	MS Lesions	PML Lesions
Location	Periventricular perpendicular to ventricles (Dawson's fingers), deep white matter, isolated U fibers, cerebellum, and spinal cord	<ul style="list-style-type: none"> <li>➤ Subcortical WM in parietal, occipital, or frontal lobes</li> <li>➤ May involve precentral or postcentral gyrus (motor/sensory cortex) or insular region</li> <li>➤ Follows WM tracks. Can cross the corpus callosum to contralateral hemisphere (butterfly pattern) or extend through internal capsule</li> <li>➤ Rarely brainstem or cerebellar WM</li> <li>➤ No spinal cord involvement</li> </ul>
Appearance	Well-defined borders	➤ Infiltrating, ill-defined, confluent WM lesions which can be multifocal
Mass effect	Large lesions can have a mass effect	➤ Rare even in large lesions
FLAIR	Flair = T2	➤ Flair more sensitive for detection of PML lesions in subcortical location
T1W pre-contrast	Isointense or mildly hypointense to Grey matter	➤ Isointense with progressive hypointensity
T1 post contrast	Homogeneous or ring-enhancement—resolves in 1-2 months	➤ Patchy, punctate, or linear

Adapted from Yousry TA et al. *N Eng J Med.* 2006;354(9):924-933.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



## JCV DNA testing to confirm diagnosis

- Plasma assessment
  - Presence of JCV DNA in plasma has not been correlated with the development of PML
  - Plasma JCV DNA test positivity is highly variable, so the sensitivity and predictive value of this screening method are unclear
  - Plasma JCV DNA testing is not included in the TOUCH Prescribing Program
- CSF assessment
  - The detection of JCV DNA in the CSF of a patient with clinical and MRI features suggestive of PML establishes the diagnosis of PML
  - If clinical suspicion of PML remains despite a negative CSF, testing should be repeated
  - It is recommended to test samples using a validated ultrasensitive quantitative PCR test that has a lower limit of quantification of 50 copies per mL or lower
- Brain biopsy
  - If diagnosis remains uncertain and suspicion of PML remains high, a brain biopsy may be considered to establish a definitive diagnosis

**Note:** TYSABRI dosing should only be resumed if the diagnosis of PML is excluded and if deemed appropriate for the ongoing treatment of MS.

## PLEX

- Three sessions of plasma exchange (PLEX) over 5 to 8 days were shown to accelerate TYSABRI clearance in a study of 12 patients with MS who did not have PML, although in the majority of patients,  $\alpha$ 4-integrin receptor binding remained high—a potential sign of continued inhibition of  $\alpha$ 4-integrin-mediated leukocyte activity
- Additional plasma exchanges (up to a total of 5 over a 10-day period) may more consistently reduce TYSABRI plasma concentration and  $\alpha$ 4-integrin receptor binding to below subtherapeutic levels
- Adverse events that may occur during PLEX include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema
- Although PLEX has not been prospectively studied in TYSABRI treated patients with PML, it has been used in such patients in the postmarketing setting to remove TYSABRI more quickly from the circulation
- There is no evidence that PLEX has any benefit in the treatment of opportunistic infections such as PML
- Physicians should use medical judgment when considering the use of PLEX to treat PML

Adapted from Khatri BO et al. *Neurology*. 2009;72(5):402-409.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

## Immune Reconstitution Inflammatory Syndrome (IRIS)

- IRIS has been reported in the majority of patients who developed PML and subsequently discontinued TYSABRI
- In almost all cases, IRIS occurred within days to several weeks after plasma exchange was used to accelerate TYSABRI clearance
- IRIS usually presents as an unanticipated clinical decline which may be rapid and severe, and may be fatal
- At the time of IRIS, MRI may show additional changes including Gd enhancement
- Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken

**For the latest scientific information about our products or to report an adverse event, contact:**

### Biogen Medical Information

**Telephone:** 1-800-456-2255 (8:30 AM to 8:00 PM ET)

**Fax:** Send Medical Information Request Form to  
1-877-462-1530

**Web:** <http://medinfo.biogen.com>

**E-mail:** [medinfo@biogen.com](mailto:medinfo@biogen.com)

**To report an adverse event, contact:**

### Biogen

**Telephone:** 1-800-456-2255

Please see the Prescribing Information, including **BOXED WARNING**, for more information

  
**TYSABRI**<sup>®</sup>  
(natalizumab)

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including **BOXED WARNING**, for more information



## Understanding PML for Gastroenterologists

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This information is provided as an educational resource for healthcare providers and should be considered current as of the date listed herein. It is not intended to be a substitute for consultation and review of reference materials and medical literature pertaining to individual clinical circumstances. Healthcare providers should make all treatment decisions based on the context of the situation and their own clinical judgment.



# Understanding PML for Gastroenterologists

The following information should be considered when undertaking the assessment and management of progressive multifocal leukoencephalopathy (PML) in adult patients treated with TYSABRI for moderately to severely active Crohn's disease (CD). During clinical trials for TYSABRI, 3 cases of PML were identified (2 in multiple sclerosis and 1 in Crohn's disease). Both multiple sclerosis patients were receiving concomitant immunomodulatory therapy and the Crohn's disease patient had been treated in the past with immunosuppressive therapy. In the postmarketing setting, additional cases of PML have been reported in multiple sclerosis and Crohn's disease patients who were receiving no concomitant immunomodulatory therapy.<sup>1</sup>

## About PML

PML is a demyelinating disease that attacks the central nervous system.<sup>2</sup> It is an opportunistic infection caused by the JC virus that typically occurs in patients who are immunocompromised.<sup>1</sup> The virus removes myelin that surrounds the nerves, and without this protection the nerves cannot transmit signals.<sup>3</sup> There are no known interventions that can reliably prevent PML or adequately treat PML if it occurs.<sup>1</sup>

## How to Recognize PML

Typical symptoms associated with PML are diverse, progress over days to weeks, and include<sup>3,4</sup>:

