Risk Evaluation and Mitigation Strategy (REMS) Document

Tysabri (natalizumab) REMS Program

Tysabri Outreach: Unified Commitment to Health (TOUCH) Prescribing Program (Multiple Sclerosis & Crohn’s Disease)

I. Administrative Information

Application Number: BLA 125104
Application Holder: Biogen, Inc
Initial REMS Approval: 10/2011
Most Recent REMS Update: 12/2021

II. REMS 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.

REMS Requirements

Biogen must ensure that health care providers, patients, pharmacies, infusion sites, and wholesalers-distributors comply with the following requirements:

1. Health Care Providers who prescribe Tysabri must:

   To become certified to prescribe

   1. Review the drug’s Prescribing Information.

   2. Review the following: Educational Slide Set, Overview, and Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI (Multiple Sclerosis) or Understanding PML for Gastroenterologists (Crohn’s Disease).

   3. Enroll in the REMS by completing the Prescriber/Patient Enrollment Form - Multiple Sclerosis or Prescriber/Patient Enrollment Form - Crohn’s Disease and submitting it to the REMS Program.

   Before treatment initiation (first dose)

   4. Counsel the patient using the Medication Guide and Prescriber/Patient Enrollment Form – Multiple Sclerosis or Prescriber/Patient Enrollment Form – Crohn’s Disease. Provide a copy of the materials to the patient.
5. Enroll the patient by completing and submitting the Prescriber/Patient Enrollment Form – Multiple Sclerosis or Prescriber/Patient Enrollment Form – Crohn’s Disease to the REMS Program.

6. Assess the patient’s risk factors that increase the risk of progressive multifocal leukoencephalopathy.

During treatment, 3 months after the first infusion

7. Assess the patient’s signs, symptoms and risk factors for progressive multifocal leukoencephalopathy.

During treatment, 6 months after the first infusion and every 6 months thereafter

8. Assess the patient’s signs, symptoms and risk factors for progressive multifocal leukoencephalopathy and whether the patient should continue treatment. Document and submit the results to the REMS Program using the Patient Status Report and Reauthorization Questionnaire – Multiple Sclerosis or Patient Status Report and Reauthorization Questionnaire – Crohn’s Disease.

After treatment discontinuation; initially

9. Assess the patient’s signs and symptoms for progressive multifocal leukoencephalopathy. Document and submit to the REMS Program using the Initial Discontinuation Questionnaire - Multiple Sclerosis or Initial Discontinuation Questionnaire - Crohn’s Disease.

After treatment discontinuation; 6 months later

10. Assess the patient’s signs and symptoms for progressive multifocal leukoencephalopathy. Document and submit to the REMS Program using the 6-Month Discontinuation Questionnaire - Multiple Sclerosis or 6-Month Discontinuation Questionnaire - Crohn’s Disease.

At all times

11. Report cases of progressive multifocal leukoencephalopathy, hospitalizations due to opportunistic infection, or deaths to the Manufacturer.

2. Patients who are prescribed Tysabri:

Before treatment initiation

1. Review the Medication Guide and the Prescriber/Patient Enrollment Form - Multiple Sclerosis or Prescriber/Patient Enrollment form - Crohn’s Disease.

2. Receive counseling from the prescriber on the benefits and risks of treatment, need to promptly report any new or worsening symptoms that persist over several days, especially nervous system symptoms.

3. Enroll in the REMS Program by completing the Prescriber/Patient Enrollment Form - Multiple Sclerosis or Prescriber/Patient Enrollment form - Crohn’s Disease with the prescriber. Enrollment information will be provided to the REMS Program.

4. Be monitored for risk factors that increase the risk of progressive multifocal leukoencephalopathy.

During treatment, before each infusion

5. Review the Medication Guide.

6. Bring a list of medicines and treatments taken during the last month.
7. Be monitored for signs, symptoms, and risk factors for progressive multifocal leukoencephalopathy.

<table>
<thead>
<tr>
<th>During treatment, 3 months and 6 months after the first infusion, and every 6 months thereafter</th>
<th>8. Be monitored for signs, symptoms, and risk factors for progressive multifocal leukoencephalopathy and the appropriateness of continuing Tysabri.</th>
</tr>
</thead>
<tbody>
<tr>
<td>After treatment discontinuation; initially and 6 months later</td>
<td>9. Be monitored for signs and symptoms of progressive multifocal leukoencephalopathy.</td>
</tr>
<tr>
<td>At all times</td>
<td>10. Notify the REMS Program if you switch physicians or infusion sites.</td>
</tr>
<tr>
<td>11. Inform the prescriber of new or worsening symptoms that last several days especially nervous system symptoms including new or sudden change in thinking, eyesight, balance, or strength, and other new or worsening symptoms.</td>
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3. **Pharmacies that dispense Tysabri must:**