- Progressive weakness on one side of the body or clumsiness of limbs
- Disturbance of vision
- Changes in thinking, memory, and orientation, leading to confusion and personality changes
- Seizures

The progression of deficits usually leads to death or severe disability over weeks or months.<sup>3</sup> Since these symptoms are very different from those of Crohn's disease, the appearance of any symptom of PML, including those listed above, should be investigated immediately.<sup>4</sup> In Crohn's disease patients, a baseline brain MRI may also be helpful to distinguish pre-existent lesions from newly developed lesions, but brain lesions at baseline that could cause diagnostic difficulty while on TYSABRI therapy are uncommon.<sup>1</sup>



## Action Steps if PML Is Suspected

- TYSABRI dosing should be suspended immediately in all cases in which PML is suspected<sup>1</sup>
- Immediate referral to a neurologist for assessment, potentially including<sup>1</sup>:
  - A brain MRI to determine if lesions that could be due to PML are present
  - Cerebrospinal fluid evaluation for the presence of JCV DNA
- Potential cases of PML should be reported immediately to Biogen at 1-800-456-2255, or to the FDA's MedWatch reporting system at 1-800-FDA-1088, or via the MedWatch Web site at [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

**Note: TYSABRI dosing should be restored only if the diagnosis of PML is excluded and if deemed appropriate for the ongoing treatment of CD in patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF- $\alpha$ , and who are not taking concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, or methotrexate) or concomitant inhibitors of TNF- $\alpha$ .**

## Indication

TYSABRI is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF- $\alpha$ . TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF- $\alpha$ .

## Important Safety Information

### **WARNING: Progressive Multifocal Leukoencephalopathy (PML)**

TYSABRI (natalizumab) increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability. Risk factors for the development of PML include the presence of anti-JCV antibodies, duration of therapy, and prior use of immunosuppressants. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. TYSABRI dosing should be withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation including a gadolinium-enhanced MRI scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended.

Because of the risk of PML, TYSABRI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the TOUCH Prescribing Program.

Important Safety Information continued on next page.



## Important Safety Information (continued)

### Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus (JCV) is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- After plasma exchange (PLEX), wait at least two weeks to test for anti-JCV antibodies to avoid false negative test results caused by the removal of serum antibodies. After infusion of intravenous immunoglobulin (IVIg), wait at least 6 months (5 half-lives) for the IVIg to clear in order to avoid false positive anti-JCV antibody test results.
- There are no known interventions that can reliably prevent PML or that can adequately treat PML if it occurs. It is not known whether early detection of PML and discontinuation of TYSABRI will mitigate the disease.
- MRI findings may be apparent before clinical signs or symptoms suggestive of PML. Periodic monitoring for radiographic signs consistent with PML should be considered to allow for an early diagnosis of PML. Consider monitoring patients at high risk for PML more frequently. Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis.
- PML has been reported after discontinuation of TYSABRI in patients who did not have findings suggestive of PML at the time of discontinuation. Patients should continue to be monitored for any new signs or symptoms that may be suggestive of PML for approximately 6 months after discontinuation of TYSABRI.
- In MS patients, an MRI scan should be obtained prior to initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of PLEX over 5 to 8 days were shown to accelerate TYSABRI clearance in a study of 12 patients with MS who did not have PML, although in the majority of patients, alpha-4 integrin receptor binding remained high. Adverse events that may occur during PLEX include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although PLEX has not been prospectively studied in TYSABRI-treated patients with PML, it has been used in such patients in the postmarketing setting to remove TYSABRI more quickly from the circulation. There is no evidence that PLEX has any benefit in the treatment of opportunistic infections such as PML.
- JCV infection of granule cell neurons in the cerebellum, i.e., JCV granule cell neuronopathy (GCN), with symptoms similar to PML, has been reported in patients treated with TYSABRI. JCV GCN can occur with or without concomitant PML and can cause cerebellar dysfunction. Diagnosis and management of JCV GCN should follow guidance provided for PML.
- Immune reconstitution inflammatory syndrome (IRIS) has been reported in the majority of TYSABRI treated patients who developed PML and subsequently discontinued TYSABRI. In almost all cases, IRIS occurred after plasma exchange was used to eliminate circulating TYSABRI. It presents as a clinical decline in the patient's condition after TYSABRI removal (and in some cases after apparent clinical improvement) that may be rapid, can lead to serious neurological complications or death and is often associated with characteristic changes in the MRI. TYSABRI has not been associated with IRIS in patients discontinuing treatment with TYSABRI for reasons unrelated to PML. In TYSABRI-treated patients with PML, IRIS has been reported within days to several weeks after plasma exchange. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken.

Important Safety Information continued on next page.



### **Contraindications**

- TYSABRI is contraindicated in patients who have or have had PML.
- TYSABRI is contraindicated in patients who have had a hypersensitivity reaction to TYSABRI.

### **TYSABRI TOUCH Prescribing Program**

- TYSABRI is available only through a restricted program under a REMS called the TOUCH® Prescribing Program because of the risk of PML.
- For prescribers and patients, the TOUCH® Prescribing Program has two components: MS TOUCH® (for patients with multiple sclerosis) and CD TOUCH® (for patients with Crohn's disease).
- Prescribers must be certified and comply with the following:
  - Review the TOUCH Prescribing Program prescriber educational materials, including the prescribing information.
  - Educate patients on the benefits and risks of treatment with TYSABRI, ensure that patients receive the Medication Guide, and encourage them to ask questions.
  - Review, complete, and sign the Patient-Prescriber Enrollment Form.
  - Evaluate patients three months after the first infusion, six months after the first infusion, every six months thereafter and for at least six months after discontinuing TYSABRI.
  - Determine every six months whether patients should continue on treatment, and if so, authorize treatment for another six months.
  - Submit to Biogen the "TYSABRI Patient Status Report and Reauthorization Questionnaire" six months after initiating treatment and every six months thereafter.
  - Complete an "Initial Discontinuation Questionnaire" when TYSABRI is discontinued and a "6-Month Discontinuation Questionnaire," following discontinuation of TYSABRI.
  - Report cases of PML, hospitalizations due to opportunistic infections, and deaths to Biogen at 1-800-456-2255 and to the Food and Drug Administration's MedWatch Program at 1-800-FDA-1088 as soon as possible.
- Patients must be enrolled in the TOUCH Prescribing Program, read the Medication Guide, understand the risks associated with TYSABRI, and complete and sign the Patient-Prescriber Enrollment Form.
- Pharmacies and infusion centers must be specially certified to dispense or infuse TYSABRI.

**Important Safety Information continued on next page.**



### **Herpes Infections – Encephalitis, Meningitis and Acute Retinal Necrosis**

- TYSABRI increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses.
- Serious, life-threatening, and sometimes fatal cases have been reported in the postmarketing setting in multiple sclerosis patients receiving TYSABRI.
- The duration of treatment with TYSABRI prior to onset ranged from a few months to several years.
- Monitor patients receiving TYSABRI for signs and symptoms of meningitis and encephalitis. If herpes encephalitis or meningitis occurs, TYSABRI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered.
- Patients being administered TYSABRI are at a higher risk of acute retinal necrosis (ARN), a fulminant viral infection of the retina caused by the family of herpes viruses. Patients with eye symptoms such as decreased visual acuity, redness or eye pain should be referred for retinal screening as serious cases of ARN can lead to blindness of one or both eyes.
- Following clinical diagnosis of ARN consider discontinuation of TYSABRI.

### **Hepatotoxicity**

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting.
- Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose; signs of liver injury have also been reported for the first time after multiple doses.
- In some patients, liver injury recurred upon rechallenge, providing evidence that TYSABRI caused the injury.
- The combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients.
- TYSABRI should be discontinued in patients with jaundice or other evidence of significant liver injury (e.g., laboratory evidence).

### **Hypersensitivity/Antibody Formation**

- Hypersensitivity reactions have occurred in patients receiving TYSABRI, including serious systemic reactions (e.g., anaphylaxis) which occurred at an incidence of <1%.
- Reactions usually occur within 2 hours of the start of the infusion. Symptoms associated with these reactions can include urticaria, dizziness, fever, rash, rigors, pruritus, nausea, flushing, hypotension, dyspnea, and chest pain. Generally, these reactions are associated with antibodies to TYSABRI.
- If a hypersensitivity reaction occurs, discontinue administration of TYSABRI, and initiate appropriate therapy. Patients who experience a hypersensitivity reaction should not be re-treated with TYSABRI.
- Hypersensitivity reactions were more frequent in patients with antibodies to TYSABRI compared with patients who did not develop antibodies to TYSABRI in both MS and CD studies.
- Patients who receive TYSABRI for a short exposure (1 to 2 infusions) followed by an extended period without treatment are at higher risk of developing anti-natalizumab antibodies and/or hypersensitivity reactions on re-exposure, compared to patients who received regularly scheduled treatment.

**Important Safety Information continued on next page.**



### Immunosuppression/Infections

- The immune system effects of TYSABRI may increase the risk for infections.
- In Study MS1, certain types of infections, including pneumonias and urinary tract infections (including serious cases), gastroenteritis, vaginal infections, tooth infections, tonsillitis, and herpes infections, occurred more often in TYSABRI-treated patients than in placebo-treated patients. One opportunistic infection, a cryptosporidial gastroenteritis with a prolonged course, was observed in a patient who received TYSABRI in Study MS1.
- In Studies MS1 and MS2, an increase in infections was seen in patients concurrently receiving short courses of corticosteroids. However, the increase in infections in TYSABRI-treated patients who received steroids was similar to the increase in placebo-treated patients who received steroids
- Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections over the risk observed with use of TYSABRI alone. The safety and efficacy of TYSABRI in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established.
- In Studies MS1 and MS2, the rate of any type of infection was approximately 1.5 per patient-year in both TYSABRI-treated patients and placebo-treated patients
- In Study MS1, the incidence of serious infections was approximately 3% in TYSABRI-treated patients and in placebo-treated patients. Most patients did not interrupt treatment with TYSABRI during infections.
- In postmarketing experience, serious herpes infections have occurred.

### Laboratory Test Abnormalities

- In clinical trials, TYSABRI was observed to induce increases in circulating lymphocytes, monocytes, eosinophils, basophils, and nucleated red blood cells. Observed changes persisted during TYSABRI exposure, but were reversible, returning to baseline levels usually within 16 weeks after the last dose. Elevations of neutrophils were not observed. TYSABRI induces mild decreases in hemoglobin levels (mean decrease of 0.6g/dL) that are frequently transient.

### Thrombocytopenia:

- Cases of thrombocytopenia, including immune thrombocytopenic purpura (ITP), have been reported with the use of TYSABRI in the postmarketing setting.
- Symptoms of thrombocytopenia may include easy bruising, abnormal bleeding, and petechiae.
- Delay in the diagnosis and treatment of thrombocytopenia may lead to serious and life-threatening sequelae. If thrombocytopenia is suspected, TYSABRI should be discontinued.

### Adverse Reactions

- The most common adverse reactions reported at an incidence of  $\geq 10\%$  with TYSABRI and  $\geq 2\%$  difference with placebo were headache (38% vs 33%), fatigue (27% vs 21%), infusion reactions (24% vs 18%), urinary tract infections (21% vs 17%), arthralgia (19% vs 14%), depression (19% vs 16%), pain in extremity (16% vs 14%), rash (12% vs 9%), gastroenteritis (11% vs 9%), and vaginitis\* (10% vs 6%).

\*Percentage based on female patients only.