<table>
<thead>
<tr>
<th>To become certified to dispense</th>
<th>1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Take training provided by Biogen.</td>
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<tr>
<td>3. Have the authorized representative enroll in the REMS Program by completing the Pharmacy Enrollment Form and submitting it to the REMS Program.</td>
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<tr>
<td>4. Establish processes and procedures to verify the infusion site is authorized.</td>
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<tr>
<td>Before dispensing</td>
<td>5. Verify that the infusion site is authorized through the processes and procedures established as a requirement of the REMS Program.</td>
</tr>
<tr>
<td>At all times</td>
<td>6. Maintain records of the pharmacy’s Site Authorization Confirmation.</td>
</tr>
<tr>
<td>7. Comply with audits carried out by Biogen or a third party acting on behalf of Biogen to ensure that all processes and procedures are in place and are being followed.</td>
<td></td>
</tr>
</tbody>
</table>

4. **Infusion sites that dispense Tysabri must:**

<table>
<thead>
<tr>
<th>To become certified to dispense</th>
<th>1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the infusion site.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Take training provided by Biogen.</td>
<td></td>
</tr>
</tbody>
</table>
3. Have the authorized representative enroll in the REMS Program by completing the **Infusion Site Enrollment Form** and submitting it to the REMS Program.

Before administering

4. Obtain authorization to dispense each infusion for administration by contacting the REMS Program or confirm receipt of a Notice of Patient Authorization and no Notice of Patient Discontinuation to verify the patient is authorized to receive the drug.

5. Provide the patient with the **Medication Guide**.

6. Assess the patient’s health status for signs, symptoms and risk factors of progressive multifocal leukoencephalopathy. Document using the **Pre-Infusion Patient Checklist**.

During treatment, within 1 business day of the patient visit for infusion

7. Submit the **Pre-Infusion Patient Checklist** to the REMS Program regardless of whether the patient receives the infusion.

At all times

8. Maintain records of the infusion site’s Site Authorization Confirmation.

9. Comply with audits carried out by Biogen or a third party acting on behalf of Biogen to ensure that all processes and procedures are in place and are being followed.

### 5. Wholesaler-distributors that distribute Tysabri must:

To be able to distribute

1. Establish processes and procedures to ensure that the drug is distributed only to certified pharmacies and infusion sites.

2. Train all relevant staff involved in distributing on the REMS Program requirements.

At all times

3. Distribute only to certified pharmacies and infusion sites.

4. Maintain records to support that all processes and procedures are in place and are being followed.

5. Comply with audits carried out by Biogen or a third party acting on behalf of Biogen to ensure that all processes and procedures are in place and are being followed.

**Biogen must provide training to health care providers who prescribe Tysabri.**

The training includes the following educational materials: **Educational Slide Set**, **Overview**, and either **Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI (Multiple Sclerosis)** or **Understanding PML for Gastroenterologists (Crohn’s Disease)**. The training must be provided online or in a hard-copy format via mail or fax.

**Biogen must provide training to pharmacies and infusion sites that dispense Tysabri.** The training includes the following educational materials: **Educational Slide Set**, **Overview**, **Pre-Infusion Checklist**. The training must be provided online, or in a hard-copy format via mail or fax.
To support REMS Program operations, Biogen must:

1. Authorize dispensing for each patient based on receipt of the Prescriber/Patient Enrollment Form-Multiple Sclerosis or Prescriber/Patient Enrollment Form-Crohn’s Disease; and Patient Status Report and Reauthorization Questionnaire-Multiple Sclerosis or Patient Status Report and Reauthorization Questionnaire-Crohn’s Disease on the following schedule:

   Authorize the first dispensing based on receipt of the Prescriber/Patient Enrollment Form-Multiple Sclerosis or Prescriber/Patient Enrollment Form-Crohn’s Disease. If a completed Prescriber/Patient Enrollment Form-Multiple Sclerosis or Prescriber/Patient Enrollment Form-Crohn’s Disease is not received, the patient is not authorized to receive the drug.

   For subsequent dispensings, authorize dispensing based on receipt of a valid Patient Status Report and Reauthorization Questionnaire-Multiple Sclerosis or Patient Status Report and Reauthorization Questionnaire-Crohn’s Disease. The Patient Status Report and Reauthorization Questionnaire-Multiple Sclerosis or Patient Status Report and Reauthorization Questionnaire-Crohn’s Disease must be completed every 6 months. If a valid Patient Status Report and Reauthorization Questionnaire-Multiple Sclerosis or Patient Status Report and Reauthorization Questionnaire-Crohn’s Disease is not on file, the patient is not authorized to receive the drug until the completed forms are received.