- The most frequently reported serious adverse reactions in Study MS1 were infections (3.2% vs 2.6% placebo), including urinary tract infection (0.8% vs 0.3%) and pneumonia (0.6% vs 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% vs 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% vs 0.3%]), and cholelithiasis (1.0% vs 0.3%).

- Based on animal data, TYSABRI may cause fetal harm. TYSABRI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.



**References:**

1. TYSABRI prescribing information. Cambridge, MA: Biogen.
2. Yousry TA, Major EO, Ryschewitsch C, et al. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. *N Engl J Med.* 2006;354:924-933.
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4. Project Inform. Progressive multifocal leukoencephalopathy (PML). Available at: <http://www.projectinform.org/info/pml/index.shtml>. Accessed February 14, 2008.
5. What is Crohn's Disease? Crohn's & Colitis Foundation of America. <http://www.cdfa.org/what-are-crohns-and-colitis/what-is-crohns-disease/?referrer=https://www.google.com/>. Accessed June 24, 2016.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



> TOUCH On-Line Login

> How do I enroll in the TOUCH Prescribing Program?

> TOUCH Prescribing Program Resources

> Learn more about TYSABRI

> Prescribing Information

> Patient Medication Guide

> Patient Medication Guide - Spanish

> Important Safety Information

**Not a TOUCH On-Line user?**

To learn more about becoming a TOUCH On-Line user, call a TYSABRI Support Specialist at Biogen:  
1-800-456-2255  Monday-Friday,  
8:30 AM to 8:00 PM (ET)

## TYSABRI® (natalizumab) is available only through the TOUCH Prescribing Program, which stands for TYSABRI Outreach: Unified Commitment to Health.

The TOUCH Prescribing Program is a restricted distribution program focused on safety and developed with the help of the Food and Drug Administration (FDA):

- Only prescribers and patients enrolled in the TOUCH Prescribing Program can prescribe and receive TYSABRI
- Only certain pharmacies and infusion sites authorized by the TOUCH Prescribing Program can dispense and infuse TYSABRI

### The TOUCH Prescribing Program is designed to:

- Inform prescribers, infusion center healthcare providers, and patients about the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI including the increased risk of PML with treatment duration and prior immunosuppressant use.
- Warn against concurrent use with antineoplastic, immunosuppressant, or immunomodulating agents and in patients who are immunocompromised.
- Promote early diagnosis of PML and timely discontinuation of TYSABRI in the event of suspected PML.

**TOUCH On-Line is a web-based tool designed to assist TOUCH Prescribing Program participants in fulfilling their TOUCH Prescribing Program Requirements.**

### TOUCH On-Line Login

TOUCH On-Line Username

Password

*Please note that the password is case sensitive.*

My password is not working, please e-mail me my password - [click here](#)

**Login**

#### Having trouble logging in?

Check with your Site Administrator or call us toll free:  
1-800-456-2255 , Monday through Friday, 8:30 AM to 8:00 PM (ET)

## How do I enroll in the TOUCH Prescribing Program?

**Prescribers, infusion sites, certified pharmacies associated with infusion sites and patients must all enroll in the TOUCH Prescribing Program in order to prescribe, infuse, dispense or receive TYSABRI.**

- **Prescribers:** The first step in enrolling in the TOUCH Prescribing Program is receiving educational materials provided by Biogen.
  - Requirements include:
    - Review the TYSABRI Patient Medication Guide with each patient and discuss the risks and benefits of starting therapy.
    - Review, complete, and submit a Prescriber/Patient Enrollment Form for each patient to acknowledge the therapy discussion and the TOUCH Prescribing Program requirements, and document the patient's consent to enroll in the program.
    - Review the Pre-Infusion Patient Checklist to make sure each patient understands the questions that will be asked prior to every infusion.
    - Evaluate the patient 3 months after the first infusion, 6 months after the first infusion, at least 6 months thereafter for as long as the patient receives TYSABRI, and for 6 months after TYSABRI has been discontinued.
    - Determine every 6 months whether a patient should continue on TYSABRI and if so, authorize treatment every 6 months.
- **Infusion Sites:** An infusion site must participate in a mandatory training program provided by a Biogen representative and complete an Infusion Site Enrollment Form documenting the site agrees to abide by the requirements of the TOUCH Prescribing Program.
  - Requirements prior to each infusion include:
    - Administer TYSABRI only to patients who are currently authorized in the TOUCH Prescribing Program. Patient authorization must be confirmed.
    - Provide each patient a copy of the TYSABRI Patient Medication Guide.
    - Complete a TYSABRI Pre-infusion Patient Checklist. The Pre-infusion Patient Checklist must be submitted to Biogen within 1 business day of the patient visit.
- **Certified Pharmacies** associated with infusion sites: A certified pharmacy must participate in a mandatory training program provided by a Biogen representative and complete a Certified Pharmacy Enrollment Form documenting the certified pharmacy agrees to abide by the requirements of the TOUCH Prescribing Program.
  - Dispense TYSABRI only to authorized infusion sites.

To learn more about enrolling in the TOUCH Prescribing Program, contact a TYSABRI Support Specialist at Biogen, call toll free: 1-800-456-2255,  Monday-Friday, 8:30 AM to 8:00 PM (ET).



**Biogen**

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## TOUCH Prescribing Program Resources

There are several resources available to assist in educating healthcare providers, and thus patients, of the known risks and potential benefits of TYSABRI treatment. Distribution of TOUCH Prescribing Program forms is controlled and available only from Biogen directly. The educational materials below are available for your convenience.

### Educational Tools

- TOUCH Prescribing Program Overview
  - This material provides an overview of the TOUCH Prescribing Program requirements and important participant responsibilities.
    - [TOUCH Prescribing Program Overview](#)
- TOUCH Prescribing Program Educational Slide Set
  - Presentation to provide education necessary to execute TOUCH Prescribing Program, intended for prescribers, infusion sites, and certified pharmacies.
    - [TOUCH Prescribing Program Educational Slide Set](#)
- Diagnosing PML (progressive multifocal leukoencephalopathy)
  - Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI is a resource for Neurology specialists treating TYSABRI patients. Key topics included in this tool are the importance of careful evaluation of any new or recurrent symptoms, differentiating between the signs and symptoms typical of MS and PML, PML diagnostic algorithm incorporating MRI and CSF assessment, and action steps if PML is suspected.
    - [Helpful Information for the Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI](#)
  - Understanding PML for Gastroenterologists material is a resource for Gastroenterologists, Internists, or other non-Neurology specialists treating TYSABRI patients. Key topics included in this tool are the characteristics of PML, guidance on recognizing PML in the context of Crohn's disease, and action steps if PML is suspected.
    - [Understanding PML for Gastroenterologists](#)

To learn more about enrolling in the TOUCH Prescribing Program, contact a TYSABRI Support Specialist at Biogen, call toll free: 1-800-456-2255,  Monday-Friday, 8:30 AM to 8:00 PM (ET).

## Change Prescriber Authorization

By Facsimile

### PRESCRIBER AUTHORIZATION REQUESTED

Date:	<Current_Date>	Patient Enrollment Number:	<Alt_ID>
New Prescriber:	<Phys_First_Name> <Phys_Last_Name>	Patient Name:	<Pat_First_Name> <Pat_Last_Name>
Address:	<MD_Address>	Patient DOB:	<Pat_DOB>
	<MD_City>, <MD_State> <MD_Zip>	Patient Enrollment Period:	Pat Auth Begin through <Pat Auth_End>
Phone:	<MD_Phone>	Infusion Site:	
Fax:	<MD_Fax>	Infusion Site Address:	
Prescriber DEA:		Prescriber State License Number:	

Our records indicate that <Pat\_First\_Name> <Pat\_Last\_Name> will continue his/her TYSABRI (natalizumab) therapy under your care. If you agree to accept this patient, please sign this form and fax it to Biogen at 1-800-840-1278.

If you do not accept this patient or have questions about the TOUCH® Prescribing Program Requirements, please call the TOUCH Prescribing Program at 1-800-456-2255. We are available Monday through Friday.

***I accept <Pat\_First\_Name> <Pat\_Last\_Name> under my care for TYSABRI (natalizumab) treatment.***

#### Prescription for TYSABRI

**Dose: TYSABRI® (natalizumab) 300 mg    Dispense: 1 vial    Refills: 12    Directions: IV infusion per Prescribing Information every 4 weeks**

I authorize Biogen as my designated agent and on behalf of my patient to (1) use the information on this form to continue the enrollment of the above-named patient in the TOUCH Prescribing Program, (2) forward the prescription by fax or by another mode of delivery to a pharmacy, if applicable, and (3) coordinate delivery of TYSABRI on behalf of the above named patient.

\_\_\_\_\_  
 Prescriber Signature

\_\_\_\_\_  
 Date

**FAX this signed form to 1-800-840-1278**

For full Prescribing Information including Boxed Warning, please see [www.TYSABRI.com](http://www.TYSABRI.com)

# TYSABRI Patient Status Report and Reauthorization Questionnaire-MS

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

<Date>  
 <Prescriber Name>  
 <Prescriber Address>  
 <MD Number>

Re: <Patient Name>  
 Patient Enrollment Number: <Patient TOUCH ID>  
 Patient date of birth: <DOB>  
 Authorization expiration date: <MM/DD/YYYY>

Dear <MD Name>,

Our records indicate that <Patient name>'s authorization to receive TYSABRI will expire on <MM/DD/YYYY> and he/she will no longer be able to receive TYSABRI. Please submit the completed form to Biogen via TOUCH On-Line (www.touchprogram.com) **OR** fax (1-800-840-1278) on <expiration date> and place a copy in the patient's record.

**A** Is the patient still under <MD name>'s care?  
 Yes  No/I don't know  
 If No, please provide name and phone number for new prescriber, if available \_\_\_\_\_  
 \_\_\_\_\_

**B** Is the patient alive?  
 Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have **not** reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)  
 Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized  
 Yes  No or  Under investigation

**E** MALIGNANCY  
 Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?  
 Yes  Not performed  
 If performed, since <last authorization>, test result:  
 Positive  Negative  Pending  
 If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_

**G** Is the patient currently receiving or has the patient received intermittent courses of steroids for the treatment of MS relapse in the previous 6 months?  
 Yes  No  
 If Yes, please circle the number of months of use:  
 1 2 3 4 5 6 >6

**H** Is the patient currently receiving or has the patient received any IMMUNOMODULATORY or IMMUNOSUPPRESSANT THERAPIES in the previous 6 months?  
 Yes  No  
 If Yes, please indicate the type of therapy.

- |                                     |  |
|-------------------------------------|--|
| <input type="checkbox"/> Aubagio®   | <input type="checkbox"/> Rebif®  |
| <input type="checkbox"/> AVONEX®    | <input type="checkbox"/> TECFIDERA®  |
| <input type="checkbox"/> Betaseron® | <input type="checkbox"/> Azathioprine  |
| <input type="checkbox"/> Copaxone®  | <input type="checkbox"/> Chronic systemic steroids                           |
| <input type="checkbox"/> Extavia®   | <input type="checkbox"/> Cyclophosphamide                                    |
| <input type="checkbox"/> Gilenya®   | <input type="checkbox"/> Methotrexate  |
| <input type="checkbox"/> Lemtrada®  | <input type="checkbox"/> Mitoxantrone  |
| <input type="checkbox"/> Mavenclad® | <input type="checkbox"/> Mycophenolate                                       |
| <input type="checkbox"/> Mayzent®   | <input type="checkbox"/> Other immunomodulatory or immunosuppressant therapy |
| <input type="checkbox"/> Ocrevus®   |  |
| <input type="checkbox"/> PLEGRIDY®  |  |

**I** If the patient is still under <MD name>'s care **DO YOU AUTHORIZE the continuation of TYSABRI treatment for the next 6 months for the patient?**  
 Yes  No  
 If you answer No, Biogen will contact the patient and the infusion site to STOP TYSABRI TREATMENT. The patient will not be eligible to receive TYSABRI treatment, and you will receive a final questionnaire for this patient in 6 months.