2. Establish and maintain a REMS Program website, TOUCH On-Line. The REMS Program website must include the capability to complete prescriber, pharmacy, and infusion site certification or enrollment online, the capability to enroll and manage patients online, and the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).

3. Make the REMS Program website fully operational and REMS materials available through website or call center.

4. Establish and maintain a REMS Program call center for REMS participants at 1-800-456-2255.

5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the Tysabri REMS Program.

6. Ensure health care providers, patients, pharmacies, and infusion sites, are able to complete prescriber, patient, pharmacy, and infusion site certification or enrollment, complete pre-infusion checklists, report patient status, reauthorize patients, report patient discontinuation, or report a change in prescriber online or via a paper-based process.

7. Ensure infusion sites are able to obtain patient authorization before each infusion online and by fax:

   a. For TOUCH On-Line infusion sites: obtain the patient authorization status through TOUCH On-Line
   b. For paper-based/fax infusion sites: provide the current Notice of Patient Authorization or Notice of Patient Discontinuation

8. Notify prescribers after they become certified in the REMS Program.

9. Notify pharmacies and infusion sites after they become certified in the REMS Program by providing a Site Authorization Confirmation.

10. Provide certified prescribers access to the database of certified pharmacies, certified infusion sites, and enrolled patients.

11. Provide certified pharmacies access to the database of certified infusion sites and enrolled patients.

12. Provide certified infusion sites access to the database of enrolled patients.

To ensure REMS participants’ compliance with the REMS Program, Biogen must:

13. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: drug distribution and dispensing; certification of prescribers, pharmacies,
and infusion sites; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.

14. Establish a plan for addressing noncompliance with REMS Program requirements.

15. Monitor certified prescribers, pharmacies, infusion sites, and wholesaler-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including de-certification.

16. Audit infusion sites, certified pharmacies, specialty pharmacies, and the wholesaler-distributor(s) in accordance with the audit plan each year to ensure compliance with respective REMS requirements.

17. Take reasonable steps to improve implementation of and compliance with the requirements in the Tysabri REMS Program based on monitoring and evaluation of the Tysabri REMS Program.

III. REMS Assessment Timetable

Biogen must 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 calendar days before the submission date for that assessment. Biogen must submit each assessment so that it will be received by the FDA on or before the due date.

IV. REMS Materials

The following materials are part of the Tysabri REMS:

**Enrollment Forms**

**Prescriber:**

1. Prescriber/Patient Enrollment Form - Multiple Sclerosis
2. Prescriber/Patient Enrollment Form - Crohn’s Disease

**Patient:**

3. Prescriber/Patient Enrollment Form - Multiple Sclerosis
4. Prescriber/Patient Enrollment Form - Crohn’s Disease

**Pharmacy:**

5. Pharmacy Enrollment Form

**Infusion sites:**

6. Infusion Site Enrollment Form

**Training and Educational Materials**

**Prescriber:**

7. Educational Slide Set
8. Overview
9. Helpful Information for Evaluation of New Neurologic Symptoms in Patients Receiving Tysabri (Multiple Sclerosis)
10. Understanding PML for Gastroenterologists (Crohn’s Disease)
Patient:
  11. Medication Guide

Pharmacy:
  12. Educational Slide Set
  13. Overview

Infusion sites:
  14. Educational Slide Set
  15. Overview

**Patient Care Forms**
  16. Pre-Infusion Patient Checklist
  17. Patient Status Report and Reauthorization Questionnaire - Multiple Sclerosis
  18. Patient Status Report and Reauthorization Questionnaire - Crohn’s Disease
  19. Initial Discontinuation Questionnaire - Multiple Sclerosis
  20. Initial Discontinuation Questionnaire - Crohn’s Disease
  21. 6-Month Discontinuation Questionnaire - Multiple Sclerosis
  22. 6-Month Discontinuation Questionnaire - Crohn’s Disease

**Other Materials**
  23. REMS Program website
  24. Change Prescriber Authorization Form
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)

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

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

Patient name: ___________________________ Date of birth: ______ / ______ / ______ (MM/DD/YYYY)

Patient signature (or personal representative): ___________________________ Date: __________

Authority of personal representative (if applicable): ___________________________
Patient History

Patient name: ___________________________ DOB: __________ / __________ / ________

Date of first MS symptoms: __________ / __________ / ________

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

Aubagio® □ AVONEX® □ Azathioprine □ Bafiertam® □ Betaseron® □ Copaxone® □ Cyclophosphamide □

Dimethyl Fumarate □ Extavia® □ Gilenya® □ Kesimpta® □ Lemtrada® □ Mavenclad® □ Mayzent® □