\*OPPORTUNISTIC INFECTION is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, pneumocystis carinii pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# TYSABRI Patient Status Report and Reauthorization Questionnaire—Crohn’s Disease

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

<Date>  
 <Prescriber Name>  
 <Prescriber Address>  
 <MD Number>

Re: <Patient Name>  
 Patient Enrollment Number: <Patient TOUCH ID>  
 Patient date of birth: <DOB>  
 Authorization expiration date: <MM/DD/YYYY>

Dear <MD Name>,  
 Our records indicate that <Patient Name>’s authorization to receive TYSABRI will expire on <MM/DD/YYYY> and he/she will no longer be able to receive TYSABRI. Please submit the completed form to Biogen via TOUCH On-Line (www.touchprogram.com) **OR** fax (1-800-840-1278) and place a copy in the patient’s record.

**A** Is the patient still under <MD Name>’s care?  
 Yes  No/I don’t know  
 If No, please provide name and phone number for new prescriber, if available \_\_\_\_\_

**B** Is the patient alive?  
 Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have **not** reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)  
 Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized  
 Yes  No or  Under investigation

**E** MALIGNANCY  
 Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?  
 Yes  Not performed  
 If performed, since <last authorization>, test result:  
 Positive  Negative  Pending

**G** Is the patient currently receiving or has the patient received systemic steroids for the treatment of Crohn’s flare in the previous 6 months?  
 Yes  No  
 If Yes, please circle the number of months of use:  
 1 2 3 4 5 6

**H** Within the past year, and since starting TYSABRI, has the patient received greater than 6 consecutive months of systemic steroids for the treatment of Crohn’s disease?  
 Yes  No

**I** Is the patient currently receiving or has the patient received any IMMUNOMODULATORY or IMMUNOSUPPRESSANT THERAPIES in the previous 6 months?  
 Yes  No  
 If Yes, please indicate the type of therapy.

- Cimzia®
- Entyvio®
- Humira®
- Remicade®
- Azathioprine or Mercaptopurine or Thioguanine
- Methotrexate
- Other immunomodulatory or immunosuppressant therapy†

†Not including aminosalicylates.

**J** If the patient is still under <MD Name>’s care **DO YOU AUTHORIZE the continuation of TYSABRI treatment for the next 6 months for the patient?**  
 Yes  No  
 If you answer No, Biogen will contact the patient and the infusion site to **STOP TYSABRI TREATMENT**. The patient will not be eligible to receive TYSABRI treatment, and you will receive a final questionnaire for this patient in 6 months.

\***OPPORTUNISTIC INFECTION** is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, *pneumocystis carinii* pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_  
**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# TYSABRI Initial Discontinuation Questionnaire-MS

Prescriber name: \_\_\_\_\_  
First MI Last

Prescriber address: \_\_\_\_\_  
Street City State ZIP

Patient: \_\_\_\_\_ Patient enrollment number: \_\_\_\_\_  
First MI Last

Patient date of birth (MM/DD/YYYY): \_\_\_\_/\_\_\_\_/\_\_\_\_

- This TYSABRI Patient Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH® Prescribing Program for all patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed TYSABRI Patient Discontinuation Questionnaire to Biogen via TOUCH On-Line (www.touchprogram.com) **OR** fax (1-800-840-1278) and place one copy in the patient's record. This form is mandatory for all discontinued patients.

**A** Is the patient still under <MD name>'s care?

Yes  No/I don't know

If No, please provide name and phone number for new prescriber, if available \_\_\_\_\_

**B** Is the patient alive?

Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have *not* reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized

Yes  No or  Under investigation

\*OPPORTUNISTIC INFECTION is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, *pneumocystis carinii* pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**E** MALIGNANCY

Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?

Yes  Not performed

If performed, since <last authorization>, test result:

Positive  Negative  Pending

If an anti-JCV antibody index value is available, please record it here: \_\_\_\_ . \_\_\_\_ \_\_\_\_

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



<Date>  
<Prescriber Name>  
<Prescriber Address>  
<MD Number>

Dear <MD Name>,

Our records indicate that <Patient Name> received a final dose of TYSABRI on <MM/DD/YYYY>.

# TYSABRI Initial Discontinuation Questionnaire–Crohn’s Disease

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-840-1278

Re: <Patient Name>  
Patient Enrollment Number: <Patient TOUCH ID>  
Patient date of birth: <DOB>

- This Initial Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH® Prescribing Program for Crohn’s disease patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed Initial Discontinuation Questionnaire to Biogen via TOUCH On-Line (www.touchprogram.com) **OR** fax (1-800-840-1278) and place one copy in the patient’s record. This form is mandatory for all discontinued patients.

**A** Is the patient still under <MD Name>’s care?  
 Yes     No/I don’t know  
 If No, please provide name and phone number for new prescriber, if available \_\_\_\_\_

**B** Is the patient alive?  
 Yes     No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have *not* reported to Biogen:

**C** **PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)**  
 Yes     No    or     Under investigation

**D** **OPPORTUNISTIC INFECTION\*** for which they have been hospitalized  
 Yes     No    or     Under investigation

**E** **MALIGNANCY**  
 Yes     No    or     Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?  
 Yes     Not performed  
 If performed, since <last authorization>, test result:  
 Positive     Negative     Pending  
 If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_

**G** Since <MM/DD/YYYY> is the patient currently receiving or has the patient received systemic steroids for the treatment of a Crohn’s flare?  
 Yes     No  
 If Yes, please circle the number of months of use:  
 1    2    3    4    5    6

**H** Within the past year, and since starting TYSABRI, has the patient received greater than 6 consecutive months of systemic steroids for the treatment of Crohn’s disease?  
 Yes     No

**I** Since <MM/DD/YYYY> is the patient currently receiving or has the patient received any **IMMUNOMODULATORY** or **IMMUNOSUPPRESSANT THERAPIES**?  
 Yes     No  
 If Yes, please indicate the type of therapy.  
 Cimzia®  
 Entyvio®  
 Humira®  
 Remicade®  
 Azathioprine or Mercaptopurine or Thioguanine  
 Methotrexate  
 Other immunomodulatory or immunosuppressant therapy

†Not including aminosalicylates.