Methotrexate □ Mitoxantrone □ Mycophenolate □ Ocrevus® □ PLEGRIDY® □ Ponvory™ □ Rebif® □

TECFIDERA® □ TYSABRI® □ VUMERITY® □ Zeposia® □ Other □

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

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 _______ M I _______ Last _______

Street address

City __________________ State _______ ZIP _______

Telephone □□□□-□□□□-□□□□
Fax □□□□-□□□□-□□□□
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: ________/______/______ (MM/DD/YYYY)

Prescriber signature: ___________________________ Date: ___________________________
Date of birth: ___________ / ___________ / ___________ (MM/DD/YYYY)  
Patient name: ____________________________________________ 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: __________________________

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**Infusion Site Information***

1. **Prescriber will administer TYSABRI** and request the following services (check only one):
   - [ ] No services required
   - [ ] Forward this prescription to a specialty pharmacy provider to investigate pharmacy coverage and coordinate delivery to prescriber’s office
   - [ ] 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
   - [ ] I am referring the patient to the following infusion site or healthcare provider:

   Name of infusion site: __________________________
   Name of healthcare provider (First, Last): __________________________
   Street address or site Authorization Number: __________________________
   City: __________________________ State: __________________________ ZIP: __________________________

   Office contact:
   Telephone: __________________________
   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.

If you are a California resident, California law provides you with additional rights regarding our collection and use of your personal information. This includes providing you with information about the categories of personal information that we collect and how we use it, described in more detail at: https://www.biogen.com/en_us/california-policy.html.
### Patient Information

<table>
<thead>
<tr>
<th>Date of birth: __________ / __________ / __________</th>
<th>(MM/DD/YYYY)</th>
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<tbody>
<tr>
<td>Patient name: ___________________________________</td>
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<tr>
<td>First</td>
<td>MI</td>
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<td>Street address: ___________________________________</td>
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<tr>
<td>City</td>
<td>State</td>
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<td>Work Telephone: ________<strong>-</strong>_____<strong>-</strong>_____<strong>-</strong>_______</td>
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<tr>
<td>Home Telephone: ________<strong>-</strong>_____<strong>-</strong>_____<strong>-</strong>_______</td>
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<tr>
<td>Patient may be contacted at Home [ ] Work [ ] Best time: __________</td>
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<tr>
<td>Female [ ] Male [ ]</td>
<td>E-mail address: ____________________________</td>
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### 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): __________________________

TSD-US-0025 V6
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: ________________ /________ /________  (MM/DD/YYYY)

Patient signature (or personal representative): ________________________________  Date: ________________

Authority of personal representative (if applicable): ________________________________
Prescriber/Patient Enrollment Form—Crohn’s Disease
Completion of all pages required.

Patient History

Patient name: ___________________________ DOB: __________/________/________

First    MI    Last

Date of first Crohn’s disease symptoms: __________/________/________

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.)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Ongoing</th>
<th>OR</th>
<th>Stopped</th>
<th>Medication</th>
<th>Ongoing</th>
<th>OR</th>
<th>Stopped</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Methotrexate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remicade®</td>
<td></td>
<td></td>
<td></td>
<td>Systemic steroids</td>
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</tr>
<tr>
<td>Humira®</td>
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<td></td>
<td>Entyvio®</td>
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<td></td>
</tr>
<tr>
<td>Azathioprine or Mercaptopurine or Thioguine</td>
<td></td>
<td></td>
<td></td>
<td>Other immunomodulatory therapy or immunosuppressant therapy (not including aminosalicylates)</td>
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<td></td>
</tr>
<tr>
<td>Cimzia®</td>
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</tr>
</tbody>
</table>

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 Thioguine ☒
- 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

City    State    ZIP

Telephone ☐ ☐ ☐-☐☐☐☐-☐☐☐☐

Fax ☐ ☐ ☐-☐☐☐☐-☐☐☐☐
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: _______ / _______ / _______ (MM/DD/YYYY)

Prescriber signature: ___________________________ Date: _____________

Reference ID: 4902920
## Prescriber/Patient Enrollment Form—Crohn’s Disease

Completion of all pages required.

### Patient Information

**Date of birth:** __________/________/________  
**Patient name:** ______________________________________________________________________

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  
   - [ ] Forward this prescription to a specialty pharmacy provider to investigate pharmacy coverage and coordinate delivery to prescriber’s office  
   - [ ] 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  
   - [ ] I am referring the patient to the following infusion site or healthcare provider

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

**Street address or Site Authorization Number**

**City** __________  
**State** __________  
**ZIP** __________

**Office contact**

**Telephone** __________-________-________

**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.

If you are a California resident, California law provides you with additional rights regarding our collection and use of your personal information. This includes providing you with information about the categories of personal information that we collect and how we use it, described in more detail at: [https://www.biogen.com/en_us/california-policy.html](https://www.biogen.com/en_us/california-policy.html).
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 pharmacy is defined as a certified pharmacy 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.

### Pharmacy Enrollment Form

**Certified Pharmacy Shipping Address**

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

<table>
<thead>
<tr>
<th>Name of Certified Pharmacy</th>
<th>Contact name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address 1</td>
<td></td>
</tr>
<tr>
<td>Address 2</td>
<td></td>
</tr>
<tr>
<td>City</td>
<td>State</td>
</tr>
</tbody>
</table>

**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**
   - Contact name
   - Address
   - City State ZIP

2. **Name of Infusion Site**
   - Contact name
   - Address
   - City State ZIP

3. **Name of Infusion Site**
   - Contact name
   - Address
   - City State ZIP

4. **Name of Infusion Site**
   - Contact name
   - Address
   - 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
- 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.
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

Address 1

Address 2

City State ZIP

Contact name

Telephone

Fax

**Method of acquiring TYSABRI**

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

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

Address 1

Address 2

City State ZIP

Contact name

Telephone

Fax

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

TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.
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.
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.
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).
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.
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.
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.

- Cases of neonatal thrombocytopenia, at times associated with anemia, have been reported in newborns with in utero exposure to TYSABRI. A CBC should be obtained in neonates with in utero exposure to TYSABRI.
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%).
The most common adverse reactions reported at an incidence of ≥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 ≥ 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
Receive TYSABRI
There are 3 main components of the TOUCH Prescribing Program:

- **Enroll**
  - Prescribers and Patients
  - Infusion Sites
  - Pharmacies

- **Infuse**
  - TYSABRI® is only administered to enrolled patients with a current status of ‘Authorized’
  - Pre-infusion Patient Checklist is completed and submitted to the TOUCH Prescribing Program

- **Track**
  - Patients are tracked longitudinally to gather important safety information

NOTE: This overview of the TOUCH Prescribing Program components does not include a complete list of the program requirements.
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?
Tools to Support the TOUCH Prescribing Program – MS

- Enrollment Forms
  - Prescriber/Patient
  - Infusion Site
  - Pharmacy
- Patient Medication Guide
- Notice of Patient Authorization
- 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
  - 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**

TouchOn-Line
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

➤ 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?
Prescriber/Patient Enrollment
How do prescribers and patients enroll?

**Education**

Prescriber and Patient discuss TYSABRI® as a treatment option

- Prescriber and patient discuss TYSABRI® as a treatment option.
- Patient reads the Patient Medication Guide and discusses the benefits and risks of TYSABRI with his/her prescriber.

**Treatment Decision**

- Prescriber reviews Pre-infusion Patient Checklist with the patient.
- Patient reads the Patient Medication Guide and discusses the benefits and risks of TYSABRI with his/her prescriber.

**Enrollment**

- Prescriber and patient complete, sign, and fax ALL PAGES of the Prescriber/Patient Enrollment Form to the TOUCH Prescribing Program to initiate therapy.
- TOUCH Case Manager confirms that all paperwork is complete and updates patient status to ‘Authorized’.

**Authorization**

- Touch Case Manager sends a Notice of Patient Authorization and a copy of the Prescriber/Patient Enrollment Form to the authorized Infusion Site.

Reference ID: 4902920
Enrollment Tools

- Enroll
- Infuse
- Track
Helpful Information for Evaluation of New Neurological Symptoms in Patients Receiving TYSABRI®

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.
Enrollment Tools

Enroll

Infuse

Track
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

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.
Infusion Site Enrollment
How does an Infusion Site enroll?

A Biogen representative provides mandatory indication-specific TOUCH Prescribing Program training to Infusion Site*

TOUCH Prescribing Program confirms that all paperwork is complete, assigns a Site Authorization Number, and provides Site Authorization Confirmation to the Infusion Site

Infusion Site completes and faxes the Infusion Site Enrollment Form to TOUCH Prescribing Program

* NOTE: Infusion Sites must select to receive training and education materials on MS TOUCH, CD TOUCH, or both.

A patient will be matched **ONLY** with Infusion Sites that have been trained on the program materials related to his/her indication.
Certified Pharmacy Enrollment
A Biogen representative provides training to the Certified Pharmacy regarding the TOUCH Prescribing Program.

TOUCH Prescribing Program confirms that all paperwork is complete, assigns a Site Authorization Number, and provides Site Authorization Confirmation to the Certified Pharmacy.