\***OPPORTUNISTIC INFECTION** is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, *pneumocystis carinii* pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete this form and submit on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

# TYSABRI 6-Month Discontinuation Questionnaire—MS

Prescriber name: \_\_\_\_\_  
First MI Last

Prescriber address: \_\_\_\_\_  
Street City State ZIP

Patient: \_\_\_\_\_ Patient enrollment number: \_\_\_\_\_  
First MI Last

Patient date of birth (MM/DD/YYYY): \_\_\_\_/\_\_\_\_/\_\_\_\_

- This TYSABRI Patient Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH® Prescribing Program for all patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed TYSABRI Patient Discontinuation Questionnaire to Biogen via TOUCH On-Line (www.touchprogram.com) **OR** fax (1-800-840-1278) and place one copy in the patient's record.  
This form is mandatory for all discontinued patients.

**A** Is the patient still under <MD name>'s care?

Yes  No/I don't know

If No, please provide name and phone number for new prescriber, if available \_\_\_\_\_

**B** Is the patient alive?

Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have *not* reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized

Yes  No or  Under investigation

\*OPPORTUNISTIC INFECTION is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, *pneumocystis carinii* pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**E** MALIGNANCY

Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?

Yes  Not performed

If performed, since <last authorization>, test result:

Positive  Negative  Pending

If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the TOUCH Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# TYSABRI 6-Month Discontinuation Questionnaire–Crohn’s Disease

Please submit this form to:  
Biogen  
www.touchprogram.com  
Fax: 1-800-840-1278

<Date>

<Prescriber Name>

<Prescriber Address>

<MD Number>

Re: <Patient Name>

Patient Enrollment Number: <Patient TOUCH ID>

Patient date of birth: <MM/DD/YYYY>

Dear <Prescriber Name>,

Our records indicate that <Patient Name> received a final dose of TYSABRI on <MM/DD/YYYY>.

- This Discontinuation Questionnaire is necessary to fulfill the tracking requirements of the TOUCH® Prescribing Program for Crohn’s disease patients treated with TYSABRI. You may also be contacted for additional information in response to answers provided on this form.
- Submit the completed 6-Month Discontinuation Questionnaire to Biogen via TOUCH On-Line ([www.touchprogram.com](http://www.touchprogram.com)) **OR** fax (1-800-840-1278) and place a copy in the patient’s record. This form is mandatory for all discontinued patients.

**A** Is the patient still under <Prescriber Name>’s care?

Yes  No/I don’t know

If **No**, please provide contact information for new prescriber, if available.

Name and phone of new prescriber: \_\_\_\_\_

**B** Is the patient alive?

Yes  No

Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have **not** reported to Biogen:

**C** PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)

Yes  No or  Under investigation

**D** OPPORTUNISTIC INFECTION\* for which they have been hospitalized

Yes  No or  Under investigation

**E** MALIGNANCY

Yes  No or  Under investigation

**F** Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?

Yes  Not performed

If performed, since <last authorization>, test result:

Positive  Negative  Pending

If an anti-JCV antibody index value is available, please record it here: \_\_\_\_\_

\***OPPORTUNISTIC INFECTION** is defined as an infection due to an organism that generally does not cause disease, or causes only mild or self-limited disease in people with normally functioning immune systems, but causes more significant disease in people with impaired immunity. These infections are frequently severe, prolonged, or disseminated. Examples include esophageal candidiasis, systemic fungal infections, pneumocystis carinii pneumonia, mycobacterial infections (including pulmonary and extra-pulmonary tuberculosis), chronic intestinal cryptosporidiosis, and disseminated viral infections (such as disseminated herpes or cytomegalovirus infections).

**TOUCH Certified Prescriber or Delegate Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**(If applicable) Print TOUCH Certified Prescriber or Delegate Name:** \_\_\_\_\_

**Please Note:** A TOUCH certified prescriber or delegate may complete and submit this form on behalf of the certified Prescriber of record. The certified TOUCH Prescriber of record is responsible for compliance with the TOUCH Prescribing Program requirements, including monitoring, evaluation, and management of each patient under his/her care. This questionnaire will be used consistent with the Touch Prescriber/Patient Enrollment Form signed by you and your patient with HIPAA and applicable privacy rules. If you have questions, or if you need additional information, please call 1-800-456-2255.

Please see the Prescribing Information, including **BOXED WARNING**, for more information

# Certified Pharmacy\* Enrollment Form

Please submit this form to:

Biogen

www.touchprogram.com

Fax: 1-800-840-1278

The TOUCH® Prescribing Program was developed as part of the Biogen commitment to patient safety. Only authorized certified pharmacies may dispense to authorized infusion sites. A certified pharmacy may become authorized after it has taken part in compulsory training conducted by Biogen and faxed a completed Enrollment Form to Biogen. Upon receipt of this Enrollment Form, Biogen will send an Authorization Confirmation Letter to provide your Pharmacy Authorization Number and confirm your Shipping Address. This letter will also provide you with the Site Authorization Numbers of any of your associated infusion sites that have been authorized to infuse TYSABRI.

\*A certified pharmacy is located within a hospital, group practice, or infusion site and is associated with an infusion site. Retail pharmacies and wholesalers are excluded from holding inventory and dispensing TYSABRI.