Certified Pharmacy completes and faxes the Pharmacy Enrollment Form to TOUCH Prescribing Program.

*A pharmacy is defined as a certified pharmacy located within a hospital, group practice, or infusion site and is associated with an infusion site.
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?
Infusion Overview

- Enroll
- Infuse
- Track
**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:

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 patients during all infusions. Post-infusion, for the first 12 infusions, observe patients for 1 hour after the infusion is complete. For patients who have received 12 infusions without evidence of a hypersensitivity reaction, observe patients post-infusion for the 13th and subsequent infusions according to clinical judgment.

Submit completed Pre-infusion Patient Checklist via TOUCH On-Line* within 1 business day.
Checking Patient Authorization Status

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
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

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

What is the TOUCH Prescribing Program?

What tools support the TOUCH Prescribing Program?
- MS TOUCH Educational Materials
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What is the enrollment process?

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How are patients tracked?

What is TOUCH On-Line?
Tracking Overview

- Enroll
- Infuse
- Track
Since starting TYSABRI therapy has the patient been diagnosed with any of the following that you have not reported to the TOUCH Program:

- THERAPEUTIC: Infections (including disseminated herpes or cytomegalovirus infections).
- THERAPEUTIC: Demyelinating disease, or other conditions that generally does not cause disease, or causes only mild or self-limited fungal infections, or self-limited disease in people with normally functioning immune system.

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

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

Enroll
Infuse
Track
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)  

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

Initial and 6-Month Discontinuation Questionnaire*

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

- Enroll
- Infuse
- Track
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)

Patient Status Report and Reauthorization Questionnaire (Every 6 months)

Initial and 6-Month Discontinuation Questionnaire*

*NOTE: Discontinuation Questionnaires are ONLY sent upon notification of discontinuation and again six months following discontinuation of TYSABRI.
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?
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
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.
Overview of the TOUCH Program

Please see the Prescribing Information, including BOXED WARNING, for more information.
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-α. TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine or methotrexate) or inhibitors of TNF-α

Why the program was developed
Biogen is committed to patient safety. The TOUCH® 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.

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

- Patients advise prescribers of any new signs and symptoms and keep track of any concurrently used medications
- Prescriber and patient discuss the potential benefits and known risks of TYSABRI, including PML, and enroll in TOUCH Prescribing Program
- TOUCH Prescribing Program assures that the patient is assigned to an authorized infusion site
- Pre-infusion Patient Checklist is administered at every infusion visit to determine whether patient can be infused
- Every 6 months, the prescriber determines whether the patient will be reauthorized to receive TYSABRI for the next 6 months

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.
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.

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

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


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.
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

<table>
<thead>
<tr>
<th></th>
<th>MS relapse</th>
<th>PML</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ONSET</strong></td>
<td>Acute</td>
<td>Subacute</td>
</tr>
<tr>
<td><strong>EVOLUTION</strong></td>
<td>➢ Over hours to days</td>
<td>➢ Days to weeks</td>
</tr>
<tr>
<td></td>
<td>➢ Normally stabilize</td>
<td>➢ Progressive</td>
</tr>
<tr>
<td></td>
<td>➢ Resolve spontaneously or with treatment</td>
<td></td>
</tr>
<tr>
<td><strong>CLINICAL</strong></td>
<td>➢ Diplopia</td>
<td>➢ Cortical symptoms/signs</td>
</tr>
<tr>
<td><strong>PRESENTATION</strong></td>
<td>➢ Paresthesia</td>
<td>➢ Behavioral and</td>
</tr>
<tr>
<td></td>
<td>➢ Paraparesis</td>
<td>neuropathological alteration</td>
</tr>
<tr>
<td></td>
<td>➢ Optic neuritis</td>
<td>➢ Retrochiasmal visual deficits</td>
</tr>
<tr>
<td></td>
<td>➢ Myelopathy</td>
<td>➢ Seizures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>➢ Hemiparesis</td>
</tr>
</tbody>
</table>

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

New neurological symptoms suggestive of non–MS-related disease

1 SUSPEND DOSING

* If PML is suspected based on clinical presentation and an MRI is not readily available, cerebrospinal fluid (CSF) assessment to exclude PML should be considered prior to MRI.

2 MRI assessment

- PML excluded
- JCV not detected and low clinical suspicion

Dosing may be resumed

3 CSF assessment

- JCV detected and high clinical suspicion

Treat as PML

- Monitor for IRIS

4 JCV not detected

Repeat assessment

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.
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 — 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**

<table>
<thead>
<tr>
<th>T1-weighted imaging</th>
<th>T2-weighted imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
</tr>
<tr>
<td>Large hypointense lesion in the region of the right occipital lobe (angular gyrus and intraparietal sulcus).</td>
<td>Typical multifocal affection of PML, with additional lesions in the white matter of the left frontal temporal and occipital lobes. Note sparing of gray matter.</td>
</tr>
</tbody>
</table>


Please see the Prescribing Information, including **BOXED WARNING**, for more information.
Table 2. MRI lesion characteristics typical of PML and MS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MS Lesions</th>
<th>PML Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Periventricular perpendicular to ventricles (Dawson’s fingers), deep white matter, isolated U fibers, cerebellum, and spinal cord</td>
<td>Subcortical WM in parietal, occipital, or frontal lobes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Follows WM tracks. Can cross the corpus callosum to contralateral hemisphere (butterfly pattern) or extend through internal capsule</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No spinal cord involvement</td>
</tr>
<tr>
<td><strong>Appearance</strong></td>
<td>Well-defined borders</td>
<td>Infiltrating, ill-defined, confluent WM lesions which can be multifocal</td>
</tr>
<tr>
<td><strong>Mass effect</strong></td>
<td>Large lesions can have a mass effect</td>
<td>Rare even in large lesions</td>
</tr>
<tr>
<td><strong>FLAIR</strong></td>
<td>Flair = T2</td>
<td>Flair more sensitive for detection of PML lesions in subcortical location</td>
</tr>
<tr>
<td><strong>T1W pre-contrast</strong></td>
<td>Isointense or mildly hypointense to Grey matter</td>
<td>Isointense with progressive hypointensity</td>
</tr>
<tr>
<td><strong>T1 post contrast</strong></td>
<td>Homogeneous or ring-enhancement—resolves in 1-2 months</td>
<td>Patchy, punctate, or linear</td>
</tr>
</tbody>
</table>

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, α4-integrin receptor binding remained high—a potential sign of continued inhibition of α4-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 α4-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

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

To report an adverse event, contact:

Biogen

Telephone: 1-800-456-2255
Please see the Prescribing Information, including BOXED WARNING, for more information.
Understanding PML for Gastroenterologists

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.¹

About PML

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

How to Recognize PML

Typical symptoms associated with PML are diverse, progress over days to weeks, and include³⁴:
- 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.³ 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.⁴ 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.¹
Action Steps if PML Is Suspected

➤ TYSABRI dosing should be suspended immediately in all cases in which PML is suspected.
➤ Immediate referral to a neurologist for assessment, potentially including:
  — 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

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-α, and who are not taking concomitant immunosuppressants (e.g., 6-mercaptopurine, azathioprine, or methotrexate) or concomitant inhibitors of TNF-α.

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-α. TYSABRI should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

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.
- 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.
- 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 ≥10% with TYSABRI and ≥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:

Please see the Prescribing Information, including **BOXED WARNING**, for more information.
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 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
  - 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
  - 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
  - strength
  - weakness on 1 side of your body
  - balance
  - 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. TYSABRI may cause low platelets, and in some cases also low red blood cells (anemia), in your newborn baby if you take TYSABRI while you are pregnant. It is not known if TYSABRI can cause birth defects.
- 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
  - 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
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 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
### Pre-infusion Patient Checklist

**As a condition of your site’s authorization to infuse TYSABRI® (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) 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® On-Line (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).

<table>
<thead>
<tr>
<th>Is the patient currently authorized to receive TYSABRI?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

**Note:** If authorization cannot be verified on-line at 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 |

**Note:** If the patient has not read the Patient Medication Guide, 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?

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 your body is not able to fight infections well?

3. **Crohn’s disease ONLY**
   - 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.)

3. **MS ONLY**
   - 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.)

#### 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.

- 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

<table>
<thead>
<tr>
<th>Not infused</th>
<th>Date infused (MM/DD/YYYY):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>__________________________</td>
</tr>
</tbody>
</table>

| Next Scheduled Appointment (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 OR fax to 1-800-840-1278.

Reference ID: 4902920
Examples of Immunosuppressants, Antineoplastics, and Immunomodulators

### Multiple Sclerosis

- **Approved MS Therapies:**
  - Alemtuzumab (Lemtrada®)
  - Cladribine (Mavenclad®)
  - Dimethyl fumarate (TECFIDERA®)
  - Dipsomel fumarate (VUMERTY®)
  - Fingolimod (Gilenya®)
  - Gilatam acetate (Copaxone®)
  - Interferon beta-1a (Rebi®)
  - Interferon beta-1b (Betaseron®, Extavia®)
  - Mitoxantrone