## Certified Pharmacy Shipping Address

Please note that this is the ONLY address to which TYSABRI will be shipped.

Name of Certified Pharmacy \_\_\_\_\_

Contact name \_\_\_\_\_

Address 1 \_\_\_\_\_

NCPDP \_\_\_\_\_

Address 2 \_\_\_\_\_

Title/position \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

Telephone    -    -

Fax    -    -

## Authorized Infusion Site Name

Please list all potential infusion sites that your pharmacy supports. If you need additional space, please attach a separate page.

**1** Name of Infusion Site \_\_\_\_\_

**2** Name of Infusion Site \_\_\_\_\_

Contact name \_\_\_\_\_

Contact name \_\_\_\_\_

Address \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

**3** Name of Infusion Site \_\_\_\_\_

**4** Name of Infusion Site \_\_\_\_\_

Contact name \_\_\_\_\_

Contact name \_\_\_\_\_

Address \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_ ZIP \_\_\_\_\_

I confirm that the above information is correct. I understand that by signing this form this pharmacy agrees to dispense TYSABRI only to authorized infusion sites that have been authorized according to the TOUCH Prescribing Program.

I understand that I am to contact Biogen if my pharmacy name or shipping address changes. By signing below, I understand that I am the TOUCH Trained Representative at the certified pharmacy and am responsible for what is outlined in the "Certified Pharmacy Acknowledgment" below.

## Certified Pharmacy Acknowledgment

- The pharmacy has received training and educational materials on the TOUCH Prescribing Program for use in the following indication(s):  
 MS  CD (check all that apply)
- Certified pharmacies may dispense TYSABRI only to authorized infusion sites
- I understand that, per the requirements of the TOUCH Prescribing Program, this certified pharmacy's compliance may be reviewed by the Food and Drug Administration (FDA), and/or audited by Biogen, and/or a third party designated by Biogen
- I understand that noncompliance with the requirements of the TOUCH Prescribing Program may result in my pharmacy no longer being enrolled and termination of our participation in the program

Responsible party acknowledgment: \_\_\_\_\_ Date: \_\_\_\_\_

Name: \_\_\_\_\_ Title: \_\_\_\_\_

Please see the Prescribing Information, including **BOXED WARNING**, for more information



# Infusion Site Enrollment Form

Please submit this form to:  
 Biogen  
 www.touchprogram.com  
 Fax: 1-800-840-1278

The TOUCH® Prescribing Program was developed as part of the Biogen commitment to patient safety. Only authorized infusion sites may receive shipments of and infuse TYSABRI. An infusion site may become authorized only after it has taken part in compulsory training conducted by Biogen and faxed a completed Enrollment Form to Biogen. Upon receipt of this Enrollment Form, Biogen will send an authorization confirmation letter to provide your Site Authorization Number and confirm your Shipping Address.

## Infusion Site Address (address where patient is infused)

Name of Infusion Site _____			Contact name _____		
Address 1 _____			Telephone <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>		
Address 2 _____			Fax <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>		
City _____	State _____	ZIP _____			

## Method of acquiring TYSABRI

**1** Infusion site will acquire TYSABRI directly. If YES, check all that apply:  Buy/Bill  Assignment of Benefits/Specialty Pharmacy

OR

**2** Infusion site will acquire through a certified pharmacy.\*

\*A certified pharmacy is located within a hospital, group practice, or infusion site and is associated with an infusion site. Retail pharmacies and wholesalers are excluded from holding inventory and dispensing TYSABRI.

## Shipping Address (address to which drug will be shipped)

Check here if address is same as above. Please note that this is the ONLY address to which TYSABRI will be shipped.

Name of Infusion Site or Certified Pharmacy _____			Contact name _____		
Address 1 _____			Telephone <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>		
Address 2 _____			Fax <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>		
City _____	State _____	ZIP _____			

I understand that I am to contact Biogen if my infusion site name, administration address or shipping address changes. By signing below, I understand that I am the TOUCH Trained Representative at the infusion site and am responsible for what is outlined in the "Infusion Site Acknowledgment" below.

## Infusion Site Acknowledgment

- The infusion site has received training and educational materials on the TOUCH Prescribing Program for use in the following indication(s):  MS  CD (check all that apply)
- I understand that TYSABRI will be administered only to patients who are currently authorized in the TOUCH Prescribing Program. Patient authorization must be confirmed *prior to each infusion* by:
  - For TOUCH On-Line infusion sites: Patient Authorization Status must be "Authorized" or
  - For paper-based infusion sites: Receipt of current Notice of Patient Authorization and verification that no Notice of Patient Discontinuation is on file
- I understand that each patient will receive a copy of the TYSABRI Patient Medication Guide *prior to each infusion*
- I understand that a TYSABRI Pre-infusion Patient Checklist must be completed *prior to each infusion*. The Pre-infusion Patient Checklist must be submitted to Biogen within 1 business day of the patient visit regardless of whether or not the patient received the infusion by:
  - For paper-based infusion sites: sending a copy of the completed Pre-infusion Patient Checklist to Biogen. A copy must also be placed in the patient's medical record
  - For TOUCH On-Line infusion sites: the infusion nurse can read, complete and submit the Pre-Infusion Patient Checklist directly in TOUCH On-Line
- I understand that, per the requirements of the TOUCH Prescribing Program, this infusion site's compliance may be reviewed by the Food and Drug Administration (FDA), and/or audited by Biogen and/or a third party designated by Biogen
- I understand that noncompliance with the requirements of the TOUCH Prescribing Program will result in de-enrollment of the infusion site and termination of the authorization to infuse TYSABRI

Responsible party acknowledgment: \_\_\_\_\_ Date: \_\_\_\_\_

Name: \_\_\_\_\_ Title: \_\_\_\_\_

Please see the Prescribing Information, including **BOXED WARNING**, for more information