- **Immunosuppressants/Antineoplastics:**
  - Azathioprine (Imuran®, Azasan®)
  - Cladribine (Leustatin®)
  - Cyclophosphamide (Cytoxan®, Neosar®)
  - Cyclosporine (Sandimmune®, Neoral®)
  - Fludarabine phosphate (Fludara®)
  - Leflunomide (Arava®)
  - Methotrexate (Methotrex®)
  - Mycophenolate mofetil (CellCept®)
  - Pemetrexed (Alimta®)

- **Additional Immunomodulators and Immunosuppressants:**
  - Other interferons (Actimmune®, Infergen®, Intron® A, Pegasys®, PEG-Intron®, Rebetron®, 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-α inhibitors for Crohn’s disease:**
  - Infliximab (Remicade®)
  - Adalimumab (Humira®)

- **Immunosuppressants/Antineoplastics:**
  - Approved TNF-α inhibitors
  - Azathioprine (Imuran®, Azasan®)
  - Chlorambucil (Leukeran®)
  - Cladribine (Leustatin®)
  - Cyclophosphamide (Cytoxan®, Osol®)
  - Cyclosporine (Sandimmune®, Neoral®)
  - Fludarabine phosphate (Fludara®)
  - Leflunomide (Arava®)
  - Mercaptopurine (Purinethol®)
  - Methotrexate (Methotrex®)
  - Mycophenolate mofetil (CellCept®)
  - Pemetrexed (Alimta®)
  - Thioguanine (Tabloid®)

- **Additional Immunomodulators and Immunosuppressants:**
  - Interferon beta-1a (Rebi®, 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®, Rebetron®, Roferon®-A)
  - Rituximab (Rituxan®)
  - Trastuzumab (Herceptin®)
  - Vedolizumab (Entyvio®)

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**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.

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

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)
☐ Yes  ☐ No or ☐ Under investigation

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

MALIGNANCY
☐ Yes  ☐ No or ☐ Under investigation

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: ___  ___  ___  ___  ___  ___  ___  ___

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.

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:

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:

Aubagio®
AVONEX®
Bafiertam®
Betaseron®
Copaxone®
Extavia®
Gilenya®
Kesimpta®
Lemtrada®
Mavenclad®
Mayzent®
Ocrevus®
PLEGRIDY®
PonvyrtM
Rebia®
TECFIDERA®
VUMERITY®
Zeposia®
Azathioprine
Chronic systemic steroids
Cyclophosphamide
Dimethyl fumarate
Methotrexate
Mitoxantrone
Mycophenolate
Other immuno-modulatory or immuno-suppressant therapy

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).
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

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: _____ _____ _____

**F** 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

**G** 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.

**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.


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

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)
- Yes
- No
- Under investigation

OPPORTUNISTIC INFECTION* for which they have been hospitalized
- Yes
- No
- Under investigation

MALIGNANCY
- Yes
- No
- Under investigation

Since <last authorization>, has the patient been tested for the presence of anti-JCV antibodies?
- Yes
- No
- 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: ____________

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.

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: __________________________________________

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:

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).

*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).
Dear <MD Name>,

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

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

- PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)
  - Yes
  - No or
  - Under investigation

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

- MALIGNANCY
  - Yes
  - No or
  - Under investigation

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: ______._____._____.

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:

- PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)
  - Yes
  - No or
  - Under investigation

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

- 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.
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) 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
   *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).

   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® (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).

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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).

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# Change Prescriber Authorization

**PRESCRIBER AUTHORIZATION REQUESTED**

<table>
<thead>
<tr>
<th>Date:</th>
<th>&lt;Current_Date&gt;</th>
<th>Patient Enrollment Number:</th>
<th>&lt;Alt_ID&gt;</th>
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<td>&lt;Phys_First_Name&gt; &lt;Phys_Last_Name&gt;</td>
<td>Patient Name:</td>
<td>&lt;Pat_First_Name&gt; &lt;Pat_Last_Name&gt;</td>
</tr>
<tr>
<td>Address:</td>
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<td>Patient DOB:</td>
<td>&lt;Pat_DOB&gt;</td>
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<td>&lt;MD_City&gt;, &lt;MD_State&gt; &lt;MD_Zip&gt;</td>
<td>Patient Enrollment Period:</td>
<td>Pat_Auth_Begin&gt; through &lt;Pat_Auth_End&gt;</td>
</tr>
<tr>
<td>Phone:</td>
<td>&lt;MD_Phone&gt;</td>
<td>Infusion Site:</td>
<td></td>
</tr>
<tr>
<td>Fax:</td>
<td>&lt;MD_Fax&gt;</td>
<td>Infusion Site Address:</td>
<td></td>
</tr>
<tr>
<td>Prescriber DEA:</td>
<td></td>
<td>Prescriber State License Number:</td>
<td></td>
</tr>
</tbody>
</table>

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